ICMx 2022, **10**(Suppl 2):40
https://doi.org/10.1186/s40635-022-00469-0

Intensive Care Medicine
Experimental

MEETING ABSTRACTS

Open Access

ESICM LIVES 2022: part 2

Paris, France. 22–26 October 2022

Published: 19 October 2022

Health services research & outcome 1

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Impact of admission SOFA score and 48-h delta SOFA on clinical outcomes of critically ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000010

Introduction: Multiple organ dysfunction syndrome (MODS) is an important cause of morbidity and mortality in the Intensive Care Unit (ICU). Sequential Organ Failure Assessment (SOFA) scores, determined upon ICU admission, can identify patients at risk of unfavorable outcomes and trigger assessment and application of interventional approaches, of which effectiveness can be evaluated by determining the SOFA score trend after 48 h.
Objectives: To assess the impact of a SOFA score equal to or greater than two at ICU admission, and the 48-h delta SOFA, on ICU and hospital mortality.
Methods: This retrospective, observational cohort study included 1101 patients admitted to three ICUs of a tertiary hospital, from January 01 to December 31, 2020. SOFA scores—determined upon ICU admission and 48 h thereafter—denoted three patient groups: those with admission SOFA scores below 2 (Group 1, $n = 348$), those with admission SOFA scores ≥ 2 whose 48-h delta SOFA reflected improvement (SOFA after 48 h < admission SOFA) (Group 2, $n = 415$), and those with admission SOFA scores ≥ 2 that had increased or remained unchanged after 48 h (SOFA after 48 h $\geq$ admission SOFA) (Group 3, $n = 338$).
Results: Group 1 patients were significantly younger and less severely ill (based on SAPS 3 score and admission SOFA) than those in Groups 2 and 3, and their length of ICU stay was shorter. Furthermore, both their ICU (3.4%) and hospital (8.6%) mortality was significantly lower, compared to that of Group 2 and 3 patients. Among these, patients in Group 3 were older and had significantly higher mortality, both in the ICU (27.3 vs. 10.1%, $p < 0.001$) and hospital (53.8 vs. 14.9%, $p < 0.001$), compared to Group 2 patients. We discovered an independent association between age $\geq$ 66 years, the Charlson Comorbidity Index, prolonged vasopressor use, and hospital mortality.
Conclusion: We demonstrated that the admission SOFA score and 48-h delta SOFA are predictors of prognosis in a non-selective cohort of critically ill patients.

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Systematic literature review on the effects of early vs late initiation of Renal Replacement Therapy in patients with AKI

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Introduction: Acute Kidney Injury (AKI) is a syndrome of abrupt onset renal dysfunction characterised by reduced urine output, increase in serum creatine, and electrolyte disturbance. In the Intensive Care Unit, the development of AKI heralds adverse patient outcomes. One of the hallmarks of treating severe AKI is Renal Replacement Therapy (RRT). RRT initiation was traditionally started late in the natural history of AKI, where uraemia and severe electrolyte disturbances (hyperkalaemia and metabolic acidosis) are developed. Nevertheless, after the development of several observational and cohort studies exploring the early initiation of RRT, evidence suggested that it can provide favourable long- and short-term patient outcomes. On the other hand, there is contradicting evidence proposing that early initiation of RRT may, in fact, be harmful, leading to further collapse of the renal apparatus. In order to assess this, we performed systematic review of Randomised Controlled Trials (RCTs) comparing the mortality rates of early vs late initiation of RRT in patients diagnosed with AKI.
Objectives: We reviewed the randomised controlled trials (RCT) available through a systematic literature search, looking at the effect of early compared to late initiation of RRT on the mortality rates of patients diagnosed with AKI.
Methods: Our review was based on the PubMed, Embase and Cochrane databases, searching for RCT with the primary outcome of investigating the effects of early vs late initiation of RRT on patient mortality. The Cochrane Collaboration and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used as a template throughout the process. Furthermore, we performed a qualitative assessment of the selected literature using the Revised Cochrane risk-of-Bias tool for RCTs (ROB 2).
Results: Our systematic literature search identified 287 studies, from which 55 were screened for eligibility and five were eventually selected for evaluation and qualitative analysis. In the study of Gaudry et al. the 60-day mortality between patients receiving RRT initiated within 6 h of diagnosis of AKI compared to late initiation varied by 1.2% (48.5 vs. 49.7%). Similar results are portrayed d by Wald et al. where the 90-day mortality rate differed by less than 1% between the

two groups (37 vs. 38%). Moreover, kindred results are seen in the RCTs conducted by Barbar and Bagshaw et al. with a 90-day mortality difference of 4% (58 vs. 54%) and 0.2% (43.9 vs. 43.7%), respectively. Interestingly, Zarbock et al. reported a 90-day mortality decrease of 14.8% in favour of early initiation of RRT (39.3 vs. 54.7%). Using the ROB2 tool, the risk of bias was assessed and found to be low to moderate for all five studies.

Conclusion: The inconsistent methodology between studies, including the: timing of initiation of therapy, type of RRT (haemodialysis vs hemofiltration), length of patient follows up, and the variance in patient characteristics (age, frailty, pre-admission co-morbidities, reason for ICU admission) do not allow for objective comparison between the studies. Based on the analysed data, there is insufficient evidence suggesting that early RRT initiation results in improved mortality rates.

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Vasoactive inotropic score (VIS) predicts 30-day mortality in intensive care patients

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Introduction: Vasoactive inotropic score (VIS) is a scoring system aiming to standardise the dosages of different vasoactive agents on a single scale to estimate their net effect. As such, it provides an indirect way to measure the severity of circulatory failure. Previous studies have confirmed its association with unfavourable outcomes in cardiac surgical patients (1, 2), but it has not been studied in the general intensive care unit population. We aimed to study whether replacing the cardiovascular component of the Sequential Organ Failure Assessment (SOFA) score with a VIS based component would improve the predictive value of the total SOFA score.

Methods: We performed a retrospective study on adult medical and non-cardiac surgical emergency patients admitted to the intensive care unit at Kuopio University Hospital in Kuopio, Finland between 1.1.2013 and 31.12.2019. We studied maximum (VISmax) and mean (VISmean) VIS values during the first 24 h after admission. We categorized the patients in five groups regarding the VIS values using cubic spline analysis. We compared the 30-day mortalities in different VIS categories to those in different cardiovascular SOFA score categories. Area Under the Receiver Operating Characteristic (AUROC) analysis and DeLong´s test were employed as primary statistical methods to compare the discrimination ability between conventional and VIS based SOFA scores.

Results: We included 8 079 patients. The 30-day mortality was 13.7%. The mortality was 8.6%, 16.4%, 24.0%, 33.4%, and 44.1% in VISmax categories 0–4, and 9.0%, 18.1%, 23.9%, 33.8%, and 51.3% in the VISmean categories 0–4, respectively. Replacing the cardiovascular SOFA component by VIS based points improved the predictive value of SOFA: AUROC was 0.777 for conventional SOFA score, 0.789 for VISmax based, and 0.788 for VISmean based SOFA scores ($p < 0.001$). The difference between VISmax and VISmean based SOFA scores was not statistically significant ($p = 0.46$).

Conclusion: An increase in VIS categories was associated with increased risk of 30-day mortality in general ICU patients. Replacing the conventional cardiovascular SOFA points with VIS based points improved the predictive accuracy of the SOFA score.

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Impact of COVID-19 pandemic on severity of illness and resources required during intensive care in 11 healthcare systems across the United States

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Introduction: SARS-CoV-2 (COVID-19) has increased the burden on ICUs leading to a rise in patient admissions, severity of illness, length of stay (LOS), and mortality.

Objectives: The objectives are to investigate the effects of COVID-19 on patient demographics, clinical outcomes, and treatments for a large dataset spanning 11 US health systems with 75 hospitals and 168 ICU units.

Methods: Numbers of COVID-19 cases in the areas within 70 miles of each hospital were derived from the Johns Hopkins Coronavirus Resource Center (CRC) [1]. They were used to segment the COVID-19 periods until September 2020 and match them to 2019 data. Only ICUs used before and during the COVID-19 periods were considered. Features extracted per ICU-day were: percentage occupancy, median ICU/hospital length of stay (LOS), percent of bed hours with invasive and non-invasive ventilation, the mean of the Discharge Readiness score (DRS) which estimates the risk of death within 48 h [2], the mean of the automated acuity (AA) score—a patient stability indicator [3], percentage of males and race (classified as Caucasian or African American). COVID-19 periods were compared to matched periods in 2019 using Wilcoxon rank-sum test. This retrospective study was exempt from IRB oversight as there was no patient level or identifiable information used for analysis.
Results: Results are summarized per health system rather than combining all data as there were differences in the start of COVID-19 as well as the patterns for cases in the vicinities of the hospitals considered. There were significant differences in percent occupancy for eight of the 11 health systems. (Table 1) Significant differences were also observed in gender percentage (more males during COVID-19) except in one healthcare system. (Table 1). Both ICU and hospital length of stay significantly increased across all health systems during COVID-19. (Table 2) There was an increase in invasive ventilation and a decrease in non-invasive ventilation (except for 3 health systems). (Table 3) The Discharge Readiness Score also showed a significant increase, except for system 10. A significant increase in Automated Acuity across all systems was also observed. (Table 4). In terms of race analysis, there was a significant increase in the percentage of African American patients across 6 of the systems, and a significant reduction in the percentage of Caucasian patients across almost all systems. (Table 5).
Conclusion: The increases in occupancy [4–6], percentage of males [7–9], hospital and ICU LOS [10] are consistent with previous studies done on smaller datasets. The indices DRS and AA were used for the first time to observe changes due to COVID-19 and increased in most health systems. In terms of patient race distribution, our observations confirm previous findings with a larger population of African American patients during the COVID-19 periods, compared to prior periods [12].

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Association between timing of medical intensive care unit admission and outcome of emergency department patients: a retrospective cohort study

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Introduction: Cost-effective care, without compromising quality of care, is a hot topic in research. Because ICU beds are rather scarce, while their services are estimated at up to 20% of the total hospital budget, ICU admission should not be taken lightly (1). On the other hand, patients should receive appropriate medical care at all times and delay can lead to poor outcome.
Objectives: To study if there is a difference in outcome between patients who were directly admitted from the ED to ICU (DICU) and patients who were indirectly admitted from the ED to ICU (IDICU, from ED via general ward to ICU). Main outcomes: length of stay (LOS) (total and ICU), mortality (ICU and post-ICU in hospital) and SAPS-II score associated expected mortality rate.
Methods: Setting: az Sint-Blasius, Dendermonde, Belgium, a 438 beds general hospital with university affiliation, with a 12 bed mixed medical-surgical ICU. Inclusion: unplanned ICU admissions between 01/01/2015 and 31/12/2019. Exclusion: surgical patients, patients with pathologies that were not represented in both groups and patients who were not admitted via the ED. Subgroups: patients with LOS < 48 h and > 48 h in ICU. Demographics, LOS and mortality were analyzed. Statistics: Chi-square and Mann–Whitney; $p < 0.05$ is statistically significant. The study was approved by the Committee for Medical Ethics of az Sint-Blasius (n° B0122021000008). EU-GDPR requirements were met.
Results: Results are shown in Table 1. IDICU-pts were older than DICU pts. Gender did not differ. Overall, LOS and mortality was higher in IDICU pts. IDICU pts who stayed < 48 h in ICU had a nearly 3 times higher ICU and post-ICU in hospital mortality. For patients staying > 48 h in ICU, SAPS-II-score and ICU mortality did not differ between DICU and IDICU patients. The post-ICU in hospital mortality was significantly higher in IDICU patients.
Table 1

	ALL PATIENTS			LOS-ICU ≤ 48H			LOS-ICU > 48H		
	DICU	IDICU		DICU	IDICU		DICU	IDICU	
n Patients	2073	707		1174	326		899	381	
Median age (med-IQR)	70–17 y	73–22 y	$p < 0.0001$	69–25 y	74–20 y	$p < 0.0001$	71–19 y	72–16 y	$p = 0.03$
Gender (M/F)	1146/927	390/317	$p = 1$	645/529	162/164	$p = 0.096$	501/398	228/153	$p = 0.195$
LOS—ICU (med-IQR)	1.82–2.2 d	2.16–3.15 d	$p < 0.0001$	1 d	1 d	$p = 1$	3.64–2.95 d	3.99–3.87 d	$p < 0.0001$
LOS—Hosp (med-IQR)	9–10 d	16–17 d	$p < 0.0001$	7–10 d	9–12 d	$p < 0.0001$	12–11 d	21–19 d	$p < 0.0001$
Mortality—ICU	140 (6.8%)	94 (13.3%)	$p < 0.0001$	74 (6.3%)	58 (17.8%)	$p < 0.0001$	66 (7.3%)	36 (9.4%)	$p = 0.245$
Mortality—post-ICU	132 (6.8%)	107 (17.4%)	$p < 0.0001$	50 (4.5%)	34 (12.7%)	$p < 0.0001$	82 (9.8%)	73 (21.2%)	$p < 0.0001$
SAPS II-score							35	35	$p = 0.970$

Conclusion: DICU patients have better outcomes than IDICU patients. IDICU patients staying < 48 h in ICU have a marked higher ICU mortality, possibly due to the continued deterioration of patients on the ward, late ICU referral and delay in ICU care. Once patients have passed this first 'critical' 48 h, there is no significant difference between the two groups in ICU mortality, demonstrating the added value of ICU.

However, post-ICU mortality is two to threefold higher in IDICU in both groups. Reasons why ICU offers limited added value in post-ICU mortality is subject for further research.

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Assessing predictors for ultimate outcome in COVID-19 patients in a UK District General Hospital critical care unit using Markov Chain Monte Carlo (MCMC) sampling

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Introduction: There have been multiple studies on epidemiological and clinical risk factors related to severe disease and mortality in COVID-19 patients. However there are only a few studies using Markov Chain Monte Carlo (MCMC) sampling in COVID-19 patients and there are no available publications assessing the ultimate outcome using MCMC.
Objectives: Our aim was to assess predictors of ultimate outcome (survived, did not survive) in a UK District General Hospital (DGH) critical care unit during our first and second waves of the COVID-19 pandemic.
Methods: Complete deidentified data for 162 patients diagnosed with COVID-19 were collected for the first and second COVID-19 waves (23/05/2020–30/05/2020 and 09/09/2020–24/04/2021 respectively). Age (years), APACHE II score, length of stay (days) and worst values within the first 24 h of admission were analysed—lowest systolic blood pressure, lowest sodium, lowest potassium, lowest creatinine, highest lactate, lowest pO2 on any gas, and lowest haemoglobin and white blood cell count. Markov Chain Monte Carlo (MCMC) sampling was performed using a random walk Metropolis algorithm to produce a sample from the posterior distribution of a logistic regression model based upon ultimate outcome at discharge from hospital. Inferential testing was performed using a Wilcoxon rank sum test with continuity correction and Fisher's exact test using a significance level of 0.05. All statistical analyses were performed using open source R (version 4.1.3, Vienna, Austria).

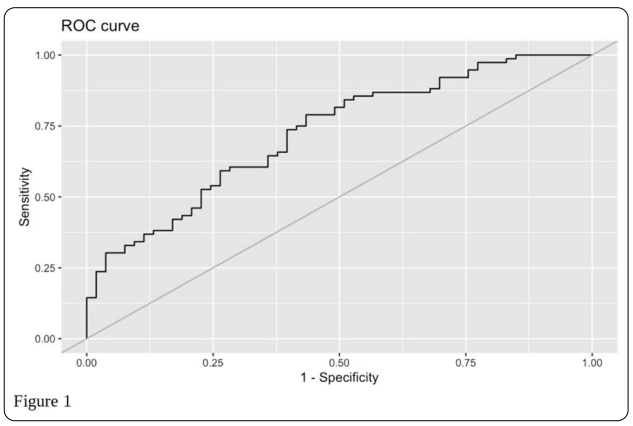

Figure 1

Results: MCMC logistic multivariate regression demonstrated that the only significant variable was age (OR 0.94 [0.91–0.97]). This suggests that the odds of surviving are multiplied by a factor of 0.94 for every year increase in age (i.e. an increase in age is associated with a decrease in survival). The AUC-ROC was 0.738, and suggests the performance of using the full model is fair (see Figure 1). Univariate analysis suggested that there were significant differences between age ($p = 0.0001$), highest lactate ($p = 0.036$), and APACHE II score ($p = 0.004$) between survivors and non-survivors. No significant difference was observed between gender and ultimate outcome.
Conclusion: Our study is the first to assess predictors of ultimate outcome using an MCMC approach. Although multiple studies suggested that an increase in age increases the risk of severe disease and mortality, no previous studies have taken an MCMC approach in estimating the odds of surviving for every year increase in age. Contrary to other studies, our findings did not demonstrate gender as a risk factor for COVID-19 outcome. Further work will involve extending our study to involve all critical care units of the South West region in the UK.

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Near-death experience in all categories ICU survivors: incidence, influencing factors, and long-term impact

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Intensive Care Medicine Experimental 2022, **10(2)**:000178

Introduction: Near-death experience (NDE) are episodes of disconnected consciousness with prototypical features such as out-of-body experience and seeing a bright light. In critical care setting, they were described mainly after cardiac arrest or brain trauma.
Objectives: To describe the incidence of NDE in survivors of a prolonged stay in intensive care unit (ICU), independently of their primary organ failure. Secondary aims were to search for influencing factors, and to assess impact of NDE on 1-year quality of life (QOL).
Methods: From July 2019 to March 2020, all adults discharged from ICU after a stay > 7 days were screened. Non-French speakers and patients detected with confusion or delirium according to the Confusion Assessment Method tool were excluded. During the 3 weeks following discharge, included patients were assessed in a face-to-face interview for NDE memories (Greyson NDE scale ≥ 7). Their dissociative tendency (28-item Dissociative Experience Scale, DES) and spirituality (World Health Organization Quality of Life—Spirituality, Religiousness and Personal Belief, SRPB) prior to ICU admission were also evaluated. Socio-demographics and ICU-related data were also collected from medical charts. One year after the interview, patients were contacted by phone to assess their QOL (using the EQ-5D-3L visual analogic scale). Data are expressed as median and interquartile range, or count and percent.
Results: From the 126 included patients (age 63 (55–70) years, SAPS II 34 (25–40), ICU stay 11.5 (9–18) days), 19 (15.1%) experienced NDE during ICU stay (NDE group). The percentage of recorded cardiac arrest episodes was not different between the two groups. Compared to the non-NDE group, a significantly higher proportion of NDE experiencers were mechanically ventilated (respectively 62/107 (57.9%) vs 16/19 (84.2%), $p = 0.039$) during respectively 5 (2–10) and 4.5 (2–9) days ($p = 0.5$), sedated (respectively 67/107 (62.6%) vs 17/19 (89.5%), $p = 0.022$) and received analgesia (respectively 65/107 (60.7%) vs 16/19 (84.2%), $p = 0.049$). The minimal arterial pressure, arterial partial pressure in oxygen, pH, and the maximal arterial partial pressure in carbon dioxide did not differ between the two groups. DES total score was significantly higher in NDE experiencers (10 (8–12) vs 2 (1–3), $p < 0.001$), as well as SRPB total score (15 (11.6–17.5) vs 10.3 (8–12.6), $p < 0.001$), compared to non-NDE group respectively. Only DES and SRPB total scores were significantly associated with NDE occurrence in a stepwise multivariate logistic regression model ($p = 0.005$ and $p = 0.001$,

respectively). At 1 year, 11 NDE and 51 non-NDE patients were contacted by phone. No difference in QOL was observed between the two groups.
Conclusion: NDEs were observed in different categories of ICU survivors. Physiological parameters were not discriminant, while dissociative tendency and spiritualty were associated with NDE occurrence. The 1-year QOL was not impacted by the fact to have experienced a NDE.

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Oncology and ICU Committee in our Hospital. Do our patients benefit?

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Introduction: In our hospital since 2019 there has been an Oncology and ICU Committee where the cases of oncology patients who are admitted are evaluated with the aim of programming our attitude if necessary. We will evaluate the data obtained during follow-up.
Methods: Patients with oncological pathology admitted to the Surgical Medical Hospital of Jaén from 2019 to 2021. Demographic data, cause of admission, type of tumor, treatment received and its prognosis have been collected. We have performed a descriptive analysis with SPSS.
Results: A total of 140 patients presented, 61% male ($N=85$) and a median age of 62 years (20–79). 64% had a personal history: 32% hypertension, 17% COPD (four of them with home oxygen), 17% smokers, 16% dyslipidemia, and 15% DM. The most frequent type of tumor was pulmonary 28% ($N=40$), followed by digestive: colorectal 18% ($N=25$) and esophagogastric 13% ($N=19$). Of the overall sample, the treatment administered: Surgery: 46%, chemotherapy 91% (at the time of consultation, 61%), radiotherapy 19%, immunotherapy 9% and only one case presented for palliative treatment. 14% were in total remission.
The cause of admission and therefore reason for consultation was in most cases respiratory I. 14% ($N=21$), chemotherapy toxicity 14% ($N=18$), pulmonary infection 8% ($N=11$), sepsis 10% ($N=14$) and febrile neutropenia 8% ($N=11$). The Committee agreed on a candidate for ICU: 24% rejected (N = 33), candidates for non-invasive measures 29% ($N=40$) and candidates for invasive measures 48% ($N=67$). Of the total number of patients mentioned, 7 patients were admitted to the ICU.
Conclusion: Advances in the treatment of cancer patients have caused a change of direction in the Intensive Medicine Units, considering their admission according to their prognosis and the pathologies they present. Clearly our patients have benefited from this committee since it has allowed us to know in advance the situation of these patients and make a decision in a consensual manner with the ICU team and oncology professionals who know exactly the prognosis and survival.

001218

Implementing and evaluating a therapeutic music program in the intensive care unit

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Intensive Care Medicine Experimental 2022, **10(2)**:001218

Introduction: Therapeutic music has been shown to provide significant physical and mental health benefits to patients, yet limited information is available on the impact of live classical music in the intensive care unit (ICU) setting.
Objectives: The purpose of this practice improvement initiative was to implement and evaluate a therapeutic music in the ICU program. Pre-pandemic, live classical music was provided at the patient's bedside by musicians using a variety of instruments including piano, flute, viola, cello and violin. The program was transitioned to a virtual format using a large iPad on wheels due to COVID-19-related visitation restrictions.
Methods: A descriptive survey methodology was used to obtain information from volunteer musicians, clinical nurses, patients, and family members. Researchers used a 12-item anonymous web-based survey to collect information on the therapeutic music program's benefits, acceptability, appropriateness, and feasibility. The Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM) statements developed by Weiner et al. (2017) was used to evaluate the music program. The AIM, FIM, and IAM are four-item measures of implementation outcomes that are often considered indicators of implementation success (Proctor et al., 2011). Responses are provided on a 5-point Likert scale ranging from completely agree to completely disagree. The survey also included questions addressing potential barriers to and facilitators of implementing therapeutic music in the ICU. Participants were recruited through convenience sampling via workplace email using a Research Electronic Data Capture (REDCap) survey. Descriptive statistics were used to analyze the data. Data were summarized and reported in aggregate.
Results: Clinical ICU staff (n = 20), volunteer musicians (n = 6) and patients (n = 20) and family members (n = 10) identified that therapeutic music was acceptable in the ICU. Similarly, a majority (73.3%) indicated that therapeutic music was appropriate and feasible. Of the volunteer musicians, all (n = 6, 100%) identified having a mobile piano as a facilitator, most (n = 5, 83.3%) identified having a patient and family-centered care environment and supportive ICU staff as facilitators, and four (66.7%) identified private ICU rooms and trained musicians as facilitators. Several barriers were also identified, including severity of patient illness and infection prevention concerns (n = 5, 83.3%), space limitations in the ICU and patient privacy concerns (n = 2, 33.35), and patients being asleep (n = 1, 16.75).
Conclusion: The results of this initiative indicated that therapeutic music in the ICU was rated as acceptable, appropriate and feasible. ICU staff, patients and family members reported benefits from hearing the live music including feelings of relaxation, the music being a pleasant experience, and a welcomed interruption to the busy ICU environment. Volunteer musicians reported the ability to provide live music in the ICU to be a beneficial and enjoyable experience.

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Acknowledgements: The project described was supported by the National Center for Research Resources, Grant UL1 RR024975-01, and is now at the National Center for Advancing Translational Sciences, Grant 2 UL1 TR000445-06. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

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VVECMO retrieval teams in the region of Madrid. Bringing extracorporeal respiratory life support to the patient. First results

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Intensive Care Medicine Experimental 2022, **10(2)**:000027

Introduction: In the midst of the COVID-19 pandemic, the region of Madrid created its first veno-venous ECMO (VVECMO) retrieval team (two hospitals, on a one week-on/one week-off roster), in order to provide extracorporeal respiratory support to patients with severe acute respiratory distress syndrome (ARDS).
Objectives: To describe the first results of the program in our hospital, which is one of the two centers of the VVECMO retrieval team.
Methods: Retrospective study (Nov 2020–Feb 2022). We included all patients evaluated as VVECMO candidates by our center during our weeks-on. The inclusion/exclusion criteria for VVECMO are described in Figure 1. We studied all patients retrieved and recorded their demographic data, ARDS etiology, duration of VVECMO run, ICU and hospital length of stay (LOS) together with ICU and hospital mortalities. Results are expressed as mean ± sd or median (IQ25–IQ75).

Figure 1

INCLUSION CRITERIA FOR VV-ECMO ARDS:

- **Severe hypoxemic respiratory failure defined as $P_aO_2/FiO_2 \leq 80$ for ≥ 6h**

With the following in-place measurements:
- FiO_2 1.
- PEEP ≥ 10 cmH_2O.
- Tidal volume 6 – 8 ml/kg.
- Neuromuscular blocking agents.
- Prone positioning ventilation.

The following measures are also recommended:
- Recruitment maneuvers.
- A trial of selective pulmonary vasodilators: inhaled NO.

- **Severe hypercapnic respiratory failure defined as $P_aCO_2 \geq 80$ and arterial pH ≤ 7.20**

With the following in-place measurements:
- Respiratory rate ≥ 35 bpm.
- Adjusted tidal volume aiming at Pp ≤ 32 cmH_2O and/or driving pressure ≤ 20 cmH_2O.

RELATIVE EXCLUSION CRITERIA FOR VV-ECMO ARDS:

- Aggressive mechanical ventilation (Pp ≥ 30 cmH_2O, driving pressure ≥ 20 cmH_2O, $FiO_2 \geq 0.9$) for more than 7 days.
- Advanced COPD or pulmonary fibrosis in a patient not suitable for lung transplantation.
- Multiorgan failure (> 2 extra-pulmonary organs; SOFA > 15).
- Recent or active hemorrhagic event.
- Advance and/or severe neurological conditions.
- Immunosuppression.
- Advanced age.

Results: During the period studied, a total of 91 patients were referred for VVECMO, with 49 being considered as non-suitable due to different reasons and 42 considered suitable for VVECMO treatment. In 22 out of the 42 cases, retrieval was performed under VVECMO due to poor gas exchange, while the other 20 patients were retrieved without VVECMO. Nine out of the 20 patients retrieved without VVECMO ended up with extracorporeal respiratory support after arrival to our center. There were two hemorrhagic complications during canulation. No other complications were reported during patient retrieval, either with or without VV-ECMO. Of the 31 actual VVECMO patients, 20 were males (64.5%) and mean age was 47.6 ± 13.1 years. ARDS etiologies were: SARS-CoV-2 pneumonia [27 cases (87.1%)]; mechanical ventilation associated pneumonia developed after SARS-CoV-2 infection [two cases (6.5%)] and Legionnaries´ disease and refractory asthma [1 case each (3.2%)]. The median duration of the VVECMO run was 14 [10–18] days. Twenty-one patients were weaned off ECMO, two were still on ECMO at the time this abstract was written, 1 was still in ICU and 8 patients (25.8%) died on ECMO due to futility of treatment (7) and intracranial bleeding (1). ICU LOS was 38.5 (33.7–56.2) days and hospital LOS was 58 (41–74.5) days. The 21 patients that were weaned off ECMO survived to ICU and hospital discharge, so overall survival of the series was 67.7%.
Conclusion: More than one year after the start of the program, the VV-ECMO retrieval team has averaged results that are comparable with those achieved by more experienced teams and is nowadays running without problem. The creation of this program has made it possible for patients across the region of Madrid to access a highly complex technology not available in all centers.

000086

Patient activity and workload monitoring in the intensive care using a camera-based artificial intelligence

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Intensive Care Medicine Experimental 2022, **10(2)**:000086

Introduction: Academic and commercial interest in remote patient monitoring has increased in recent years, driven partly by the need to limit patient contact associated with the COVID-19 pandemic. While the bulk of this interest focuses on remote vital sign monitoring, there also remains a need to improve monitoring of holistic aspects of patient recovery including sleep, agitation, and discomfort. By combining continuous patient monitoring using video with Convolutional Neural Networks, a so called "Ambient Intelligence" can be created, potentially accomplishing this monitoring.
Objectives: To deploy an Artificial Intelligence-trained neural network on a set of thermal images taken from an Intensive care unit to specifically monitor patient movement and caregiver interaction as a proof of concept.
Methods: 5000 images were manually annotated and then used to train You Only Look Once (YOLOv4), an open-source computer vision algorithm. Comparison of patient motion and caregiver activity was then performed between these patients. 5000 images were manually annotated and then used to train You Only Look Once (YOLOv4), an open-source computer vision algorithm. Comparison of patient motion and caregiver activity was then performed between these patients.
Results: The algorithm was deployed on fourteen patients comprising 1762800 frames of new, untrained data. There was a significant difference in patient movement throughout the day ($p < 0.005$). There was a significant difference in the standardized motion scores of High Dependency Unit (HDU) and Intensive Care Unit (ICU) patients (0.60 ± 0.008 vs 0.65 ± 0.012, $p < 0.005$), intubated and non-intubated patients ($0.40 \pm .021$ vs $0.67 \pm .007$, $p < 0.0001$) and delirious and non-delirious (0.79 ± 0.016 vs. 0.59 ± 0.007, $p < 0.005$). There was a significant difference in caregiver activity throughout the day ($p < 0.005$), HDU vs ICU patients (0.71 ± 0.24 caregivers/hour compared vs 1.04 ± 0.31 caregivers/hour, $p < 0.005$), and in delirious vs non delirious patients (1.05 ± 0.024 vs 0.79 ± 0.013 caregivers per hour, $p < 0.005$). The two most important covariates with respect to patient motion were ventilation status (coeff = −0.314 [SE = 0.020]; relative dominance = 35.6%) and the presence of delirium (coeff = 0.169 [SE = 0.024]; relative dominance = 25.9%). With respect to caregiver activity, the two most important covariates were ICU vs HDU Status (coeff = 0.497 [SE = 0.029], relative dominance 46.7%) and delirium (coeff = 0.367 [SE = 0.037]; relative dominance 23.3%).
Conclusion: Passive, contactless monitoring of the patient bedspace that is augmented by automated object recognition allows for novel insights into patient activity and caregiver workload. Increased activity and caregiver workload is associated with delirious or intubated critical care patients, and this activity is also dependent on the time of day.

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Development and external validation of a prediction model for quality of life after intensive care unit admission: a multicenter prospective cohort study

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Introduction: Due to treatment advances, more patients are surviving their critical illness. Half of these ICU survivors experience new physical, mental, and/or cognitive problems one year after ICU admission, negatively affecting their quality of life. Often, patients and their family members, and even ICU clinicians are unaware of these consequences and are mostly overoptimistic about long-term outcomes after critical illness. Prediction models for quality of life can help ICU clinicians fill this information gap and inform patients about life after the ICU. However, currently no externally validated prediction models for quality of life after ICU are available. Moreover, the vast majority of developed prediction models do not reach clinical practice.
Objectives: To develop and externally validate a prediction model for quality of life one year after ICU admission that would be suitable for use in a general ICU.
Methods: Data were acquired from a prospective multicenter cohort study (MONITOR-IC) and the Dutch National Intensive Care registry. Adults admitted to the ICU in one of seven participating hospitals between July 2016 and February 2020 were included. Patients who had died within one year after ICU admission were excluded. Outcome was defined as change in quality of life, measured using the EuroQol five-dimensional (EQ-5D-5L) questionnaire. Input variables were based on previous studies and clinical relevance, including demographics, comorbidities, quality of life pre-ICU and clinical parameters. Multiple imputation by chained equations was conducted for missing data. The developed model was based on data from an academic hospital, using multivariable linear regression analysis. To assist usability, a core set of variables was selected using least absolute shrinkage and selection operator (lasso). Geographical external validation was executed using the data of the six non-academic hospitals.
Results: Of 1804 patients included in analysis, 1057 (58.6%) patients were admitted to the academic hospital, and 747 (41.4%) patients were admitted to a non-academic hospital. 49 variables were entered into a multivariable linear regression model, resulting in an explained variance (R2) of 56.6%. Using lasso, quality of life pre-ICU, admission type and Glasgow Coma Scale were selected for the final model (R2 = 52.5%) (Table 1). Internal and external validation showed good calibration with a regression slope of 0.995 and 0.929 respectively (Figure 1). External validation also showed good predictive power (R2 = 53.2%).

Table 1: Selected variables and their coefficients in the final model

	Coefficient	Standard error	p-value
Quality of life pre-ICU (EQ-5D-5L) (range −0.446–1)	−0.7123	0.0223	< 0.0001
Admission type			
Acute surgical	−0.0180	0.0194	0.3532
Planned surgical	0.0438	0.0157	0.0054
Lowest Glasgow Coma Scale in the first 24 h (range 3–15)	0.0082	0.0021	0.0001

Conclusion: This study is the first that developed and externally validated a prediction model for change in quality of life one year after ICU. Due to the small number of predictors, the model is appealing for use in clinical practice, while the performance is comparable to previous studies. Further clinical trials are necessary to assess its clinical applicability.

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000183

Lung ultrasound and sonographic subpleural consolidation in COVID-19 pneumonia correlate with disease severity

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Intensive Care Medicine Experimental 2022, **10(2)**:000183

Introduction: Lung ultrasound (LUS) was used in COVID-19 pneumonia in case of identification, disease severity classification, and treatment allocation (1). For the severity of the disease they mainly used the B lines as percentages in each field of the examined chest area (aeration score) (2). The correlation between the number of subpleural consolidation (SPC)and severity of COVID-19 pneumonia was not studied.
Methods: The study is an observational, prospective, single-center study conducted in the intensive care unit of Adan General Hospital, Kuwait, from May 1, 2020, to June 30, 2020. Patients were included if they were age > 18 with suspicion of COVID-19 infection and had been transferred to the ICU with fever or suspected respiratory infection (3). Polymerase chain reaction (RT-PCR) had been performed; every patient admitted to ICU. We performed lung ultrasonography for every patient admitted to the ICU with suspicion of COVID-19 infection using a 12-zone method (2). The signs of the high probability of COVID-19 pneumonia on lung ultrasound evaluation are (7):

1. The patchy distribution of multiple coalesced and separated B lines with the light beam sign, Bilateral and well-demarcated separation from large "spared" areas.
2. The pleural is sliding, and maybe irregular and fragmented
3. Multiple small SPCs are limited to the periphery of the lungs (1).

We calculated the aeration score and total number of SPCs in each area of chest in 12 zones protocol and correlate it with PaO_2/FiO_2
Results: Of 109 patients with suspected COVID-19 pneumonia, 77 (71%) were confirmed. The patients' median age was 53 (82–36) years, and 81 (73.7%) were men. The clinical characteristics of the patients

with confirmed COVID-19 pneumonia are shown in Table 1. The aeration score was significantly higher COVID-19 pneumonia (P0.018) and counting SPCs in each zone was significantly higher in COVID19 pneumonia (P > 0.0001). There is an inverse relation between PO2/fiO2 and aeration score and SPC number. The higher number of SPC, the lower the ratio (Figs. 1, 2). LUS revealed the signs of the high probability of COVID-19 pneumonia in 75(97.4%) (sensitivity 96.9%, CI 85%–99.5%). Of the patients in the group without COVID-19 pneumonia and negative RT-PCR, 32 (90%) were LUS negative for COVID-19 pneumonia (specificity 91.7%, 95% CI 58.72%–99.77%).

Conclusion: The LUS aeration score, as well as the SPC score correlates with the severity of COVID-19 pneumonia at presentation in the ICU. A higher elevated LUS aeration and SPC score on admission is associated with lower PO_2/FiO_2.

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Acknowledgements: None.

000243

Infrared thermography hotspot mapping patterns of the thigh in septic shock patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000243

Introduction: To evaluate septic shock-associated early microcirculatory dysfunction, peripheral perfusion assessment through the skin parameters is of particular interest. Thermographycally perforator arteries are seen as skin hotspots in color-coded images and correspond accurately to standard diagnostic methods in free flap surgery research. In this study, we evaluated skin thermographic hotspot patterns of the anterior thigh in septic shock patients, by using infrared thermography. We hypothesized that abnormal peripheral perfusion during critical illness affects skin thermographic hotspot patterns, normally seen in hemodynamically stable individuals.

Objectives: The aim of this study was to classify skin thermographic hotspot patterns into types during septic shock and determine type association with outcomes.

Methods: We performed a prospective observational study. The study protocol was approved by the Institutional Ethics Committee (26/23.02.2017). Patients were screened for septic shock according to the Sepsis-3 definition and included in the study during the first 24 h of ICU admission. After hemodynamic resuscitation, the thermographic images of the anterior thigh were recorded using FLIR A600 (FLIR systems, Sweden) camera. Thermographic images were further visually analyzed using FLIR Researcher MAX (4.40.11.35) software and classified either into homogenous (no hotspots seen) or heterogeneous (hotspots seen) types. Clinical data, demographic data, and outcomes were collected.

Results: Eighty-one patients were included in the study. Out of them in 69% (n = 56) of cases, infrared thermography imaging of the anterior thigh has been classified as a heterogeneous type, with identified on average 11 (SD = 5) hotspots. The temperature gradient between skin hotspot temperature (M = 32.9 °C; SD = 1.5) and adjacent skin area temperature (M = 31.5 °C; SD = 1.4) was 1.2 °C (SD = 0.7). There was a statistically significant ICU survival distribution between heterogeneous and homogonous types (Log Rank test, $\chi^2(1) = 5.781$, $p = 0.02$). However, there was no significant association between 28-day survival and the type of hotspot patterns (Fisher's exact test, $p = 0.1$).

Conclusion: Thermographic absence of skin hotspots might be associated with poor early outcomes, possibly representing acute critical illness severity and peripheral perfusion abnormalities.

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000250

Predictors of postoperative outcomes in patients who underwent multiple valve surgery in a specialty hospital in the Philippines

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Intensive Care Medicine Experimental 2022, **10(2)**: 000250

Introduction: The most commonly used predictive scores (STS-PROM and EuroSCORE) have been helpful in identifying high risk patients for cardiac surgeries, however were not constructed for multiple valvular heart diseases.

Objectives: This study was conducted to determine the prevalence, postoperative outcomes and prognostic determinants for patients who underwent multivalve surgeries; and aimed to be a pre-requisite to formulating a new predictive risk score for this type of surgeries.

Methods: This is a retrospective cohort study of 118 adult patients who underwent multivalve surgeries at the Philippine Heart Center in 2019. Descriptive statistics was used for the demographic and clinical characteristics of the patients; and binary logistic regression to determine significant predictors for outcomes.

Results: Among the 118 patients who underwent multivalve surgeries, there was prevalence of rheumatic heart disease, mitral valve involvement, NYHA Class II, chronic heart failure, elective surgeries, and atrial fibrillation. Postoperative outcomes were nosocomial infection, prolonged postoperative hospital stay and low cardiac output syndrome. Less commonly seen were prolonged postoperative ICU stay, refractory arrhythmias, renal failure, stroke and reoperation. In-hospital mortality was 7.63%. On multivariate analysis, significant predictors of outcomes included advanced age (OR 4.02, CI 1.03–5.7, p 0.045), poor right ventricular dysfunction (OR 6.1712, CI 1.66–22.9, p 0.007) and elective procedures (OR 0.1070, CI 0.02–0.50, p 0.004).

Conclusion: Among patients who underwent multivalve surgeries, prolonged postoperative hospital stay and nosocomial pneumonia were the most common postoperative outcomes; and in-hospital mortality was noted at 7.63%. Advanced age, urgency of surgery and RV dysfunction were determined to be significant predictors of postoperative outcomes.

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000267

Prevalence of anxiety and depressive symptoms in the context of PICS-F: baseline results of a chilean's cohort of family members

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Intensive Care Medicine Experimental 2022, **10(2)**:000267

Introduction: The survival of critical patients has improved in recent years. However, ICU survivors may present functional, psychological and cognitive impairment (1). This multidimensional patient's decline has been recognized as the post-intensive care syndrome (PICS). Patients' relatives can develop PICS symptoms, a condition known as PICS-family (PICS-F). Symptoms of PICS-F include: anxiety, depression, post-traumatic stress, etc. (2). As intensive care professionals we should design strategies to prevent PICS and PICS-F. We reported the preliminary results of a study that aims to prevent PICS-F at Complejo Asistencial Doctor Sotero del Rio (CASR), in Santiago de Chile.
Objectives: To determine the prevalence of anxiety and depressive symptoms in a cohort of relatives of critical patients, during the ICU stay of their loved ones.
Methods: Relatives of ventilated patients hospitalized at the ICU were enrolled. They were excluded if their loved one had treatment limitations. This study includes a diagnostic phase and an interventional phase of spiritual care. During the diagnostic phase the participants were evaluated (telephone interview) using the Hospital Anxiety and Depression Scale (HADS). This instrument has a subscale for anxiety and another for depressive symptoms. A cutoff of 11 points per subscale indicates a probable case of anxiety or depression (3). Sociodemographic variables of the participants and relevant clinical data from the patients were registered. The results are reported using mean ± standard deviation (SD) and percentages, and compared using chi-square. The study was approved by the hospital ethics committee.
Results: Between November 2021 and February 2022, 106 relatives (1 relative/patient) were recruited.The majority of them were the patient's tutor (usually the spouse), who could visit the patient at the ICU and receive medical information. The patients' age was 57.3 ± 16.6 years, and 45% were women. The most common reasons for ICU admission were acute respiratory failure (40%), half of them due to COVID-19, and septic shock (23%). Table 1 shows the sociodemographic characteristics of the relatives. Seventy participants had anxiety (66%) and 25 (23%) had depressive symptoms. The mean score for the anxiety subscale was 12.6 ± 4.3 and for depression 8.3 ± 4.1. More women meet the cut-off score for anxiety (chi-square = 7.6, $p < 0.01$), whereas the prevalence of depression showed no association with sex. No other characteristic of the relatives was associated with anxiety or depressive symptoms. The baseline prevalence of anxiety in this cohort was higher than the reported by other authors after ICU discharge (4), with a lower prevalence of depression.
Table 1: Socio-demographic characteristics of the relatives.

Characteristic	Mean/ frecuency	SD/Percentage
Women	84	79%
Age	46.6	11.9
Practice any religion	83	78%
Civil status single	35	33%
Civil status married	55	52%
Civil status divorced/separated	13	12%
Civil status widowed	3	3%
Educational level < 8 years	26	25%
Educational level 8–12 years	51	48%
Educational level > 12 years	29	27%
Formal employment	54	51%
Mental health consultation during last year	22	21%
Treatment with anxiolytics/antidepressants	22	21%

Conclusion: In this cohort of ICU relatives we found a higher prevalence of anxiety than the reported by other studies, associated to female sex. Determining the most frequent baseline PICS-F symptoms can be helpful to develop strategies for preventing this condition.

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Acknowledgements: This study was founded by a grant of Pontificia Universidad Católica de Chile.

000278

Point-of-care prompting improves restocking of ICU emergency drug bags

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Intensive Care Medicine Experimental 2022, **10(2)**:000278

Introduction: In our 1000-bed quaternary referral hospital, emergency drug bags are taken from the Intensive Care Unit for use at medical emergencies, cardiac arrests, and transfers of ventilated patients. Faculty of Intensive Care Medicine (FICM) guidelines recommend that transfer bags should be standardised, checked routinely, and restocked between uses to ensure consistent availability of contents, to reduce human error and delays (1). The local hospital policy *Checking Emergency Drug Bags and Transfer Bags* extends the FICM guidelines

to mandate the contents of the drug bags (Figure 1), and a protocol for checking and sealing them with a tag by the clinician who opens them (2).

Objectives: To evaluate whether the emergency drug bags are stocked and sealed in accordance with the hospital policy. To evaluate the impact of a printed checklist in improving compliance with the policy.

Methods: A power calculation showed a sample size of 45 bags was needed to demonstrate a 20% difference in stock levels after any intervention with a 95% confidence interval. The bags were audited from October 2021–January 2022. At each check, the bag tag number was recorded before untagging, and the contents were checked against the checklist (Figure 1). All checked bags were restocked correctly and sealed with a new tag. The unique tag number was recorded. Bags were not re-checked if they had not been unsealed since the last check. An interim analysis of 15 bags showed inadequate stocking of key drugs: to ameliorate this a checklist of drugs was laminated and inserted in the bags to provide a point-of care prompt. A further 15 bags were audited. The Kruskal–Wallis test was used to test for change in bag contents pre- and post- intervention. The audit was registered with the local audit office. No personal data were recorded and ethical approval was not required according to the Health Research Authority (3).

Results: Interim analysis showed that 7 (47%) bags were not tagged and a significant proportion were missing key drugs for intubation (Figure 2). Following the introduction of a checklist of drugs in each bag there was a significant improvement in the proportion of bags correctly stocked ($p = 0.0034$) (Figure 2). The improvement in stock levels was predominantly in drugs commonly used in rapid sequence induction, and in fluid-refractory hypotension (Figure 2). 11 (73%) bags were sealed with a tag on re-audit when compared to 8 (53%) at baseline.

Drugs	Size	Number
RSI pouch		
Propofol 1%	20ml	2
Rocuronium	50mg	2
Under elastic		
Adenosine	6mg	2
Adrenaline	1mg	1
Flumazenil	0.5mg	1
Glycopyrrolate	200mcg	2
Lidocaine	5ml	2
Mag Sulphate 50%	10ml	1
Metaraminol	10mg	3
Metoprolol	5mg	1
Midazolam	10mg/2ml	1
Naloxone	400mcg	1
Noradrenaline	4mg	1
Suxamethonium	100mg	2
Equipment		
20ml syringe		1
10ml syringe		3
5ml syringe		3
2ml syringe		2
5 drawing up needles		5
Red bungs		5
NaCl 0.9%		5
Labels		PRN

Figure 1: Checklist of emergency drug bags

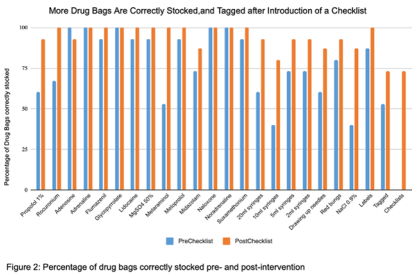

Figure 2: Percentage of drug bags correctly stocked pre- and post-intervention

Conclusion: The stocking and tagging of emergency drug bags was inadequate. The inclusion of a checklist resulted in improved stocking of the drug bags and resolved the safety concerns ad interim. The study is underpowered to demonstrate a conclusive difference post-intervention as data collection prior to intervention was terminated early due to safety concerns. Re-audit will demonstrate whether there is attrition of the checklists from the bags and allow evaluation of its impact in the longer term.

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Acknowledgements: This work received no funding.

Health services research & outcome 3

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Comparative analyses of two models of tele-critical delivery in a large multi-hospital healthcare system

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Introduction: Across the specialty of critical care medicine, there exists strong agreement that the ideal critical care delivery model is comprised of an intensivist physician and a multi-disciplinary team of ICU specialized clinicians, providing 24/7 bedside care (1). Effectiveness of these ICU specialized care teams team have been critical determinants of quality and outcomes (1-3). Though, evidence regarding maintaining the physical presence of intensivists at the bedside 24/7 effect on outcomes vary (2, 4–20). Optimal critical care delivery is also progressively reliant on advancing technologies. Technological innovations have contributed to the evolution of Tele-Critical Care (TCC) in which Tele-Intensivists (TI) with multidisciplinary teams of ICU specialists provide critical care services to patients through technology enabled live portals (21–26) TCC has enabled fluidity, accessibility, and summative cognizance of vital information across care settings (23, 27, 28).

Objectives: We hypothesized that Tele-Intensivists ICU teams would provide equivalent quality and effectiveness across the full-spectrum of routine ICU standards of care delivery. We compared outcomes between two TCC delivery models, Tele-Intensivists (TI) with 24/7 Bedside Intensivist (BI) and with Private Daytime Attending Intensivist (PI) in relation to ICU and hospital mortality, ICU and hospital length of stay (LOS), costs, and complications.

Methods: This original investigation was an observational cohort study in 12 ICUs that functioned as Medical, Surgical, Cardiac, Neuroscience, or Mixed-Units. The setting provided a naturally occurring circumstance whereby patients received care in only one of the two TCC models depending upon the quasi-random factor of which hospital they were admitted. The setting enabled a natural experiment and development of mutually exclusive cohorts for obtaining statistically meaningful comparisons.

Results: Cohort included 19,519 critical care patients, of which 71.7% ($n = 13,993$) received Tele-Intensivist with 24/7 Bedside Intensivist while 28.3% ($n = 5526$) received Tele-Intensivist with private daytime attending intensivist. We compared severity-adjusted outcomes between Tele-Critical Care models in relation to ICU and hospital mortality, ICU and hospital length of stay (LOS), costs, and complications. The rates of ICU mortality (4.8% vs. 3.1%, $p < 0.0001$), and hospital mortality (12.6% vs. 8.1% $p < 0.0001$) were higher among patients receiving with 24/7 Bedside Intensivist compared to private daytime attending intensivist. Multivariate mixed models with direct and indirect standardization revealed significantly higher odds (OR; 95% CI) of ICU mortality (1.58; 1.28–1.93), hospital mortality (1.52; 1.33–1.73), complications (1.55; 1.18–2.04), ICU LOS [3.14 vs. 2.59 (1.25; 1.19–1.51)], hospital LOS [9.05 vs. 7.31 (1.23; 1.21–1.25)] and overall higher cost per case with 24/7 bedside intensivist compared to private daytime attending intensivist. Sensitivity analyses assessed the odds of mortality between the two Tele-Critical Care delivery models for patient sub-groups with the greatest critical care needs and demonstrated significantly favorable odds ratios with Tele-intensivist with private daytime attending intensivist.

Conclusion: Results indicated ICU and hospital mortality rates and LOS, costs, and complications, were all significantly lower for patients cared for in Tele-Intensivists with Private daytime attending Intensivists compared to 24/7 Bedside Intensivists. Severity-homogeneous strata and hierarchal risk clustering allowed fair comparisons between unequal comparison groups. Our findings did not support our assumption that patients with the greatest critical needs would benefit most from BI. The sample was sufficient to compare differences in unbalanced groups through several sensitivity models with targeted strategies to adjust, stratify, and minimize bias. Our results remained consistent under routine care whilst accounting for risk and patient stays. Our results remained consistent through testing of varying patient characteristics and severity of illness across multiple ICUs and hospitals. Our comparison demonstrated Tele-Intensivist with private daytime attending intensivist ICU teams provided high quality care with significant positive effective on outcomes across the full-spectrum of routine ICU standards of care delivered in our system. Results provide supporting evidence to suggest Tele-Intensivists ICU teams have broad range applicability and benefits in routine critical care delivery necessitating progressive research.

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000152

Long term survival of direct versus indirect intensive care admission of medical emergency department patients: a retrospective cohort study

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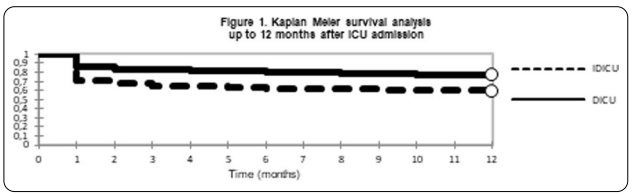
Introduction: Patients have the right to receive appropriate care at all times. Triage at the Emergency Department (ED) is aimed to identify patients that potentially need critical care, and permits to avoid delay of appropriate care, which is associated with poor outcome.
Objectives: To study if there is a difference in long term outcome between patients who were directly admitted from the ED to ICU (DICU) and patients who were indirectly admitted from the ED to ICU (IDICU, from ED via general ward to ICU). Main outcomes: length of stay (LOS) (ICU and in hospital), mortality (ICU, in hospital and long term, up to 12 months).
Methods: Setting: az Sint-Blasius, Dendermonde, Belgium, a 438 beds general hospital with university affiliation, with a 12 bed mixed medical-surgical ICU. Inclusion: unplanned ICU admissions between 01/01/2015 and 31/12/2019. Exclusion: surgical patients, patients with pathologies that were not represented in both groups, patients who were not admitted via the ED, and readmissions within the same hospitalization. Outcomes: demographics, LOS, mortality, Kaplan–Meier survival analysis. Statistics: Chi-square, Mann–Whitney and Log-rank test; $p < 0.05$ is statistically significant. Study approval by the Committee for Medical Ethics of az Sint-Blasius (n° B0122021000008). EU-GDPR requirements were met.
Results: Results are shown in Figure 1 and Table 1. 2665 admissions were included. DICU patients were younger. Gender did not differ. DICU pts had shorter LOS in ICU and in hospital. IDICU patients had a significant higher mortality in ICU and in hospital, and at 12 months. Mortality was highest in the first month after ICU admission.



	DICU	IDICU	
Patients (n)	2067	598	
Lost to follow up (n)	0	0	
Median age (med-IQR)	70y–22	73y–18	$p < 0.0001$
Gender (M/F)	1144/923	321/277	$p = 0.471$
LOS—ICU (med-IQR)	1.8d–2.2	2.1d–3.0	$p = 0.002$
LOS—Hosp (med-IQR)	8.1d–10.0	3.8d–15.9	$p < 0.0001$
Mortality—ICU (n)	132 (6.4%)	83 (13.9%)	$p < 0.0001$
Mortality—in hospital (n)	271 (13.1%)	166 (27.8%)	$p < 0.0001$
Mortality—12 months (n)	484 (23.4%)	245 (41.0%)	$p < 0.0001$

Conclusion: Indirect admission in ICU was associated with poor outcome: a longer length of stay and an up to two-fold higher mortality, that persisted even after 1 year. The importance of correct triage at admission of patients at risk of further deterioration cannot be overemphasized.

000226

Long-term cognitive performance and its relation to anti-inflammatory therapy in critically ill COVID-19 patients

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Introduction: Long-term cognitive performance data in patients who survived critical illness related to COVID-19 are sparse. Current evidence suggests that cognitive decline is related to systemic inflammation induced neuroinflammation.
Objectives: This study assessed long-term cognitive function in critically ill patients with COVID-19 and the effect of anti-inflammatory therapies on neuropsychological outcomes.
Methods: Patients admitted to the ICU due to COVID-19 ARDS were included. Six months after hospital discharge, an extensive neuropsychological assessment was performed, examining both objective cognitive function and subjective complaints. Cognitive impairment was defined as a score of < -1.5 SD on two or more cognitive tests.

Furthermore, patients were stratified in cohorts according to their anti-inflammatory treatment.
Results: Between March 2020 and June 2021, 96 patients were included (median [IQR] age 61 [55–69] years; 67% male). Mean ± SD APACHE-II-score at admission was 15·8 ± 4·1; 91% received invasive mechanical ventilation. After 6·5 ± 1·3 months, 27% scored cognitively impaired. Patients with or without cognitive impairments did not differ in ICU-admission parameters, clinical course or delirium. Patients with subjective cognitive complaints (20%) were more likely women (61% vs 26%), and had a shorter ICU stay (median [IQR] 8–[5–15] vs 18–[9–31], p = 0·002). Objective cognitive dysfunction did not correlate with subjective cognitive dysfunction. Overall, 27% received dexamethasone, 44% received additional tocilizumab and 29% received neither. Although, occurrence and severity of cognitive dysfunction were not affected by anti-inflammatory therapy, patients treated with both dexamethasone and tocilizumab had worse executive functioning scores (Trail-Making-Test-interference) than patients without anti-inflammatory treatment (T-score 40·3 ± 13·5 vs 49·1 ± 9·3, p = 0·007).
Conclusion: A relevant proportion of critically ill COVID-19 patients shows deficits in long-term cognition. While the combination of dexamethasone and tocilizumab therapy may impair executive functioning, overall, anti-inflammatory therapy was not associated with long-term cognitive performance.
Acknowledgements: ZonMw Clinical Fellowship grant 90715610.

000251

Factors affecting short and long-term outcomes of patients who underwent surgical management of congenital heart defects beyond the age of 18 at a specialty tertiary hospital in the Philippines

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Intensive Care Medicine Experimental 2022, **10(2)**:000251

Introduction: The number of adults with congenital heart disease now outnumbers children with congenital heart disease. With uncertainty on accurate operative risk, there may be a natural reluctance to recommend surgery, particularly for patients lacking overt symptoms.
Objectives: This study aims to determine the factors associated with clinical outcomes of patients with congenital heart defects who underwent surgical management beyond the age of 18 at a specialty tertiary institution in the Philippines.
Methods: This is a retrospective observational study of patients with congenital heart defects, 18 years old and above, who underwent surgical management as the first surgery at the Philippine Heart Center from 2013 to 2015. Factors associated with surgical and long-term outcomes were analyzed.
Results: Majority of the patients had atrial septal defect (37 of 53). New York Heart Association class II was also prevalent (39). Right ventricular systolic dysfunction measured by TAPSE and RVFAC were noted in seven patients and left ventricular systolic dysfunction measured by ejection fraction was seen in two patients. Only a portion of the patients (17) had normal pulmonary artery pressure, while the remaining had pulmonary hypertension ranging from mild (10), moderate (11) to severe (11). Surgical and long-term outcomes were seen in 30 of the 53 patients. The most frequent complication was postop arrhythmia (12). Among the preoperative variables with significant outcomes, prolonged bypass time was shown to be associated with surgical and long term outcomes (p-value 0.034, CI 1.1048 to 11.629). Median length of Intensive Care Unit stay was 1.8 days (1.1 to 2.3); median days from surgical procedure to discharge was seven days (6 to 9); and median length of hospital stay was nine days (8 to 12). There was no in-hospital mortality. The five-year survival probability was computed at 94.34% (95% CI: 83.47 to 98.14).
Conclusion: Patients with adult congenital heart disease who underwent surgery for the first time had high morbidity outcomes but with good recovery. Length of ICU and postoperative stay were favorable; and five-year survival probability was high.

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000269

Multicenter study evaluating prognostic bias of critical illness severity scores across the USA: a comprehensive retrospective analysis

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Introduction: Illness severity scoring systems such as the Acute Physiology and Chronic Health Evaluation IVa (APACHE IVa) and Sequential Organ Failure Assessment (SOFA) are widely used in the critical care setting for mortality prediction, risk stratification, and resource allocation [1]. However, these systems are limited by population-level prognosis estimation, leading to variation in performance across subgroups such as ethnicity [2–3]. Additional sources of bias such as age, gender, and English proficiency have not been fully explored [4–6].
Objectives: To identify the potential bias of illness severity scores in evaluating hospital mortality across subgroups divided by demographics such as age, gender, and primary language via two large intensive care unit (ICU) databases.
Methods: This multicenter, retrospective study was conducted using data from the Medical Information Mart for Intensive Care (MIMIC-IV, 2001–2019) database and the eICU Collaborative Research Database (eICU-CRD). SOFA and APACHE IVa scores were obtained via ICU admission records. The SOFA predictions of hospital mortality were fitted separately using each dataset of 10% randomly chosen data. Patients were stratified by age, gender, and

primary language and then assessed for discrimination and calibration in all subgroups. To evaluate for discrimination, area under receiver operating characteristic (AUROC) curve and area under precision-recall curve (AUPRC) were used. Standardized mortality ratio (SMR) evaluated calibration.

Results: A total of 173,930 patient encounters were studied (78,550 MIMIC and 95,380 eICU-CRD). Tests for discrimination showed that the SOFA and APACHE IVa models performed best for the youngest age range (AUROC over 0.8); AUROC decreased with increasing age (Table 1). The measurements of discrimination were similar across gender. When comparing primary language using MIMIC-IV, the AUROC for the SOFA model was higher for patients who spoke English vs patients who did not speak English. Measurements of calibration showed differences among the subgroups in Figure 1. With both databases, SOFA model consistently overestimated mortality in younger patients and male patients while underestimated mortality in older patients and female patients. Additionally, the SMR for English speaking patients was 0.85 while the SMR for non-English speaking patients was 1.4, indicating that mortality of non-English speaking patients is often underestimated. In contrast, the APACHE IVa model overestimated mortality for all patients, with greatest overestimation seen in younger patients and female patients.

Table 1. Discrimination comparison of SOFA and APACHE-IVa models when MIMIC and eICU-CRD databases are stratified by age, gender, and primary language subgroups.

Sub population		MIMIC (single center, 2001–2019)		eICU-CRD (188 hospitals, 2014–2015)	
Category (value)		AUROC (95% CI)	AUPRC (95% CI)	AUROC (95% CI)	AUPRC (95% CI)
SOFA					
Total	All	0.744 (0.739-0.75)	0.304 (0.295-0.312)	0.725 (0.721-0.729)	0.236 (0.227-0.244)
Age	16-44	0.812 (0.794-0.831)	0.257 (0.224-0.305)	0.808 (0.791-0.825)	0.21 (0.181-0.245)
	45-64	0.777 (0.768-0.786)	0.313 (0.296-0.329)	0.763 (0.756-0.774)	0.242 (0.22-0.257)
	65-79	0.732 (0.721-0.742)	0.312 (0.293-0.326)	0.706 (0.696-0.716)	0.243 (0.227-0.258)
	80-	0.705 (0.697-0.716)	0.356 (0.343-0.376)	0.673 (0.661-0.684)	0.271 (0.251-0.29)
Gender	Female	0.745 (0.735-0.751)	0.314 (0.296-0.323)	0.721 (0.713-0.731)	0.235 (0.227-0.248)
	Male	0.748 (0.741-0.759)	0.301 (0.287-0.319)	0.728 (0.724-0.734)	0.24 (0.228-0.249)
Language	English	0.771 (0.764-0.779)	0.304 (0.292-0.312)	--	--
	Non-English	0.709 (0.699-0.72)	0.33 (0.312-0.347)	--	--
APACHE-IVa					
Total	All	--	--	0.822 (0.818-0.828)	0.382 (0.372-0.397)
Age	16-44	--	--	0.882 (0.87-0.898)	0.411 (0.366-0.442)
	45-64	--	--	0.839 (0.829-0.845)	0.378 (0.359-0.397)
	65-79	--	--	0.803 (0.796-0.811)	0.395 (0.382-0.414)
	80-	--	--	0.754 (0.744-0.767)	0.367 (0.347-0.39)
Gender	Female	--	--	0.819 (0.811-0.825)	0.382 (0.37-0.393)
	Male	--	--	0.827 (0.821-0.832)	0.389 (0.369-0.401)

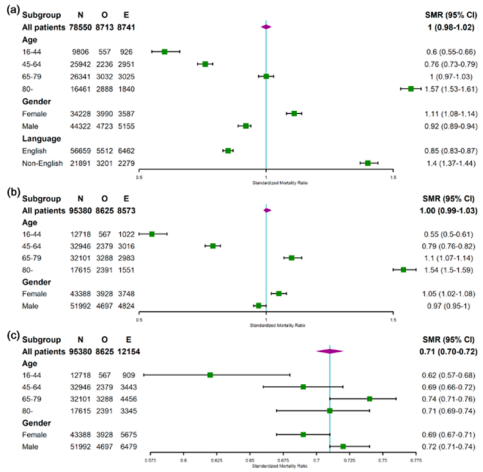

Figure 1. Calibration comparison of SOFA and APACHE IVa models when stratified by age, gender, and primary language subgroups. N: Number of ICU admissions, O: Observed mortality, E: Expected mortality. (a) Standardized mortality ratios (SMR) of SOFA model when applied to the stratified MIMIC database (b) Standardized mortality ratios of SOFA model when applied to the stratified eICU-CRD database (c) Standardized mortality ratios of APACHE IVa model when applied to stratified eICU-CRD database

Conclusion: Illness severity scores have poor discrimination for older and non-English speaking patients, and they overestimate hospital mortality in younger patients. Caution must be taken when using these illness severity scores for quality benchmarking across ICUs that have different mix of patients. Researchers must also be mindful when they adjust for illness severity using these scores as they may not reflect true probability of death.

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Acknowledgements: ZBZ is funded by the National Natural Science Foundation of China (62171471). LAC is funded by the National Institute of Health through the NIBIB R01 EB017205.

000287

Implementation of a digital early warning score (NEWS2) in a cardiac specialist and general hospital settings in the COVID-19 pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000287

Introduction: Prediction tools in acute care settings can improve patient safety and reduce pressure on health systems. Early Warning Scores (EWS) are a potential solution to decrease critical events. However, there is a gap in evidence on the performance of EWS and in the implementation of integrated EWS in Electronic health records (EHR) in specialised clinical settings (1–4). For EWS to be successful, they have to be executed accurately. Failure of EWS can be related to patients' physiology or poor adherence to the prescribed protocol for deterioration (5, 6). Errors in assessment, recording and escalation of care contribute to the occurrence of severe adverse events (7). In addition, the downsides of EHR integration and automated monitoring, i.e. false alarms (8) can challenge the progress needed. Therefore, the implementation of NEWS2 requires investigation by understanding clinicians' perceptions of the application.

Objectives: To evaluate implementation of EHR-integrated NEWS2 in a cardiac care setting and a general hospital setting in the COVID-19 pandemic.

Methods: *Objectives:* To evaluate the implementation of EHR-integrated NEWS2 in a cardiac care setting and a general hospital setting in the COVID-19 pandemic. *Design:* Thematic analysis of qualitative semi-structured interviews with purposefully sampled nurses and managers, as well as online surveys following the non-adoption, abandonment, scale-up, spread, sustainability (NASSS) framework (9) for digitally supported tools in healthcare. *Settings:* Specialist cardiac hospital (St Bartholomew's Hospital) and General teaching hospital (University College London Hospital). *Participants:* Eleven nurses and managers from cardiology, cardiac surgery, oncology, and intensive care wards (St Bartholomew's) and medical, haematology and intensive care wards (UCLH) were interviewed and sixty-seven were surveyed online.

Results: Three main themes emerged: (i) Implementing NEWS2 challenges and support; (ii) Value of NEWS2 to alarm, escalate, particularly during the pandemic; and (iii) Digitalisation: EHR integration and automation. The value of NEWS2 was partly positive in escalation, yet there were concerns by nurses who undervalued NEWS2, particularly in cardiac care. Challenges, like clinicians' behaviours, lack of resources and training and the perception of NEWS2 value, limit the success of this implementation. Changes in guidelines in the pandemic have led to overlooking NEWS2. EHR integration and automated monitoring are improvement solutions that are not fully employed yet.
Conclusion: Whether in specialist or general medical settings, the health professionals implementing EWS in healthcare face real challenges in adopting NEWS2 and related digital solutions. The validity of NEWS2 in specialised settings and complex conditions is not yet apparent and requires comprehensive validation. EHRs integration and automation are powerful tools to facilitate NEWS2 if its principles are reviewed and rectified, and resources and training are accessible.

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Acknowledgements: The research is part of a PhD study funded by the Saudi Ministry of Education.

000304

Prevalence of using landmark technique for CVC insertion within the local environment and current climate

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Introduction: With the increasing use of ultrasound (US) in the critical care and anaesthesia environment for the placement of central venous catheters (CVCs), the number of CVCs inserted via landmark technique is diminishing. Major medical societies have unanimously encouraged the use of US for elective placement of CVC as there is evidence that it is safer with less complications. However, there may still be a role for anatomical landmark techniques for CVC placement in the event of emergencies where US is unavailable. As real-time US guided CVC placement is almost universally considered to be the standard of care in most developed countries, there are diminishing opportunities to train the future generation of doctors in using anatomical landmarks in CVC insertions. An important question looms: will anatomical landmark techniques for CVC insertion soon become obsolete in the next decade or so?. Placement of a CVC in the subclavian vein (SCV) is useful in specific scenarios. For example, severely injured patients with polytrauma often present to the critical care or anaesthetic team with a cervical collar and a pelvic binder, making the SCV the most ideal site for CVC insertion. Although there is a greater chance of significant complications such as arterial puncture or pneumothorax; if performed correctly, SCV cannulation is least likely to result in infective complications compared to other commonly cannulated locations and is the most comfortable for the patient. CVC insertion in the SCV is traditionally done via anatomical landmark techniques due to difficulty in visualization with US. The fear of complications with less conventional CVC insertion techniques and subsequent litigation has resulted in lesser numbers of them being performed.
Objectives: To assess the prevalence of anatomical landmark technique CVC insertion in Singapore in the current day and age of real-time US guidance as the gold standard for CVC insertion.
Methods: We designed a simple questionnaire to sample the local practice and experience of Anaesthetists and Intensivists in Singapore. We collected data on their experience in performing anatomical landmark CVC insertion and their current practice. Senior residents and consultant specialists in all 7 restructured hospitals in the public sector were surveyed to examine the prevalence of CVC insertion via anatomical landmark technique.
Results: Our survey showed that CVC insertion via anatomical landmark is a technique that is hardly practised or taught in Singapore. Doctors who graduated before the ubiquitous use of US for CVC insertion tend to have more experience with anatomical landmark insertion of CVCs. Doctors who have performed more than 100 CVC insertions via anatomical landmark technique in their career are more comfortable performing the procedure in an emergency even though they may not done one in the last 5 years. Despite the infrequent practice of CVC insertion via anatomical landmarks, most agree that this is a skill that should be preserved. Furthermore, our survey has confirmed that the use of ultrasound does not prevent complications of CVC insertion entirely; therefore the pervasive fear of complications with the landmark technique may be unfounded.
Conclusion: The use of anatomical landmarks for CVC insertion is being less practiced in the current age. This is likely to be a result of the common use of US for CVC insertion due to increasing accessibility of US and the unanimous recommendations by major medical societies. Hence, doctors are less experienced and confident in performing anatomical landmark CVC insertions. Furthermore, the increasing litigious environment discourages doctors from practicing less conventional techniques of CVC placement. Despite so, most doctors surveyed agree that CVC insertion via anatomical landmarks is an important skill that should be retained and taught to future trainees. Therefore, there is a need to find ways to teach and train future generations of doctors this specific skill to ensure that it is not lost in the next few decades.

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Acknowledgements: None.

000316

Short-term mortality of patients ≥ 80 years old admitted to European intensive care units—a prospective cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000316

Introduction: Limited evidence indicates that mortality of older critically ill adults varies widely across Europe.
Objectives: We aimed to investigate regional differences in mortality among very old intensive care unit (ICU) patients.
Methods: Multilevel analysis of two multicentre prospective cohort studies that enrolled patients ≥ 80 years old in 16 European countries. The primary outcome was mortality within 30-days from admission to the ICU.
Results: 322 ICUs recruited 8457 patients. Crude mortality in participating countries ranged from 10.1% to 45.1% in the ICU and from 21.3% to 55.3% in 30-day follow-up. The variation in 30-day mortality between countries was substantially smaller than between ICUs (adjusted median odds ratio [OR] 1.14 vs. 1.58). Healthcare expenditure per capita (OR = 0.84 per 1000$; 95% CI: 0.75–0.94) and social health insurance framework (OR = 1.43; 95% CI 1.01–2.01) were associated with ICU mortality, but the direction and magnitude of these relationships was uncertain in 30-day follow-up. Volume of admissions was associated with lower mortality both in the ICU (OR = 0.81 per 1000 annual ICU admissions; 95% CI: 0.71–0.94) and in 30-day follow-up (OR = 0.86; 95% CI: 0.76–0.97).
Conclusion: The apparent variation in short-term mortality rates of patients hospitalised in ICUs across Europe can be largely attributed to differences in the clinical profile of admitted patients.

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Acknowledgements: Polpharma Scientific Foundation (VIII 2020/2021). Polish National Agency for Academic Exchange, Iwanowska Programme (PPN/IWA/2019/1/00106).

000378

Reproducibility and standardization of echogenicity measurements of the diaphragm in critically ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000378

Introduction: Diaphragm echogenicity assessment has gained interest as an ultrasound approach to quantify muscle quality. Lower echogenicity values (darker pixels) may indicate good muscle quality. Ventilated critically ill patients were found to have higher values compared to healthy subjects [1]. However, standardizing this method is key, as ultrasound settings have a large impact on resulting gray levels. We aimed to standardize a method for measuring diaphragm echogenicity (Part A) and studied the reproducibility (Part B).
Methods: Part A: impact of ultrasound settings on diaphragm echogenicity was studied in 3 subjects. Settings were then standardized to limit filtering/alterations by the machine (Tab1). Part B: in 15 subjects diaphragm ultrasound videos of at least 3 breaths were acquired in B-mode by 2 observers and observer 1 repeated the measurement. Probe locations were right midaxillary line (zone of apposition) and the frontal diaphragm where the muscle attaches to the abdominal wall. Each observer selected 3 inspiratory and expiratory cycles and drew a region of interest (ROI) in the muscle, not including the hyperechoic fascia (Figure 1). Intraclass correlation coefficients (ICCs) were computed from the median gray values within each ROI to determine the interobserver (2 observers acquired images and selected ROI), interrater (1 observer acquired images, 2 raters selected ROI), and intraobserver (repeated image acquisition and ROI selection) reproducibility.
Results: Part A: Figure 2 shows the effects of compress and gain settings on the histogram of echogenicity values. Part B: 5 healthy subjects (2 male, mean BMI 22 kg/m^2) and 15 invasively ventilated patients (9 male, mean BMI 26 kg/m^2, on pressure control (n = 6) and support (n = 9) mode) were included. ICCs were between 0.71 and 0.98 (Table 2), with highest ICC in the frontal diaphragm. ICCs for ROI selection only (intra-rater) were larger than ICC for the complete measurement (interobserver: image acquisition + ROI selection). There was a significant (p = 0.02) increased echogenicity in patients compared to healthy subjects, but only in the frontal region (mean (standard deviation), 74.7 (16.0) vs. 70.8 (11.7) respectively in zone of apposition and 70.0 (22.7) vs. 53.9 (2.9), in frontal region).

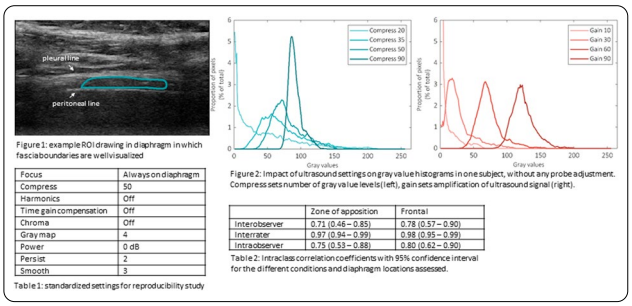

Figure 1: example ROI drawing in diaphragm in which fascia boundaries are well visualized

Focus	Always on diaphragm
Compress	50
Harmonics	Off
Time gain compensation	Off
Chroma	Off
Gray map	4
Power	0 dB
Persist	2
Smooth	3

Table 1: standardized settings for reproducibility study

Figure 2: Impact of ultrasound settings on gray value histograms in one subject, without any probe adjustment. Compress sets number of gray value levels (left), gain sets amplification of ultrasound signal (right).

	Zone of apposition	Frontal
Interobserver	0.71 (0.46 – 0.85)	0.78 (0.57 – 0.90)
Interrater	0.97 (0.94 – 0.99)	0.98 (0.95 – 0.99)
Intraobserver	0.75 (0.53 – 0.88)	0.80 (0.62 – 0.90)

Table 2: Intraclass correlation coefficients with 95% confidence interval for the different conditions and diaphragm locations assessed.

Conclusion: Reproducibility of diaphragm echogenicity measurement is acceptable and mostly impacted by image acquisition as opposed to ROI selection. Adjustment of ultrasound settings considerably influence results which has been neglected in earlier studies [1]. Our proposed standardization enables a reproducible assessment of diaphragm muscle quality. The results also indicated an increase in echogenicity in ventilated critically ill patients compared to healthy

subjects, as was also found in another study [1], although the relatively small sample size must be kept in mind.

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000400

Dummy run: use of in situ simulation is a useful tool in preparing the adult critical care team for relocation to a new unit

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Introduction: Transition into newly-built healthcare facilities is a common requirement in the UK NHS (1). Medical simulation is growing in popularity in intensive care (2). It has been studied as a means to prepare for transition to new health care facilities by several specialties, including Emergency departments (3), Obstetric units, NICUs (4,5) and PICU (6). However, it has not been studied in this context for adult intensive care.
Methods: We conducted simulation-based orientation training for healthcare workers transitioning to the newly-constructed Adult Critical Care Unit, based in John Radcliffe Hospital—a UK tertiary care hospital and trauma centre. We conducted structured focus groups, interviews, and questionnaires prior to this to inform the training content. The training course was comprised of:

- Walk-round guided tour of the new critical care unit
- Pokemon-themed treasure hunt activity aimed at locating key pieces of clinical equipment
- Fire evacuation procedure demonstration and in situ simulation
- Cardiac arrest in situ simulation, including BLS update and LUCAS device training
- Obstructed tracheostomy high-fidelity in situ simulation scenario

Feedback on the usefulness of the training as a whole, as well as each individual component, was collected immediately post-simulation. Follow-up feedback is planned 4 weeks post-transition.
Results: Several latent safety issues were identified during simulations, including an ambiguous section of the emergency tracheostomy management algorithm, and response to activation of the new bedside emergency buzzers. Post-course feedback was mostly positive—77 of 84 respondents found the training programme useful. Positive comments focused on the multidisciplinary nature of the training, and the pragmatic, high-fidelity details germane to day-to-day healthcare provision. Constructive criticism highlighted ways in which these positive elements could have been maximised.
Conclusion: Simulation-based orientation training is useful in preparing Adult Critical Care healthcare workers to transition to a new Critical Care Unit. Optimisation of this requires a focus on day-to-day tasks, and high fidelity, both of which are best achieved when the unit is fully stocked and ready for transition. However, timing complexities make this challenging.

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Health services research & outcome 4

000104

How an external team for family communication fit in the ICU team in pandemic times: Experience of a single centre

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Intensive Care Medicine Experimental 2022, **10(2)**:000104

Introduction: Collaborative practice amongst health providers in ICU is essential for safer patient care and increased satisfaction for patients and families [1]. Teambased medicine requires the expertise and coordinated efforts of different clinicians, who must successfully perform both taskwork and teamwork [2]. The visitation restrictions posed by the current Covid-19 pandemic forced ICUs to turn to non-critical care personel to aid communication with patients' family and friends (PFFs). Those family laison teams (FLTs) had to collaborate closely with ICU staff to maintain the clinician—family connection during the pandemic.
Objectives: To describe the interactions between the "established" ICU team and the newly created FLT during the two waves of the pandemic.
Methods: We evaluated the quality of collaboration between the "established" ICU team and the newly created FLT by using the Interprofessional Collaboration Scale (ICS) [3]. We compared the evolution of that collaboration between the 1st (March–May 2020) and 2nd (December 2020–March 2021) waves of the pandemic in our tertiary London hospital.
Results: The FLT consisted of 39 non-ICU healthcare professionals, the majority of which were consultant grade. Their main responsibilities are shown in table 1 and the composition of the team largely remain the same between the two waves. We focused on the 6 ICS questions that address the family's information needs: > 80% of FLT members felt welcomed and respected in both waves, whereas > 70% of both teams mostly or fully agreed that there was a mutual understanding of responsibilities. However, approximately 25% of the FLT reported that their views were not sought during the communication process, whereas only 8% of the ICU staff felt the opposite (23% and 8% in the second wave). Almost 80% of the FLT and 65% of the ICU team stated that important information was always communicated adequately (similar for both groups from 1st wave). Last, both teams reported a strong willingness to to discuss issues between the two teams (approaching 90% in both waves).

Table 1. Family Liaison Team Responsibilities

Daily medical updates
Facilitation of video calls
Information provision and support for visiting*
Obtaining social history from family, if unknown
Communicate information to the medical and nursing teams
Identification of families/friends with specific needs (young children, impending bereavement, social and psychological support) and refer them to the appropriate services

Conclusion: Non-critical care professionals have been pivotal in continuing the patient-family connection during the pandemic. Clarification of roles, communication and collaboration fostered during the first wave increased understanding and cooperation between the two teams during the second wave. The difficult of communicating critical care specific information to non-ICU staff was a recurrent theme.

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000248

Delta neutrophil index as a prognostic factor for mortality in patients with Fournier's gangrene

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Introduction: Fournier's gangrene (FG) usually causes painful swelling of the affected lesion with foul-smelling discharge, which can extend rapidly and sometimes in a fulminant fashion, causing multiple organ dysfunction, septic shock, and death. Consequently, the early detection of patients with FG who are likely to show adverse outcomes and the prevention of disease progression by aggressive treatment is a considerable issue. The delta neutrophil index (DNI) represents the fraction of circulating immature granulocytes, and is a marker of infection and sepsis. However, no studies have explored the potential role of DNI as an initial biomarker for predicting mortality in FG.
Objectives: This study aimed to determine the usefulness of the DNI as a prognostic serum biomarker and compare it with previously established markers or indices for predicting mortality in patients with FG.
Methods: We enrolled patients with FG who were admitted to the Wonju Severance Christian Hospital (Wonju, Korea) between September 2010 and December 2021. We retrospectively analyzed the patients' characteristics, factors related to management, scoring systems such as the Fournier's Gangrene Severity Index (FGSI), and laboratory data measured at initial presentation. Comparative analysis between survivors and non-survivors using Student t-test, chi-square, and Fisher's exact test. Multivariate analysis was performed using logistic regression to identify the independent risk factors. A receiver operating characteristic (ROC) curve was constructed, and the Youden index method was used to determine the optimal cutoff values for data to predict mortality.
Results: There were 58 (68.2%) survivors and 27 (31.8%) non-survivors. The initial levels of serum lactate, hemoglobin, DNI, albumin, international normalized ratio (INR), creatinine, FGSI, and prognostic nutritional index differed between survivors and non-survivors. Stoma formation was not associated with mortality. Age, INR, and DNI were independent predictors of mortality in FG. In ROC curve analysis, DNI on the day of admission was the best indicator of mortality [area under the curve (AUC), 0.804; 95% confidence interval (CI) (0.679–0.929)]. The optimal cutoff for DNI in predicting mortality was 11.25% (sensitivity, 74.1%; specificity, 91.4%). Initial DNI was the best indicator of mortality (area under the curve: 0.804; 95% CI: 0.679–0.929). AUC of INR were 0.739 (95% CI, 0.610-0.868). The optimal cutoff value for INR was 1.36 (sensitivity, 48.1%; specificity, 94.8%). *Escherichia coli* was the most common organism found in the enrolled patients in this study (n = 31, [36.9%]).
Conclusion: Our study may be meaningful in that it is the first to evaluate the usefulness of DNI in predicting mortality in patients with FG. DNI could be a promising predictor of mortality in patients with FG, and the optimal cutoff value for predicting mortality was 10.25%. INR can also be used as an independent predictor of mortality in patients with FG, with a cutoff value of 1.36. Moreover, old age was an independent predictor of mortality in FG. Additionally, since stoma formation was not associated with mortality, it may be performed after patient stabilization and wound re-evaluation. Large-scale multicenter prospective studies are needed to confirm our results.

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Acknowledgements: None.

000281

Environmental impact of plastic IV bags versus reusable glass jars

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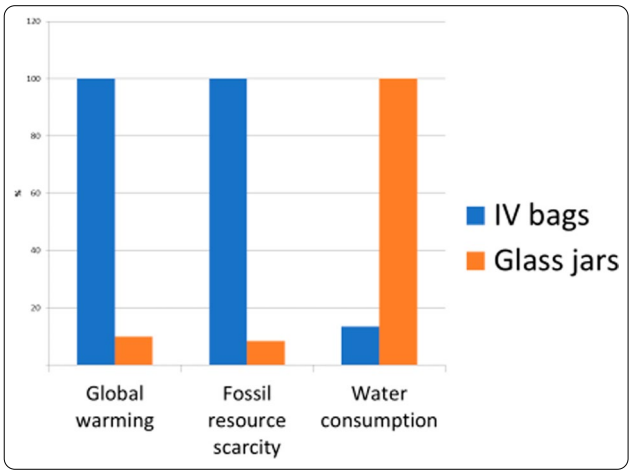
Intensive Care Medicine Experimental 2022, **10(2)**:000281

Introduction: Globally, the healthcare sector is one of the most carbon-intensive service sectors. The system is responsible for approximately 5% of the global greenhouse gas emissions, while emitting similar fractions of toxic air pollutants due to fossil fuel combustion [1]. In the Netherlands, the healthcare system is responsible for 7% of the national CO_2 footprint [2]. Europe aims to reduce overall CO_2 emissions in 2050 by 80% compared to 1990 [3]. In order to achieve this goal, the environmental impact of the healthcare sector primarily needs to be mapped out in more detail. This can be accomplished by determining the environmental impact of specific medical products and care pathways. This obtained data will contribute to an action perspective for the required sustainable transformation of the healthcare system.
Objectives: The aim of this study is to compare the environmental impact of the frequently used plastic IV bags with on-site production of infusion fluids administered in reusable glass jars.
Methods: An environmental life cycle assessment (LCA) was conducted in SimaPro 9.2.0.2 software by using ReCiPe 2016 Midpoints [4]. This method includes all environmental inputs and outputs from the harvesting of resources up to the disposal of the

product. The conducted LCA calculates the impact on several midpoints, including global warming, fossil resource scarcity and water consumption.



Results: Plastic IV bags have a 90% higher impact on the midpoints of global warming and resource scarcity, mainly caused by the plastic production, transport and hazardous waste treatment. The emitted CO_2-equivalents for one IV bag is approximately 0.9 kg, while it is 0.09 kg per glass jar used. On the other hand, glass jars have a 85% higher impact on the midpoint of water consumption which is mainly caused by the tap water used for sterilization. The calculations were performed with wind and solar energy for the sterilization of the glass jars. Interestingly, scenario analysis showed that glass jars that are cleaned and sterilized using a classical Dutch energy mix instead have a higher environmental impact on all three midpoints compared with plastic bags. Jars/bags with a larger volume and processes of re-using further decreases the environmental impact.
Conclusion: From the performed LCA it can be concluded that the environmental impact of glass jars is up to 90% lower compared with that of the plastic IV bags. The glass jars are, thus, considered to be a more environmentally-friendly alternative, provided that renewable energy for the cleaning and sterilization process is used. In 2021, more than 270,000 IV bags were administered to patients in our hospital. Switching from plastic IV bags to reusable glass jars could save approximately 225 ton CO_2 per year, which is equivalent to 1.85 million km travel by car (4.5 times around the world).

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Acknowledgements: This study was granted a ZonMw scholarship. File number: 80-86800-98-112.

000315

The impact of electronic Critical Care Information Systems in critical care medicine on work processes, job satisfaction and agency from an employee perspective—qualitative interview study on barriers and opportunities of CCIS use

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Introduction: Electronic Critical Care Information Systems (CCIS) used in intensive care medicine can increase the quality of care (1–3), e.g. by simplifying treatment through overview of different automatically taken vital signs (4, 5), saving documentation time (6–10), reducing medication errors (11–15) and decreasing adverse drug events (16, 17). In addition, they may also increase staff-perceived quality of documentation (8) and care (1–3) and increase job satisfaction (18, 19). At the same time, there are also studies showing that the introduction of a CCIS has no effects (20–24) or even negative effects on care such as an increase in documentation time (25, 26) or medication errors (27). CCIS can also potentially cause resistance (28) and "technostress" and associated decreases in job satisfaction (29–33) among staff. Problems with CCIS may differ for different occupational groups (34–36). Therefore, to avoid negative consequences for care and employee well-being, it is necessary to examine why and how negative consequences may arise. Several factors should be considered: The emergence of negative feelings such as loss of control (37) or a sense of being controlled (38), a substitution of the interaction process (39), the emergence of new tasks and needed competencies, and that employees desire more participation during the implementation process (40). Also relevant are the duration of training with the CCIS and the usability of the CCIS (36).
Objectives: The objective of the study is to identify examples of relevant factors that create resistance or problems with regard to the perceived quality of care or staff satisfaction when using a CCIS and to shed more light on how these factors take effect. Differences between occupational groups with regard to these factors will also be examined and ideas for improvement will be generated. Decision makers in hospitals can then take these factors into account when using or implementing a CCIS.
Methods: A prospective qualitative interview study (semi-structured individual interviews of 30 min) of staff members of different intensive care units of a german university hospital is planned. 15–20 persons will be interviewed, consisting of equal numbers of nurses and physicians. As far as possible, a balanced distribution in terms of age, gender and hierarchical level should be ensured. The data will be coded with MAXQDA and will be analyzed according to Corbin & Strauss (41) by elaborating thematic categories. Data collection should be completed by the end of June 2022 so that the results of the interview study can be presented in the poster session.
Results: Expected until October 2022.
Conclusion: Excpected until October 2022.

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000380

FICUS trial study protocol: a cluster-randomized trial of a multicomponent family support intervention in adult intensive care units

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Introduction: Family members of critically ill patients face uncertainty and distress during their close others' intensive care unit (ICU) stay. Up to two thirds experience adverse mental health outcomes post-ICU, such as symptoms of anxiety, depression, and posttraumatic stress. The important role of families in supporting the critically ill patient and the need to increase family inclusion and communication are gaining recognition. Recent reviews suggest promising effects of family inclusion and communication (Goldfarb et al., 2017; Kiwanuka et al., 2022, Xryichis et al. 2021; Zante et al., 2020; Kiwanuka et al., 2022), but the evidence on the clinical effectiveness of specific family support interventions is modest (Curtis et al., 2016; White et al., 2018; Kentish-Barnes et al., 2022).
Objectives: To test the clinical effectiveness and explore the implementation of a multicomponent, nurse-led family support intervention (FSI) in Swiss ICUs.
Methods: The cluster-randomized, controlled hybrid-type 1 trial with eight ICUs per study arm will be undertaken in the German-speaking part of Switzerland. The trial will include family members of adult, critically ill patients with an expected ICU stay of 48 h or longer. The projected sample size was calculated to n = 896. The FSI consists of (1) specialist family nurse support along the patient pathway, with early, proactive family engagement and follow-up care, (2) psychoeducational and relationship-focused family conversations, and (3) structured, interprofessional communication. Usual care is the control condition. The primary study endpoint is quality of family care, operationalized as satisfaction with ICU at discharge. Secondary endpoints include quality of communication, nurse support, family management of critical illness, and family members' mental health, measured at admission, discharge, and after three, six, and twelve months. Data will be analysed using linear mixed-effects models, with the individual participant as the unit of inference.

Results: Patient and family member representatives are involved in the trial implementation to ensure that participation in the FICUS trial is meaningful and feasible for family members. The trial has been approved by the responsible ethic committees, cluster baseline characteristics on family care processes have been collected, and clusters have been randomized to intervention and control arm. Study team and intervention nurses are currently trained, with participant recruitment commencing in spring 2022. A mixed-methods evaluation will investigate implementation processes and outcomes on intervention units.
Conclusion: The FICUS trial has the dual aim to examine the clinical effectiveness of the FSI in the real-world context of ICU care delivery and explore its implementation. Both types of evidence are necessary to determine the clinical effectiveness and implementability of multicomponent family support interventions in ICU.

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Acknowledgements: Funded by the Swiss National Science Foundation. Supported by the Swiss Society of Intensive Care Medicine.

000412

A comparison of echocardiographic findings in critically ill patients with COVID-19 with and without extracorporeal membrane oxygenation

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Introduction: The use of Venovenous Extracorporeal Membrane Oxygenation (VV ECMO) for refractory acute respiratory failure has been reported in more than 13 000 patients with COVID-19**.** Although respiratory failure is the cornerstone of severe COVID-19, cardiac disease has been described in up to 20% of the patients, with an increased associated mortality. Currently, there is a paucity of data regarding the echocardiographic findings in patients with COVID-19 supported with ECMO.
Objectives: This study aims to compare the baseline echocardiographic characteristics of mechanically ventilated patients with COVID-19 with and without ECMO support. A secondary aim was to describe the incidence of new echocardiographic abnormalities in these patients.
Methods: We performed a single-center, retrospective cohort study of patients admitted to the ICU with COVID-19 from March 2020 to June 2021. Patients were included if they had SARS-CoV-2 infection confirmed by reverse transcription-polymerase chain reaction (RT-PCR) test, required mechanical ventilation, and had an available echocardiogram performed in the first 72 h of admission. Follow-up echocardiograms during ICU stay were reviewed. Patient characteristics, physiological and ventilatory parameters, as well as echocardiographic findings were recorded and analyzed.
Results: During the study period, 315 patients were admitted with COVID-19 to the ICU, 242 patients were included in the analysis, amongst which 145 (60%) were supported with VV-ECMO. Patients in the ECMO group were younger (49 years vs 54 years, $p = < 0.001$) and had a higher proportion of males (80 vs 70%, $p = 0.05$). The most common comorbidity in both groups was hypertension. Median (IQR) PaO_2/FiO_2 was 76 (65–95) and 98 (85–140) in the ECMO and non-ECMO patients respectively ($p = < 0.001$). A total of 596 transthoracic echocardiograms and 179 transesophageal echocardiograms were reviewed. On average, each patient had 3 (± 2) echocardiograms performed. In the first echocardiograms, there were no significant differences in left ventricular (LV) systolic dysfunction (15 vs 9%, $p = 0.08$) and right ventricular (RV) systolic dysfunction (38 vs 27%, $p = 0.27$) between the ECMO and non-ECMO groups. However, the ECMO group had higher incidence of RV dilation (44 vs 27%, $p = 0.006$), and paradoxical septal motion (48 vs 33%, $p = 0.02$). A total of 20 patients had intracardiac structures suggestive of thrombi (9% ECMO vs 7% non-ECMO, $p = 0.6$). During their ICU stay, 122 (84%) patients in the ECMO group and 58 (60%) in the non ECMO group had follow-up echocardiograms. In the ECMO group, RV systolic function worsening occurred in 47 patients (39%), as compared to six patients (10%) in the non-ECMO group ($p = < 0.001$). ICU mortality was 53% for the ECMO group and 39% for the non-ECMO patients ($p = 0.07$).
Conclusion: Echocardiographic findings suggest that the incidence of ventricular systolic dysfunction in the COVID-ECMO patients is comparable to the non-ECMO group early upon their admission. However, a higher percentage of patients on ECMO associate RV dilation and pressure overload and will develop worsening of RV systolic function during follow-up.

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000458

Long-term impairments are most pronounced in obese critically ill patients with COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**:000458

Introduction: While obesity is a risk factor for severe COVID-19 (1), once admitted to the intensive care unit (ICU), body mass index (BMI) and short-term outcomes are no longer associated (2). Long-term symptoms in COVID-19 survivors are well recognized (3, 4), but it is unknown whether the prevalence rates of long-term symptoms differ between different BMI groups. This study aimed to examine differences between BMI groups in the occurrence of physical, mental and cognitive symptoms 3 and 12 months following ICU treatment in critically ill COVID-19 patients.
Methods: In this prospective multicenter cohort study, COVID-19 patients admitted to ICUs in 11 Dutch hospitals between March 2020 and July 2020 were included (5). Patients received three questionnaires regarding their health status: pre-ICU (baseline), 3 and 12 months following ICU treatment. Patients who completed baseline and 12-month follow-up questionnaires were included. Primary outcomes were occurrence of physical (fatigue and new physical problems), mental (symptoms of anxiety, depression, and post-traumatic stress disorder [PTSD]) and cognitive symptoms. Patients were categorized into BMI groups: underweight (< 18.5 kg/m^2), normal weight (18.5–25.0 kg/m^2), overweight (25.0–30.0 kg/m^2), obese class I (30.0–35.0 kg/m^2) and obese class II/III (≥ 35.0 kg/m^2) (6). Differences in symptom occurrence rates were adjusted for age, sex, severity of illness (APACHE-IV), and length of stay (LOS) in ICU using multivariable logistic regression analysis.
Results: A total of 239 ICU patients with COVID-19 was included. Patients with obesity class II/III were younger, less likely male and had a lower APACHE-IV score and shorter LOS-ICU compared to normal weight patients. Baseline physical, mental, and cognitive symptoms did not differ between BMI groups (Table 1). There was a significant interplay between BMI groups and the incidence of physical and mental symptoms at both 3- and 12-months. This was most pronounced for the class II/III group at 3-months for the incident symptoms of fatigue, anxiety, and PTSD (Figure 1). At 12 months post-ICU, patients in the obesity class II/III group were still significantly more likely to experience symptoms of fatigue, physical symptoms, and symptoms of anxiety, depression and PTSD compared to the other BMI groups (Figure 1). Cognitive symptoms were similar between BMI groups.

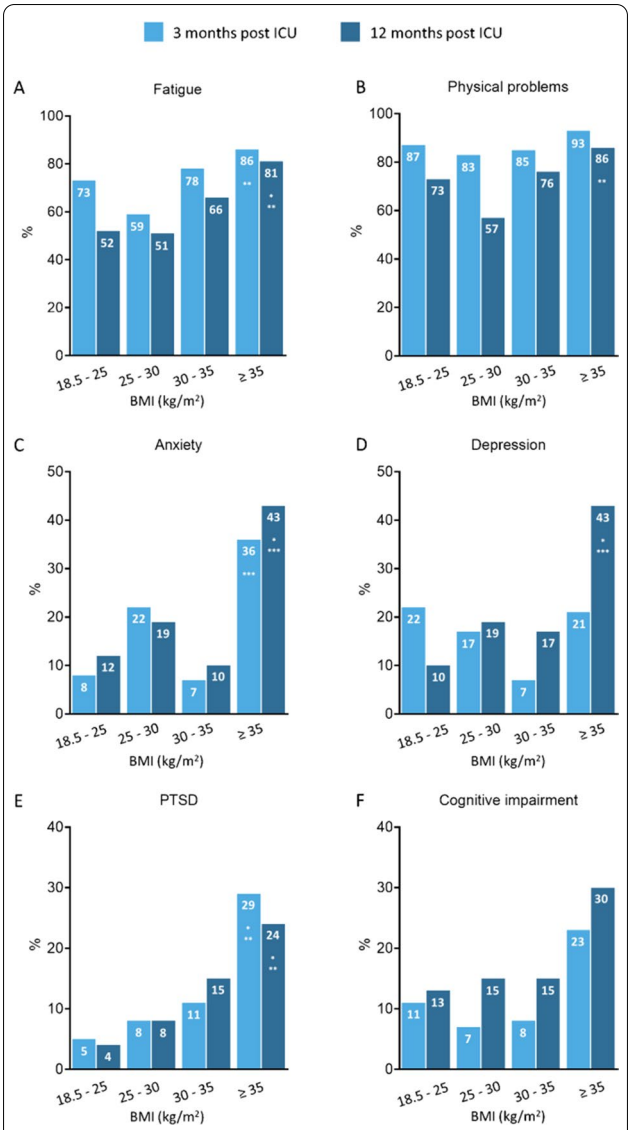

Figure 1. Prevalence of symptoms of **A)** fatigue, **B)** physical problems **C)** anxiety, **D)** depression **E)** post-traumatic stress disorder (PTSD) and **F)** cognitive impairment at 3- and 12-months post ICU in different Body Mass Index (BMI) categories in patients with COVID-19. *p < 0.05 compared to BMI 18.5-25 kg/m2. **p < 0.05 compared to BMI 25-30 kg/m2. ***p < 0.05 compared to BMI 30-35 kg/m2*

Table 1. Demographic patient characteristics

Table 1. Demographic patient characteristics.

BMI category	Normal weight 18.5-25 kg/m² (n=69)	Overweight 25-30 kg/m² (n=108)	Obesity Class I 30-35 kg/m² (n=41)	Obesity Class II/III ≥35 kg/m² (n=21)
Patient characteristics				
Age, median [IQR], y	65 [59-70]	62 [55-69]	58 [52-65][a]	57 [53-61] [a]
Sex, male, n (%)	52 (75)	84 (78)	27 (66)	9 (43)[a b]
BMI, median [IQR], kg/m²	23.9 [22.9-24.6]	27.3 [26.3-28.4][a]	32.6 [30.8-32.7][a b]	37.0 [36.4-39.1][a b]
APACHE-IV, median [IQR]	59 [49-68]	59 [49-68]	54 [43-68]	50 [42-58][a]
LOS ICU, median [IQR], days	27 [13-39]	18 [11-31]	18 [12-28]	12 [9-20][a]
LOS hospital, median [IQR], days	39 [25-54]	29 [20-44]	27 [18-43]	24 [15-35][a]
Frailty (CFS ≥ 5), n (%)	12 (17)	21 (20)	11 (27)	5 (24)
Baseline symptoms (pre-ICU)				
Fatigue (CIS ≥ 27), n (%)	43 (62)	57 (53)	28 (68)	13 (62)
Anxiety (HADS-A ≥ 8), n (%)	10 (15)	9 (8)	6 (15)	5 (24)
Depression (HADS-D ≥ 8), n (%)	12 (17)	17 (16)	6 (15)	3 (14)
Cognitive impairment (CFQ ≥ 43), n (%)	4 (6)	4 (4)	5 (13)	3 (14)

[a]p<0.05 compared to BMI 18.5-25 kg/m²

[b] p<0.05 compared to BMI 25-30 kg/m²

None of the patients had a BMI <18.5 kg/m².

IQR: interquartile range. *BMI:* Body Mass Index. *APACHE-IV:* Acute Physiology and Chronic Health

Conclusion: Higher incidence rates of long-term physical and mental symptoms were observed in obese ICU survivors with COVID-19 compared to patients in lower BMI groups, whereas no significant differences were present prior to ICU admission. In contrast with the absence of an association of BMI and ICU mortality (2), these long-term symptoms may be directly related to BMI. Regardless the underlying causes, it implicates that long-term follow-up is of explicit importance in obese patients.

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000481

The impact of the COVID19 pandemic on the number of ICU admissions to a UK district general hospital (DGH) for known end stage renal failure (ESRF) patients missing their regular dialysis sessions

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Intensive Care Medicine Experimental 2022, **10(2)**:000481

Introduction: East Surrey hospital (ESH) is a DGH covering a population of over half a million. It has renal clinics but no onsite dialysis service. When ESRF patients on dialysis present emergently requiring renal replacement therapy they are admitted to ICU for continuous venovenous hemofiltration (CVVH) if they cannot be transferred to a dialysis unit. This impacts individual patient care as well as wider availability of healthcare resources. ESH ICU has ten level 3 and six level 2 beds. During the pandemic this escalated to thirty-four level 3 beds. Studies showed decreased ED attendances and hospital admissions in patients presenting with conditions other than COVID19 during waves of the pandemic$_1$
Objectives: To assess the impact of the COVID19 pandemic on ICU admissions for patients with ESRF requiring CVVH at ESH.
Methods: ICU admitted 56 ESRF dialysis patients for CVVH only from 1st January 2018 to 31st December 2021. Using 2018–2019 as a baseline, we looked at how the number of admissions changed during the pandemic by year. We compared the number of patients admitted to hospital purely due to missed dialysis to those admitted for another reason and if this changed during the pandemic. We also looked at discharge destination. Data was analysed by Fisher's Exact Test and pairwise comparisons where appropriate, using R (version 4.1.3, Vienna, Austria).
Results: There was an absolute increase in the number of admissions per year. No significant difference was seen between reasons for admission. A significant difference was seen for discharge destination, but pairwise comparison showed this was ultimately not significant (Table 1).

Table 1: ICU admissions for ESRF patients requiring only CVVH by year

	2018	2019	2020	2021	p-value
Total admissions	8	11	16	21	
Reason for admission					
Missed dialysis	2	4	7	9	
Other reason	6	7	9	12	0.8908
ICU discharge destination					
Renal unit	4	8	7	7	
Ward	2	3	8	3	
Home	1	0	0	6	0.0423

Conclusion: Patients in this study had no critical care needs and could have been managed in a dialysis centre. While ICU bed numbers increased to accommodate the burden of COVID19, the overall number of ICU trained nurses had not. As these patients were still admitted to ICU this impacted an overburdened service. Better access to services has led to an increased number of patients on dialysis[2]. ESRF patients are prone to hospital admission due to associated co-morbidities. As patient numbers increase, admissions are likely to rise. We will repeat this study to see if similar admissions continue to rise (becoming statistically significant), or if this small increase was a result of the pandemic. While studies suggest outcomes of acutely ill ESRF dialysis

patients are similar to non-dialysis patients[3], there is little data on how dialysis needs are met when presenting to non-renal centres. Collating data from other DGHs would assess the impact on ICU services.

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000494

Adjunctive hemoadsorption in critically ill COVID-19 patients requiring extracorporeal membrane oxygenation (ECMO): The CytoSorb Therapy in COVID-19 patients (CTC) multicenter registry

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Intensive Care Medicine Experimental 2022, **10(2)**:000494

Introduction: The multicenter CTC registry was launched following FDA emergency use authorization (EUA) for the use of CytoSorb to reduce hyperinflammation in critically COVID-19 patients.
Objectives: Evaluate the clinical performance of ECMO-integrated CytoSorb hemoadsorption in critically ill COVID-19 patients. We have previously reported a 90-day survival of 73.1% in the first 52 patients enrolled in the Registry [1]. The current analysis extends the observations to the full CTC Registry cohort.

Methods: Patients on ECMO also treated with CytoSorb at 5 US centers were included in the analysis. Survival was evaluated with a time-to-event analysis. Available data on CytoSorb and ECMO treatment parameters, inflammatory markers and pulmonary function were collected and compared between survivors and non-survivors. For context, reported survival from the international COVID-19 ECMO ELSO-registry (n = 13,864; April 4, 2022) is Referenced.
Results: A total of 100 patients (63% male; median age 45 [IQR = 16]) were included. Survival rates were 86% (86/100) at 30 days and 74% (74/100) at 90 days. Compared to non-survivors, survivors had a significantly shorter interval between ECMO initiation and CytoSorb start (Median time: 64.2 [127.0] vs. 151.2 h [216.0], $p = 0.0073$), numerically lower baseline D-Dimer levels (2.81 ± 2.50 vs 8.04 ± 9.98 µg/mL; $p = 0.19$) and numerically lower baseline SOFA scores (5.72 ± 3.78 vs. 6.71 ± 4.47; $p = 0.35$). Among survivors, those who initiated CytoSorb before the median start time showed a trend towards improved 24-h PaO2/FiO2 ratio (90.66 ± 113.03 vs. 55.40 ± 84.04 mmHg; $p = 0.1007$) and had significantly shorter overall ECMO support duration (532.8 ± 533.1 vs. 800.7 ± 701.7 h; $p = 0.0213$).
Conclusion: Survival of critically ill COVID-19 patients on ECMO also treated with CytoSorb was high compared to international benchmark rates reported in the ELSO-registry. The current analysis also suggests that early initiation of CytoSorb may be a key feature underlying the high survival rates.

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Acknowledgements: None.

Health services research & outcome 5

000173

Long-term functional decline in survivors of critical COVID-19 pneumonia: comparison of the first two waves of the pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000173

Introduction: The long-term functional consequences of a critical COVID-19 pneumonia, in view of pre-illness status, are not widely described. Moreover, it is not sure that the treatment differences provided during wave 1 (W1) and wave 2 (W2) could have impacted patients outcome.
Objectives: The aim of this bicentric cohort study was to assess the 1-year functional status of survivors of a critical COVID-19 pneumonia during W1, compared to W2.
Methods: All adults who survived an intensive care unit (ICU) stay for a critical COVID-19 pneumonia in the University Hospital of Liège or in the Regional Hospital of Verviers between March 15th to April 30th 2020 (W1) and between October 1st and November 30th 2020 (W2) were included. One year after ICU discharge, a standardized assessment was conducted by phone, focused on health-related quality of life (EQ-5D-3L), autonomy for activities of daily living (Barthel Index), and physical activity quantification (IPAQ short form). Patients rated their current status and that prior to ICU admission. We also collected place of residence, return to work or leisure activities, and hospital readmissions.
Results: Among the 361 patients admitted to these two ICU during W1 and W2, 121 died in hospital and 44 W2 patients were transferred in other hospitals due to overcrowding. Among the 198 remaining survivors, 132 (66.7%) answered our phone call: 64.4% male, 64 [54–70]y. Their ICU and hospital length of stay (LOS) were respectively 8 [4.2–16.7]d and 22 [12–42.5]d. Their SAPS 2 reached 34 [26–46]. Mechanical ventilation (MV) was required in 62/132 (46.9%) patients, during 12.5 [6–23]d. None of them was treated with ECMO. At M12, 36 out the 62 active patients (58.1%) returned to work full time while 40 out of the 70 retired patients (57.1%) returned to their previous level of activities. Most of the patients (127/132, 96.2%) was living at home. Hospital readmission during the previous 12 months occurred in 25.8% (34/132) of the patients. Compared to the pre-ICU time, the visual analogic scale (VAS) part of the EQ-5D-3L decreased significantly from 86 [80–95] to 75 [60–80] at M12 ($p < 0.001$). Pre-ICU estimated physical activity decreased from 1383 [693–3066] to 888 [383–2339] MET-min/week at M12 ($p < 0.001$). Loss of autonomy (Barthel Index < 100) was observed in more patients at M12 (48/132, 36.4%) than during the pre-ICU period (16/132, 12.1%) ($p < 0.001$). Compared to W1, W2 patients had a shorter ICU LOS ($p = 0.0003$). The proportion of W2 patients supported by MV and norepinephrine was lower than during W1 ($p < 0.001$ and $p = 0.0008$, respectively). However, no difference was observed in term of functional decline between groups.

Conclusion: In our cohort of COVID-19 ICU survivors, 1-year functional status was still impaired compared to pre-ICU status, without differences between W1 and W2 survivors. Whether these results could be transposed to non-COVID-19 ICU survivors requires further investigations.

000295

Accepting psychological support in the intensive therapy team, during the pandemic, in Hungary

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Intensive Care Medicine Experimental 2022, **10(2)**:000295

Introduction: The mental health of healthcare workers affects the quality of patient care and their ability to stay in the workplace. During the waves of the COVID-19 pandemic, several mental health care professionals and organisations offered free psychological support to the caregivers in both individual and group settings. However, there was often a dismissive attitude among colleagues; feedback from psychologists indicated that only few people took advantage of these services.
Objectives: Based on the feedbacks about the lack of seek for help, our study's aim was to find out how many of the workers felt they needed psychological help during the pandemic in a department, and how many actually used psychological help before and during the pandemic. We also aimed to examine—through our questionnaire survey—the group of people who were able to express the need for psychological support but did not accept it.
Methods: Our workgroup performed surveys among caregivers in one of the intensive care units of Semmelweis University in Budapest, Hungary, designated for COVID care. Between April and May 2021, at the end of the third wave, we asked the staff to complete a package of five questionnaires: Professional Quality of Life (ProQoL), Demoralization Scale, Perceived Stress Scale-14 (PSS), Impact of Event Scale, Posttraumatic Growth Inventory. In addition, demographic data were collected, and we inquired whether the worker had used psychological support before or during the pandemic, and whether the respondent felt the need for psychological support during the pandemic. The research has accepted by the Committee of Research Ethics.
Results: Only a minority ($n=6$) of the respondents ($n=63$) had received psychological support before the pandemic, and there was no significant increase in the number of people seeking support during the pandemic ($n=8$). 72,6% of the participants were female. However, more than a third of respondents ($n=22$) reported that they felt the need of psychological support. These respondents scored significantly higher on the ProQoL total score ($U=205,5$; $p<0.001$), Burnout Subscale ($U=193$; $p<0.001$), Secondary Trauma Subscale ($U=241$; $p=0.002$); Demoralisation Scale ($U=155$; $p<0,001$); PSS total score ($U=204$; $p<0,001$); Impact of Event Scale total score ($U=167,5$; $p<0.001$), Intrusion Subscale ($U=151$; $p<0.001$) and Avoidance Subscale ($U=228$; $p=0.002$).
Conclusion: Only a small number of the intensive therapy team members had sought psychological support prior to the outbreak of the pandemic. The first year did not significantly impact this pattern. During the third wave, the third of the staff indicated the need of psychological support, but they did not accept it, despite having the opportunity. Based on the results of the surveys, the subjective perception of colleagues may also be a relevant indicator. We believe it is important to continue to investigate this attitude more widely, to understand the pattern and try to help for the colleagues getting real help.

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000410

The perioperative pathway of elective head and neck free-flap surgery: a case for change

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Introduction: Routine admission to critical care post head and neck microvascular free-flap surgery has been standard practice for many years. However, recently studies have shown that the immediate postoperative care in the Intensive Care Unit (ICU) does not reduce the incidence of flap failure or complication rates, and non-ICU nursing can provide equivalent clinical outcomes [1].
Objectives: The purpose of this audit was to analyse the postoperative course of patients undergoing free-flap surgery in our hospital. These patients are currently all admitted to critical care and we aimed to establish whether or not they require interventions that can only be provided in this setting and, if so, if this can be predicted in certain high-risk patient groups.
Methods: After registering with the local audit department, we carried out a retrospective observational study of patients who had undergone free-flap surgery at Royal Sussex County Hospital (RSCH) within the last 2 years. The clinical notes of these patients were reviewed in addition to online data systems. We then compared the postoperative course of patients who had been identified as high risk and had been seen preoperatively in the Anaesthetic Review Clinic (ARC) to those who had not.
Results: Of the 19 patients identified for review, 10 were female and 9 were male, mean age was 69 and 66 years respectively. There was a statistically significant difference in the number of comorbidities, ASA grade and frailty score between the ARC and non-ARC patients ($p=0.003$, 0.02 and 0.006 respectively). Average length of stay on critical care was similar for both groups. There was no difference in the number of patients requiring ventilation, however the number of patients requiring vasopressor support was significantly higher in the ARC patient group ($p=0.04$). The incidence of postoperative complications was similiar in both groups.
Conclusion: For patients undergoing head and neck free-flap surgery there is a need to closely monitor the flap viability for any vascular compromise in the first 72 h. This requires an appropriate environment with adequately trained nursing staff to perform frequent observations. For patients in our hospital this occurs in a critical care setting, however, we found very few patients required other critical care interventions. Furthermore, we found that all patients who did require vasopressor support had already been identified pre-operatively as higher risk. Limiting the routine post-operative critical care admission to carefully selected patients may result in a reduction in the incidence of postoperative complications as well as cost [1]. This could also reduce the burden felt by our ICU and prevent surgery delays due to bed availability. We propose that for those patients already identified pre-operatively to be lower risk, an alternative perioperative pathway could be created. This could be in a non-critical care setting, with additional nursing support, to provide equivalent intensive observations in the initial postoperative period without the need for admission to ICU.

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000430

The impact of Ramathibodi rapid response system triggered by Ramathibodi early warning score and clinical warning signs on in-hospital mortality and incidence of cardiopulmonary resuscitation in adult hospitalized patients

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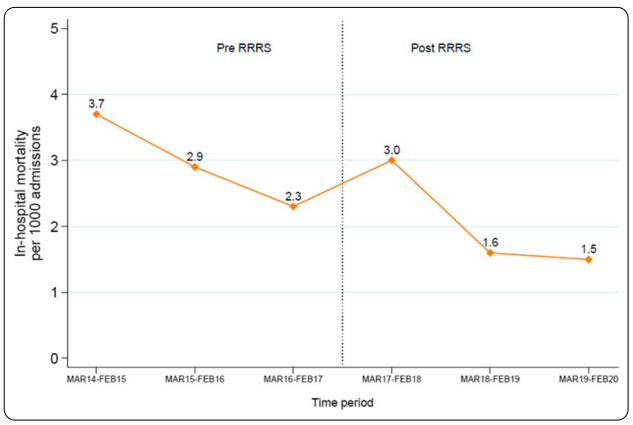
Intensive Care Medicine Experimental 2022, **10(2)**:000430

Introduction: Rapid response systems are commonly used to identify and respond to deteriorating patients outside of the intensive care unit (ICU). The Ramathibodi Rapid Response Systems (RRRS) was created and applied in March 2017 as the standard protocols in the general wards. The system comprises Ramathibodi early warning score and Ramathibodi clinical warning signs as the trigger tools to monitor all admitted patients. The response provides closed monitoring and early treatment by expert physicians to rapidly stabilize and triage the patient to a location where services meet the patient's needs. Furthermore, the fast track systems of specific diseases were activated by this system depending on the particular clinical warning signs.
Objectives: We aimed to evaluate the impact of the implementation of RRRS on in-hospital mortality and incidence of cardiopulmonary resuscitation (CPR) outside ICU.
Methods: A retrospective observational study was conducted among adult patients admitted to the general wards in Ramathibodi hospital. All adult patients with unplanned ICU admission, sudden cardiac arrest, or unexpected death from March 2014 through February 2020 were included. Clinical characteristics and outcomes were assessed with descriptive statistics. Differences in in-hospital mortality and incidence of CPR outside ICU between the pre and the post-RRRS implementation group were analyzed with a chi-square test. The association between RRRS implementation and in-hospital mortality and incidence of CPR outside ICU was assessed with multiple logistic regression analyses.
Results: Off 17,741 admissions, 9168 admissions before RRRS implementation (March 1, 2014 through February 29, 2017) and 8573 admissions after RRRS implementation (March 1, 2017 through February 29, 2020) were evaluated. In-hospital mortality decreased from 30.0% (2748 pts) to 20.8% (1787 pts) after RRRS implementation (odds ratio 0.62; 95% confidence interval (CI), 0.57 to 0.66; P < 0.0001, as shown in figure). After adjusting with age, sex and co-morbidities with P < 0.10, the reduction of in-hospital mortality remained statistically significant (adjusted odds ratio, 0.58; 95% CI, 0.54 to 0.63; P < 0.0001).The incidence of CPR outside ICU decreased from 1.8% (167 events) to 1.1% (96 events) (adjusted odds ratio 0.6; 95% CI, 0.46 to 0.77; P < 0.0001). The rate of ICU transfer increased from 85.4% (7832 events) to 92.1% (7897 events) (risk difference 6.7; 95% CI, 7.6 to 5.8; P < 0.0001).



Conclusion: The implementation of RRRS was associated with a reduction in in-hospital mortality and incidence of CPR outside the ICU.

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Acknowledgements: Not available.

000482

Assessment of quality and quantity of sleep among patients in Aster Medical ICU and viable interventions for its improvement: audit-cum-interventional study

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Intensive Care Medicine Experimental 2022, **10(2)**:000482

Introduction: Sleep is essential for healthy living and recovering from illness.So it is logical toconsider good quality sleep is essential when the patient is critical ill in an ICU.It isa fact that the sleep of ICU patients are poor because of various factors, individual factors such as pain,illness etc. and environmental factors such aslight, sound,procedure etc. So i would like to Objectively and subjectively assessthe quality and quantity of sleep of patients admitted in Aster WIMS–MICU, andto implement logical and viable action plan to improve the same.
Objectives: To assess the quality and quantity of sleep among the patients admitted inASTER WAYANAD MICU (Audit). To improve the quality and quantity of sleep among the patients admitted inASTER WAYANAD—MICU using logical and viable action plan. (QIP interventionbased on Audit) (Based on QIP plan- The Richards-CAmpbell Sleep QuestionnaireRCSQ)
Methods: To assess the quality and quantity of sleep in the MICU subjectively andobjectively via Richards Campbell sleep questionnaire –> implement the viableaction plan –> reassess, using relevant statistical tools. Patients are selected based on: A) Inclusion criteria: Adult Patients admitted inthe MICU who are provided informed consent,—Who are willing to participate andnot on any critical life supports.—GCS 15/15, normal HMF, clear state of mind andwithout aphasia—Who are unlikely to deteriorate in next 48 h B) Exclusioncriteria:—All others not fulfilling the inclusion criteria Pathway: 1) To assess thequality and quantity of sleep in the MICU subjectively and objectively via RichardsCampbell sleep questionnaire 2) To find the major causes of poor sleep and thepossible solutions for the same 3) To implement a viable action plan and to assessthe quality improvement using relevant statistical tools. Improvement measures taken after detailed analysis/discussion of my Audit withmy ES/Programme Director/MICU Incharge/Support staff:- a) Issue of Lighting inthe MICU:-—An Opaque Eye mask was given to the patients (Savaged cheap andeffectively by modifying black coloured 3ply face mask) to facilitate the sleepinghours.—Unwanted and direct lighting on patients side has been modified bedwiseas appropriate. b) Issue of Sound in the MICU:- -a pair of comfortable and cheapearplugs were given to the patients to facilitate the sleeping hours.
Results: Based on the sample data, the average duration of continuous sleep in the MICU is 4 hours 08 minutes (248 min). RCSQ average was found to be 26.72%. Lighting in the ICU, Sound in the ICU including instruments, supports, staff, fellow patients andmedication & invasive procedures are found to be the major factors contributing tothe poor sleep of the ICU patients. The major contributing factors were found to be Lighting, Sound and Invasiveprocedures & medication. The interventions on lighting and sound were found tobe the most suitable and practical in the current setup for improvement. Thus

based on Audit and Re-Audit after the QIP intervention:- a) There is animprovement in the quality of sleep by 07.41% (34.13 minus 26.72) as evident byRCSQ_Total average. b) There is an improvement in the quantity of sleep by 80 min (328–248) or 32.25% improvement from the pre-implementation (4 hrs 08 min) data.
Conclusion: The quality and quantity of sleep in the ICU can be greatly improved by simple and viable interventions like dealing with lighting and sounds in the ICU.Theseinterventions can be reproduced even in ICUs with minimum resource settings.

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Acknowledgements: No conflicts of Interests.

000502

A survey analysis of airway management and sedative choice among intensivists and anaesthesiologists. The Greek experience

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Intensive Care Medicine Experimental 2022, **10(2)**:000502

Introduction: Airway management and intubation for COVID-19 patients have been a challenge for physicians treating these patients since the start of the pandemic. These life-saving procedures have an increased risk of complications and impose the operator to great risks of contamination; therefore consensus guidelines are already available to address these issues of concern1.
Objectives: To evaluate the practices Greek intensivists and anaesthesiologists followed, during the last 2 years by distributing an online survey.
Methods: A 20 item-questionnaire was sent to Intensivists (n = 600) and Anaesthesiologists (n = 600) during the fourth pandemic wave in Greece (December 2021). The items included questions regarding demographics, the choice of sedative and neuromuscular blocking agents (NMBA) and the management of the difficult airway technique. Those who were not familiar with COVID-19 patient management were excluded from the analysis.
Results: Of the 1200 physicians asked, 146 answered (response rate 12.25%) and 15 were excluded from the analysis (not treating COVID-19 patients). All the results are presented in detail in Table 1. In regards to the use of sedatives for intubation of COVID 19 patients Intensivists used more the combination of Propofol/Midazolam/Fentanyl relative to Anaesthesiologists (P = 0.041) while the use of ketamine was low (18.3%). NMBAs were administered for the intubation regardless of phycisian (58.8%) and rocuronium was the agent of choice of both physicians (60.3%). Alternatively, suxamethonium chloride was preferred by Anaesthesiologists and cis-atracurium by Intensivists. On the matter of difficult airway management, both physicians opted for videolaryngoscope use in anticipated difficult intubation; they neither use a different blade (McCoy) nor an Eschmann bougie as a routine. The decision to intubate is based both on blood gases and clinical criteria in either physician while ROX index is only employed by 30.8% of them to guide the decision to intubate. Overall, 87.8% of the study's sample feels more comfortable with airway management for these particular patients after 1.5 year of experience.
Conclusion: It seems that there is a high level of compliance of Greek physicians to the consensus guidelines regarding the choice of sedative and NMBA agents yet this thins out in regards to difficult airway management techniques.

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000535

The effects of music on the physiology and experiences of intensive care patients: a methodology for utilising routinely-collected quantitative data in a feasibility study

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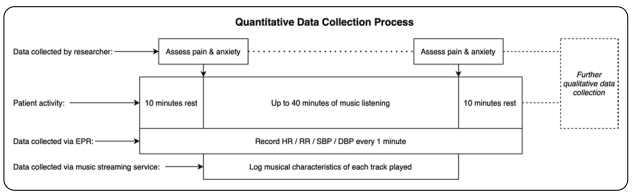
Introduction: Music has been shown to have potential benefits for patients in a number of clinical settings, including critical care (1, 2). New technology offers the potential to explore the precise mechanisms underlying this in greater depth, with sophisticated electronic patient record (EPR) systems and artificial intelligence (AI) algorithms for music classification both routinely producing detailed and accessible new datasets for research (3, 4).
Objectives: The EMPIRE study sought to establish a comprehensive workflow for analysing physiological data from electronic patient records alongside data on musical characteristics from the Spotify streaming service, and assess its feasibility for use in the context of a critical care-based research project.

Methods: The EMPIRE study took place in the ICU of Chelsea and Westminster Hospital in London, UK. Each participant took part in a music listening session of up to 40 min, with 10 min of undisturbed rest before and after. The music was played via Spotify, allowing for unlimited choice by the patient or their family and friends. Where a music pReference was not given, the researchers chose music from pre-selected playlists. Throughout the session, patients' heart rate, respiratory rate and blood pressure were recorded every minute via the EPR. Patients were also asked to assess their level of pain and anxiety pre and post the session using numerical scales. Following the session, musical characteristic data was retrieved from Spotify's application programming interface (API), including information on tempo, tonality, loudness, energy and valence (5). Further qualitative data was also subsequently collected through interviews with patients.



Results: 15 patients were recruited, with detailed sets of physiological and musical characteristic data successfully captured for 14. The two datasets could be easily aligned by time-points, allowing for future detailed analysis into the effect of specific musical characteristics on physiological processes. Of the 113 tracks played across the music listening sessions, the data on 65 (58%) required manual cleaning, with certain characteristics being misinterpreted by the AI analysis and therefore requiring verification by a musician.

Tracks played	Tracks with data requiring cleaning	Data points requiring cleaning:			
		Key	Mode	Tempo	Time signature
113	65	39	18	36	11
100%	58%	35%	16%	32%	10%

Conclusion: The EMPIRE study has demonstrated the feasibility of using routinely-collected large datasets for exploring the mechanisms of music's effect on the body, although musical expertise is necessary for the cleaning of some inaccurate data. The workflow for data

collection which was used in this project could also be extended to include other routinely collected data, such as environmental data from air quality or sound-level sensors. Future work will analyse the collected data to identify significant correlations between musical characteristics and specific physiological processes, as well as collecting other data to explore music's effect on pain, anxiety, and the qualitative experience of the intensive care setting.

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Acknowledgements: This project has been funded by CW+, the charity for Chelsea and Westminster Hospital NHS Foundation Trust.

000549

"Was the MRI performed?" A service evaluation on the provision of MRI in a tertiary centre

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Intensive Care Medicine Experimental 2022, **10(2)**:000549

Introduction: In the critical care setting, MRI has been used to characterize subacute and chronic strokes, evaluate the spinal cord, central nervous system injuries and infections and, in recent years, to aid neurological prognostication. But performing an MRI in intensive care patients is a challenging task due to high risk for patients, its more often than not remote location and MRI specificic nuisances, making the process to be carefully planned. In our institution, intensive care patients requiring an MRI are transferred to, from and cared for during the procedure by the Anaesthetic department.
Objectives: To understand provision and performance of MRI for the intensive care population in a tertiary centre in the United Kingdom.
Methods: We sought approval to conduct a service evaluation on the provision of MRI in intensive care at a tertiary centre in London, UK; including patients admitted to the intensive care units where an MRI was requested between March and August 2021. We collected the following: demographic data (including sex, age, reason for admission to intensive care, ICU length of stay (LOS) and ICU and hospital outcomes). We specifically collected indication for test, date test was requested and accepted by the Radiology team, date the MRI was performed, time from acceptance to performance and reasons for delay on performing the test or cancellation.
Results: From March to August 2021, MRI was requested in 66 patients, 29 female (43.9%), with a mean age 58yo, an ICU LOS of 26 days, 55 (42.5%) patients were discharged alive from intensive care. Reason for admission to intensive care on these patients varied from post-cardiac arrest care (27%), stroke (23%) to status epilepticus (12%) or suspected central nevous system (CNS) infection/encephalitis (11%) (Figure 1). Main reason to request the test was "Neuroprognostication" (n = 31, 47%) followed by CNS infection/encephalitis (n = 11, 17%). The median time from vetting to performing the MRI was 3 ± 3.5 days. Documentation of delay more than 3 days was not documented in 58%, while in 21% was due to lack of provision of anaesthetic/operating department practitioners. (Figure 3).

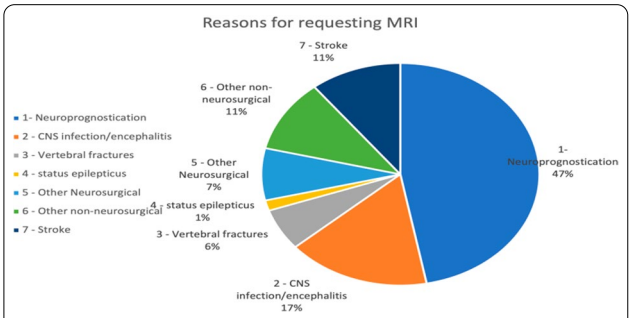

Figure 1. Reason for MRI request

Conclusion: Urgent diagnostic MRI has limited indications in the intensive care setting. Based on recent publications, an increased demand for prognostic MRI to aid decision making may occur. On either of the previous circumstances, physiological stability will determine whether the scan should proceed and appropriate medical team and support should be made available.

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000564

The Influence of obesity on outcome of severely burned patients admitted in intensive care unit

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Introduction: Obesity is described as a risk factor for morbi-mortality in patients admitted to intensive care. However, the impact of obesity on the prognosis of patients with extensive burn injuries remains unknown.
Objectives: The aim of the study was to assess the impact of obesity on the prognosis of burn patients admitted to intensive care.
Methods: A retrospective study, conducted in intensive burn care department in Tunis over a period of 14 months (January 2021–February 2022). The exclusion criteria are age < 16 years and SCB < 20%. Obesity is defined by a BMI > 30 kg/m^2.
Results: During the study period, 450 patients were admitted, 154 patients were included. Two groups were identified: G1: non-obese patients (BMI < 30 kg/m^2) (n = 114) and G2: obese patients (BMI > 30 kg/m^2) (n = 40). The comparative study of the clinical and evolutionary data of the two groups is represented respectively in tables 1 and 2. The multivariate analysis identified the predictive factors of mortality in obese patients, which are: the occurrence of acute kidney injury (p = 0.01), sepsis (p = 0.012) and the use of mechanical ventilation (p = 0.01).

Table 1. Comparison of clinical characteristics and outcome of the 2 groups

	n = 154	G1(n = 114)	G2(n = 40)	p
Age, mean (years)	43 ± 18	42 ± 19	45 ± 15	0.002
Sex ratio	1,45	2,5	0,73	0,4
TBSA (%)	36 ± 21	31 ± 21	38 ± 22	0.26
ABSI score, mean	6 ± 3	6 ± 3	6 ± 4	0.12
Diabetes (n, %)	23 (15)	14 (12)	9 (22)	0.1
Mechanical ventilation (VM) (n, %)	81 (53)	61 (54)	20 (50)	0.7
Duration of VM (days)	4	4,5	3	0,5
Sepsis (n,%)	107 (70)	77 (68)	30 (78)	0.68
Acute kidney injury (n, %)	45 (30)	28 (25)	16 (36)	0,17
Atelectases (n, %)	9 (6)	2 (3)	7 (18)	**0.049**
Thromboembolic events (n, %)	21 (14.28)	9 (8.33)	12 (30)	**0.07**
Length of stay (days)	12	11.5	13.5	0.2
Mortality (n, %)	72 (47)	53 (48)	21(50)	0.55

Conclusion: In our study, thromboembolic complications and the occurrence of atelectasis were observed more in obese patients without significantly influencing the use of mechanical ventiation, lengh of stay or mortality in burn patients hospitalized in intensive care.

000582

Validation of pictograms for communication board with intubated patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000582

Introduction: Communication is one of the most important skills during health care, it provides information to prevent diseases, integrate diagnoses and explain treatments, which is why it is essential for quality and safe care (1). The lack of communication results in poor resolution in pain management, a feeling of loss of control, depersonalization, anxiety, stress and frustration (2–4), all of these build a frightening and dehumanized experience, as well as being factors that indirectly contribute to the development of delirium and therefore an increase in the days of mechanical ventilation and stay in the ICU (4–6).
Objectives: Validate a series of pictograms designed for a communication board with intubated patients.
Methods: The pictogram development process: In a previous stage, ICU healthcare personnel (doctors, nurses and others), patients and relatives were surveyed about the most commonly used requests or expressions during their stay. A list of 213 actions, feelings or needs was obtained, which was filtered by semantic fields, synonyms or colloquial terms, obtaining 26 terms that represented 85% of the most used expressions, later the Social Communication Unit designed pictograms for each one. In this stage, an open text survey was applied to ICU staff Where requested, briefly write the meaning of each pictogram.
Results: A sample of 40 respondents was required, 65 answers were obtained (doctors 20.9%, nursing 24.9%, residents 33.8% and other personnel 23.3%), the results were analyzed by semantic group with the support of the Spanish Language Dictionary (7) and the University of Navarra Clinical Medical Dictionary. (8), all the pictograms had greater than 80% agreement with the meaning for which they were designed (Figure 1).

Conclusion: It can be established that the designed pictograms express the most common feelings and needs of critically ill patients admitted to the ICU of this hospital; It will be complemented with text in Spanish (availability of at least 1 board in other languages and regional languages) and Braille System to favor inclusivity.

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Acknowledgements: No funding or grants were obtained for this research.

Health services research & outcome 6

000260

Analysis of imaging modalities used for the assessment Sarcopenia in the Critical Care Unit using a systematic literature review

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Introduction: -During Critical illness, there is an increase in the muscle protein breakdown to muscle protein anabolism ratio (MPB: MPA) due to several mechanisms working in conjunction, namely: immobility, bioenergetic failure, neuroendocrine dysfunction and systemic inflammatory response leading to myocyte apoptosis. This inevitably results in muscle tissue loss- sarcopenia. The use of imaging to diagnose sarcopenia in the ICU setting was introduced in 1976, and since then, several different modalities have been used. Prompt diagnosis of ICU- acquired sarcopenia assists in risk stratification, predicts patient outcomes and allows for early intervention in high-risk patients.
Objectives: Our primary objective is to evaluate the current literature available for imaging tools for diagnosing sarcopenia in the context of ICU.
Methods: -Using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) system devised by Cochrane, we conducted a systematic literature search based on the Embase, Cochrane and PubMed databases. The modalities were then analysed based on the: timing of investigation after ICU admission, muscles investigated, parameters measured, and acquisition protocols used. -(PRISMA) was used as a template. After devising a research question using the PICO framework, a systematic literature search was performed using the Embase, PubMed and Cochrane databases to explore the current literature on the imaging modalities used for ICU-AW diagnosis.
Results: -A total of 113 records were identified and screened, and 41 studies were evaluated. Ten studies using MRI were identified, eight using Computerised Tomography and fourteen using Ultrasonography. Studies using Nuclear Imaging and Dual Energy X-ray absorptiometry were also identified. -Regarding Ultrasound: rectus femoris was the muscle most commonly investigated (11 out of 14 studies). Muscles of the upper limb were only investigated in 2 citations. Moreover, measured muscle thickness and muscle cross-sectional areas are the most frequently measured parameters used in 6 and 5 studies, respectively. The US assessment was done between 7 to 30 days post ICU admission in all observational studies. -In computerised tomography, 9 out of 10 studies used image slices at the L3 lumbar level analysing psoas major and quadratus lumborum. In terms of the parameters used: echogenicity was measured in 3 citations, muscle CSA in 2, muscle index in 2 and muscle density in 1. CT scans were performed upon the admission of the patients in the ICU; hence they did not directly measure ICU-acquired sarcopenia. The acquisition protocols used (voltage, current and slice thickness) were heterogeneous through literature (summarises in table). Moreover, the Hounsfield Units (HU) were used to identify muscle thickness wear variables between literature ranging from -39 to 150. -In MRI, there was heterogeneity in the muscles ranging from psoas major, erector spinae, tibialis anterior, and bicep brachii. The most common measures parameters are CSA, muscle depth, proton density fraction and Intramuscular Adipose Tissue (IMAT). Lastly: seven studies used T1 weighted image, and three used T2.
Conclusion: There are several modalities available to quantify sarcopenia in the Intensive Care Unit. Nevertheless, the muscles, parameters, and acquisition protocols used are variable within each investigation. This hinders the ability to compare the results between the available literature. We propose that developing guidelines on parameters, acquisition protocols and muscles used can assist in an objective measurement of sarcopenia

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000421

Delayed ICU admission is associated with duration of IMV and hospital stay in patients with critical COVID-19 in low-resource settings

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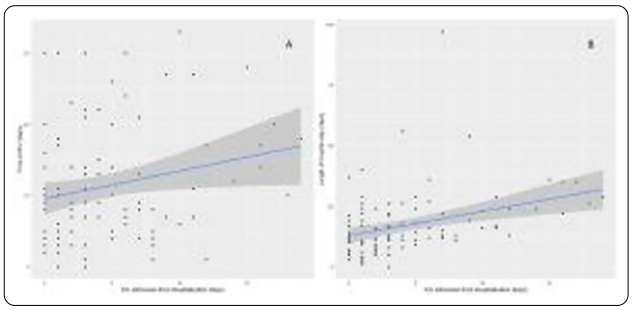
Intensive Care Medicine Experimental 2022, **10(2)**:000421

Introduction: Delays in medical care have been shown to be a risk factor for mortality in patients with COVID-19 who receive medical care in non-developed countries such as Mexico (1). The low availability of resources alongside saturation of hospitals during infectious disease outbreaks lead to delays in medical care (2). Other adverse outcomes potentially associated with delayed in-hospital medical care (i.e., delayed ICU admission) remain to be explored in low-resource hospitals to fully characterize their impact on healthcare systems (i.e., costs).
Objectives: To evaluate the association of delayed intensive care unit (ICU) admission with days on invasive mechanical ventilation (IMV), duration of hospital stay, and mortality in a cohort of hospitalized patients with critical COVID-19 from a low-resource hospital in Mexico.
Methods: We conducted a retrospective observational study in hospitalized patients with COVID-19 admitted to the Intensive Care Unit (ICU) of Hospital General de San Juan del Río (central Mexico), between 1 November 2020 and 31 December 2021. Patients with acute respiratory distress syndrome (ARDS) due to suspected COVID-19 who required invasive mechanical ventilation (IMV) were included in the study. Those with a negative test for SARS-CoV-2 were excluded. The evaluated endpoints were days on IMV, duration of hospital stay, and mortality. The main exposure was time from hospital admission to ICU admission. Linear regression and Cox regression analyses were performed to determine the association of delayed admission to the ICU with IMV days, hospitalization length, and mortality. Models were adjusted for age and sex.
Results: A total of 101 patients were included for analysis. The mean age was 49.3 (SD:1.3) years and 50.5% (n = 51) of patients were women. The most frequent comorbidities were obesity (43.6%, n = 44), type 2 diabetes (28.7%, n = 29), and hypertension (28.7%, n = 29). Mean baseline risk scores were APACHE-II, 16.9 (SD:0.7) points; SOFA, 8.9 (SD:0.3) points; NEWS-2, 9.5 (SD:0.3) points, and CO-RADS, 4.9 (SD:0.03) points. The most frequent complications during ICU stay were acute kidney injury (55%, n = 56), mortality (51%, n = 52), and delirium (36%, n = 37). Median time from hospital admission to ICU admission was 3 (IQR:1–7) days. Regarding outcomes, median hospital stay was 14 (IQR:10–22) days; days on IMV, 9 (IQR:5–17) days, and

duration of ICU stay, 11 (IQR:6–20) days. After multivariable regression analyses with adjustment, delays in ICU admission were associated with longer IMV duration (β = 0.43, IC95%:0.05–0.8, p = 0.03) (Figure 1A), and longer hospital stay (β = 1.03, 95%CI: 0.50–1.62, p = 0.001) (Figure 1B), although mortality risk was not higher (HR = 0.97, 95%CI: 0.91–1.02, p = 0.3).



Conclusion: In this single-center study, delays in ICU admission were associated with longer IMV duration and longer hospital stay in patients with critical COVID-19, but not with mortality.

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000501

Prognosis scores in COVID-19 critically-ill patients: What's the better?

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Intensive Care Medicine Experimental 2022, **10(2)**:000501

Introduction: Hospitalized patients of COVID-19 needing Intensive Care Unit (ICU) admission suffer from a high mortality rate. Accurate prognosis scores would have been helpful that allowing clinicians to identify high-risk patients using an initial risk-adapted allocation for managing medical resources and providing intensive care.
Objectives: Our study aims to compare performance characteristics of CURB-65(1), ISARIC-4C (2), NEWS 2 (3) and COVID-GRAM (4) scores, in predicting ICU mortality in the context of COVID-19.
Methods: The files of all COVID-19 patients over the age of 18, admitted to the ICU in Zaghouan' hospital (Tunisia), between September 2020 and December 2021 were retrospectively scanned and the 4 studied scores were calculated with the earliest measurement recorded at admission. Scores were assessed individually against their validated outcomes and overall, for their ability to identify people at risk of ICU-mortality. This analysis included sensitivity and specificity of each score's high- risk groups. Discriminatory ability was assessed by comparison of the corresponding receiver operating characteristic curves with computation of area under the curve (AUC).
Results: 322 patients were included. mean age was 55 ± 13 years and the gender ratio (H/F) was 1.42. Means of SAPS II and APACH scores were respectively 23 ± 8 and 7 ± 4. The most frequent comorbidities were obesity (49.7%), diabetes (37.3%) and hypertension (36,6%). The median hospital length of stay was 7(IQR 4-12) days and the globally mortality rate was 43.5%. The mean of the studied scores CURB-65, ISARIC-4C, NEWS 2 and COVID-GRAM were respectively 1.25 ± 0.97; 8.73 ± 3.46; 7.99 ± 2.12 and 36.37 ± 22.22%.
Table 1 describes score's characteristic and mortality predicting abilities.

Comparaison of scores characteristics

Score	Cut-off point	Sensitivity (%)	Sensibility (%)	VPP (%)	VPN (%)	AUC
ISARIC-4C	≥ 9	68	55	68	69	.668
NEWS2	≥ 7	89	26	48	76	.640
CURB-65	≥ 3	13	98	90	59	.638
COVID-GRAM	≥ 40,4	51	69	59	65	.632

**VPP* positive predictive value, *VPN* negative predictive value, *AUC* area under the curve.
Conclusion: AUC for mortality prediction in critically ill COVID-19 patients, were similar for the 4 score's high- risk groups. CURB-65 ≥ 3, was the most specific, while the NEWS2 ≥ 7 have proven to be the most sensitive.

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000546

The RALE–score versus the CT Severity Score in Invasively Ventilated COVID–19 patients—a retrospective study comparing their prognostic capacities

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Intensive Care Medicine Experimental 2022, **10(2)**:000546

Introduction: Radiological scores for the visual quantification of extent and severity of pulmonary infiltrates based on chest radiography (CXR) and computed tomography (CT) scan are increasingly used in critically ill invasively ventilated patients.
Objectives: To determine and compare the prognostic capacity for mortality of the 'Radiographic Assessment of Lung Edema' (RALE) score and the chest CT Severity Score (CTSS) in a cohort of invasively ventilated patients with acute respiratory distress syndrome (ARDS) due to COVID–19.

Methods: Two-center retrospective observational study, including consecutive invasively ventilated COVID-19 patients. Trained scorers calculated the RALE score of first available CXR and the CTSS of the first available CT scan during first 14 days of stay. The primary outcome was ICU mortality; secondary outcomes were duration of ventilation in survivors, and length of stay in ICU, and hospital-, 28-, and 90-day mortality. Prognostic accuracy for ICU death was expressed using odds ratios and receiver operating characteristic curves (ROC).
Results: 82 invasively ventilated patients with COVID-19 ARDS were included. The median APACHA score was 12.0 [10.0–20.0], with the most common comorbidities being hypertension and diabetes. Oxygenation parameters were not different between ICU survivors and ICU non–survivors, and most patients had moderate or severe ARDS. ICU mortality was 42.7%.The median RALE score (22 [15–37] *vs* 26 [20–39]; P = 0.34) and the median CTSS (18 [16–21] *vs* 21 [18–23]; P = 0.022) were both lower in ICU survivors compared to ICU non–survivors, albeit that only the difference in CTSS reached statistical significance. The RALE score of the first available CXR had no association with ICU mortality (OR, 1.35 [95%–confidence interval 0.64–2.84]; P = 0.417; area under the ROC, 0.50 [0.44–0.56]. The CTSS was independently associated with death in ICU (OR, 2.31 [1.22–4.38]; P = 0.010) but with a poor prognostic capacity (area under ROC 0.64 [0.57–0.69]).
Conclusion: In this cohort of COVID–19 patients, the CTSS of the first chest CT scan but not the RALE score of the first CXR was associated with ICU mortality. The prognostic capacity of the CTSS, however, was poor.

000573

Exploring the experience of simulation training amongst members of an intensive care unit (ICU) multidisciplinary team (MDT)

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Introduction: Safe clinical management in critical care requires a combination of procedural skills, time-sensitive decisions, and effective teamwork. The value of simulation training in developing skills and improving healthcare professionals' response to acute scenarios has been widely documented (1). Improvement in outcomes following multidisciplinary simulation in the management of critically unwell patients has been demonstrated (2). The Guidelines for the Provision of Intensive Care Services state that ICUs should have a regular MDT educational programme incorporating simulation (3). However, simulation training is not equally accessible to all healthcare professionals working in ICU (4,5).
Objectives: To establish the availability of simulation training, barriers to access, and attitudes to future opportunities from MDT members in one National Health Service district general hospital (DGH) ICU.
Methods: A structured quantitative and qualitative survey was distributed to MDT members of a range of grades in one busy DGH ICU over a 3-week period. Team members surveyed included doctors, nurses, physiotherapists, dieticians, healthcare assistants and psychologists. Questions ascertained frequency of simulation training, aspects found to be useful, barriers, and pReferences regarding future training. All responses were anonymous and obtained with informed verbal consent.
Results: A total of 55 responses were collected (22 doctors, 25 nurses, 7 other MDT members). Forty percent (N = 21) received zero annual simulation sessions and thirty-eight percent (N = 22) received one training session annually. On average, doctors received twice the amount of simulation sessions as compared to nursing staff. Participants found simulation training useful, 64% giving a rating of 8-10 out of 10. Respondents reported finding hands on skill practice the most useful aspect. Barriers to accessing training included lack of opportunity (85%) and lack of time (65%). Only 1 participant reported avoidance of simulation due to personal pReference. Most wanted more frequent simulation sessions with involvement of other MDT members, and ideal frequency of training was monthly (N = 21) or three times per year (N = 15).
Conclusion: ICU simulation training needs to be made more available in line with GPICSv2 standards. Our study indicates that achieving this would be welcomed by the whole MDT. Lack of time and opportunity were highlighted as barriers suggesting that policymakers need to invest in supporting simulation training by allocating time and resources for education.

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Acknowledgements: Nothing to disclose.

000590

Initial levels of inflammatory markers and it's association to mortality and organ failure in severe COVID-19 patients under invasive mechanical ventilation

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Intensive Care Medicine Experimental 2022, **10(2)**:000590

Introduction: The main effort behind the early identification of severity of patients with COVID-19 related ARDS (C-ARDS) has relied on the initial grade of hypoxemia, tomographic findings and dependance of oxygen supplementation in it's diverse modalities. With the heterogenous relation of this features to the prognosis reported in the literature, inflammatory markers like Interleukine-6 (IL6), C Reactive Protein (CPR), Procalcitonin (PCT), D-dimer (DD) and Ferritin (SF) have risen much interest. Measurements of these biomarkers aren't available in developing-countries. There are few publications in Mexico that address these topics and clarify the value of the different biomarkers may improve the development of an early severity score.
Objectives: To find the specific threshold levels of initial inflammatory markers (IL-6, CPR, PCT, DD and SF) in C-ARDS patients under invasive mechanical ventilation that are the most sensitive to detect organ failure (OF) and mortality.
Methods: A retrospective and longitudinal cohort study was carried out in adult patients admitted to the respiratory intensive care unit with C-ARDS and use of invasive mechanical ventilation (IVM) in the first 48 h of admission. Electronic records were reviewed to obtain demographic characteristics and admission levels of inflammatory markers to associate with initial OF assessment through SOFA, APACHE-II, SAPS-II and mortality. Number of ventilation days, length of stay (LOS) days in ICU and hospital LOS days were accounted. Only patients with all inflammatory markers on admission were included. The association for primary and secondary outcomes was made with each biomarker and by group (≤ 2 high biomarkers and ≥ 3 high biomarkers). The statistical analysis was made in SPSS.

Results: A sample of 218 patients was obtained with a male gender in 77.5% and mean age of 60.3 years (±12.8). Mortality rate of 24.7%, mean hospital-LOS 24.8 days (±17.2), ICU-LOS 19.4 days (±13.2) and ventilation days 14.6 (±11.3) was reported. For OF, median SAPS-II, APACHE and SOFA were 28 points (22–43), 12 points (8–19) and 6 points (3–9) were found respectively. Higher OF defined by SAPS-II ≥ 50pts, APACHE-II ≥ 25pts and/or SOFA ≥ 10pts was present in 20.2, 11.5 and 21.6%, respectively. Initial PaO2/FiO2 was 128.5 mmHg (83.3–204) and $PaCO_2$ 45 mmHg (38.9–53.2). Median inflammatory marker's levels were: CRP 14.8 mg/mL (7.2–25.7), PCT 0.4 ng/mL (0.2–1.2), DD 1.211 ng/mL (760–2101), IL6 175 pg/mL (51.4–363.5) and SF 1.461 ng/mL (912–2493). Primary and secondary outcomes are in table 1.
Table 2

Outcome. n (%)	≤ 2 High Markers	≥ 3 High Markers	OR	95% CI	P
Mortality.	16 (7.3)	52 (23.8)	1.15	(0.96–1.35)	0.46
Organ Failure					
SAPS II > 50pts.	2 (0.91)	36 (16.5)	2.67	(0.37–19.43)	0.46
APACHE II > 25pts.	2 (0.91)	14 (6.4)	0.99	(0.14–6.83)	1.00
SOFA > 10pts.	2 (0.91)	34 (15.6)	2.53	(0.35–18.43)	0.47
Hospitalization-LOS ≥ 15 days. 124 (56.9) 184 (84.4)			2.72	(1.31–5.62)	0.02
ICU-LOS ≥ 10 days.	124 (56.9)	185 (85)	2.86	(1.37–5.96)	0.01
ICU-LOS ≥ 15 days.	140 (64.2)	192 (88)	3.02	(1.3–7)	0.03
IMV ≥ 7 days.	140 (64.2)	192 (88)	3.02	(1.3–7)	0.03

Conclusion: The initial measurement of inflammatory markers in C-ARDS has a direct relationship with OF and mortality, but with low specificity and sensitivity. Having ≥ 3 initial inflammatory markers with high levels may be used in the prediction of mortality, with non-significant in OF. Multiple markers with higher levels had better power to detect LOS days and ventilation days than OF and mortality.

000631

Challenges in care of critically ill patients in the emergency department: Perceptions from intensive care and emergency department providers

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Intensive Care Medicine Experimental 2022, **10(2)**:000631

Introduction: Care for intensive care unit (ICU) patients boarded in the emergency department (ED) can be provided by the ED or ICU team. The choice between these different models of care is context-specific, but leads to distinct challenges. Our center uses a model of care based on an ICU consult team composed of an ICU staff, ICU fellows and residents. Team members are also responsible for the care of ICU patients in other locations.
Objectives: To explore perceptions from both the ICU and ED teams regarding the quality of care provided to ICU patients boarded in the ED, and identify potential solutions for gaps in quality of care.
Methods: We conducted a qualitative analysis of interprofessional staff perception of quality of care for ED-boarded patients using semi-structured interview questions. We sampled using a snowballing method, and interviewed providers until thematic saturation was reached. Interview transcripts were analyzed using thematic analysis.
Results: We interviewed 13 participants, consisted of seven physicians and six nurses. All providers agreed that quality of care was affected by an insufficient nurse-to-patient ratio. Major challenges identified were inadequate monitoring, poor coordination of care, and suboptimal transition of care from ED to ICU service. Potential solutions included adjusting workflow, improving communication and standardizing handover.

Three major challenges in care of ICU patients boarded in the ED

Challenges	Causes	Potential Solutions
Inadequate monitoring of ICU patients	-Insufficient nurse-to-patient ratio -Unpredictable number of ICU patients	-Identifying high risk patients and communicating concerns -Simplifying labor-intensive protocols (e.g. subcutaneous insulin for DKA protocol) -Optimize workload (e.g. generating standardized assessment note focusing on most common diagnoses)
Poor coordination of care	-Insufficient nurse-to-patient ratio -ICU team not always present -Unfamiliarity with ED flow sheet	-Adjusting workflow during rounds. For example, rounding with the charge nurse who received issues and concerns from bedside nurses -Communication with charge nurses to facilitate understanding of disposition plans. -Incorporating electronic flowsheet
Suboptimal transition of care from ED to ICU, including inappropriate ICU referral and inadequate handover	-Unawareness of consultation policy -Responsibilities of the ICU team in the ED and upstairs -Workload of ED providers -Suboptimal handover skill	-Training of policy/procedures regarding the transition of care -Two-way communication between ICU and ED regarding patients' conditions -Training handover skill or standardizing handover

Conclusion: Conclusions: Several challenges in care of critically ill patients in the ED were identified. Involvement of both ICU and ED teams in solving problems could optimize care of these patients.

000607

Echographic imaging of the Inferior Vena Cava for fluid responsiveness: a systematic review of comparison between subcostal and transhepatic approach

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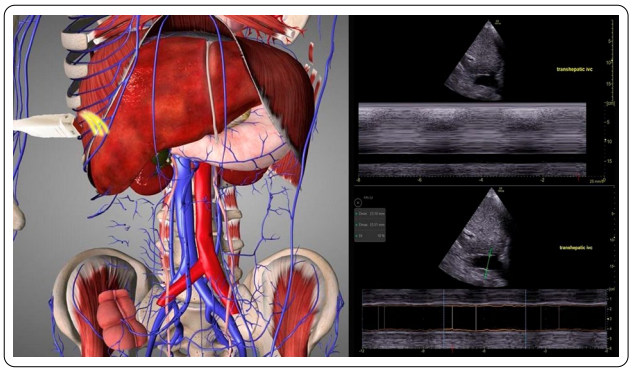
Introduction: Assessment of fluid-responsiveness is a key aspect of daily management in critically ill patients. Non-invasive evaluation of the variation of inferior vena cava (IVC) diameter during ventilation may provide useful information. However, sagittal IVC visualization from the subcostal (SC) region is not always feasible. Alternatively, IVC can be visualized with coronal trans-hepatic (TH) approach.

Methods: We performed a systematic search to explore the interchangeability of IVC evaluation with SC and TH views. We searched Medline and EMBASE up to December 8th, 2021 to identify prospective studies on the topic. We focused mainly on feasibility, correlation, intra/inter-rater reliability.

PICOS

1. Participants	*Volunteers or adult hospitalized patients, self-breathing and/or in positive pressure ventilation*
2. Intervention	*Assessment of the IVC with trans-hepatic coronal approach*
3. Comparison	*Assessment of the IVC with subcostal sagittal approach*
4. Outcomes	*Agreement (bias), correlation and differences between measurements of IVC diameters and IVC variability indexes (collapsibility and distensibility) during respiratory cycle; feasibility of imaging acquisition*
5. Study design	*Prospective observational studies*

Results: We included seven studies (population range: 14–131). Four studies were conducted on spontaneously breathing patients/volunteers, two on fully mechanically ventilated patients, and one in a mixed population. We found large heterogeneity regarding the analyses reported. Feasibility of TH imaging was reported between 81 and 100% (four studies). Limits of agreement between SC and TH were large (three studies). Concordance of the IVC collapsibility/distensibility indices are not interchangeable between SC and TH view (four studies). Correlation between diameters measured with SC and TH approach and intra/inter-observer correlation produced variable results (four studies). Two studies described the change of the IVC axes during ventilation, and both reported that most patients had a horizontal elliptical IVC shape.



Conclusion: Despite paucity of data and large heterogeneity, an overview of the included studies suggests that TH and SC assessment of IVC size and respiratory variation are not interchangeable. New studies are needed to define the proper cut-offs for fluid responsiveness using TH approach.

000641

Clinical characteristics and mortality of critically ill elderly patients with invasive mechanical ventilation and COVID-19 in a Mexican public hospital

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Introduction: Elderly patients have been more vulnerable to serious illness from COVID-19, which implied a therapeutic challenge in those who developed a critical condition and used mechanical ventilation.
Objectives: To describe the clinical characteristics at admission to ICU (Intensive Care Unit) and mortality of critically ill elderly patients with invasive mechanical ventilation and COVID-19 in a Mexican public hospital.
Methods: We conducted a single-center, retrospective, observational study with all patients admitted to ICU equal or older than 65 years old with mechanical ventilation and COVID-19 infection to ICU. We enrolled patients from April 2020 to June 2021. The demographic and clinical conditions at admission to ICU, pre-hospital therapeutic interventions, the degree of severity of the disease by APACHE II and SOFA was recorded. Finally, fatality to ICU discharge was recorded and the end point of follow-up.
Results: During the analysis period, there was a total of 635 admissions, from which 221 were elderly patients, 58.4% of them were men. The observed rate mortality was of 71.9% (n = 159). The median age was 62 (IQR 68–77). The severity of the disease by APACHE II, the median score was 19 (IQR 15.5–21) and the degree of organic failure by SOFA was 14 points (IQR 13–14), the median duration of invasive mechanical ventilation was 11 days (IQR 4.5–20) The median length of stay in the ICU was 14 days (IQR 5–15). The most frequent comorbidities were diabetes mellitus 49.3%, obesity 42.5% and arterial hypertension 40.3%. When the living and the dead were compared, the clinical characteristics, in the subjects who died in the ICU, dyspnea on admission was more frequent (60.4% vs 41.9% $p = 0.01$) and active smoking (10.1% vs 1.6% $p = 0.03$). Regarding the laboratory, the lymphocyte count was higher in dead patients ($0.86 \times 103/\mu L$ (IQR 0.63–1.31) vs $0.68 \times 103/\mu L$ (IQR 0.54–0.98) vs $p = 0.03$), and in the same way fibrinogen (686.5 mg/dL (IQR 588–778) vs 566 mg/dL (IQR 549–732) $p = 0.009$) and serum ferritin (1255.5 ng/dL (IQR 796.1–1740) vs 831.55 ng/dL (IQR 494.7–1480) $p = 0.006$). In the case of live ICU discharges, abdominal pain occurred more frequently (27.4% vs 15.1% $p = 0.03$), presence of bacterial coinfection (71.2% vs 55.8% $p = 0.04$) and Neutrophil count was higher in living patients ($9.75 \times 103/\mu L$ (interquartile range (IQR) 7.53–11.23) vs $9.55 \times 103/\mu L$ (IQR 6.09–14.25) $p = 0.04$). In the multivariate analysis we observed that the SOFA score at admission (OR 1.29 (95% CI 1.09–1.53)) the lymphocyte count (OR 3.02 (95% CI 1.00–9.10)) and fibrinogen concentration (OR 1.00 (95% CI 1.00–1.01)) at admission to the ICU.
Conclusion: The critically ill elderly patient with mechanical ventilation and COVID-19 infection has a high mortality. The increase in the SOFA score, lymphocyte concentration and fibrinogen at admission are risk factors that can predict death in this group of patients.

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000615

Implementation of videocalls in caregivers of patients admitted to intensive care: a prospective evaluation of the psychological effects

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Intensive Care Medicine Experimental 2022, **10(2)**:000615

Introduction: The coronavirus pandemic has caused over 280 million infections and over 5 million deaths to date, with a high percentage of hospitalizations and intensive care unit (ICU) admissions. In the context of the contagiousness of the coronavirus disease (COVID-19), visits by relatives to their loved ones admitted to ICU for severe COVID-19 have been prohibited. Furthermore, considering the ongoing period of restrictions, visits have been also limited for ICU admitting patients negative for COVID-19. This situation has led to an inevitable detachment between patients and their families as a preventive measure to limit further spread of the pandemic. However, the resulting physical detachment could negatively impact on caregivers' anxiety, depression, and post-traumatic stress disorder (PTSD). In this context, video communication between patients and their loved ones could reduce the negative effects of such detachment, but the impact of this strategy on levels of anxiety, depression and PTSD disorder are not well-known.
Methods: In this prospective study conducted at the ICU of the Policlinico Hospital (Catania), we evaluated the effects of the introduction of a weekly video-call on the incidence of depression, anxiety and PTSD in the caregivers of hospitalized patients. We initially included caregivers of COVID-19 patients. For subsequent conversion of our ICU to "non-COVID", we subsequently included caregivers of patients negative for COVID-19 for whom a direct visit to their loved one was not feasible. Assessment of anxiety, depression and PTSD was done using the following validated questionnaires (filled online): Impact of Event Scale (Revised IES-R), Center for Epidemiologic Studies Depression Scale (CES-D) and Hospital Anxiety and Depression Scale (HADS). Caregivers who answered twice to the questionnaire were included. In particular, the first questionnaire was completed before the initial video-call, while the second was completed before the second video-call, at least one week apart.
Results: We included 20 caregivers (of them n = 12 COVID-19 patients) from 17 patients (of them n = 11 COVID-19 patients). A total of 11 patients survived (n = 9 in the COVID-19 group and n = 2 in the "non-COVID" group). The average results of the questionnaires completed by caregivers between the two video calls showed no significant difference in terms of depression (CES-D and HDAS-D), anxiety (HDAS-A) and PTSD (IES-R). These results were observed both in the entire study population as well as in the two subgroups analyzed according to admission diagnosis (separated into COVID-19 and "non-COVID", Table 1).

TEST		T1	T2	p value
CES-D	COVID	15.3 ± 7.8	18.3 ± 8	0.13
	NON-COVID	26 ± 9.8	27.4 ± 9.7	0.69
HADS-Anxiety	COVID	8.3 ± 2.2	7.2 ± 4	0.37
	NON-COVID	9.4 ± 2.7	10.1 ± 2.8	0,47
HADS-Depression	COVID	9 ± 0.9	7.4 ± 3.5	0.15
	NON-COVID	10.1 ± 2.2	11.4 ± 3.3	0.34
IES-R	COVID	17.1 ± 9.9	18.2 ± 10	0.45
	NON-COVID	26.6 ± 10	30.4 ± 11.5	0.31

Conclusion: Our preliminary results showed that a video call implementation strategy between caregivers and patients admitted to the ICU did not show an improvement in terms of the risk of depression, anxiety and PTSD. The results appear similar regardless of ICU admission diagnosed with COVID or not. Our pilot study remains exploratory and limited to a small sample. Studies of larger samples of caregivers in the context of the pandemic could be helpful.

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Comparison of clinical characteristics and outcomes of covid-19 patients admitted to the intensive care unit during the first and second wave of the pandemic in Brazil: a single center retrospective cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000321

Introduction: The second wave of coronavirus disease 2019 (COVID-19), caused mainly by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) P.2 and P.1 (Gamma) variants, has been reported to be associated with increased morbidity and mortality (1). Nevertheless, studies on epidemiological characteristics and outcomes during the first two waves of the pandemic in private hospitals in Brazil are limited (2).
Objectives: To compare clinical characteristics and outcomes of patients admitted to the intensive care unit (ICU) at a private hospital in São Paulo, Brazil during the first and second waves of COVID-19 pandemics, and to identify predictors of in-hospital mortality.
Methods: Retrospective single-center cohort study. We compared clinical characteristics, resource use, and outcomes between patients admitted to the ICU during the first (May 01, 2020 to August 31, 2020) and second (March 01, 2021 to June 30, 2021) waves, and performed a multivariate logistic regression analysis to identify predictors of in-hospital mortality.
Results: A total of 1427 patients with COVID-19 were admitted to the ICU during the first (421 patients) and second (1006 patients) waves. Compared to the first wave [median (IQR)], patients admitted during the second wave were younger [57 (46–70) *vs.* 67 (52–80) years; $p < 0.001$], presented a lower SAPS 3 score [45 (42–52) *vs.* 49 (43–57); $p < 0.001$], and a lower SOFA score on ICU admission [0 (0–3) *vs.* 2 (0–5); $p < 0.001$]. During ICU stay, patients admitted during the second wave used more noninvasive ventilation (81.3% *vs.* 53.4%; $p < 0.001$) and more high flow nasal cannula (63.2% *vs.* 23.0%; $p < 0.001$), while the proportion of patients that used mechanical ventilation (35.5% *vs.* 32.5%; $p = 0.315$) and renal replacement therapy (11.3% *vs.* 8.3%; $p = 0.108$) did not differ between the groups. ICU (11.3% *vs.* 10.5%; $p = 0.696$) and in-hospital mortality (12.3% *vs.* 12.1%; $p = 0.998$) did not differ between patients admitted to the ICU during the second and first waves respectively. After adjusting for confounders, independent predictors of in-hospital mortality included: age older than or equal to 74 years (OR: 4.64; 95%CI: 2.21–9.71; $p < 0.001$); higher SAPS 3 score (OR: 1.03; 95%CI: 1.00–1.07; $p < 0.43$); higher SOFA score (OR: 1.22; 95%CI:1.12–1.33; $p < 0.001$); higher Charlson Comorbidity Index (OR: 1.32; 95%CI: 1.17–1.50; $p < 0.001$); the need for vasopressors (OR: 2.62; 95%CI: 1.49–4.60; $p < 0.001$) and the need for high flow nasal cannula (OR: 2.05; 95%CI: 1.36–3.09; $p < 0.001$).
Conclusion: During the second wave, patients with severe COVID-19 exhibited similar mortality rates and a need for invasive organ support compared to patients admitted during the first wave, despite being younger and less severely ill at the time of ICU admission.

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Acknowledgements: We thank the intensive care unit physicians, nursing staff, physical therapists, and all members of the multidisciplinary team of Hospital Israelita Albert Einstein, who managed patients during the SARS-CoV-2 pandemic.

000505

There is no such thing as routine blood tests

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Intensive Care Medicine Experimental 2022, **10(2)**:000505

Introduction: Intensive care patients frequently have bloods taken for various tests, many of which are clinically indicated but frequent testing often continues even when patients have clinically improved. Blood tests such as full blood count(FBC), urea and electrolytes (U&Es), liver function test (LFT), coagulation screen (CS), and C-reactive protein (CRP) are often thought of as 'routine' tests and done daily despite having no clinical indication. Frequent phlebotomy has been found to be associated with iatrogenic anaemia and increased healthcare cost (1,2).
Objectives: We aim to reduce unnecessary blood tests in a High Dependency Unit (HDU) and an Intensive Care Unit (ICU) in a UK district general hospital.
Methods: We surveyed ITU nurses and consultants on their opinions regarding regular blood tests. We then carried out a quality improvement project from 1 November 2017 to 31 July 2021. Data was collected from the clinical information system used in our unit. Data collected included patient demographics, duration of HDU/ICU stay, SOFA scores on admission and on day 7/discharge (whichever earlier), and number of blood tests sent including FBC, LFT, and CS. We carried out interventions using the Plan-Do-Study-Act (PDSA) cycles involving different versions of blood request proformas on electronic ward round templates intended as a prompt for clinicians to make conscious decisions whilst requesting blood tests. We calculated costs of total blood tests using private sector rates as of March 2022.
Results: 25% of nurses and 45% of consultants felt all blood tests(FBC, U&Es, LFT, CS, CRP) are not necessary on a regular basis. 80% of consultants felt that only FBC and U&Es are necessary if patient's SOFA score is > 8 or requiring organ support. In Nov 2017, our baseline data showed median SOFA scores on admission was 7, on Day 7/discharge was 3, mean(SD) total blood tests(FBC, LFT and CS) sent was 2.28(0.83) tests per patient-day, mean(SD) cost of £131.92(£49.57) per patient-day. As part of our first PDSA cycle, we introduced a proforma specifying blood test requests into our morning ward round documentation. In Dec 2019, median SOFA scores on admission was 5, on Day 7/discharge was 4, total blood tests sent increased to 2.53(0.76) tests per patient-day, cost £146.27(£49.06) per patient-day. We updated the blood request proforma to included explanations of usual indications for regularly requested blood tests. Following this, in July 2021, the total number of blood tests sent decreased to 2.14(0.93) tests per patient-day, cost £123.10(£63.78) per patient-day, median SOFA score on admission was 6, on day 7/discharge was 4.
Conclusion: Initially, despite clinical improvement as reflected in improvement in SOFA scores, 'routine' blood tests were still done frequently. The introduction of blood test request proforma on our electronic ward round notes and education on its use has resulted in a decrease in unnecessary blood tests in HDU/ICU patients.

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Acknowledgements: This project received no grant or funding.

000589

Development and validation of an automatic algorithm to calculate Sequential Organ Failure Score Assessment (SOFA) score from electronic health record data

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Intensive Care Medicine Experimental 2022, **10(2)**:000589

Introduction: SOFA score is routinely used in Intensive Care to quantify multiorgan failure, as an outcome parameter in clinical trials, and for the diagnosis of sepsis. Lambden et al recently published guidance to facilitate the consistent and valid assessment of SOFA score for sepsis trials. Due to the amount of data recorded during intensive care, accurate manual calculation of SOFA score according to this guidance is time consuming and requires training of staff. An automated algorithm is thus useful to reduce the labor requirement and increase the quality and accuracy of SOFA score.
Objectives: To develop and validate an automatic algorithm to calculate accurate SOFA score directly from electronic health record data, without any manual data cleaning, and to assess the ability of automatically calculated SOFA score to predict post-ICU mortality.
Methods: Data was extracted from the database underlying the electronic medical record system in Karolinska University Hospital ICUs (Centricity Critical Care). Patient data from all adult patients admitted to the ICU at Karolinska University Hospital Huddinge during 2018 was used as development cohort. For the CNS component, all periods of continuous sedation during mechanical ventilation, as calculated from the rates of infusion pumps containing sedative drugs, was used to carry forward GCS values and fill in missing data on days when GCS was not assessed due to continuous sedation. For the respiratory components, imputation of PaO2 from SpO2 according to Ellis' inversion of Severinghaus' formula was used when no arterial catheter was present. For the circulatory component, the maximum simultaneous rate of norepinephrine, epinephrine and vasopressin, according to the dose equivalence suggested by Lambden et al, was used. To reduce errors from invasive blood pressure measurements during zeroing of the arterial line, blood sampling or flushing, a two-step unsupervised outlier algorithm was used, first applying a Hampel filter over rolling time windows, then using the Local Outlier Factor. For the validation, data from all adult patients admitted to the ICU in Karolinska Huddinge between 2015 and 2017, and all adult patients admitted to the ICUs in Karolinska Solna between 2015–2018 was extracted and SOFA score calculated according to the algorithm described above. Then, 300 ICU days were randomly selected, and SOFA calculation by manual chart review, including tables extracted directly from the ICU database, was performed by an independent specialist physician in Intensive Care. The inter-rater reliability between the algorithm and the manual review was calculated according to Cohen's Kappa and Spearman's rank correlation. Finally, the ICU data from between 2015–2018 (excluding the development cohort) was linked to the Swedish population registry, and the univariate association between admission SOFA score and mortality was investigated with logistic regression. The SOFA algorithm was written in R and C++. All statistical analyses were performed in R.
Results: The inter-rater reliability according to Cohen's kappa was 0.94 (95% CI 0.9–0.97) for the respiratory component, 0.99 (0.97–1.0) for the coagulation component, 0.99 (0.97–1.0) for the liver component, 0.94 (0.90–0.97) for the circulation component, 1.0 (1.0–1.0) for the renal component, and 0.89 (0.84–0.93) for the central nervous system component. Spearman's rank correlation for the full SOFA score was 0.9832. The algorithm was able to calculate full SOFA score on 93.2% of patient days. A univariate logistic regression model for mortality at 30 days from ICU admission, based on admission SOFA score, was developed in 5068 patient admissions and tested in 1276 patient admissions. The area under the ROC curve in the test set was 0.7848 (95% CI 0.7506–0.8191).

Conclusion: Automatic calculation of SOFA score from electronic health records has excellent inter-rater reliability compared to manual chart review, and the SOFA score calculated by the algorithm has predictive performance similar to what has previously been reported from manually calculated admission SOFA score.

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000608

Dysnatremia in COVID patients—an analysys of the COLOS study

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Intensive Care Medicine Experimental 2022, **10(2)**:000608

Introduction: Hyponatremia is the most common electrolyte imbalance found in COVID-19 patients, with its prevalence ranging up to 9,9% [1]. It has also been observed that hyponatremia in COVID patients may be associated with detrimental outcomes, such as ICU admission or death [2]. Hypernatremia is less common than hyponatremia but seems to result in even worse clinical outcomes in COVID-19 patients [3].
Objectives: To elucidate the prevalence of dysnatremia among COVID patients and its impact on 30- and 90-day mortality and the need for the admission to Intensive Care Unit (ICU).
Methods: The single-center, retrospective, observational study included 2026 adult patients with proof of SARS-CoV-2 infection, who were admitted to Wroclaw University Hospital between February 2020 and June 2021. Using electronic records, patients were divided into three groups on admission: normonatremic (N group), hyponatremic (L group), and hypernatremic (H group), based on their natremia. To identify predictors of adverse outcomes a Cox Hazards regression and logistic regression were implemented.
Results: Hyponatremia on admission has occurred in 17.47% (n = 354) of patients and hypernatremia in 5.03% (n = 102). Mean sodium levels equaled: 130.39 ± 5.27 in L group, 150.14 ± 5.45 in H group, and 139.04 ± 2.55 in the N group. Dysnatremic patients presented with more comorbidities, used more drugs in a long-term manner, had higher CRP and creatinine values on admission and were statistically more often admitted to the ICU. Results of the multivariable analysis of predictors of ICU admission are presented in *Table 1*. The level of consciousness was the strongest predictor of ICU admission (OR = 1.21; CI: 1.16–1.27, p < 0.0001), followed by: male sex (OR = 1.055), white blood cell count (WBC) (OR = 1.0037) and CRP concentration (OR = 1.0005). Neither hypo- nor hypernatremia was found significant in this analysis. The 30-day mortality was significantly higher in both L- and H-groups (28.52%, p = 0.0001 and 47.95%, p < 0.0001 respectively) in comparison to 17.67% in N group. The 90-day mortality showed a similar trend in all study groups: 34.37% in the L group (p = 0.0001), 60.27% (p < 0.0001) in the H group, and 23.32% in the N group. In multivariable analysis, both hypo- and hypernatremia were found to be independent predictors of in-hospital mortality. Hypernatremia was a strong mortality predictor for both 30-day (HR = 1.60, CI: 1.14–2.24, p = 0.006) and 90-day (HR = 1.61; CI: 1.15–2.25 p = 0.0050) mortality, independently from the ICU admission. Hyponatremia on admission was also a 30-day mortality predictor (HR = 1.30, CI 1.02–1.66, p = 0.037).
Table 1 Results of univariable and multivariable analysis of predictors of ICU admission

Feature	univariable p-value	adjusted OR	lower 95% CI	upper 95% CI	multivariable p-value
Sex (male)	0.0001	1.055	1.023	1.088	0.0006
Systolic blood pressure [mmHg]	0.0099	1.0014	1.0005	1.0023	0.0018
Diastolic blood pressure [mmHg]	< 0.0001	0.9949	0.9934	0.9964	< 0.0001
Consciusness	< 0.0001	1.205	1.1556	1.256	< 0.0001
WBC [1000/ul]	< 0.0001	1.0037	1.0024	1.0050	< 0.0001
CRP [mg/dL]	< 0.0001	1.0005	1.0003	1.0007	< 0.0001
Hyponatremia	0.3598	1.0061	0.9664	1.0474	0.7682

Feature	univariable p-value	adjusted OR	lower 95% CI	upper 95% CI	multivariable p-value
Hypernatremia	0.0026	1.002	0.09313	1.0782	0.9565

Conclusion: Both hypo- and hypernatremia are strong predictors of mortality and disease severity in COVID-19 patients. Extraordinary care should be taken when dealing with hypernatremic, COVID-positive patients, as this group exhibits the highest mortality rates.

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000632

Reporting of implemented and proposed sound reduction measures in intensive care units: an online survey

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Intensive Care Medicine Experimental 2022, **10(2)**:000632

Introduction: Sound levels in the intensive care unit (ICU) are known to consistently surpass recommended levels1. This is problematic both for patients and healthcare professionals who experience negative health consequences associated with these elevated sound pressure levels1. Despite studies investigating interventions to reduce sound levels, it is not clear what measures are being implemented in real life1.

Objectives: The goal of this study was to better understand what types of strategies are already in place, and what types of strategies healthcare professionals propose could be beneficial to tackling the elevated sound pressure levels in the ICU.

Methods: Data was collected via an online survey sent to ICU staff in hospitals in Germany, Austria, and the German speaking part of Switzerland. All healthcare professionals were allowed to complete the survey. The survey contained questions about sound-reduction measures, asking participants what types of measures are currently being implemented (n = 91), and what types of measures they propose (n = 106) for reducing sound pressure levels.

Results: In total, 158 healthcare professionals (women: n = 93, 58.8%) took part in the survey (mean age 45 ± 11 years). Participants included nurses (n = 93, 58.8%), physicians (n = 62, 39.2%), and others such as physiotherapists (n = 3, 1.9%). Participants' responses indicated not enough being done by the hospital managers (n = 104, 65.8%) and co-workers (n = 79, 50%), with not enough equipment and infrastructure in place (n = 90, 60%), to reduce the sound pressure levels. Sound reduction measures currently being implemented, and those proposed by the participants, were grouped into four main categories (Table 1). Not everyone who participated in the survey completed both parts, resulting in 91 responses about what is currently being implemented, and 106 about proposed measures.

Table 1: Implemented and proposed sound reduction measures. Measures were grouped into four main categories. The number of responses can be higher than the number of participants as they could indicate multiple implemented or proposed measures.

Groupings	Sound reduction measure	Implemented Measures *(Number of responses)*	Proposed Measures *(Number of responses)*
Minimization of equipment and alarms	Alarm Management	17	37
	Telephone/Door Ringing	2	2
Modification of staff behaviour and procedures	Relocation of talks and work	7	10
	Staff sensitisation and motivation	25	24
	Noise measurements and display	39	14
	Changes in work processes	2	11
	Markings/rest periods	8	11
Optimizing design of the ICU	Structural Measures	21	29
Protection of the patient	Individual measures	2	1

Conclusion: Within ICUs, the greatest sound reduction measure currently implemented focuses on noise measurements and displays, as well as staff sensitization and motivation. This differs from what participants proposed as being useful measures, which focused more on alarm management and structural measures to reduce sound pressure levels.

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000647

From friend to foe—alarm fatigue in ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000647

Introduction: Alarms provide vital information about the patient's physiologic status. A significant factor to alarm-related adverse events is the excessive number of alarms, which can be as high as 150 alarms per Intensive Care Unit (ICU) patient per day. Research suggests that only 5–13% of alarms are clinically relevant. Most of these alarms are set by default to a generalized population (high sensitivity, low specificity). However, individualization of the alarm thresholds can mitigate nuisance alarms and alarm fatigue. Educational interventions are one of the recommended strategies.

Objectives: The aim of this study is to evaluate the impact of educational interventions on the establishment of safer alarm thresholds.
Methods: Cross-sectional study in a Portuguese ICU. During 3 random days, the following alarm thresholds of all patients hospitalized, excluding only potential organ-donor, where gathered: heart rate (HR), systolic (SP), diastolic (DP), mean blood pressure (MAP), peripheral oxygen saturation (SpO_2), temperature (Temp), end-tidal of CO_2 (EtCO2), respiratory rate (RR), tidal volume (Vt), respiratory minute volume (RMV), apnoeic time (AT) and airway peak pressure (Ppeak). A clinical education action, with doctors and nurses, was made after the first data collection. Same alarm threshold data were collected one month later. We categorized alarm threshold as safe or unsafe, according to literature, and compared pre-education to post-education intervention data. Statistical analysis, with significance of 0.05, included descriptive statistics and univariable analysis using Chi-Square test or Fischer's Exact test.
Results: Overall, 314 alarm thresholds were collected in the first period and 240 in second. Of those, in pre-education period, 71% were categorized as safe alarms and 66,7% in post-intervention period. Only SP, MAP, Vt, RMV, AT and Ppeak had a greater number of safe alarms thresholds after clinical education action(SP 84,8% vs 88,5%, MAP 84,8% vs 92,6%, Vt 68,4% vs 71,4%, RMV 15,8% vs 21,4%, AT 95% vs 100% and Ppeak 42,1% vs 64,3%). In univariable analysis, results didn't show a statistically significant difference in any of the alarm thresholds. Multivariable analysis wasn't possible due to sample size.
Conclusion: To our knowledge there are numerous studies regarding alarm fatigue but few of them address the safety of alarm threshold setting by clinicians in ICUs. The educational intervention was insufficient to change the usual practice regarding alarm management in our reality. We hypothesize that the intervention did not reach a significant number of staff either through live sessions or visualization of the video. Reduced sample size also limits statistical analysis and conclusions. Nevertheless, this study revealed vulnerabilities that led to prompt reflection. A careful plan to improve this issue should be addressed with training, development of institutional protocols and definition of safer opening thresholds with manufacturers.

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Acknowledgements: This research received no specific grant from any funding agency.

000674

Prognosis of the elderly patients in a regional ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000674

Introduction: The admission of elderly patients to the ICU is often limited. The prognosis of those patients may depend on factors such as diagnosis at admission.
Objectives: To analyze the clinical and epidemiological features of elderly patients (defined as more than 85 years) admitted to a regional intensive care unit (ICU); as also analyze the factors related to mortality in elderly patient admitted in our ICU.
Methods: Retrospective descriptive analysis was performed using a prospective cohort obtained from a 15-beds ICU collected between 2019 and 2021. Demographic outcomes, comorbidities, severity scores (APACHEII and SAPSII), ICU admission diagnoses and their origin (community, ward or another ICU), risk factors, ICU and hospital length of stay (LOS) and mortality were collected. Statistical analysis: continuous variables (mean and standard deviation or median and interquartile range), categorical variables (percentages and frequencies). Comparisons: Chi- square test (percentages) and T-student test (mean). Multiple logistic regression. Statistical significance was set at p-value < 0.05.
Results: 989 patients were included. Elderly patients (n = 54) were compared to non-elderly patients (n = 935). Gender (p < .001): female (57.4% vs. 32.9%), male (42.6% vs. 67.1%). Age (p < .001): 87.4 (± 3.8) vs. 62 (± 14.4). Prognosis scores: APACHE II (13.5 [10;19.5] vs. 12 [7;17], p = .015), SAPSII (35.5 [29.25;48] vs. 28 [18;42], p < .001). Comorbidities: DM 46.3% vs. 31.2% (p = .031), Renal chronic disease (RCD) 22.2% vs. 12.1% (p = .049). Risk factors: Mechanical ventilation (MV) 27.8% vs. 44.3% (p = .025), central venous catheter (CVC) 48.1% vs. 62.9% (p = .041). ICU LOS (days) 3 [1.25;5] vs. 4 [2;8], p = .039. Hospital LOS (days) 8.5 [3;17] vs. 11 [6;22], p = .017. Mortality (p = .365): 38.9% vs. 31.9%. Survivors and dead were compared: Female 20 (60.6%) vs. 11 (52.4%), p = .754. SAPS II (35 [26;42] vs. 43 [31;56], p = .057). Diagnosis at admission (p = .022): cardiopathy (60.3% vs. 33.3%); acute respiratory failure (3% vs. 23.8%); Complicated intra-abdominal pathology (15.1% vs. 9.5%); sepsis (12.1% vs. 9.5%). Risk factors: CVC 36.4% vs. 66.7%, (p = .058); urinary catheter (UC) 63.3% vs 90.5%, (p = .053). Mechanical ventilation (MV) 18.2% vs. 38.1%, (p = .19). Time of MV (days): 0 [0;0] vs, 1 [0;1], p = .031.
Conclusion: In our ICU the mortality of elderly patients was 38.9%, similar to control group. Patients who survive were mainly admitted due to cardiopathy. Days of MV were related to mortality in these patients.

000699

Worldwide clinical intensive care registries response to the pandemic: an international survey

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Intensive Care Medicine Experimental 2022, **10(2)**:000699

Introduction: The COVID-19 pandemic presented a major challenge to Intensive care units (ICU). ICU registries responded by capturing and reporting findings that guided resource allocation, informed policy, and generated time-critical data via observational and clinical research. The LOGIC (Linking of Global Intensive Care) is an independent consortium of ICU national registries to provide benchmarking, quality improvement, and clinical research to improve outcomes.
Objectives: To describe the changes in structure, data, funding as well the role of ICU registries for public reporting, data sharing and research during the pandemic.
Methods: An electronic questionnaire was developed by the authors and iterated by pilot-testing by 4 registry coordinators. An invitation was sent by email to a single member of each national registry. Standard descriptive statistics were used.
Results: Sixteen registries (representing 19 countries) were collecting data on COVID-19 patients in the ICU, ten from high-income countries (HICs) and six from low-and-middle income countries (LMICs). Most (55%) registries (6 of 10 from HICs) reported no specific funding and only one received governmental funds. Data from eight registries (80%) from high-income countries were used by scientific societies or government agencies for strategic planning, while only one (16.7%)

from LMICs used it. All registries provided data for research; All 16 registries used data in clinical research, six (three in LMICs) shared data for Randomized Control Trials (RCTs), and two for systematic reviews.
Conclusion: The response of existing quality registries during the pandemic shows their potential value in times of crisis. Funding, legal aspects, transparency use of data for research purposes and governmental use, varied, with even greater variation when LMICs and HICs are compared. Global initiatives such as this survey can help registers to learn and show possibilities for the use of their data in the post-pandemic to support the worldwide critical care community.

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000742

Towards a predictive software for management of cardiogenic shock patients in ICU

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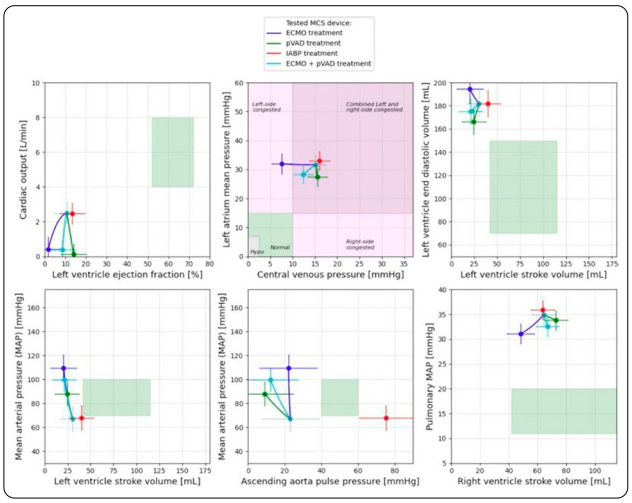
Intensive Care Medicine Experimental 2022, **10(2)**:000742

Introduction: Cardiogenic shock (CS) is a multisystemic pathological condition with a high mortality and complex aetiology and pathogenesis. Prognosis may vary greatly from one patient to another, depending on severity of the leading cause, anatomical and age differences and presence of additional pathological conditions or comorbidities making thus management of CS a cumbersome task, requiring a high level of experience and multidisciplinary skills.
Objectives: We introduce preliminary results obtained through a novel, proprietary ICU information system that relies on predictive computational models of human whole body physiology for supporting clinical decisions and management of CS patients. In this study, we will focus on the cardiovascular applications of this software, testing its reliability in 1) calibrating its underlying models on a specific patient's condition and 2) providing predictive insights on patient's global hemodynamics in response to treatment with three different mechanical circulatory support (MCS) devices at various functioning rates and configurations.
Methods: The cardiovascular module of this software relies on a predictive multiscale mathematical model of the whole cardiovascular system and on lumped parameter models of MCS devices. Advanced machine learning algorithms are adopted to calibrate the cardiovascular model on the specific hemodynamics of a real CS patient as reported in a published clinical case report. Subsequently, the calibrated model is employed to test the use of three different MCS devices at various functioning rates and configurations: a VA-ECMO (0 to 5 L/min), a pVAD (0 to 4 L/min), a IABP (inflating at every cardiac cycle) and concomitant use of VA-ECMO and pVAD (from 0 to 2 and 3 L/min respectively).
Results: The cardiovascular model was successfully calibrated on patient's hemodynamics with a satisfactory low degree of uncertainty. Predictions on the use of the different MCS devices allowed a qualitative and quantitative characterization of the impact of each MCS on global hemodynamics and the identification of the expectable differences between available treatments (Figure 1, each result as mean ± standard deviation).



Conclusion: The proposed models could be easily and rapidly calibrated to simulate the hemodynamic condition of a specific CS patient, starting from his clinical records and on measurements of monitoring systems commonly put in place after admission in ICU. This allowed an in-depth assessment of the impact that different administrable treatments can exert on the patient's specific hemodynamics. Further developments are ongoing to extend calibration algorithms to whole body physiology models, while next steps will be directed towards testing the applicability of this solution in a clinical environment and validating the models against a cohort of real cases.

000755

Assessing the association between APACHE II score and outcome at 6 months

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Intensive Care Medicine Experimental 2022, **10(2)**:000755

Introduction: The Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system is one of several ICU scoring systems for predicting in-hospital mortality that has been in use for nearly four decades.1 It is still used in critical care units throughout the world despite the subsequent APACHE III and IV systems being developed. The APACHE II scoring system utilises several biochemical and patient signs whilst taking both acute and chronic disease into consideration. It was originally suggested that it can be used to evaluate the efficacy of critical care units over time. Several studies have validated the APACHE II score for predicting mortality in different critical care patient populations.2
Objectives: To assess if an association exists between the APACHE II score and outcome at 6 months over a 22-year period in a district general hospital ICU in the UK.

Methods: From a total of 13,637 patients, we examined deidentified data for 5205 patients admitted to the East Surrey Hospital critical care unit between the years 2000 and end of 2021 (22 years) where the outcome at 6 months was known. We used generalised linear mixed-effects regression (GLMER), fitting a random-slope and random-intercept nested model, to determine if the APACHE II score has a significant effect on outcome at 6 months after controlling for variation in years and gender. Both a full and reduced model were compared via a likelihood-ratio test. Analysis was performed using R (version 4.1.3, Vienna, Austria).
Results: A likelihood-ratio test indicated that the model including the APACHE II score provided a better fit for the data than a model without it, $X2(1) = 26.88$, $p < 0.001$. The random effect of years accounted for over 95% of the variance. The model suggested that for each point increase in APACHE II score, the risk of death at 6 months increases by 19% ($p < 0.001$).
Conclusion: This analysis has demonstrated that the APACHE II score can potentially be used to help predict the outcome of critical care patients at 6 months following admission (e.g. an APACHE II score of 20 would estimate the probability of death at 34.2%). This can be used by clinicians to manage the expectations of patients and their relatives. To the best of our knowledge, we believe this is the first study that has assessed the APACHE II score in predicting 6 month outcomes over a consecutive 22 year period using GLMER. With the advent of 'big data', it may be possible to evaluate the APACHE II score in larger datasets over similar periods of time using GLMER to confirm these findings. Therefore, further research to investigate the association of the APACHE II score on long term outcomes, especially in different critical care patient populations, may justify the continued use of this score without the need to spend resources on APACHE III and IV scoring systems.

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Health services research & outcome 8

000480

How effective are interventions to reduce sound levels in the ICU, a systematic review

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Intensive Care Medicine Experimental 2022, **10(2)**:000480

Introduction: Intensive care units (ICU) have become complex workplaces due to advanced medical technology with accompanying excessive noise exceeding the WHO recommended noise levels of max 35 A-weighted decibel (dBA) by far. This not only results in a stressful environment for patients and family members, but also negatively affects proper work performance of caregivers including increased potential for errors (1). Despite that many studies focused on lowering this noise burden in various ways, a concise overview is lacking.
Objectives: The aim of this study was to systematically review the literature to evaluate the effectiveness of interventions aiming to reduce sound levels in the ICU.
Methods: PubMed, EMBASE, Psych INFO, CINAHL and Web of Science were systematically searched from inception to March 9th, 2022. Two independent reviewers assessed titles and abstracts against study eligibility criteria. Noise mitigating ICU studies were included when having at least one quantitative acoustic outcome measure in decibel (dBA), with an experimental, quasi-experimental or observational design. Discrepancies were resolved by consensus, and a third independent reviewer adjudicated as necessary. After title, abstract and full-text selection, two reviewers independently assessed each studies quality using the Cochrane's Risk of Bias in Non-randomized Studies (ROBINS-I) tool and extracted data.
Results: A total of 11,749 articles were screened, and 24 articles were included comprising a mixed group of healthcare professionals ($n = 17$) or only nurses ($n = 7$) from different adult or pediatric ICU settings. Noise reduction interventions were categorized into education ($n = 3$), warning devices ($n = 3$), multicomponent programs ($n = 15$) and architectural redesign ($n = 4$). Overall, the methodological quality of the studies was low. A statistically significant reduction ($p < 0.05$) of mean sound levels was reported in 14 (58%) studies. Education, a noise warning device and an architectural redesign, decreased the sound levels significantly ranging from 1 or 2 dBA up to 16 dBA but the effect was only measure in the short-term.
Conclusion: Single interventions as staff education and visual alert systems, as a noise warning device, seems promising interventions to achieve noise reduction with a short-term effect. The evidence of multicomponent intervention studies that may have a longer term effect, remains uncertain, and therefore high-quality studies with a long-term follow up are warranted.

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Acknowledgements: None.

000594

Bedside visualisation tool for prediction of deviation from intended dosage in multi-infusion therapy

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Intensive Care Medicine Experimental 2022, **10(2)**:000594

Introduction: In multi-infusion therapy multiple infusion pumps are connected to the same vascular access point. The different pumps in such a system influence each other [1], which leads to deviations from the set flow. Resulting under- or overdosing of medication, for instance when administering inotropics, can be very harmful to the patient [2,3]. It is known that these errors occur, however clinicians tend to find it hard to estimate an order of magnitude of these errors [4].
Methods: This research uses an analytical model to create a bedside prediction tool that is able to show clinicians what dosing errors will occur in multi-infusion therapy. The model, created in previous research [5], predicts these errors based on hardware parameters and pump flow settings. A panel of experts was gathered consisting of both nurses and doctors. To obtain an indication of the level of knowledge about multi-infusion, the panel is presented a number of multi-infusion systems where the set flow is changed. The panel is asked to predict what happens to the dosing. Afterwards the panel is shown the prediction tool.
Results: In Figure 1 the prediction tool is shown, including the two pump multi-infusion system that is used. A large fraction (44%) of the panel of experts wrongly predicted the impact of changing the set flow of liquid A on the flow of liquid B that reaches the patient. None of the members of the panel (0%) were able to correctly predict the dosing deviation when a very small catheter is used. The deviations caused by changes in set flow when using these high resistance catheters was seen as counter-intuitive by the panel. After the model was shown, the experts indicated they had a better understanding of what deviations to expect. The panel indicated that the prediction tool would be a useful tool to improve the understanding of multi-infusion dosing errors.

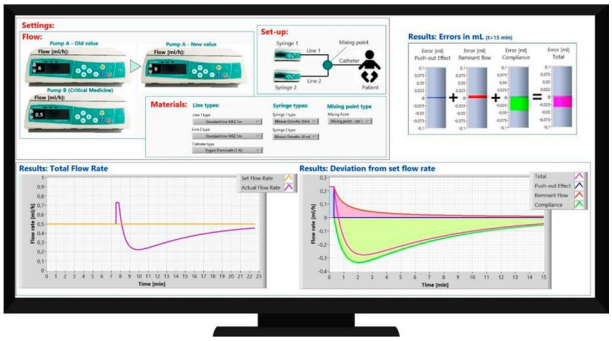

Figure 1 Impression of the predictive tool. In the top-left the two-pump system is described. The set flowrate of pump A is changed. In 'Materials' the syringes and mixing points that are used can be selected from the drop-down menus. The impact of changing the set flowrate on pump A on the resulting flow of the substance in pump B at the vascular access point is presented in the different figures. In the top-right the total dosing errors is shown. The bottom-left figure shows the set flowrate (yellow) and the actual flowrate (purple) of the substance in pump B. The bottom-right figure shows the contribution of different factors to the deviation.

Conclusion: Using a predictive tool to visualise the deviations from the set flow is a good opportunity to create more insight for clinicians in deviations from the set dosage in multi-infusion therapy. This knowledge can be used to reduce the amount of expected dosing errors in the clinical situation. Future research needs to expand the tool to allow it to simulate more complex setups and more different syringes, lines and mixing points.

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Acknowledgements: This work has received funding from the EMPIR programme co-financed by the Participating States and from the European Union's Horizon 2020 research and innovation programme.

000646

Predictive modelling of neurocognitive outcomes

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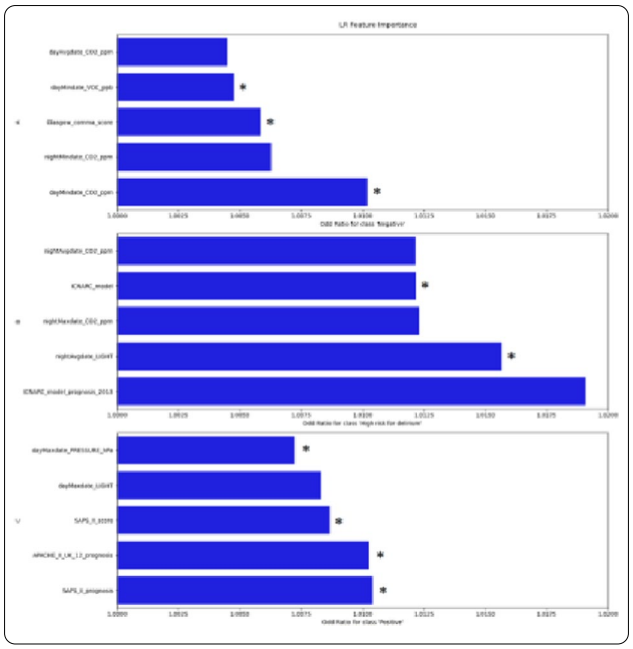
Introduction: Delirium is a serious disturbance in mental abilities that often develops over a short period of time. It can occur in up to 69% of ventilated patients in the UK and ICU has been reported to have the highest incidence rates of delirium of all clinical departments in the hospital [1]. Clinical risks factors for delirium have been identified in many research [2–12]. However, the influence of environment on delirium is less well studied in the field. In the past only the direct effects of light intensity and noise level at affecting patient's delirium have been investigated but their results were inconclusive [13–18].
Objectives: The aim of the project was to identify the primary clinical variables and environmental variables that can independently predict multiclass delirium outcomes of adult ICU patients using logistic regression.
Methods: Anonymised clinical data of patients admitted to adult ICUs of CWFT, between April 5th 2021 and March 29th 2022, were extracted using SQL from Cerner EPR and Acubase database. A final study cohort of 257 patient encounters was selected. Environmental data used in the study were recorded by Airthings devices. Clinical data of the patients and the environment were matched together based on recorded time and location. The data were then processed and cleaned before being fed into logistic regression for delirium prediction (Positive, Negative, High risk for delirium). In the end, we collected and processed a total of 90 different clinical and environmental features, of which 89 were testing features and CAM-ICU was the delirium outcome prediction (Table 1). The results of logistic regression were expressed as odd ratios. Statistical analysis was performed on the odd ratios by bootstrapping half of the dataset 1000 times to examine whether the features could strongly predict different delirium outcomes at $p = 0.05$ significance level.

Clinical features (48)	
Non-modifiable factors	17
Age	18-89
Sex	Male or Female
Ethnicity	White, Asian, Black, Others
Frailty score	Rockwood, PRISMA, Charlson
Severity score	APACHE II, SAPS II, ICNARC model, GCS
Neuropsychiatric history	Yes or No
Modifiable factors	30
Methods of ventilation	CAPA, HFNC, BiPAP, Ventilator
BMI	14.57-46.28
Drugs	Atropine, Diazepam, Fentanyl, Midazolam, Morphine, Propofol, Tramadol, Diamorphine
Primary reason for admission	Abdominal/liver/GI, Cadiovascular, Drug/iatrogenic, Endocrine, Infection, Neurological, OB/GYN, Renal/urinary, Respiratory, Others
Comorbidities	Diabetes, Hypertension, COPD, Cancer, Heart failure, Obesity
Admission Method	Elective or Emergency
Outcome measures	1
CAM-ICU scores	Positive, Negative or High risk for Delirium
Environmetal features (42)	
Name	Per Aggreagation
Air radon short term average	per Daytime maximum
Room temperature	per Daytime miminum
Air humidity	per Daytime average
Air pressure	per Night time maximum
CO2 Concentration	per Night time minimum
Air volatile organic compounds cncenrtation	per Night time average
Light intensity	

Results: High Glasgow coma score was shown to be a significant protector for delirium. On the other hand, high SAPS II score, high APACHE II UK 12 prognosis score, high ICNARC model score were all significant predictors for positive delirium. Additionally, the use of propofol, invasive ventilator, and HFNC could significantly increase the risk of delirium. In terms of environmental variables, high air pressure and high room temperature could increase the odds of patients being delirious. On the other hand, low radon gas level and VOC were protectors for delirium (Figure 1).



Conclusion: Severity scores including Glasgow coma score, SAPS II score and its prognosis score, ICNARC model and APACHE II UK 12 prognosis score should be considered as key clinical variables when predicting patient's delirium outcomes. Liberation from HFNC and invasive ventilator for AICU patients should be actively encouraged since they could significantly increase the risk of delirium. This research is also the first study to suggest air quality such as radon gas level and air pressure have an impact on delirium outcomes.

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Acknowledgements: My gratitude extends first to Dr Marcela P. Vizcaychipi who has been supportive throughout the project. She has informed me the relevant developments and trends in the world of medical data research, kindly providing useful literatures and ideas to support the progression of the project. I am also sincerely grateful for all the support David Fukum (day-to-day mentor) and Giles Rolph (data analyst) had provided me. They had helped me immensely at understanding how Cerner is used to store and process patient's clinical data in the Trust. Additionally, they had also taught me the data manipulation skills in SQL server required for this research. Alex Brown (Co-supervisor) had helped me greatly at building and troubleshooting the machine learning models. I also want to thank Dr Lothaire Gerard for helping me understood the clinical risk factors for delirium as well as helping me categorise diseases and drug classes. Last but not least, I would like to thank Dr Matthieu Komorowski who had provided statistical support in machine learning and had helped me understood the clinical significance of the outputs in the two models. I cannot express in words how much grateful I am to all of their help in the past six months.

000677

Lung sequelae after critical COVID-19: An analysis of long-term outcomes at follow-up post-Intensive Care consultation

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Intensive Care Medicine Experimental 2022, **10(2)**:000677

Introduction: Survivors of Coronavirus Disease 2019 (COVID-19) are known to sustain a variety of sequelae after Intensive Care Medicine (ICM) admission that may influence recovery, with lung injury as a major concern. A number of critical COVID-19 survivors report sustained symptoms, and some demonstrate persistent detrimental lung imaging findings that may be associated with worse patient outcomes.

These alterations have been widely described at short-term post-discharge follow-up. However, there are limited reports on the full range of long-term pulmonary sequelae after critical COVID-19 and whether these changes may be progressive or reversible. Therefore, we aimed to evaluate long-term post-ICM lung sequelae in COVID-19 survivors.
Methods: Adult COVID-19 ICM survivors admitted to a Portuguese University Hospital between March 2020 and March 2021 (1st to 3rd "waves") were included. Lung sequelae were assessed at "short-term" [3 months(M)] and "long-term" (6/12 M) post-discharge using chest computerized tomography (CT).
Results: Study included 254 patients: 66% male, median age = 64y; mean Charlson Comorbidity Index = 2,91, Acute Physiology and Chronic Health Evaluation (APACHE)-II score = 16 and Simplified Acute Physiology Score (SAPS)-II = 35. Median ICU and hospital length of stay was 10 and 26D, respectively. 30% of patients underwent high-flow nasal O2 therapy and 18% non-invasive ventilation. 39% received invasive mechanical ventilation (median duration = 21D) and 13% required therapy with Extracorporeal Membrane Oxygenation (ECMO). Most patients presented at least one CT lung abnormality post-discharge, with similar incidence on short- and long-term follow-up (72% at 3 M vs 76% at 12 M, $p = 0.777$). Frequency of ground glass opacities (GGO, 55,7% 3 M vs 42,8% 12 M, $p < 0.001$) and fibrosis (32,3% 3 M vs 19,2% 12 M, $p < 0.001$) demonstrated significant improvement. Conversely, presence of bronchiectasis (20,8% 3 M vs 26% 12 M), bronchiolectasis (18,6% 3 M vs 16,3% 12 M) and small-airway disease (7,2% 3 M vs 10,3% 12 M) did not differ significantly, and rate of fibrotic atelectasis increased (14,9% 3 M vs 28,4% 12 M, $p < 0.001$). Improvement in evidence of fibrosis at long-term follow-up was significantly associated with younger age ($p = 0.023$), shorter hospital and ICU stay ($p < 0.001$), lower Charlson ($p = 0.004$) and lower APACHE ($p = 0.012$), absence of restrictive pattern ($p = 0.004$) and normal CO diffusion capacity ($p = 0.004$) at 3 M post-discharge pulmonary function testing. GGO improvement was associated with chronic obstructive pulmonary disease patients ($p = 0.045$).
Conclusion: These results suggest that most COVID-19 ICM survivors maintain some lung abnormality at both short- and long-term post-discharge, with a progressive improvement in GGO and fibrosis and sustained bronchiectasis, bronchiolectasis and small-airway disease. These results underline the importance of follow-up post-ICM evaluation for assessment and management of long-term lung sequelae.

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000763

One year mortality of mechanically ventilated patients with COVID-19: A multicenter cohort study

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Introduction: The COVID-19 pandemic is being a major challenge for health systems around the world (1). Great demand for intensive care units and therefore mechanical ventilation was observed in several locations. Mortality by ventilated patients was excessively high in several regions of the world, with great variability ranging from 26–97%, depending on the outcome studied—ICU or 30-day mortality (2–7). However, studies that assess later mortality as well as post-hospital discharge are scarce (8,9).
Objectives: Describe one year outcomes of mechanically ventilated patients with COVID-19
Methods: Retrospective cohort study in 3 tertiary private hospitals in Rio de Janeiro, Brazil from March to June 2020. Patients admitted to general intensive care units (ICU) with a diagnosis of COVID-19 were included. Clinical and outcomes data were collected from Epimed Monitor System (10). Outcomes after hospital discharge was collected from the Rio de Janeiro State Public Database of births and deaths (http://cgj.tjrj.jus.br). The study was approved by The Ethics Committee of InstitutoD´OR: CAAE: 41734621.1.0000.5249 and the need for informed consent was waived.
Results: From 653 ICU admissions, 260 (39,8%) needed mechanical ventilation (MV) and were analyzed. Median age was 73(IQR 61–82) years, modified frailty index (MFI) 2(IQR 1–3), Charlson 1 (IQR 0–3), SAPS3 59(IQR 51–70) e SOFA 6 (3–9) points. 248(95,4%) used vasoactive drugs and 118(45,4%) renal replacement therapy (RRT). Hospital mortality was 48% and 53% after 1 year. RRT, age, MFI, SOFA and SAPS 3 were higher in non survivors. In a multivariate analysis RRT (OR 3,33[1,78–6,25]), age (OR 1,05 [1,02–1,08]) and Charlson (OR 1,3[1,08–1,58]) were associated to increased mortality in 1 year.
Conclusion: One year mortality of patients with COVID-19 and mechanical ventilation was high in the analyzed populaton with no significant difference among hospital mortality. Renal replacement therapy, age and Charlson score were associated to increased mortality in 1 year

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Acknowledgements: No grants were used.

000799

NEWS2 trigger for Peri-arrest calls: the effect of varying the NEWS threshold on frequency of calls

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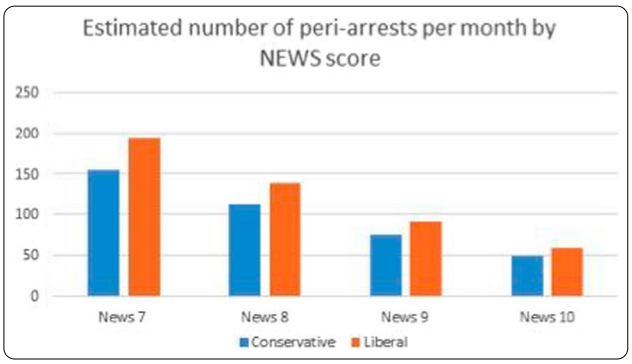
Intensive Care Medicine Experimental 2022, **10(2)**:000799

Introduction: The National Early Warning Score 2 (NEWS2) is used to identify deteriorating ward patients in the UK. NEWS of 7 or above is the "emergency response threshold", recommending emergency assessment by a team with critical care competencies (Figure 1). However there is no national guidance on response time for this assessment or on when to make a peri-arrest call for immediate assessment by the entire peri-arrest/medical emergency team. At Southend Hospital we have introduced a protocol that mandates a peri-arrest call at NEWS 10 for immediate assessment by the medical emergency team.
Objectives: To estimate the number of peri-arrest calls generated by varying the NEWS threshold in the range NEWS 7–10.
To define an optimal trigger score for peri-arrest calls by balancing the sensitivity of low NEWS against increasing the workload on the emergency team through high frequency of calls.
Methods: The total number of ward inpatients who recorded a NEWS score of 7 or more in the month of December 2021 was recorded, excluding patients in A&E and critical care. Electronic patient records were manually reviewed to assess their treatment escalation plan at the time the NEWS score of 7 and above was recorded. Based off these plans we could determine if a peri-arrest call would be generated, or if treatment limitation decisions already made would rule out a peri-arrest call, thus produce conservative and liberal estimates for the number of peri-arrest calls for the month.
Results: In December 2021, 244 unique patients scored a NEWS 7 on at least one occasion. 50.8% (124) of these were recorded 'in hours' (08:00–18:00) vs 49.2% (120) recorded 'out-of hours' (18:00–08:00). The use of a NEWS 10 threshold generated an estimated 49–60 peri-arrest calls. The use of a NEWS 7 threshold would have generated 155–193 calls (conservative vs liberal estimate – full results see Figure 3). The total number of actual peri-arrest calls at Southend Hospital in December made was 103; this number includes calls made from clinical decisions as well as automatic NEWS score calls.
Conclusion: When deciding on the threshold for peri-arrest calls it is important to balance the higher sensitivity of a low NEWS2 threshold for detection of deteriorating patients with the increased workload for the emergency medical team. Our current pathway uses NEWS 10 as the threshold for peri-arrest calls. Based on these results, changing the NEWS2 threshold for peri-arrest calls from NEWS 10 to NEWS 7 would generate an additional 106 calls per month in busy winter months (conservative estimate). Although NEWS 7 is recommended as a criteria for assessment by critical care teams, based on these estimates we do not feel NEWS 7 is a feasible threshold for peri-arrest calls at current medical staffing. We will continue to use NEWS 10 as the threshold for peri-arrest calls for medical emergency team activation as we feel it provides optimal compromise between sensitivity and increased workload.

Chart 4: Clinical response to the NEWS trigger thresholds

NEW score	Frequency of monitoring	Clinical response
0	Minimum 12 hourly	• Continue routine NEWS monitoring
Total 1–4	Minimum 4–6 hourly	• Inform registered nurse, who must assess the patient • Registered nurse decides whether increased frequency of monitoring and/or escalation of care is required
3 in single parameter	Minimum 1 hourly	• Registered nurse to inform medical team caring for the patient, who will review and decide whether escalation of care is necessary
Total 5 or more Urgent response threshold	Minimum 1 hourly	• Registered nurse to immediately inform the medical team caring for the patient • Registered nurse to request urgent assessment by a clinician or team with core competencies in the care of acutely ill patients • Provide clinical care in an environment with monitoring facilities
Total 7 or more Emergency response threshold	Continuous monitoring of vital signs	• Registered nurse to immediately inform the medical team caring for the patient – this should be at least at specialist registrar level • Emergency assessment by a team with critical care competencies, including practitioner(s) with advanced airway management skills • Consider transfer of care to a level 2 or 3 clinical care facility, ie higher-dependency unit or ICU • Clinical care in an environment with monitoring facilities



	Conservative	Liberal
News 7	155	193
News 8	113	139
News 9	76	91
News 10	49	60

Reference
1. NEWS2 Chart 4—https://www.rcplondon.ac.uk/file/9437/download
Acknowledgements: No grants received.

000832

Characterization of ICU-acquired weakness: proof of concept

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Introduction: Critical illness-associated weakness (ICU-AW) can be caused by critical illness polyneuropathy, critical illness myopathy, or muscle disuse atrophy alone or in combination (1). The loss of myofibrillar protein, predominantly myosin loss in myofibrils is associated with prolonged immobilization (> 5 days) (2), in addition the loss of diaphragmatic myosin due to mechanical ventilation (3). Thus, critical illness-associated weakness is a frequent entity in the intensive care unit that can reach an incidence of 50% in critical ill patients and up to 67% in patients with sepsis (4); this leads to prolonged hospital stay, difficult weaning of mechanical ventilation and many derived complications. Early identification and accurate diagnosis of this disease is important to make interventions in nutrition status, promote constant mobilization and timely rehabilitation to reduce the risk of morbidity and mortality.
Objectives: Characterize by ultrasound (US), electromyography (EMG) and biochemical nutritional parameters the ICU-AW of the critically ill patient.
Methods: This is a prospective cohort where ICU patients were included, interviewed with EMG, US of the diaphragm and vastus medialis muscles (VMM), as well as serum prealbumin at admission and at day 5 and nitrogen balance.
Results: Of the 45 patients admitted to the ICU since the beginning of the protocol, only three met the sample selection criteria are presented; two presented ICU-AW on day 5. Patients who had decreased prealbumin below normal ranges on the 5th day developed ICU-AW documented by EMG; No significant changes were observed in the mean maximum or minimum diameter of the vastus medialis of the quadriceps (Graph 1).

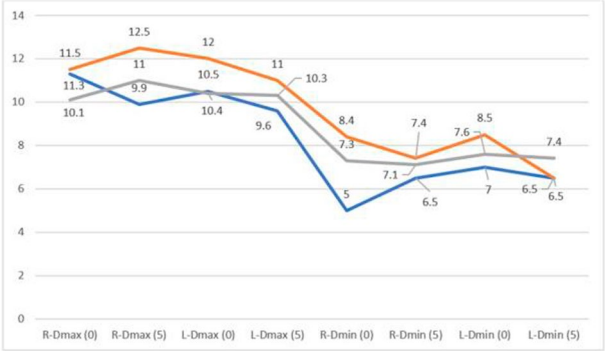

Figure 1. Maximum (max) and minimum (min) diameters (D) of the vastus medialis of the right (R) and left (L) quadriceps.

Conclusion: ICU-AW is a clinical diagnosis where the Medical Research Council sum score and handgrip dynamometry constitute the gold standard and require patients´ cooperation, therefore can't be used in some patients undergoing mechanical silencing- that is, the complete loss of mechanical stimuli in patients who are mechanically ventilated or deeply sedated o receiving neuromuscular blocking agents or who are undergoing a combination of these (1), and is likely to be underdiagnosed. It seems that some biochemical parameters, more than the ultrasound ones (operator dependent) can predict the EMG changes related to ICU-AW.

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Acknowledgements: No funding or grants were received for the development of this protocol.

000863

Breaking the glass ceiling: A scoping review and framework proposal to achieve gender equity in intensive care

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Intensive Care Medicine Experimental 2022, **10(2)**:000863

Introduction: Despite women's best efforts to reduce the gender gap in professional and academic spheres, the *glass ceiling* still needs to be addressed. This metaphor represents an invisible barrier that prevents women from rising beyond a certain level in a hierarchy, whether in training programs, the workforce, academic positions, or leadership roles.Literature concerning this topic has grown substantially in the past five years—allowing greater recognition and understanding of its foundations, which has led to various policies and strategies to reduce the gap at different levels. However, the data used are derived from developed countries that differ from low-income regions in political, academic, social, and medical structures.
Objectives: To analyze available data regarding the gender gap in different roles in critical care, focusing on Latin America, and present a framework proposal of strategies and goals to achieve gender equity in critical care settings in low- and middle-income countries.
Methods: Five major search engines (Embase, PubMed, Medline, SciELO, and Google Scholar) were reviewed to identify published information regarding gender disparities in critical care. After careful selection, 29 papers were read and discussed among the investigators. The information was organized in a flow chart, identifying current biases and limitations. Strategies and goals that focus on the Latin American situation were developed.
Results: Twenty-nine articles were selected for the review. Only two of the selected studies were conducted in Latin America. Even though in Latin America overall gender gap findings were consistent with international literature, a wider disparity was reported regarding leadership roles. The main issues concerning low- and middle-income countries were grouped and organized in a framework (Figure 1). Historically, social, and cultural traditions that have prevented women from achieving equity in intensive care were reported and classified into cultural bias, self-perception bias, and lack of information. The primary limitations were economic divergence, little academic motivation, and a lack

of support from medical institutions, which are thought to be more pronounced in Latin America. Based on this, strategies were proposed, like educational programs to encourage sorority; Organizational policies for women and men with children; Zero tolerance for harassment and promotion for women in leadership roles. Also, some goals were reshaped to this population, such as the creation of a safe environment, equitable number of women and men in leadership positions, and, finally, social, economic, and political equity within institutions.

Conclusion: In the past decade, there has been a growing literature on gender equity and the strategies targeted at improving it in high-income countries. However, to date, this data is nearly nonexistent in most Latin American countries. Available data suggest that a gender gap is still in place, as women are still under-represented in critical care, whether in training programs, the workforce, academic positions, or leadership roles. Since low- and middle-income countries have evolved at different rates, it is imperative to address this issue regionally and adapt or create new strategies and realistic goals.

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000873

Critical care nurse work environments in five European countries

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Intensive Care Medicine Experimental 2022, **10(2)**:000873

Introduction: Healthy work Environment (HWE) is the cornerstone for quality patient care and nurses' wellbeing (Ulrich et al., 2018). The HWE standards, of the American Association of Critical Care Nurses (AACN), have been identified as an important tool that organizations and nurses can use to foster a workplace that promotes optimal patient outcomes and where nurses and other members of the healthcare team are fulfilled in their work (AACN, 2016).

Objectives: To evaluate the current state of the critical care nurse work environment in five European countries (Cyprus, Spain, Poland, Croatia, and Romania), to identify areas for improvement and provide a baseline for future documentation.

Methods: A multinational descriptive correlational survey was used with a convenience sample of all Registered Nurses (RNs) working in adult ICUs in the five countries. The Critical Care Nurse Work Environment survey, based on the AACN HWE standards (Ulrich et al., 2018), was translated and used with permission. The survey was distributed over one year, November 2020–2022. Descriptive statistics (N, % or Mean (SD) were used. Comparisons across countries were conducted with an ANOVA and Chi-square tests. The six HWE standards were calculated as mean scores.

Results: 1413 RNs participated (Cyprus: n = 264, Spain: n = 437, Croatia: n = 290, Poland: n = 105, and Romania: n = 317). With respect to their gender, 15% were Male, 52% Female, and 33.3% preferred not to answer. Their mean age was 37.4 years (SD = 10.1). More than half (53%) stated they are aware of some HWE Standards in ICU and 25.2% stated that their unit**,** similarly with their organisation (24.2%), is well on its way or has fully implemented some HWE standards. Overall, 83% of the RNs are Very satisfied (28%) or somewhat satisfied (55%) with their current job. However, almost one third (32%), have plans to leave within the next 1 or 3 years with significant differences across the countries, (Cyprus:30%, Spain:49%, Croatia:34.2%, Poland:51%, Romania:14.7%). With respect to the HWE standards (table 1), the mean Skilled Communication level in the RN's unit is 2.3 (SD = 0.7) (scale of 1—4, with 4 being "Strongly agree" and 1 "strongly disagree), True collaboration mean level is at 2.5 (SD = 0.7), Effective Decision Making is at 2.4 (SD = 0.6), Appropriate staffing is at 2.5 (SD = 0.7), Meaningful recognition at 2.5 (SD = 0.7) and Authentic leadership is at 2.5 (SD = 0.7). Similar results of the state of HWE were stated for their organisation. There were statistically significant differences across the five countries in all six standards for both, RNs' unit and organisation.

Table 1 Mean level of AACN standards—Unit and Organisation

AACN Standard	Overall, N = 1.2051		Cyprus, N = 2281		Spain, N = 3091		Croatia, N = 2771		Poland, N = 871		Romania, N = 3041		p-value2	
	Unit	Org	Unit	Org	Unit	Org	Unit	Org	Unit	Org	Unit	Org	Unit	Org
Skilled Communication	2.2 (0.7)	2.3 (0.7)	2.2 (0.6)	2.3 (0.7)	2.3 (0.6)	2.4 (0.6)	2.4 (0.6)	2.5 (0.6)	2.5 (0.6)	2.7 (0.6)	1.9 (0.7)	2.0 (0.6)	< 0.001	< 0.001
True Collaboration	2.4 (0.7)	2.5 (0.7)	2.2 (0.6)	2.4 (0.6)	2.7 (0.6)	2.8 (0.6)	2.5 (0.6)	2.5 (0.6)	2.8 (0.6)	2.9 (0.5)	2.1 (0.7)	2.1 (0.7)	< 0.001	< 0.001
Effective Decision-Making	2.3 (0.6)	2.4 (0.6)	2.1 (0.5)	2.2 (0.5)	2.4 (0.6)	2.5 (0.6)	2.4 (0.6)	2.4 (0.6)	2.5 (0.5)	2.7 (0.5)	2.1 (0.7)	2.2 (0.6)	< 0.001	< 0.001
Appropriate Staffing	2.4 (0.7)	2.5 (0.7)	2.3 (0.7)	2.4 (0.7)	2.6 (0.6)	2.8 (0.6)	2.4 (0.7)	2.4 (0.7)	2.9 (0.7)	3.1 (0.6)	2.1 (0.7)	2.2 (0.7)	< 0.001	< 0.001
Meaningful Recognition	2.4 (0.7)	2.5 (0.7)	2.3 (0.6)	2.4 (0.6)	2.5 (0.6)	2.6 (0.6)	2.7 (0.7)	2.7 (0.7)	2.6 (0.5)	2.8 (0.4)	2.1 (0.7)	2.2 (0.7)	< 0.001	< 0.001
Authentic Leadership	2.4 (0.7)	2.5 (0.7)	2.3 (0.6)	2.4 (0.6)	2.6 (0.7)	2.7 (0.7)	2.5 (0.7)	2.5 (0.7)	2.6 (0.6)	2.7 (0.6)	2.0 (0.7)	2.1 (0.7)	< 0.001	< 0.001

[1]Mean (SD)
[2]One-way ANOVA
Note: Mean of scores ranging from 1 (strongly disagree) to 4 (strongly agree); a higher score indicates a higher level of the standard

Conclusion: The status of HWE for the participating countries is moderate. The results indicate pressing challenges and offer a starting

point for dialogs that can lead to solutions and a baseline for future measurement.

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Acknowledgements: This study was a joint effort of the consortium of the Erasmus + project entitled: 'Improving Working Environments for Critical Care Nurses -HWE4CCN. Find more about this project: https://sites.google.com/view/hwe4ccn/home?authuser=4.

Health services research & outcome 9

000559 Defining the problem: prevalence of psychological distress and required interventions in COVID-19 and non-COVID-19 patients following Intensive Care Unit (ICU) admission

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Intensive Care Medicine Experimental 2022, **10(2)**:000559

Introduction: The prevalence of psychological difficulties amongst survivors of critical illness is well documented (1), with high rates of depression (29%), anxiety (33%) and post-traumatic stress disorder (PTSD; 22%) (2). COVID-19 patients appear to be as psychologically affected as non-COVID-19 patients (3). The psychological sequelea of patients admitted to ICU is recognised as an important target to address (4). UK national guidelines now recommend specialist psychological provision during ICU follow-up clinics (5).
Objectives: To assess if an association exists between COVID-19 and increased prevalence of psychological distress and to describe interventional pathways provided to those patients.
Methods: We examined deidentified data for 139 patients attending ICU follow-up clinic between 10/2020 to 03/2022. Patients were assessed by our resident ICU clinical psychologist. We divided patients into treatment (admitted for COVID-19 illness) and control (not admitted for COVID-19 illness) groups. Inferential testing used Fisher's Exact test or Wilcoxon's test. Psychological conditions assessed included anxiety, depression, PTSD and other (e.g. cognition, adjustment or sleep). All analyses were performed using R (version 4.1.3, Austria, Vienna) using an alpha level of 0.05.
Results: Treatment and control groups consisted of 70 and 69 patients respectively. A statistically significant difference was observed for the male:female ratio between groups ($p = 0.0396$). From the total sample, 58% of patients presented with psychological concerns: anxiety, 15%; low mood, 16%; PTSD, 12%; and 15% with other conditions. No psychological concerns were reported in 42% of patients. Significant differences in the prevalence of each psychological domain were not found between groups. However, the increased prevalence of anxiety symptoms in COVID-19 patients was approaching significance ($p = 0.056$) with OR (95% CI) 2.9 (1.04–7.9). In the 80 patients with psychological concerns, 34% were referred to the ICU clinical psychologist for outpatient intervention, with a further 16% offered but declining referral. Finally, 19% of patients were provided with in-clinic psychological input, and 31% of patients were referred to other services.
Conclusion: This study describes the significant burden of psychological distress following ICU, further supporting the need for specialist psychological services at follow-up. The absence of significant difference in psychological distress between COVID-19 and non-COVID-19 cohorts highlights the role of the ICU admission itself on psychological outcomes, rather than the admitting physical diagnosis. Future work should explicate the long-term psychological consequences of COVID-19 to understand whether the trajectory of persisting distress differs from non-COVID-19 critical illness. This small study is limited by potential bias whereby those without psychological concerns may be less inclined to uptake invitation to clinic.

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000665 COVID-19 related changes in outcomes in a regional ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000665

Introduction: COVID-19 infection has change the world in the last 2 years. Risk factors related to mortality in ICU may have changed too.
Objectives: To analyze the differences observed between patients diagnosed with Covid and patients admitted for other pathologies from June 2019 to December 2021 in an ICU of a regional hospital.
Methods: Retrospective descriptive analysis was performed using a prospective cohort obtained from a 15-beds ICU collected between 2019 and 2021. Demographic outcomes, comorbidities, prognosis scores (APACHE II and SAPS II), risk factors (central venous catheter [CVC], mechanical ventilation [MV], urinary catheter [UC]), ICU and hospital length of stay (LOS), microorganism isolated and antimicrobial therapy used and mortality were collected. Statistical analysis: continuous variables (mean and standard deviation or median and interquartile range), categorical variables (percentages and frequencies). Comparison: Chi- square test (percentages) and T-student test (mean) or Wilcoxon-test (median). Multiple logistic regression. Statistical significance was set at p-value < 0.05.
Results: 989 patients were included. SARS-CoV2 (n = 142) vs. No SARS-CoV2 (n = 847). Origin: community (11.3% vs. 59.7%, p < .001), ward (88% vs. 37.1%, p < .001). CU-acquired infections (52.8% vs.15.9%, p < .001). Previous antimicrobial therapy (46.5% vs. 71.7%, p < .001). Risk factors: Need for renal replacement therapy (RRT) (13.4% vs. 5.5%, p < .001), CVC (83.1% vs. 58.7%, p < .001), MV (74.6% vs. 38.1%, p < .001). UC (95.8% vs. 70%, p < .001). Tracheostomy (17.6% vs. 3.3%, p < .001). Days of CVC (10 [16] vs. 1 [5], p < .001). Days of MV (8 [15] vs. 0 [2], p < .001). Days of UC (13 [15] vs. 3 [5], p < .001). ICU LOS (days) (13 [15] vs. 3 [4], p < .001) and hospital LOS (days) (20 [20] vs. 9 [13], p < .001). First antimicrobial therapy used: ceftriaxone (73.6% vs. 23.9%, p < .001). First ICU-adquired infection: Ventilator-associated pneumonia (VAP) (8.5% vs. 2.6%, p < .001); Catheter-related bloodstream infection (CRBSI) (9.9% vs. 2.7%, p < .001); secundar y bloodstream infection (BSIs) (12.7% vs. 6.1%, p < .001). First microorganism isolated (p < .001): *Staphilococcus* spp. (16%) vs *E. coli* (25%). Second ICU-adquired infection: VAP (12.7% vs. 1.8%, p < .001); CRBSI (7% vs. 1.1%, p < .001). Second microorganism isolated (p < .001): *C. albicans* (16.7%) vs. *Klebsiella spp* (18.7%). Time until ICU-adquired infection (9.5 [7] vs. 2 [6], p < .001). Mortality (69% vs. 26.1%, p < .001).
Conclusion: Patients diagnosed with COVID19 infection in our ICU exhibit more incidence of ICU-adquired infections (VAP, CRBSI, BSIs), need for CVC, MV, UC and RRT. ICU length of stay and mortality were also higher with statistical significance.

000761

Clinical profile of deceased COVID 19 patients in ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000761

Introduction: It has been documented a high mortality in ICU of patients due to SARS COV 2 pneumonia, especially in mechanical ventilated patients.
Objectives: To describe clinical characteristics and support therapy requirements of patients deceased during ICU stay due to SARS CoV2 pneumonia.
Methods: Retrospective, single-center case series of patients with SARS CoV2 pneumonia deceased in ICU. Setting: 19-beds medical-surgical ICU of a community hospital. Time of study: 2 years. APACHE II and SOFA at admission, medical history, age, invasive mechanical ventilation requirement and ICU length of stay were collected. Statistical analysis: Data were analyzed by SPSS 18 and quantitative variables were expressed as a mean $\pm$ standard deviation.
Results: 198 consecutive patients were admitted in ICU during time of study. Mortality was 56%. Clinical characteristics of deceased patients were: mean age of 68 years old, 66,6% were man. Hypertension was the most common preexisting medical condition, 69,37%. 36,94% had diabetes mellitus. Body mass index was 31,02 kg/m^2. APACHE II at admission was 13 and SOFA score of 5 points. Most of the patients required mechanical ventilation 91,89%. And most of these patients were ventilated in prone position at admission 85,59%. 90,99% were treated with vasoactive drugs. In 32,43% haemofiltration was indicated. ICU lenght of stay was 18 days.
Conclusion: Deaths due to COVID-19 affected obese patients aged $\geq$ 65 years with risk vascular factors. Most of patients were admitted with organ failure and invasive treatment requirements.

000827

Emergency endoscopy: the role of intensivists in the emergency department in a multidisciplinary environment

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Introduction: Emergency endoscopies are an important procedure frequently required in the setting of an active upper gastrointestinal bleeding, enabling both diagnostic and appropriate treatment approaches, as well as providing prognostic information. In this setting, the intensivists' role is assumed as vital in the management of these clinical challenges within the emergency department, encompassing multitasking to ameliorate the patient's condition and warrant a successful treatment and outcome. Appropriate knowledge and clinical recognition of critical situations, advance airway skills, haemodynamic management and anticipate emergency consequences or unfavourable outcomes are paramount. In Portugal there is no specialization in emergency medicine. Therefore, the emergency department is mainly governed by the intensive care unit, although it is covered by different specialities during night shifts, weekends and in certain regions of the country. Since 2008 that Centro Hospitalar Universitário Porto (CHUPorto) is the only tertiary emergency hospital in the North region of Portugal, that is responsible for receiving all the cases that warrant an urgent endoscopy approach during the nightshift and weekends.
Objectives: Evaluate the necessity of having an intensivist in the emergency department during the management of an emergency endoscopy in a country without a specialization in emergency medicine.
Methods: Unicentric retrospective observational study conducted in a large tertiary university hospital. Data was gathered from 333 patients between January 2019 and December 2020. Data was obtained from medical records of those patients who received emergency endoscopy at CHUPorto. The information was screened further and submitted to basic statistical analysis.
Results: During 2019 and 2020 it was registered the admission of 188 and 145 patients, respectively. In this cohort, 56,4% were referred to the CHUP emergency department from other hospitals and 46,7% discharged to a highly dependent facility. In this study, upper gastrointestinal bleeding was registered as the primary clinical emergency for endorsing emergency endoscopy. Secondary treatment was required, such as red blood cells transfusions (18,3%), administration of fluids (13,5%) and vasopressors (2%) and advanced airway management (35,6%). The majority (63%) of the emergent endoscopy procedures were taken in the emergency department with the supervision of an intensivist.
Conclusion: The contribution of intensive care in the management of emergency endoscopies is essential within the emergency department, assuming a vital multitasking approach of this challenging clinical emergencies.

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Acknowledgements: The stated study provides important evidence of the supreme position of intensive care within the emergency department. Furthermore, it propels for more clinical research considering protocols and precise guidelines regarding the admission and management of this specific clinical presentations.

000872

Reporting and interpreting missing health-related quality of life data in intensive care trials—a systematic review

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Intensive Care Medicine Experimental 2022, **10(2)**:000872

Introduction: Health-related quality of life (HRQoL) is a frequently assessed patient-important outcome in ICU trials (1, 2), and included in a core outcome set for patients with acute respiratory distress syndrome (3). Missing data is a known challenge in trials with long-term HRQoL outcomes (4–6). The extent and handling of missing data in randomised trials in the ICU setting are unknown, but currently under investigation (7).
Methods: We performed a systematic review exploring the extent and handling of HRQoL data in ICU trials according to a pre-published protocol and statistical analysis plan (8), and Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement (9). We systematically searched the Cochrane Library, PubMed, EMBASE and CINAHL. Three authors independently screened and extracted data for the included trials in duplicate. We included any published randomised trials in adult ICU patients reporting HRQoL as an outcome by any score as defined in the trial without limitation to language or intervention. We followed the recommendations by the Cochrane Collaboration and assessed risk of bias (ROB) according to the second version of the ROB tool (10). Our primary outcome was the proportion of missing HRQoL data due to death before follow-up and due to non-respondents, and if missing data were reported in quantity and discussed. Our secondary outcomes were whether there was a comparison between respondents and non-respondents and if there was,

then which analytic strategy was used for handling missing data. All data was handled descriptively. We also compared outcomes between trials with low vs high risk of bias and between small ($n \leq 100$) vs larger trials with a Fisher's exact test. Finally, we will explore heterogeneity with subgroup analyses.
Results: Of 10,971 articles screened, we assessed the full text of 137 trials. Sixty-four eligible randomised trials met all inclusion criteria. The ROB assessment showed 7 trials with low, 8 with some concerns and 49 with high ROB. Ten trials assessed HRQoL as the primary outcome and 36 as a secondary outcome. The final 18 trials did not specify HRQoL as a primary or secondary outcome.
Conclusion: This systematic review will provide valuable information regarding the extent and handling of missing data for HRQoL outcomes in randomised trials in ICU. The study is still in progress, thus providing limited and preliminary results, but we expect all results to be ready for presentation at LIVES2022.

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000891

ABCDEF bundle mesures in the critically ill patient care, a cross-sectional study

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Intensive Care Medicine Experimental 2022, **10(2)**:000891

Introduction: In the last 20 years, the focus of intensive care medicine has shifted from mere patient survival to looking more and more at how the patient survives. The ABCDEF strategy, which focuses on the objectives of sedation time, optimization of analgesia, physiotherapy, treatment and prevention of delirium and the presence of the family, seeks to improve care quality and has shown benefits in terms of mortality, days of hospital stay and sequelae at discharge.
Objectives: To determine the current situation in an intensive care unit regarding the ABCDEF measures.
Methods: Cross-sectional study in a 35-bed medical intensive care unit of a third level care hospital in Madrid. Data were collected weekly during July 2021 using medical and nursing notes, and the nursing care chart, using only validated scales. Data on analgesia, sedation, mechanical ventilation, delirium, physiotherapy, relatives, nutrition, and antibiotic therapy were collected. Finally, a descriptive analysis of the data was performed.
Results: 103 questionnaires were collected from 58 patients. ANALGESIA: pain was registered > 6 times/day in 5.1%. Only 78% had the fixed plus rescue analgesia regimen (the most recommended one). There is a medical note in 73% and a nursing note in 43.7% (all three shifts). SEDATION: recorded > 3 times/day in 48%, and > 6 times/day in 7%. In sedated patients, sedation was recorded once per shift in 63% of them. Medical note was written in 88% and nursing note in 88%. Benzodiazepines were used in 29% of the total. MECHANICAL VENTILATION: 68 patients. Both medical and nursing note in > 95% of them. Weaning attempt was made in 53% of these patients. DELIRIUM: 23.3% of patients developed symptoms, and 37% received treatment (40.5% in a prophylactic way). There is only a medical note in 41.7% and a nursing note in 26.7%. None of them was recorded with validated scales (CAM-ICU). PHYSIOTHERAPY: clinical situation allowed physiotherapy in 67% of the patients. Of these, 69.5% were candidates for active physiotherapy. Only 26% of them received physiotherapy. RELATIVES: 84.3% of family members received information (the reason is not specified). The visit of relatives was considered beneficial por the patient in 68% of the cases. This is recorded in medical notes only in 19.6%. NUTRITION: intestinal functioning was assessed in 68.6% of patients and 87.3% of them received nutritional support (considered appropriate in 92%). INFECTION: 67% of the patients had antimicrobial treatment, most of them antibiotics (66.7%). Most empirical (61%), and targeted only 36%. Adjustments are made according to isolation in 69%, with a clear target in 91%. There is justification registered in 95% of cases, being considered appropriate in 95%.
Conclusion: To this day, the benefits of improving the care quality and caring are evident. With this study we show what our current situation is and what aspects need to be improved within all these areas that are so important in intensive care.

000908

Fluid de-resuscitation among critically ill patients requiring intravenous fluid administration

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Intensive Care Medicine Experimental 2022, **10(2)**:000908

Introduction: Intravenous fluid overprescribing might carry significant risks to critically ill patients. Large-volume fluid administration often results in considerable fluid overload. Several studies have shown that a persistent cumulative positive fluid balance negatively impacts intensive care unit (ICU) patients' outcomes. A retrospective study conducted on 2631 septic ICU patients found that every 1 L (L) increase in cumulative fluid balance at 72 h of ICU admission was associated with hospital mortality. Two other studies found that a cut-off of $\geq$ 10% fluid overload, defined as dividing total fluid balance/ admission body weight multiplied by 100, was associated with mortality. However, a subsequent study found that as low as $\geq$ 5% fluid overload was associated with increased mortality. Previous studies established the association between percent fluid overload and mortality; however, it's unclear if percent fluid overload could guide fluid de- resuscitation among ICU patients.
Objectives: To assess the association between the percent fluid accumulation at 72 h of ICU admission and the need for fluid

de-resuscitation by diuretics or/ and renal replacement therapy in critically ill patients.
Methods: A Prospective cohort study was conducted in a tertiary care hospital in Saudi Arabia. The study included adult critically ill patients admitted to ICU and started on intravenous (IV) fluid for resuscitation, replacement, or part of IV medications fluid. The study excluded patients under 18 years of age with end-stage renal disease on renal replacement therapy, patients on diuretics upon ICU admission, and those who could not measure fluid output. The primary outcome of this study is the mean percent fluid accumulation in patients who were de-resuscitated with diuretics or/and RRT compared to those who were not de-resuscitated. Other outcomes include ICU and hospital mortality and length of stay.
Results: A total of 393 patients were screened since September 2021. Sixty-seven patients are included in the preliminary analysis with a mean age of 59.7 ± 17.4. The mean APPATCHI II score upon ICU admission was 16.5 ± 7.99. Forty-five (67.1%) patients required fluid de-resuscitation (DR) by diuretics or/ and RRT, and 22 (32.8%) patients didn't require fluid de-resuscitation (NDR) during their ICU stay. Mean percent fluid accumulation at 72 h was 7 ± 11.5 and 7.2 ± 6.3 in patients requiring de resuscitation (DR) and those who didn't need it (NDR), respectively (P-value NS). ICU mortality was found in 14 (31.1%) patients with DR and 4 (18.1%) in those with NDR; (P-value NS).
Conclusion: In the preliminary data, the mean percent fluid accumulation on day 3 was not statistically different between the group of patients who required fluid de-resuscitation and those who didn't. Even though we did not see a statistical difference in the ICU mortality between the two groups, there was a clear signal toward a worse outcome in those patients who required fluid de-resuscitation. A larger sample size is needed to confirm the lack of association between percent fluid overload and the need for fluid de-resuscitation.

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000910

Mental Health Assessment Among COVID-19 Patients Survivors of Critical Illness

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Intensive Care Medicine Experimental 2022, **10(2)**:000910

Introduction: Critically ill survivors are at increased risk of developing post-intensive care syndrome (PICS). Anxiety and depression at three to twelve months following intensive care unit (ICU) discharge are two of three main psychological components of PICS that occur in 46% and 29% of ICU survivors, respectively. A matched cohort study of more than 200,000 patients found a significant increase in mood, anxiety, or psychotic disorders in COVID -19 patients compared with influenza patients. Few published prospective data assessing the psychological status of COVID-19 patients post ICU discharge.
Objectives: Using a validated assessment tool, this study aimed to evaluate anxiety or depression among COVID -19 patients who survived the critical illness.
Methods: A questionnaire-based study for adult COVID- 19 patients admitted to ICU or under ICU consultation for ≥ 24 h and discharged alive. The study excluded patients with language barriers or those not willing to participate. Six months post ICU discharge, we communicated with each eligible patient through a telephone call to assess their psychological status using the Hospital Anxiety and Depression Scale (HADS). A cut-off score of > 7 for either HADS anxiety or depression scales defined the caseness of the respective condition. The primary outcome is the mean HADS score six months after discharge from the ICU.
Results: Over eight months, a total of 518 COVID 19 ICU patients were screened. Among 390 patients who met the inclusion criteria, 49 patients completed the questionnaire. The mean age was 56.5 ± 17.1 years, 30 (61%) were male, and the mean length of ICU stay of 13.7 days. The main comorbid conditions were endocrine (49%) and respiratory diseases (43%). The mean HADS score was 11.24 (SD ± 8.4). A total of 18 patients (36%) and 15 patients (30%) were found with HADS scores > 7 for depression and anxiety, respectively.
Conclusion: HADS score confirmed positive for almost one-third of COIVD-19 ICU survivors. These findings highlighted the necessity of a structured follow-up plan for critically ill COVID-19 survivors to ensure optimal care is continued post ICU discharge.

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000918

Rapid response system in a primary hospital: a 3-year retrospective analysis

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Intensive Care Medicine Experimental 2022, **10(2)**:000918

Introduction: The concept of a Rapid Response System (RRS) mainly integrates two major components: the afferent limb, including ward physicians and nurses that identify critical patients and activate an emergency response; the efferent limb, including an emergency team of critical care doctors and nurses, the rapid response team (RRT). The RRS has been created to detect and respond to deteriorating patients outside the intensive care unit (ICU). In our country, formal guidelines for its implementation were created in 2010, with an important switch from a traditional code team to an integrated RRS with other precise activation criteria. This study describes the RRS activity and organization at a primary care hospital of our center, from 2018 to 2021.

Methods: We performed a descriptive statistical analysis of all RRS activations from January 2018 until December 2021, since our RRS registry database was formally implemented.
Results: In the study period, a total of 207 activations were performed. 53.6% of the patients were female, with a mean age of 78.7 ± 11.8. There was no specific pattern of activations throughout the study period, with a total of 30 activations in 2018, 95 activations in 2019, 52 activations in 2020 and 30 activations in 2021. The mean time between activation and the emergency team arrival was 5.52 ± 0.03 min and the mean duration from activation until the end of approach was 34.5 ± 0.13 min. 82.1% of RRS activations originated from the internal medicine ward, 12.1% from a Convalescent Unit, and the remaining 3.86% equally distributed through outpatient services and radiology department. The most frequent activation criteria were tachycardia with heart rate > 140 (23.7%) followed by oxygen desaturation (18.4%) and cardiac arrest (CA) (10.6%). Other activation criteria were altered mental status (including Glasgow Coma Scale (GCS) decrease of two or more points and repeated/sustained seizures), and airway obstruction. Immediately after the RRT approach, death was declared on site in 12.1% of patients. Nine patients were promptly transferred to a secondary or tertiary hospital. In CA cases, the predominant arrest rhythm was asystole (60.0%) followed by pulseless electrical activity (8.00%). A non-successful cardiopulmonary resuscitation occurred in 24.0% of the cases. In 56.0% of the cases a do-not-resuscitate (DNR) order had been previously established by the assistant medical team.
Conclusion: At this primary hospital, RRS is formed by a RRT composed of a Emergency Room nurse and an Internal medicine physician active on a 24/7 basis. This study aimed to study the RRS activations in an attempt to understand the context for the different outcomes. Having recognized a limitation in the medical records, we are planning subsequent changes and protocols for registry and auditing RRS in order to ensure the quality of medical records, and allow future studies with more detailed information.

000900

Evaluating a novel critical care inter-hospital transfer course for HEMS clinicians

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Intensive Care Medicine Experimental 2022, **10(2)**:000900

Introduction: Air Ambulance Kent Surrey and Sussex (AAKSS) is a UK pre-hospital emergency medicine service. An area in which AAKSS aimed to expand its service was to inter-hospital transfers of intensive care patients. This was with the aim of reducing the burden on local hospitals to provide transfer teams and providing a time critical service for those who need it. Thus, a Critical Care Transfer Course was developed by AAKSS's governance and education teams to adequately prepare all HEMS clinicians for this new role. This novel program consisted of online lectures, workshops and simulation training.
Objectives: To evaluate the course in terms of participants' views and experiences, and by their self-assessed knowledge and competencies pre- and post-course.
Methods: This study used mixed methods and recruited doctors and paramedics currently working for AAKSS. Participants completed questionnaires pre- and post-course with Likert scales to rate their competence with different pieces of equipment and scenarios. Post-course they rated the value of different teaching methods. Semi-structured group interviews and open-ended questionnaires were used to collect qualitative data, and a thematic analysis was performed.

Results: Pre-course, doctors felt significantly more competent than paramedics in the management of patients with most of the equipment and all of the scenarios ($p < 0.05$). Participants from both professional backgrounds rated themselves significantly more competent across all fields after the course ($p < 0.05$). Participants rated the value of all the styles of teaching as 'valuable' or 'very valuable'. From the thematic analysis, four superordinate themes broken down into ten subthemes were identified. 1) Consistent high-quality care: Equipment, drugs and logistics; Structure and troubleshooting; AAKSS specific. 2) Learning styles and pReferences: Further learning; Mixed teaching methods; Simulation. 3) The educational journey: Previous experience; Ongoing development. 4) Collaboration and cooperation: Reputation and respect; Interpersonal communication; New relationships.
Conclusion: This course was well received by participants, with an increase in confidence seen across several domains and for all types of doctors and paramedics suggesting the multi-disciplinary teaching approach is successful. All the educational strategies were deemed valuable, and participants approved of the predominance of simulation training. However, participants were anxious to be familiarised with the kit, and felt their simulation-based learning would be improved if this had been achieved first. Participants were aware of their ongoing learning needs and some of the challenges that come with offering a new service. Future plans include developing the course further and researching which educational strategies are most economical and which are more likely to lead to retention of skills.

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000775

Comparison of the clinical course and long-term follow-up between COVID-19 and non-COVID-19 patients with critical illness

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Intensive Care Medicine Experimental 2022, **10(2)**:000775

Introduction: A subset of patients (4–32%) affected by COVID-19 develops severe to critical symptoms requiring ICU treatment.(1) Especially those patients suffer from severe long-lasting symptoms. In a cohort of ICU survivors, 74% reported physical impairment even one year after infection.(2) In general, long-term physical and psychological impairment is common after critical care admission.(3)
Objectives: To compare the clinical course and long-term follow up of COVID and non-COVID patients after prolonged ICU treatment.
Methods: After discharge from ICU, patients were recruited at the Schoen Clinic Bad Aibling in Germany, a clinic for acute neurology and neurorehabilitation. Patients were included in this cohort study, if they had been mechanically ventilated for ≥ 5 days. Investigations took place at discharge from neurorehabilitation and 1 year after disease onset. Assessments regarding health related quality of life (EQ-5D-5L), mental health (Hospital Anxiety and Depression Scale), fatigue (Fatigue-Severity-Scale-7), frailty (Clinical Frailty Scale) and dyspnea (modified Medical Research Council dyspnea scale) were conducted.
Results: A total of 40 patients were included in this interim analysis. Non-COVID patients were initially hospitalized due to internal (15%), cardiovascular (10%), respiratory (7.5%) or cerebral (5%) diseases or viral/bacterial infections (5%). Four patients (3 COVID patients) died before or shortly after discharge. Table 1 visualizes the comparison between COVID and non-COVID patients. Patients did not differ regarding their duration of ICU treatment or mechanical ventilation. However, total length of hospitalization (ICU + neurorehabilitation) was significantly higher in non-COVID patients. At discharge and 1 year after disease onset, health state between groups did not differ in any assessment ($p > .112$). Patients of both groups showed a limited health related quality of life and a substantial level of frailty. At follow-up, non-COVID patients had a significantly worse mental health in terms of anxiety ($p = .032$) and depression ($p = .012$) compared to discharge. Fatigue symptoms increased until follow-up in both the COVID ($p = .036$) and the non-COVID group ($p = .063$). Symptoms of

depression, fatigue and anxiety were similarly frequent in both groups (35.7%-57.1%) 1 year after disease onset.

Table 1 Clinical course and long-term outcome compared between COVID and non-COVID patients

	At discharge from neurorehabilitation				At follow-up (1 year after disease onset)			
	Non-COVID (n=17)	COVID (n=23)	p-value	Statistical value	Non-COVID (n=16)	COVID (n=20)	p-value	Statistical value
Gender, female	6 (35.3%)	6 (26.1%)	.530	X^2=.395				
Age [years]	68.6±10.2	62.9±11.9	.118	t=1.597				
Total hospital stay [d]	187.5±74.5	140.4±56.4	**.028**	t=2.280				
ICU length of stay [d]	72.2±38.7	64.5±32.8	.497	t=.685				
Mechanical ventilation [d]	34.4±26.5	45.0±31.1	.664	t=-.461				
ECMO								
N treated	2 (11.8%)	7 (30.4%)	.256	X^2=1.954				
Length [d]	5.5±6.4	41±19.7	**.047**	t=-2.411				
Health related quality of life	0.61±0.25	0.72±0.15	.149	t=-1.492	0.62±0.33	0.62±0.27	.887	t=-.220
Frailty	5 (5-6)	5 (4.5-6)	.542	U=149.5	5 (4-6)	5 (3-6)	.473	U=138.0
Anxiety	2 (1-8)	3.5 (1-7)	.400	U=138.0	7 (3-10)	7.5 (4-10)	.945	U=96.5
Depression	3 (2-6)	3 (1-5)	.755	U=155.0	6.5 (3.5-9)	4 (3-9.5)	.518	U=84.0
Fatigue	2.5±1.2	2.7±1.5	.669	t=-.431	4.0±2.1	3.9±1.9	.891	t=.138
Dyspnea	1 (1-2)	2 (1-4)	.112	U=32.5	0.5 (0-3)	2 (0-3)	.247	U=125.0

ICU: Intensive Care Unit; ECMO: Extracorporeal membrane oxygenation; Anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HADS). Health related quality of life was measured by the health index of the EQ-5D-5L. Frailty by the Clinical Frailty Scale, Fatigue by the Fatigue-Severity-Scale-7 and Dyspnea by the modified Medical Research Council dyspnea scale. Values are displayed as mean (±Standard deviation) or as median (quartile 1-quartile 3).

Conclusion: Although the length of the ICU treatment was comparable in COVID and non-COVID patients, COVID patients required less rehabilitation time. Patients of both groups were discharged with a similar but limited health state, which did rather deteriorate than improve until the follow-up 1 year after disease onset. At that time, patients frequently reported symptoms of fatigue, mental health issues, frailty and their health related quality of life was still limited compared to the health population of a similar age (0.92 ± 0.13).(4) This data underlines the urgent need of adapted therapies and supportive structures to improve long-term physical and mental health in ICU survivors.

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Acknowledgements: Else Kröner-Fresenius-Stiftung: 2020_EKEA-94.

000875

Characteristics and outcomes of 2223 adults admitted to critical care units: preliminary findings from the Kenya Critical Care Registry

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Intensive Care Medicine Experimental 2022, **10(2)**:000875

Introduction: Scarce information is available regarding the epidemiological, management and outcome characteristics of patients admitted to Kenyan critical care units [1].
Objectives: We aimed to leverage on the recently born Kenya Critical Care Registry to describe case-mix information, clinical management and outcomes of critically ill patients who received care in Kenyan intensive care units (ICUs) and high dependency units (HDUs).
Methods: This was a registry-based prospective observational study performed between January 2021 and October 2021 in 7 ICUs and 3 HDUs in six public and private hospitals in Kenya. Consecutive adult patients admitted to participating units were inserted in real-time on a cloud-based platform, based on a minimum dataset collected at admission, first 24 h of care and discharge. The registry quality control processes were detailed previously [2–4]. Study outcomes included demographic characteristics, acute physiology and chronic health evaluation (APACHE II) score, ventilation status, organ support, antibiotic exposure and tracheostomy rate; patient centred outcomes included ICU mortality, ICU length of stay and duration of mechanical ventilation. Patients in ICUs were compared to patients in HDUs.
Results: A total of 2223 adult patients were included in the Kenya critical care registry (**Table 1**). The ICU versus HDU model is well established in the country with six out of ten patients being registered from HDUs. One fifth of patients were admitted due to COVID-19, while 19% were surgical admissions. Overall readmission rate was 4.9%. ICU patients were younger but more severe when compared to HDU patients (APACHE II 22 [18–28] vs 19 [16–22]; $p < 0.01$). While hypertension and diabetes were the most frequent comorbidities, 2.7% of the patients had simultaneous HIV disease. 40% of ICU patients needed invasive mechanical ventilation, with a median duration of ventilation of less than 3 days. Invasive ventilation was rare in the HDUs, while non-invasive ventilation was used in both settings in roughly one in twenty patients. While there was an equal use of renal replacement therapy (RRT) across ICUs and HDUs, vasopressor support was infrequent. Half of patients admitted received one or more antibiotics on admission. Length of stay was higher in ICU, with crude ICU mortality being 34.7% versus 10.5% in HDUs. ICU mortality for the COVID-19 group of patients was 166/454 (36.6%).

	All patients (n=2223)	Patients in ICU (n=935)	Patients in HDU (n=1288)	P-value
Demographics				
Age, years mean (SD)	55 (18)	53 (18)	56 (18)	<0.01
Female, n(%)	869 (39.1)	324 (34.7)	545 (42.3)	<0.01
COVID-19 admissions, n(%)	504 (22.7)	362 (38.7)	142 (11.0)	<0.01
APACHE II score, median (IQR)[$]	20 (17-24)	22 (18-28)	19 (16-22)	<0.01
Surgical admissions, n(%)	424 (19.1)	186 (19.9)	238 (18.5)	
Emergency surgery, n(%)	259/424 (61.1)	119/186 (64.0)	140/238 (58.8)	0.280
Comorbidities, top 4, n(%)				
Hypertension	839 (37.74)	299 (32.0)	540 (41.9)	<0.010
Diabetes, unclassified	247 (11.11)	96 (10.27)	151 (6.6)	0.281
Type 2 diabetes	156 (7.02)	71 (7.59)	85 (5.6)	0.365
Type 1 diabetes	150 (6.8)	40 (4.3)	110 (8.5)	<0.01
Management				<0.01
HFNT, n(%)	10/2163 (0.5)	7/895 (0.8)	3/1268 (0.2)	
NIV, n(%)	100/2163 (4.6)	54/895 (6.0)	46/1268 (3.6)	
Invasive ventilation, n(%)	427/2163 (19.7)	355/895 (39.7)	72/1268 (6.7)	
Use of vasopressors, n(%)	103/2163 (4.76)	62/895 (6.9)	41/1268 (3.2)	<0.01
Renal replacement therapy, n(%)	93/2163 (4.30)	37/895 (4.1)	56/1268 (4.42)	0.419
Antimicrobial use, n(%)	1105/2163 (51.09)	629/895 (70.3)	476/1268 (37.5)	<0.01
Outcomes				
Death in ICU/HDU, n(%)	432/2105 (20.52)	303/873 (34.7)	129/1232 (10.5)	<0.01
Length of stay, days, median (IQR)	3 (1-7)	4 (1-10)	2 (1-5)	<0.01
Tracheostomy, n(%)*	35/542 (9.5)	32/425 (10.7)	19/117 (9.4)	-

Abbreviations: ICU, intensive care unit; HDU, high dependency unit; APACHE, acute physiology and chronic illness health evaluation; HFNT, high flow nasal therapy; NIV, non-invasive ventilation.
[$]data available on 1831 patients (713 in ICUs and 1118 in HDUs); *data available in 542 patients

Conclusion: These preliminary findings provide the first large multicenter mixed cohort of Kenyan critically ill patients admitted to ICUs and HDUs in both private and public hospitals participating in the Kenya Critical Care Registry.

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Acknowledgements: The Kenya Critical Care Registry is funded by a research grant from United Kingdom Research and Innovation (MR/V030884/1).

000906

Factors associated with mental health outcomes among health care workers in Chile during of COVID-19 pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000906

Introduction: The COVID-19 global pandemic has put a tremendous strain on healthcare systems and healthcare professionals (HCPs). In the pandemic, HCPs have been one of the most affected groups: have had to work long hours, multiple shifts, and under extreme stress. Studies have demonstrated that psychological distress during COVID-19 is prevalent, especially among HCPs (1). The persistence of these symptoms can affect the quality of life in the long term (2). Furthermore, psychological distress in HCPs can negatively impact the health of patients. Depression or anxiety in HCPs has been associated with increased medical errors (3). Understanding the association between risk factors and psychological distress may provide preliminary insights for future intervention development and evaluation areas that would stem the burden of psychological distress among HCPs during the COVID-19 pandemic and future pandemics.
Objectives: The study aimed to assess the mental health of healthcare professionals working with critical patients with COVID-19 and identify demographic and social determinants that may increase the risk of negative outcomes.
Methods: This is a preliminary report of the "Impact of an Early and Comprehensive Communication Strategy in the Prevention of Depressive Symptoms in Patients With Severe Covid-19, Their Families and Health Personnel study" (NCT05035563). HCPs complete a survey screening for anxiety and depression symptoms (Hospital Anxiety and Depression Scale—HADS), post-traumatic stress disorder (Event Impact Scale-Revised – EIS-R), and a sleep disorder (Pittsburgh Sleep Quality Index – PSQI). In addition, HCPs complete a socio-demographic questionnaire. The results are reported using mean ± standard deviation (SD) and percentages. The associations between risk factors and outcomes were presented as odds ratios (ORs) and 95% CIs, after adjustment for selected potential confounders. The study was approved by the ethics committee.
Results: A total of 303 HCWs were included in the current analysis. Participants were 69% female, 57% married/living with partner and 50,8% declared they had at least one child. Most of the participants were nurses (29,7%). Regarding your mental health, 36% have received some type of mental health care during this time, while 25,7% had a medical license for this reason. About the use of drugs to treat mental health symptoms, 32% of the respondents state that they are using pharmacological treatment. The prevalence of poor sleep quality was 80,6%. Overall, 29,5% of participants screened positive for elevated anxiety symptoms, 10,7% screened positive for elevated depressive symptoms, and 50,4% screened positive for likely post-traumatic stress disorder. Multivariable logistic regression analysis showed that age (odds ratio [OR]: 0.96; CI 0.94–0.99) and gender (OR, 0.55; CI 0.34–0.89) were associated with PTSD; in addition, years of work experience (OR, 0.96; CI 0.93–0,98) and ICU experience (OR, 0.95; CI 0.92–0.99) were associated with PTSD. Age (OR, and having some spiritual beliefs were associated with depression and anxiety symptoms. Poor sleep quality was associated with all investigated outcomes. Other work-related factors were not associated with the outcomes of interest.
Conclusion: In this preliminary report of mental health status among health care workers in hospitals in Chile, participants reported high rates of symptoms of posttraumatic stress, anxiety, depression, and poor sleep quality. The health care workers should be given more effective interventions to relieve their stress and improve mental symptoms.

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Acknowledgements: COVID-0921 PROJECT. Fondecyt 1201772

000958

Improving temperature management post-cardiac arrest in a District General Hospital Intensive Care Unit

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Intensive Care Medicine Experimental 2022, **10(2)**:000958

Introduction: NHS ambulances attend 30,000 out-of-hospital cardiac arrests (OOHCA) in the UK each year with a 9% survival rate. Return of spontaneous circulation (ROSC) is achieved in approximately 30% with the majority being unconscious and needing ICU admission, and with only 30–50% being discharged alive. Therapeutic hypothermia showed promising results in significant clinical trials and was the management of choice for many years but the recent Targetted Temeprature Management 2 (TTM2) trial concluded that there was no benefit to cooling patients to 36 °C following OOHCA if the arrest was due to cardiac/unknown cause.
Objectives: Patients post-ROSC currently should be maintained at 36 °C or below for the first 36 h post-ROSC followed by prevention of pyrexia (defined as > 37 °C in the local guidance) for the following 36 h. Regular temperature monitoring is essential to achieve this. Our aim was to compare current targeted temperature management at Torbay ICU with the hospital and national guidance. Outcomes measured included whether regular hourly temperature management was

recorded, adherance to 36 °C for 36 h, if pyrexia (defined as > 37 °C) was avoided through measures such as regular paracetamol and invasive cooling.
Methods: Looking at data from February 2020 to March 2022, our inclusion criteria included adults admitted with OOHCA of cardiac/unknown cause who were unconscious unable to follow verbal commands post-ROSC. We excluded patients with in-hospital arrests, hypothermia (< 30 °C) on presentation, low blood pressure despite adequate resuscitation, pregnant or presumed pregnant, severe COPD with long-term oxygen, and those with intracranial bleeds. Fourty patients fit our criteria, with one being excluded due to very early palliation within the hour.
Results: Results that were not entirely representative of our performance were also calculated and interpreted on the basis of a majority, defined as > 90% of the time. Our results showed that 20.5% of patients at Torbay ICU had a temperature of 36 °C or below in the first 36 h post-ROSC the majority of the time (with only actually 10.3% having all recorded temporatures below 36). Only 22.2% of patients who made it past the initial 36 h and required temperature control were adequately maintained at < 37 °C for the following 36 h. Hourly temperature monitoring were recorded more in the first 36 h period. These were done in 66.6% of patients the majority of the time (only 28.2% had all hourly readings) and it was noted that only 16.7% of all patients had all temperatures recorded throughout (with 77.8% having the majority of readings). 89.7% of patients had t > 36 °C for more than one hour; of these patients, 75% of them had t ≥ 37.8 °C for over 2 h. Only 20.5% of patients received invasive cooling and 38.5% received regular paracetamol.
Conclusion: Following TTM2, recent guidance from ERC/ESICM has confirmed that avoidance of pyrexia (defined as 37.8 °C and above) is the new aim post cardiac arrest. We propose to improve temperature monitoring in our patients by updating our local guidance in line with these changes. We aim to reduce pyrexia through regular paracetamol and earlier initiation of invasive cooling by monitoring temperature readings at least hourly. Patients who reach ≥ 37.8 °C for ≥ 2 h will be cooled with a target of 37.5 °C. Education for nursing staff and doctors will also be undertaken through clinical effectiveness meetings, journal clubs, MDTs and reminders through admission paperwork targets and daily handovers when these patients are present on the unit so that we can all work together to achieve better care for them.

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000973

Predicting mortality in sepsis and septic shock: a retrospective comparison of APACHE-II and SOFA, with an assessment of SOFA-defined organ failures contribution to mortality

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Intensive Care Medicine Experimental 2022, **10(2)**:000973

Introduction: Predictive scoring systems are measures of disease severity that are used to predict outcomes, typically mortality, of patients in the intensive care unit (ICU) (1). Sepsis has a high mortality rate (10% to 52%). One of the most widely used predictive scoring systems used to predict mortality in general ICU patients is the Acute Physiologic and Chronic Health Evaluation (APACHE) scoring system (2). In the case of septic shock, the Sequential (sepsis-related) Organ Failure Assessment (SOFA) score was designed to sequentially assess the severity of organ dysfunction in patients who were critically ill from sepsis (3).
Objectives: To determine the utility of APACHE-II and SOFA scores to predict mortality in sepsis and septic shock patients. To assess the relative contribution of each organ failure to mortality.
Methods: We conducted a retrospective, observational, single-centre study in the ICU of a University Hospital in Spain, over 2 years (2018–2019). We included all the patients who were admitted to the ICU with sepsis or septic shock. We recorded relevant clinical data, including APACHE-II and SOFA scores on ICU admission. Results are expressed as median (interquartile range) or frequency (%). We applied Chi-square, Mann–Whitney U test and ROC analysis, as appropriate. We built a logistic regression model to explore the association of mortality with each organ failure, as defined by SOFA Score (i.e. ≥ 3 points *vs* < 3 points).
Results: We included 191 patients, 53% men, aged 68 (59–76), APACHE-II 20 (16–25) points, SOFA on ICU admission 7 (4–9) points. ICU length of stay (LOS) 3 (2–7) days, hospital LOS 15 (8–30) days. ICU mortality 13.6%, without differences according to sex (male 16% *vs* female 11%, p = 0.30), age [survivors 68 (59–76) years *vs* non-survivors 70 (61–75) years, p = 0.81] or source of infection (respiratory 23%, urinary 6%, abdominal 15%, others 20%; p = 0.09). Sepsis origin was community-acquired in 60% of the patients, while the remaining 40% was hospital-acquired; ICU mortality was different between groups (10% *vs* 19%, p = 0.05). We found an association between the requirement of life support therapies and mortality: norepinephrine (OR 9.09, p < 0.01), mechanical ventilation (OR 11.53, p < 0.01), renal replacement therapy (OR 10.2, p < 0.1). APACHE-II score (survivors *vs* non-survivors): 19 (15–23) *vs* 31 (26–39) points, p < 0.01. AUC ROC 0.87 (95%CI 0.78–0.96) to predict ICU mortality. A cut-off point ≥ 25 has a sensitivity of 81% and a specificity of 83% to predict ICU mortality. SOFA score on admission (survivors *vs* non-survivors): 6 (4–8) *vs* 11 (10–13) points, p < 0.01. AUC ROC 0.86 (95%CI 0.78–0.94) to predict ICU mortality. A cut-off point ≥ 10 has a sensitivity of 81% and a specificity of 85% to predict ICU mortality. The association between each organ failure and mortality is analysed with a logistic regression model (Table 1).

SOFA Organ failure	OR	95%CI	p
Neurological	2.12	0.14–31.32	0.58
Renal	2.30	0.67–7.81	0.18
Hepatic	3.77	0.75–18.87	0.11
Haemostatic	8.02	2.01–32.07	**< 0.01**
Respiratory	21.20	6.65–67.60	**< 0.01**
Haemodynamic	1.21	0.33–4.48	0.77
cons	0.03	0.01–0.11	**< 0.01**

Conclusion: Both APACHE-II and SOFA scores are useful to predict mortality in septic and septic shock patients on ICU admission. In our series, respiratory and haemostatic failures on ICU admission are independent predictors of mortality.

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001014

Clinical features, management and outcome of COVID-19 patients in a Tunisian intensive care unit

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Introduction: The coronavirus disease 2019 (COVID-19) has spread from China to many other countries leading to a great threat to public health. Severe COVID-19 needs frequently intensive care management.
Objectives: The aim of this study was to report the clinical characteristics, laboratory findings, management and outcome of COVID 19 patients in a Tunisian intensive care unit (ICU).
Methods: It was a descriptive, prospective and monocenter study, including all confirmed COVID-19 patients hospitalized in intensive care between March 2020 and August 2021. We recorded data about demographic characteristics, clinical presentation, laboratory findings, ICU management and outcome.
Results: During the study period, 536 patients were included, with a mean age of 59 ± 14 years and a gender-ratio of 1.68. Among women, 12 were pregnant. Most frequent comorbidities were: arterial hypertension (38,8%), diabetes (36,6%) and obesity (39%). Acute respiratory distress syndrome (ARDS) was diagnosed on admission in 496 patients, it was severe (n = 192), moderate (n = 238) and mild (n = 66). High flow nasal therapy (HNFT) was conducted for 211 patients and non-invasive ventilation (NIV) was indicated for 448 patients. Endotracheal intubation was performed in 306 patients. The median duration of mechanical ventilation was 7 days [3–13]. Prone position was necessary in 274 patients with 79.4% of response. Inhaled nitric oxide (NO) was set up in 96 patients. Chloroquine was prescribed in 26 patients, low-dose corticosteroids in 484 patients, solumedrol boli in 79 patients and tocilizumab in 80 patients. The most frequent complications were respiratory worsening (n = 288), acute renal failure (n = 261), nosocomial infections (n = 245) and shock (n = 214). The median length of stay in ICU was 10 days [6–17]. The overall ICU mortality rate was of 54.7%. Independent predictive factors of ICU mortality were: advanced age (OR = 11.26; CI 95% [3.26–38.96]; p < 10–3), need of mechanical ventilation (OR = 660; CI 95% [128–3431]; p < 10–3), use of inhaled nitric oxide (OR = 5.42; CI 95% [1.41–20.82]; p = 0.014), occurrence of shock (OR = 4.24; CI 95% [1.76–11.39]; p = 0.004), and occurrence of metabolic complications (OR = 6.57; CI 95% [2.08–20.75]; p = 0.001).
Conclusion: COVID-19 in intensive care unit was common and associated to a high morbidity and mortality. Independent predictive factors of ICU mortality were advanced age, need of mechanical ventilation and inhaled NO and ICU complications such as shock and metabolic ones.

001025

Design and implementation of a resource-agnostic tele-ICU service to provide critical care expertise in remote regions of Asia and East Africa during the COVID-19 era

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Introduction: Till December 2021, there have been over 290 million confirmed cases of COVID-19 with over 5 million of these cases resulting in death.(1) There is a global deficit of critical care resources, particularly in lower-middle-income-countries with most of these resources concentrated in metropolitan cities leaving limited availability in districts and smaller towns.(2) These gross shortages have escalated during the COVID-19 pandemic, leaving patients in remote and resource-limited settings without access to skilled personnel.(3)
Objectives: To leverage existing technology to deliver free peer-to-peer consultations to healthcare workers in resource-limited regions for the diagnosis, management, and monitoring of COVID-19 patients.
Methods: This Tele-ICU service utilizes a Scheduled and Responsive Care Model delivered through a centralized and decentralized structure. Using existing two-way audio-visual technology, the Tele-ICU provides critical care expertise to clinical teams in rural and remote hospital settings across four lower-middle-income-countries in Asia and East Africa. End-to-end encrypted text-based applications or telephone calls are utilized. Initially, this service provided consultations exclusively for the management of COVID-19 patients; however, coverage was expanded to include other surgical, medical, and paediatric patients requiring intensive care.
Results: Between June 2020 and December 2021, 1011 patients have been managed during 4220 teleconsultations. These include 605 COVID-19 patients, of which 338 presented with severe and 131 presented with critical COVID-19 symptoms. An estimated 48,838 min of consultative services have been provided covering 52 medical facilities across Pakistan, East Africa, and Afghanistan. The mean call duration of each teleconsultation was 16.59 min. Outcome data was available for 405 (40.3%) of patients. Tele-ICU mortality was 34.3% (n = 139), with 37.5% (n = 152) of patients transferred safely home.
Conclusion: To combat the exiguous critical care capacity in remote and resource limited regions, Aga Khan University Hospital implemented a novel resource-agnostic Tele-ICU service. This provided an innovative solution for coordination of critical care and 24/7 availability of intensivists in remote settings across four countries in Asia and East Africa.

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Acknowledgements: This study was funded by the Bill and Melinda Gates Foundation.

001050

Protocol for management of pregnant women with severe covid-19

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Introduction: The impact of SARS-CoV-2 in pregnancy remains to be determined, and a concerted, global effort is required to determine the effects on implantation, fetal growth and development, labor, and neonatal health
Objectives: To describe the experience in the application of a multidisciplinary protocol for the management of distressed pregnant[sg1] women due to Covid-19 in a tertiary hospital in the Community of Madrid.
Methods: Prospective, observational study, performed in pregnant women who required ICU admission during August-September 2021 (5th Spanish pandemic wave). Treatment decisions were made according to a multidisciplinary protocol developed by obstetricians, neonatologists and intensivists. **Protocol**: Daily cardiotocographic record, operating room enabled 24 h and: 1) for women of 32 weeks gestation: elective Caesarean

section, 2) women of less than 28 weeks gestation: maintain pregnancy until week 32, prioritizing maternal well-being and performing urgent caesarean section if necessary, 3) women of 28–32 weeks gestation: assess the need for caesarean section based on the situation of the mother-child binomial, tending to elective caesarean section. Descriptive analysis: expressed as a means (standard deviation) for normally distributed quantitative variables, medians (interquartile range) for non-normally distributed variables, and as percentages for categorical data.
Results: Of the eighty-eight patients admitted to the ICU, 11.4% (10 patients) were pregnant. Age 33 (26–39) years, without comorbidities (I. Charlson 0), obesity (30%). **Severity at admission**: APACHE II 7 ± 1.4 and SOFA 3 ± 1.1. **Admission respiratory support**: NC 10%, HFNC 80%, IMV 10%. Finally, 60% (6 patients) required IMV lasting 4 days (0–16). Initial PO2/FiO2 80 (67–162), 83% (5 patients) required prone position ventilation, 1 session median (0–5). **Complications**: pneumothorax (10%), pneumonia associated with mechanical ventilation (10%) and bacteraemia (10%). Of the total, 90% (9 patients) completed pregnancy during their hospital stay: 11% prior to admission to the ICU, 67% at the ICU, and 22% after discharge from the ICU. Vaginal delivery 22% (2 patients), caesarean Sect. 88%. ICU stay 9 days (4–21), hospital stay 26 days (13–40). All pregnant women survived. **Neonatal outcomes**: Gestational age 30 ± 7 weeks, weight 1700 g (1075–2445), 89% of neonates required resuscitation: 22% type III resuscitation (Nasal CPAP/mask IPP) and 33% type IV (OTI ± CPR). Apgar at birth 6 (2–8). All neonates survived.
Conclusion: In our experience, the development and application of a multidisciplinary protocol for pregnant women with severe Covid-19 has had very positive results, without any deaths in either pregnant women or neonates

000917

Quality of life in survivors of severe COVID-19: comparing outcomes of two distinct strategies for the management of acute respiratory failure

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Intensive Care Medicine Experimental 2022, **10(2)**:000917

Introduction: Post-Intensive Care Syndrome is defined as the spectrum of physical, emotional and cognitive sequelae potentially derived after severe illness requiring Intensive Care Unit (ICU) admission [1]. Recent studies have stressed the importance of quality of life assessment in COVID-19 survivors [2]. The paramount of early Invasive Mechanical Ventilation (IMV) has shifted to initial trials of Non-Invasive Ventilatory Support (NIVS) in selected patients. Data is lacking regarding whether the type of ventilatory support impacts the quality of life with which survivors return to society.
Methods: Single-center retrospective study including adult survivors of ICU admission in a portuguese Intensive Care Medicine Department (ICMD) presenting with severe acute respiratory failure due to critical COVID-19 disease, from October 1st 2020 to 31st March, 2021. Patients were divided into two groups, according to the strategy of respiratory support within the first 24 h: 1) IMV; 2) NIRS with HFNC and/or conventional NIV combined with pharmacological management of respiratory overdrive. Patients with ICU lengh of stay (LOS) inferior to 24 h and those who required rescue with extracorporeal membrane oxygenation were excluded. Data regarding demographics, *Age-Adjusted Charlson Comorbidity Index* (aaCCI), length of IMV and NIVS, ICU and hospital LOS were collected by electronic process revision. Our ICMD has a follow-up clinic, from which electronic records data regarding quality of life (QoL) assessment were extracted. The EQ-5D-5L and EQ-VAS tools were used [4] in three appointments: 30–45 days, 6 months and 12 months after hospital discharge.
Results: 107 patients were included in the first quality of life assessment (3 lost to follow-up), with no significant differences regarding age, gender or aaCCI. Length of ventilatory support, ICU and hospital LOS were significantly lower in the NIRS group. Self-care, daily activities and pain and discomfort related problems were particularly noteworthy in the IMV group in the first evaluation. Moderate to severe impairments (score > 3) in all domains of quality of life were more frequent in the IMV group 6 and 12 months after hospital discharge, with self-care reaching statistical significance in the 6 months evaluation. Patients' self-perception of health status was satisfactory, with a median of 70 out of 100 points in the first evaluation, slightly higher 6 months after hospital discharge in the NIRS group.

	NIVS group	IMV group	*p* value
Number of patients, no. (%)	76 (69,1%)	34 (30,9%)	–
Evaluation 30–45 days after hospital discharge (n = 107)			
EQ-5D-5L, moderate to extreme problems			
Mobility, % (no.)	25.0 (18)	34.3 (11)	0.269
Self-care, % (no.)	13.3 (10)	28.1 (9)	0.067
Daily activities, % (no.)	32.0 (24)	56.3 (18)	0.019
Pain and discomfort, % (no.)	20.0 (15)	37.5 (12)	0.056
Depression and anxiety, % (no.)	29.3 (22)	34.4 (11)	0.605
EQ-VAS, (median; IQR), no. from 0 to 100	70; 20	70; 31	0.948
Evaluation 6 months after hospital discharge (n = 98)			
EQ-5D-5L, moderate to extreme problems			
Mobility, % (no.)	21.7 (15)	45.0 (9)	0.329
Self-care, % (no.)	2.9 (2)	13.8 (4)	0.040
Daily activities, % (no.)	17.4 (12)	31.0 (9)	0.133
Pain and discomfort, % (no.)	13.0 (9)	38.1 (8)	0.083
Depression and anxiety, % (no.)	24.6 (17)	31.8 (7)	0.958
EQ-VAS, (median; IQR), no. from 0 to 100	80; 25	80; 37	0.352

Conclusion: Critically ill COVID-19 patients who underwent non-invasive ventilatory support reported lower incidence of self-care, daily activities and pain and discomfort related problems up until 12 months after hospital discharge. This study highlights the importance of considering medium and long-term outcomes and quality of life outcomes in critical patients.

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000722

Are anxiety and the Burn-out syndrome the new pandemic within the ICU?

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Intensive Care Medicine Experimental 2022, **10(2)**:000722

Introduction: In the current period of global health crisis due to the COVID-19 pandemic, healthcare workers are more exposed to physical and mental exhaustion—burnout—due to making difficult decisions, the pain of losing patients and colleagues, and the risk of infection, for themselves and their families. This leads to raise awareness of those challenging working conditions and the need to address burnout by identifying possible solutions.
Objectives: The aim of the present study is to describe the incidence of burn-out syndrome and anxiety/depression within the ICU workers now that the admission of covid-19 patients has slowed down and compare it to a previous study in 2020; also, to inspect if the workers suffering from the syndrome are prone to search help or limit their work presence.
Methods: This is an observational, cross-sectional study. All of the health workers working in an adult Intensive Care Unit in a Regional

Hospital, were invited to participate through an anonymous online questionnaire, after the first 6 months of slowing the rate of admission of Covid-19 patients. Two validated tests have been used: Maslach Burnout Inventory—MBI for the burn-out syndrome diagnostic and the Hospital Anxiety and Depression Scale—HADS for the screening of anxiety and depression, as well as asked for demographic data. Statistical analysis with SPSS v22.

Results: A total of 175 workers were invited to participate obtaining a feed-back response of the 38.8% (68) after two weeks in March and April 2022. Of the participants, the 54.4% (37) were Nurses, 27.9% (19) Care Assistants, 13.2% (9) Attending physicians and 2.9% (2) of Resident physicians. Of all of them the 72.1% (49) were women with a mean age of 43.5 ± 10.4 years and the 27.9% (19) were men with mean age of 45.8 ± 7.6 years. Out of all the participants, 32.4% (22) present all the criteria to diagnose them of the burn-out syndrome, a percentage that has increased given that in 2020 it was 24.1%. Furthermore, the 47.1% (32) present at least 2 of the 3 defining criteria, thus being assigned as "potential cases", number that has decreased (previously the 53%). When asked if the workers willingly reduced work hours, the 7.4% (13) chose to do so, and even 2 of them preferred to retire from the profession; in this subgroup the 90.9% (11) presented Burn-out syndrome; the reasons behind this decision were mostly to enjoy more free time (7) and because of the pandemic (4). Regarding the HADS scale, 58.8% (40) of the participants were diagnosed with anxiety, finding that yet again the number has increased (previously, 48.3%). In the depression scale, we have detected 7 cases (10.3%) and 16 possible cases (9.1%). Of the participants, 36.8% (25) have developed a new habit as an escape route such as: more exercise 19.1% (13), start smoking 5.9% (4), avoiding social gatherings 5.9% (4), new hobbies 5.9% (4) and even doing drugs 1.5% (1). It's worth noting that 19.1% (13) of the participants have asked for help and are receiving psychological counsel. Most of the workers diagnosed with the syndrome have not asked for help, 72.7% (16), but all of them when asked if they would receive it as a program formed within the ICU, answered that they would happily attend the sessions.

Conclusion:

- - In our series, we have found that the percentage of burn-out cases has increased from 2020 to 2022 but also the cases of anxiety, while the depression rate kept steady.
- - While most of the participants did not cut working hours, there's some of them who have preferred to work less due to the pandemic, being a group in which the burn out syndrome is heavily represented.
- - This questionnaire shows the arising need of forming mental health programs within the ICU to promote a healthy work space.

000893

A comparison of mortality prediction scales accuracy in a single-center ICU during 4th Coronavirus wave

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Intensive Care Medicine Experimental 2022, **10(2)**:000893

Introduction: The World Health Organization (WHO) on March 11, 2020, has declared the novel coronavirus (COVID-19) outbreak a global pandemic [1]. Since then, health care system was under pressure and Intensive Care Units (ICU) were overwhelmed by huge influx of patients. Disease severity scoring systems were used to help predict patients' death at the time on admission to ICU.

Objectives: The aim of this study was to compare three disease severity scoring systems and estimate which one is the most accurate for predicting mortality in ICU patients with COVID-19 disease.

Methods: We retrospectively evaluated 167 patients, who were admitted to tertiary hospital ICU from 2021 September to 2022 January (4th COVID-19 wave in Lithuania). Patients' inclusion criteria were age 18 or older and tested positive for SARS-CoV-2 infection, patients who stayed in the ICU less than 24 h were excluded from the study. The Simplified Acute Physiology Score (SAPS) II, Acute Physiology and Chronic Health Evaluation (APACHE) II and 4C ISARIC (4 ISARIC) Mortality Score was calculated upon admission to the Intensive Care Unit. Data was processed by SPSS 26.0 software. The receiver operating characteristic area under the curves (ROC-AUCs) were used to measure the accuracy of disease severity scoring systems.

Results: Study cohort included 94 (56.3%) males, age was 60 ± 16 years [range 19–91]. Upon admission to ICU 51 (30.5%) patients were vaccinated. Length of stay in ICU was 5 days [1–50], total length of stay in hospital was 11 days. [1–111]. 106 (63.5%) patients required mechanical ventilation support and 73 (43.7%) patients were treated with renal replacement therapy. All-cause mortality was 54.5%. Median SAPS II, APACHE II, and ISARIC 4C scores on the day of admission were 30.5, 13, 11, respectively. SAPS II AUC value of 0.744 (95% CI 0.669–0.819; $p < 0.001$). APACHE II AUC value of 0.784 (95% CI 0.715–0.853; $p < 0.001$). ISARIC 4C value of 0.690 (95% CI 0.610–0.77; $p < 0.001$).

Conclusion: In our study the APACHE II score had the highest accuracy of predicting mortality on first day on admission to the ICU subpopulation with COVID-19 disease during 4th wave of Covid-19 pandemic.

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Acknowledgements: The authors received no financial support for the research, authorship and publication of this abstract.

000932

Routine vs. on-demand blood sampling in critically ill patients—a scoping review

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Introduction: Blood testing is common in intensive care units (ICUs). The Choosing Wisely initiative for critical care settings states that diagnostic testing should be based on clinical indication rather than routine intervals. (1) As much as 50% of blood work may be redundant. (2) Excessive blood sampling without clinical indication may distort clinical decision making, and may result in increased patient morbidity and wasted resources. (3–5)

Objectives: We aimed to describe the current body of evidence regarding routine vs. on-demand blood sampling practices in critical care settings.

Methods: This scoping review was conducted according to the PRISMA-ScR guidelines. (6) The protocol was pre-published. (7) We used a PICO-based approach to define eligibility criteria and systematically searched EMBASE, Medline, and Cochrane Library for relevant literature. Two authors independently screened titles and abstracts and extracted data from the selected papers. Multiple reports on the same study were collated. If necessary, authors were contacted for additional data. We assessed the overall certainty of evidence for all clinical outcomes according to the GRADE approach. (8)

Results: We identified 12,270 unique References and included 76 papers and abstracts representing 22 observational and 50 interventional studies. Most studies were conducted in ICU settings, including in trauma settings, and high dependency units. The included studies were published between 1985 and 2022 and conducted in five continents. We found that patients in medical ICUs were more frequently subjected to blood testing compared to those in mixed ICUs and surgical ICUs. Patients in paediatric ICUs were less frequently subjected to blood testing. Furthermore, teaching hospital status, presence of an arterial line, mechanical ventilation, and male gender were associated with more frequent blood testing. Multiple studies reported on blood loss due to

routine phlebotomies. Two studies reported a reduction in transfusion rates associated with less blood testing. No studies reported on the association between routine blood sampling and changes in mortality, length of stay, or patient-important outcomes. Adjusted for inflation the estimated annual savings associated with an intervention to reduce unnecessary routine blood sampling in ICU settings ranged from €587 to €58,459 per ICU bed. (9, 10)

Conclusion: In this scoping review of routine versus on-demand blood sampling in critically ill patients, we found that most studies found that a substantial reduction in blood testing and associated costs had no detrimental effects on patient-related outcomes (low certainty of evidence).

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Acknowledgements: This research project has not received any funding. C.J.S.H. has received salary funding from the Research Council of Rigshospitalet and Novo Nordisk Fonden.

001002

Impact of ambient air pollution on incidence of out-of-hospital cardiac arrest is observable even in a small urban/rural population

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Intensive Care Medicine Experimental 2022, **10(2)**:001002

Introduction: A number of studies have shown an increase in incidence of out-of-hospital cardiac arrest corresponding to increasing concentrations of ambient air pollutants. These studies have mostly been performed in large, densely populated urban centres. There is very little data on impact of ambient air pollutants in smaller urban/rural areas.

Objectives: The objective of our study was to assess the impact of ambient air pollution on incidence of out-of-hospital cardiac arrest in a small central European city and corresponding area.

Methods: We performed a retrospective observational study in patients who suffered out-of-hospital cardiac arrest from 2018–2019 in an area with 125.000 inhabitants (of those 60.000 living in an urban area, others in rural/urban settings) over 820 km2 (average population density 152/km^2). We used concentration of PM10 particles (particulate matter 10 µm) as a measure of ambient air pollution.

Results: The incidence of cardiac arrest in our patient population was 63/100.000 inhabitants/year. In all, 157 patients suffered out-of-hospital cardiac arrest, 144 (92%) died or survived to hospital discharge with unfavourable neurological outcome, and 13 (8%) survived to hospital discharge with good neurological outcome. We observed significantly higher concentration of PM10 particles on days when out-of-hospital cardiac arrests occurred (34 ± 26.5 µg/m^3 vs. 19.2 ± 16.5 µg/m^3, $p < 0.0001$). Return-of-spontaneous circulation or survival to hospital discharge with good neurological outcome were not associated with different concetrations of PM10 particles (34 ± 18.2 µg/m^3 vs. 35.9 ± 13.9 µg/m^3, $p = 0.69$ and 34.2 ± 18.2 µg/m^3 vs. 35.9 ± 13.9 µg/m^3, $p = 0.82$).

Conclusion: To conclude, firstly, ambient air pollution is affecting the incidence of out-of-hospital cardiac arrest in way that is detectable even in a small urban/rural population with low population density. In future, environmental issues such as ambient air pollution will need to be addressed vigorously as a modifiable factor in order to decrease mortality attributed to out-of-hospital cardiac arrest. Second, local (and, if possible, continuous) data collection of out-of-hospital cardiac arrest parameters is paramount in order to clearly present a catastrophic loss of lives and measure improvement efforts.

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001033

healthy working environment for critical care nurses: the experience of a blended training solution—lessons learned from a focus group analysis

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Intensive Care Medicine Experimental 2022, **10(2)**:001033

Introduction: There is a positive correlation between healthy work environments (HWE) and nurse job satisfaction, retention, and patient outcomes. The uptake of such initiatives in Europe remains limited. Through an Erasmus + project, a training course about HWE was created. It included 48 h of training using the standards from the American Association of Critical-Care Nurses. It was tested in Poland, Croatia, Cyprus and Spain. Despite the course was planned to be face-to-face, Covid-19 forced to conduct some lessons on-line.

Objectives: To analyse the experience of trainees and trainers who took part in the pilot course to identify strengths and weaknesses of the course.
Methods: 9 online focus groups were conducted from January to April 2021. All participants, who attended at least one module of the training and were working as critical care nurses (CCN), were invited to participate voluntarily. 8 focus groups were held with trainees (n = 40) (2/country) and 1 with trainers (n = 4). 4 more trainers from Cyprus (n = 1) and Poland (n = 3), completed the questions via an online questionnaire. The mean duration of the focus groups was 60 min and were video-recorded and used a semi-structured interview guide. Questions addressed to trainees were grouped in 4 categories: a.Evaluation of the training course, b.Challenges and suggestions for training improvement, c.Suggestions and opinions for implementing such a training course in the educational curricula for CCN, and d.Transferability potential. Questions addressed at trainers included also an additional category: Identification of best practices. Focus groups were transcribed verbatim and the national ones translated into English. A thematic analysis was performed.
Results: Trainees considered that the course was useful, highly applicable and helped them to become aware of different situations they encounter. They enjoyed the combination of theoretical aspects, examples and practical exercises. They considered positively the provision of scientific evidence to support statements. They highlighted that the inclusion of this kind of training would be positive for the curricula and the team as it is necessary to improve working environments, however they pointed out the need to include managers and other healthcare professionals. Trainers coincided with the perceptions from trainees. Moreover, they felt that the training course was well developed having great detail which helped the conduction of the lessons. They considered that this course could be transferred to other areas of healthcare not just ICU.
Conclusion: Trainees and trainers were highly satisfied with the training course highlighting the type of activities performed and the transferability to clinical practice. The proposed blended training, developed within the Erasmus project will serve as an educational intervation to improve HWE.

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Acknowledgements: This study was a joint effort of the consortium of the Erasmus + project entitled: 'Improving Working Environments for Critical Care Nurses -HWE4CCN. (Erasmus + KA2 ref. number 2019-1-CY01-KA202-058401).

001059

The impact of organizational culture and moral distress on burnout during the COVID-19 pandemic: a multicenter cross-sectional survey study

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Introduction: The COVID-19 pandemic has increased burnout symptoms in intensive care unit (ICU) professionals [1–3].
Objectives: Pre-COVID-19, organizational culture and moral distress were associated with burnout symptoms in ICU professionals.[1] We explore whether these associations can be validated in the context of the enduring COVID-19 pandemic.
Methods: A survey was sent to ICU professionals in eleven Dutch hospitals between September and November 2021. The Utrecht Burnout Inventory was used to measure burnout symptoms. The burnout cut-off score by Azoulay et al. was used to classify professionals as either burnt out or not [3]. Team climate and organizational culture were measured using the Safety Attitude Questionnaire and Culture of Care Barometer respectively. Morally distress was measured using the moral distress scale. The intraclass correlation (ICC), the degree to which the outcome (burnout) is clustered within hospitals, was 0.02 and statistically significant (p = 0.02). A multilevel logistic analysis did not statistically improve on a normal multivariable logistic analysis. Therefore, we carried out a normal multivariable logistic regression analysis to assess the association between moral distress, team climate and organizational culture versus burnout. We adjusted for confounding variables, including personality, work-home balance and profession. A forward selection procedure was used to build the most statistically significant model.
Results: 696 of 1752 ICU professionals returned the survey (response rate: 39.7%). Overall, 37.1% of the ICU professionals experienced burnout symptoms. Burnout symptom prevalence ranged from 20.7% to 51.2% between hospitals. In the multivariable model, we identified four variables that are associated with a significantly lower risk of burnout: a supportive organization (OR .57, p = .01), a pleasant relational atmosphere among colleagues at work (OR .49, $p = .03$), an agreeable personality (OR .30, $p = .00$) and extraversion (OR .55, $p = .00$). Three variables were associated with a significantly higher risk of burnout symptoms: provision of futile treatment (OR 1.34, $p = .00$), negative work-to-home spillover (OR 6.24, p = .00) and neurotic personality (OR 2.08, $p = .00$) (Table 1).
Conclusion: Organizational culture and moral distress are associated with burnout symptoms during COVID-19. Differences in organizational culture contribute to wide variation in burnout symptom prevalence rates across hospitals. To mitigate symptoms of burnout, organizations need to support and explicitly appreciate ICU professionals, as well as facilitate and stimulate a good relational atmosphere among colleagues. Moreover, perception of provision of futile treatment among ICU professionals may be addressed by multidisciplinary moral case deliberation about patients' prognostics. Lastly, hospitals are wise to mitigate negative work-home spillovers, for instance, by debriefing ICU professionals after each shift.

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Acknowledgements: The research was supported by ZonMw, Project Number 516012513.

001086

Is severity of disease a good predictor of functional capacity after discharge?

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Intensive Care Medicine Experimental 2022, **10(2)**:001086

Introduction: Traditionally, the assessment of critical care was focused on mortality. During recent years, the increased post ICU survival, has led to a shift of the interest in the long term sequels of critical illness. However, the information about post-intensive care syndrome (PICS) is still very scarce. Regarding the function component, there isn´t any established measure or time point for follow-up. However it has been accessed that multi organ failure and severity of the disease are associated with poor prognosis.
Objectives: To study the association between the severity of disease and the functional outcome six months after hospital discharge.
Methods: This is a single center, prospective study that was conducted in patients aged $\geq$ 18 years and admitted for more than 5 days in the Intensive Care Units (ICU) of Centro Hospitalar e Universitário de São João, a tertiary hospital. A total of thirty three patients were consecutively selected. To access disease severity, APACHE II score was used at ICU admission, then it was correlated with different functional variables at 6 months after discharge from hospital. Functional variables included questionnaires such as SF-36 physical functioning, Barthel Index, International Physical Activity Questionnaire (IPAQ) and physical tests such as 6 min walking test (6MWT), handgrip strength, 1 min sit-to-stand (1MSTS), Timed Up and Go (TUG) test and Short Physical Performance Battery (SPPB). Correlations were estimated using Spearman correlation. A p-value inferior to 0.05 was considered statistically significant. Bonferroni correction was applied to control for multiple comparisons. R2 was also calculated in order to understand how much of the functional capacity variation between patients was explained by disease severity (APACHE II score). Statistical analysis was performed in IBM SPSS Statistics 28 (IBM, Armonk, NY).
Results: The median APACHE II score was 19 (percentile 25;75: 10.0;26.5). All variables except handgrip strength ($r = -0.48$, $p = 0.01$) showed a non-statistically significant correlation between severity of disease at ICU admission and functional capacity at 6 months after discharge, with spearman correlation between -0.174 and 0.102. Moreover, even handgrip strength did not survive to Bonferroni correction, with results becoming non-significant. R2 values of the correlation between APACHE II score and functional variables were between 0.003 and 0.030 (except for handgrip strength—0.228).
Conclusion: Unlike what was expected, correlation was poor between disease severity and functional capacity 6 months after hospital discharge. Only 0.3% to 3.0% of the functional variables variation (except handgrip strength) was explained by APACHE II. Clinical gravity at ICU admission seems to be a very poor predictor of functional capacity. This emphasizes that even patients with severe disease may have a good quality of life, without any major limitations in activities of daily living.

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Acknowledgements: The authors thank the department of Physical Medicine and Rehabilitation of São João University Hospital Center for the time, expertise and materials provided.

001104

Optimising multidisciplinary team input into admission clerkings and subsequent workflows on an ITU informatics system: a survey of the end users of admission documentation

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Intensive Care Medicine Experimental 2022, **10(2)**:001104

Introduction:

- The admission clerking is the foundational document in any patient's journey through the ITU. The information contained, historically collated by doctors and arranged under the traditional medical headings (presenting complaint, PMHx etc.), inform subsequent investigations and management plans for the entire team (1).
- As a multidisciplinary team with a variety of complementary roles, the relative importance of information categories varies in their professional management plans.
- Clinical informatics systems enable the automated pull through and population of information between documents. This can enhance efficiency and accuracy of information collation and transfer.

Objectives:

- To investigate if the needs of nurses and allied healthcare professionals are met by current medically authored admission clerkings on the critical care informatics system.
- We hope to use this knowledge to develop and improve the transfer of information and workflow within a fully digital healthcare system.

Methods:

- The work force on the unit on a given day is c. 5 doctors, 16 nurses and 7 AHPs.
- We conducted 22 guided surveys to doctors (6), nurses (10) and AHPs (6) in a teaching hospital ITU aiming to represent a typical shift.

Results:

- Nursing staff were heavier users of the document than other groups—reviewing daily as part of their handover process.
- Nurses and AHPs tended to value clarity, efficiency and accuracy in documentation. Surveyed doctors preferred thoroughness and completeness.
- Nursing staff were less likely to approve of direct copy and pasting from previous external documentation(5/10). Universally

medical staff AHPS thought it acceptable with caveats i.e. "If clearly cut & paste e.g. scan is reported as "…", or surgeons have stated "…" (A consultant intensivist).
- AHPs wanted more information pertaining to their subspecialty i.e. swallowing / communication baselines.

Conclusion:

- The MDT use this document for a variety of reasons at different times, during a patients journey through the ITU.
- Different professional groups need for overlapping information at separate points during an ITU admission. This could be enhanced by the effective set up of an informatics system that can anticipate their needs.
- Medical, AHP and nursing documentation requirements are not mutually exclusive. ITU residents should be cognisant of their audiences needs when admitting patients.
- There is scope locally for a multi-author / MDT clerking on our digital platform which could improve transfer of information and optimize workflow
- Given their high frequency usage (greater than daily), access of pertinent admission information could be automatically populated into a bespoke bedside nursing handover tool.
- Attention needs to be paid to the accuracy of information input – concerns were raised about the use of copy and paste and the pull through of information that was inaccurate or incomplete. This highlights the tension between efficiency and accuracy if incorrectly utilised.

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Acknowledgements: Not applicable.

001136

The quantitative effects of music on the physiology and experiences of intensive care patients: a feasibility study

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Intensive Care Medicine Experimental 2022, **10(2)**:001136

Introduction: Using music as an intervention is being explored in an increasing number of studies due to its anxiolytic effects and stimulation of multiple brain regions. Research has shown that music could potentially have analgesic effects through autonomic modulation of physiological parameters [1, 2]. Therefore, musical interventions may benefit critically ill patients, particularly those in pain or distress.
Objectives: This feasibility study aimed to evaluate the effect of listening to music on objective and subjective measures of anxiety and pain in Adult Intensive Care Unit (AICU) patients and explore the relationship between musical characteristics and physiological response.
Methods: After obtaining ethical approval, 15 patients with Richmond Agitation Sedation Scale (RASS) score ≥ -2 were recruited from Chelsea and Westminster Hospital AICU in London, UK. The intervention consisted of up to 40 min of music listening, with 10 min of undisturbed rest pre- and post-intervention. Music was chosen by the patient, or when required by their next of kin or from pre-made playlists by the researchers. Heart rate (HR), blood pressure (BP) and respiratory rate (RR) were recorded throughout the session. Alongside anxiety and pain, these were the primary outcome measures. Pain and anxiety were measured at baseline and after the intervention, using the Oral Numeric Rating Scale (NRS-O) or Critical-Care Pain Observation Tool (CPOT), and the Verbal Anxiety Rating (VAR) respectively. The musical characteristics of each song was recorded by the Application Programming Interface (API) of Spotify.
Results: Following the music intervention there was a significant reduction in patient anxiety, with median VAR decreasing from 4.5 to 0 ($p < 0.05$). However, there was no significant change in pain, evaluated with NRS-O and CPOT, or sedation depth, measured by RASS, after the intervention ($p > 0.05$). Similarly, there was no significant difference in median HR, RR, and DBP before, during or after the intervention ($p > 0.05$). Median SBP increased significantly from 109 pre-intervention to 113 mmHg during the intervention ($p < 0.05$). No significant difference was seen in median SBP pre- and post-intervention, or during and after the session ($p > 0.05$). Spectrograms were used for preliminary analysis of variation in physiological response and music over time, with patients' physiological parameters plotted against the pitch of music played.

Measurement	Pre-Intervention Score	Pre-Intervention Score	Difference	*p*-value
VAR	4.5 (0.25 – 8)	0 (0 – 2.5)	4.5	0.027 *
NRS-O	2 (0 – 4.5)	0 (0 – 4.5)	2	0.098
CPOT	1.5 (0.75 – 1.5)	0 (0 – 0)	1.5	0.18
RASS	0 (0 – 0)	0 (0 – 0)	0	1

Table 1 - Comparison of median anxiety, pain and sedation scores pre- and post-intervention was performed and analysed in 14 patients using SPSS.
Pre-test and post-test data is presented as median (LQ – UQ).
VAR (n = 12). NRS-O (n = 12). CPOT (n = 2). RASS (n = 14).
The Wilcoxon Signed-Rank Test was used to identify significant differences in pre- and post-intervention scores ($p \leq 0.05$), with significance denoted by *.

Physiological Parameter	Pre-Intervention	Music Intervention	Post-Intervention	Friedman (χ^2)	*p*-value
SBP / mmHg	109 (102 – 122)*	113 (108 – 124)*	110 (100 – 127)	6	0.05 †
DBP / mmHg	57 (49 – 65)	55 (50 – 71)	58 (50 – 73)	0.429	0.807
HR / bpm	90 (78 – 90)	91 (72 – 98)	92 (74 – 99)	0.383	0.826
RR / breaths per minute	18 (14 – 21)	17 (14 – 22)	20 (16 – 23)	2.596	0.273

Table 2 - Comparison of median SBP, DBP, HR and RR pre-intervention, during the intervention and post-intervention was performed and analysed in 12 patients using SPSS.
Data is presented as median (LQ – UQ).
The Friedman Test was used to determine if differences in median physiological parameter were statistically significant ($p \leq 0.05$) as denoted by †.
The Wilcoxon Signed-Rank Test was used to identify which time periods were significantly different ($p \leq 0.05$). $p \leq 0.05$ for pre-intervention and intervention data denoted by *, $p \leq 0.05$ for intervention and post-intervention data denoted by **, $p \leq 0.05$ for pre- and post-intervention data denoted by ***.

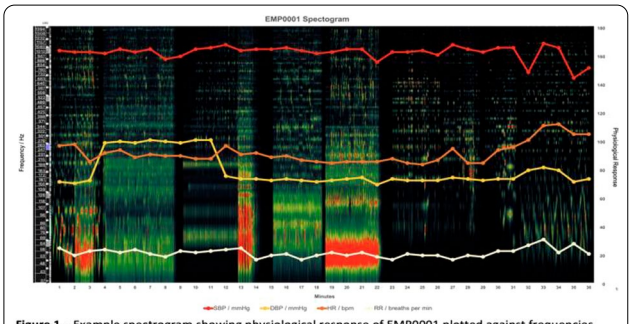

Figure 1 – Example spectrogram showing physiological response of EMP0001 plotted against frequencies (pitch) of the music played.
Pitch, or sound wave frequency, plotted on left y axis.
Physiological response plotted on right y axis.
Red indicates the loudest pitch, with green representing the quietest pitches.

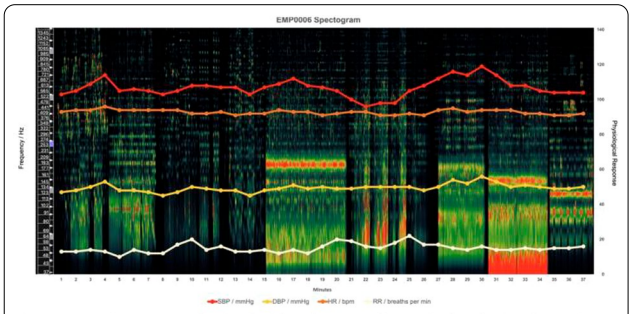

Figure 2 – Example spectrogram showing physiological response of EMP0006 plotted against frequencies (pitch) of the music played.
Pitch, or sound wave frequency, plotted on left y axis.
Physiological response plotted on right y axis.
Red indicates the loudest pitch, with green representing the quietest pitches.

Conclusion: Initial findings suggest that music can significantly reduce anxiety but does not affect pain. The results also seem to suggest that music significantly affects SBP, although DBP, HR and RR were unaffected. The novel findings of this study, which used previously unexplored parameters, demonstrated the feasibility and necessity of further, large-scale investigation. Other outcomes that will be analysed in the future to evaluate the relationship between physiological response and music characteristics include key, mode, tempo and energy.

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Acknowledgements: This project has been funded by CW+, the charity for Chelsea and Westminster Hospital NHS Foundation Trust.

001182

Comparison of GCS recordings for ICU patients by doctors and nurses

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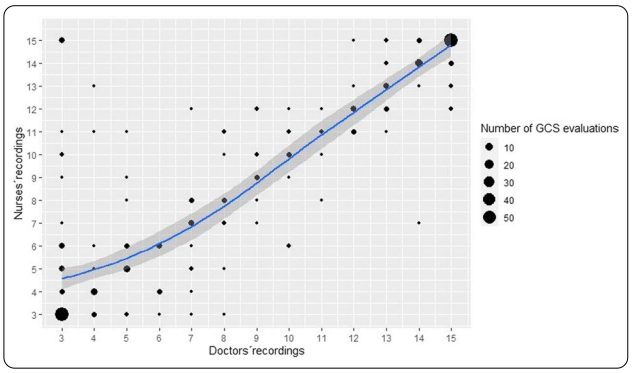
Intensive Care Medicine Experimental 2022, **10(2)**:001182

Introduction: The Glasgow Coma Scale (GCS) is a practical tool to describe a patient's level of consciousness. Impaired consciousness because of an illness or trauma heavily affects prognosis. Furthermore, the GCS is an essential component in severity-of-illness scores, such as the Simplified Acute Physiology Score (SAPS) II or the Sequential Organ Failure Assessment (SOFA). The documentation of GCS should be precise and reliable.
Objectives: The objective of this study was to investigate whether GCS is systematically documented in the medical records by Finnish intensive care doctors and if that documentation is consistent with the GCS documentation by nurses in the intensive care unit (ICU) database.
Methods: Our study population was made of 1379 adult patients treated for medical or emergency surgical reasons in the ICU in Kuopio University Hospital, Finland, in 2019. We evaluated whether the level of consciousness was documented in the written medical records by an ICU physician during the admission day, and whether the description was consistent with the GCS registered by nurses in the ICU database. We defined precise documentation as the exact GCS score or a verbal description that enabled deduction of the GCS.
Results: The level of consciousness at admission to the ICU was precisely documented by an intensivist in the medical records for 272 (19.7%) patients. For 677 (49.1%) patients there was a narrative description of the level of consciousness in the medical record, but the precise GCS was not recorded and could not be deduced. For 430 (31.2%) patients, level of consciousness was not described at all. The level of consciousness was described more precisely when the admission diagnosis implied lower GCS. The precise GCS was recorded in 48.7% of the medical records for patients with intracerebral hemorrhage, in 47.9% for intoxication, and in 44.7% for cardiac arrest, $p < 0.001$ in comparison with other admission diagnoses. GCS was recorded by nurses in the ICU database for all patients. For patients with a precise documentation of GCS in the medical records, it matched exactly the GCS recorded by nurses in the ICU database in 61.8% of cases. Doctors' GCS recordings and the corresponding nurses' recordings are presented in Figure 1.



Conclusion: The level of consciousness is insufficiently documented in the medical records by Finnish ICU physicians, and the recordings are often inconsistent with nurses' recordings.

Health Services Research & Outcome 12

000837

Long-term clinical outcomes in COVID-19 ICU survivors compared to non-COVID-19 ICU survivors: A prospective cohort study

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Introduction: A better understanding of the differences in long-term outcomes between COVID-19 and non-COVID-19 Intensive Care Unit (ICU) survivors is needed for tailored intensive care treatment and post ICU treatment to specific needs and problems.
Objectives: To determine the differences in prevalence of physical, mental or cognitive impairments and Quality of Life (QoL) between COVID-19 and non-COVID-19 ICU survivors.
Methods: A prospective, multicenter, cohort study was conducted. ICU survivors completed validated questionnaires concerning their health before and one year after ICU admission. Occurrence rates of physical (frailty, fatigue, physical symptoms), mental (anxiety, depression, post-traumatic stress disorder) and cognitive impairments and Quality of Life (QoL) in COVID-19 ICU survivors, admitted between March, 1st and July, 1st 2020, were compared to a matched cohort of ICU survivors, admitted between July, 11th 2016 and December, 31st 2019, with similar causes of respiratory distress, including ARDS, pneumonia or pulmonary sepsis.
Results: Of the 302 included COVID-19 ICU survivors, 246 (81.5%) completed the one-year follow-up, and were meticulously matched with 154 non-COVID-19 ICU survivors. One year after ICU treatment,

COVID-19 ICU survivors experienced significantly less physical (74.3% vs. 86.2%, $p < 0.01$) and mental (26.2% vs.45.5%, $p < 0.001$) symptoms, whereas cognitive symptoms did not significantly differ (16.2% vs. 15.6%, $p = 0.80$). However, COVID-19 ICU survivors experienced a decline in QoL between pre-ICU and one year after treatment, while the comparator group reported no change in QoL (SF-12; change in physical component score: −4.6 vs. 0.3; $p < 0.001$, change in mental component score: −2.4 vs. 0.4; $p = 0.03$).

	Baseline		1-year outcomes		
	COVID-19 ICU cohort	Comparator ICU cohort†	COVID-19 ICU cohort	Comparator ICU cohort†	P-value*
Physical domain—no. (%)					
≥ 1 physical symptom	155 (63.0)	83 (86.4)	182 (74.3)	131 (86.2)	< 0.01
Frail	50 (20.4)	42 (27.5)	15 (6.1)	30 (19.6)	0.001
Fatigue	144 (58.5)	128 (83.1)	138 (56.1)	114 (74.5)	0.001
New physical problem(s)	NA	NA	165 (67.1)	115 (74.7)	0.11
Mental domain—no. (%)					
≥ 1 mental symptom	52 (21.1)	61 (39.4)	64 (26.2)	70 (45.5)	< 0.001
Anxiety	30 (12.2)	46 (29.9)	44 (17.9)	46 (29.9)	0.04
Depression	38 (15.4)	48 (31.2)	45 (18.3)	54 (35.1)	0.008
PTSD	NA	NA	24 (9.8)	20 (13.0)	0.15
Cognitive domain—no. (%)	17 (7.1)	8 (6.3)	39 (16.2)	22 (15.6)	0.80
Quality of life, SF-12					
Physical component scale, mean (SD)	50.5 (7.8)	40.3 (11.5)	45.9 (9.8)	40.6 (10.9)	< 0.001
Mental component scale, mean (SD)	52.8 (10.0)	44.0 (12.4)	50.4 (10.3)	44.4 (12.2)	< 0.001

*1-year outcomes COVID-19 vs. Comparator cohort

Conclusion: COVID-19 ICU survivors experienced equal or less physical, mental and/or cognitive symptoms one year after ICU admission compared to non-COVID-19 ICU survivors with similar disease characteristics. However, these impairments seem to have a greater impact on QoL in COVID-19 ICU survivors compared to the comparator group.

000964

Association between histological diaphragm atrophy and ultrasound diaphragm thickness in ventilated patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000964

Introduction: In recent years, ultrasound has become a useful tool in intensive care to evaluate diaphragm anatomy. Ultrasound diaphragm thickness (Tdi) has been used to describe diaphragm fiber atrophy which has been evidenced after short periods of mechanical ventilation. But association between decreased Tdi with histological atrophy measured by fiber cross-sectional area (CSA) in human diaphragm biopsies remains unknown due to the difficult to obtain these samples in clinics.
Objectives: To evaluate the ability of diaphragm thickness (Tdi) measured by ultrasound to predict diaphragm atrophy, defined by a decrease in diaphragm fiber cross-sectional area (CSA) obtained through diaphragm biopsy (the gold standard technique) in ventilated patients.
Methods: This is a prospective observational unicentric study performed in a University Hospital ICU including all admitted organ donors during a period of 3 years. Diaphragm biopsies and diaphragm ultrasound were performed in all patients the donation day and control subjects admitted for thoracic surgeries were also included. Demographic variables, comorbidities, severity on admission, treatment, laboratory test results and evolution variables were evaluated. Immunohistochemical analysis (CSA) and ultrasound measurements (Tdi) were evaluated and median values of the control group were used as thresholds for further analysis. Sensitivity, specificity, and positive and negative predictive values of an ultrasound Tdi cutoff for detecting histologic atrophy by CSA were calculated. Agreement between two ultrasound observers was also assessed. Continuous variables were described as means and standard deviation (SD) or medians and interquartile range [IQR (25–75)]. Statistical significance at $p \leq 0.05$. Clinical Research Ethics Committee: CEIC PSMAR (2017/7183/I).
Results: Thirty-five ventilated organ donors and 5 ventilated controls were included, without differences in basic characteristics. CSA were lower in donors than in controls [1513 (1150–1807) μm^2 vs 2851 (1743–3587) μm^2, $p \leq 0.001$] and Tdi tend also to be lower in this group [1.4 (1.3–1.7) mm vs 1.7 (1.3–1.8) mm, $p > 0.05$]. Regarding the control group thresholds, all donors presented lower CSA, but only 74% lower Tdi. The cutoff value for lower diaphragm thickness (Tdi < 1.7 mm) presented a sensitivity of 73%, a specificity of 67%, a positive predictive value of 96% and a negative predictive value of 17% for determining the presence of diaphragm atrophy (CSA < 2851 μm^2). Measurements of Tdi showed a very good intra-observer agreement (0.93 (CI 0.8–0.96) and 0.96 (CI 0.94–0.98)) and inter-observer agreement (Rho 0.89, $p \leq 0.001$).
Conclusion: Mechanical ventilation generates both diaphragm atrophy and thickness reduction. While a lower Tdi in diaphragm ultrasound is a good tool for diagnosing atrophy, normal or increased Tdi cannot rule atrophy out showing that both parameters should not be considered as synonymous.
Acknowledgements: Supported by a grant from Instituto de Salud Carlos III-Fondo Europeo de Desarrollo Regional (FEDER) (PI18/00025).

001056

Environmental impact of individual patient trajectories: paving the way for a sustainable intensive care through Life Cycle Assessments

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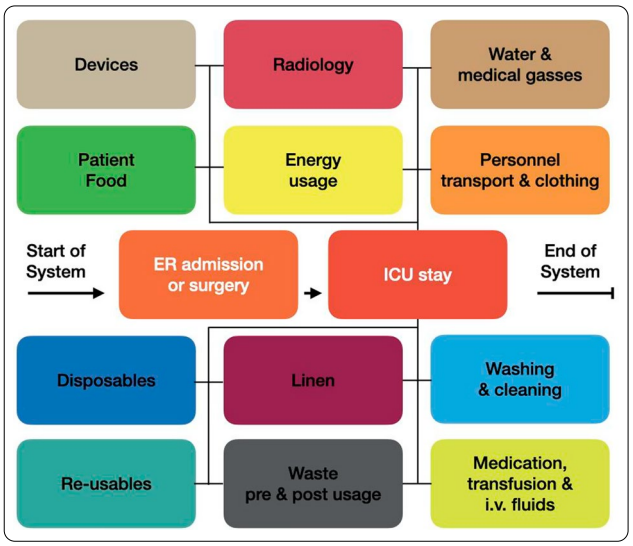
Intensive Care Medicine Experimental 2022, **10(2)**:001056

Introduction: Climate change is the biggest public health threat of the twenty-first century [1]. Reduction of negative human environmental impact is required to protect the health of current and future populations [2,3]. Paradoxically, the healthcare sector makes a substantial contribution to global CO_2-emissions [4]. The intensive care unit (ICU), emergency room (ER), and operating room (OR) constitute a substantial share of the hospital carbon footprint [5,6]. Fundamental understanding of the environmental impact of individual patient trajectories is currently lacking, but is essential to guide sustainability progress in acute care delivery [7].
Objectives: This study aims to quantify the environmental impact through life cycle assessment (LCA) of individual patient trajectories from the ER and OR onto the ICU. Obtained insights will provide an action perspective for future efforts in healthcare sustainability.
Methods: A single center observational study will be executed in a tertiary academic hospital, observing three frequent trajectories of

ICU patients. Included trajectories: 1) septic shock and 2) high-energy trauma admissions from the ER and 3) post-operative coronary artery bypass grafting admissions from the OR. A convenience sample of 10 patients will be included per trajectory, which is considered to provide sufficient variability regarding the associated environmental impact, similar to previous studies [8,9]. An overview of all measurements is shown in figure 1. If product data cannot be obtained directly, public databases, previous studies, and manufacturers will be consulted. Where necessary, economical value will be used as a proxy for environmental impact. Process-based LCAs will be performed to analyze the environmental impact of trajectories in accordance with international standards [10], using the ReCiPe2016 methodology. All stages from the production of materials to final destruction will be considered15. Outcomes will be reported in several domains, including CO2-equivalent emissions, loss of biodiversity, deforestation, and freshwater usage.

Results: This is the first study conducting an environmental life cycle assessment for individual patient trajectories in the intensive care in Europe. Data collection is currently on-going and the first results are expected by September 2022.



Conclusion: Outcomes will illustrate the environmental impact per patient trajectory and expectedly pinpoint a number of hotspots to reduce the environmental impact of the intensive care. Findings will be both relevant and timely, considering the European Green Deal and unanimously agreed upon urgent need for reduction of carbon emissions.

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Acknowledgements: This study was granted a ZonMw scholarship. File number: 80-86800-98-112

001102

Resources consumption in patients admitted to the icu for Covid-19 in the 6th wave in Spain according to SARS-CoV-2 vaccination

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Intensive Care Medicine Experimental 2022, **10(2)**:001102

Introduction: Despite the fact that at the end of December 2021, 90% of the population over the age of 12 in Spain was fully vaccinated, the sixth wave of the coronavirus had an explosive growth during the Christmas holidays in this country.

Objectives: To analyze the characteristics and resource consumption of adult patients admitted to the ICU for Covid-19 according to their vaccination status.

Methods: The study was realized in an intensive medicine department of a tertiary university hospital, with 3 ICUs, 2 polyvalent with 20 beds each, and one with 8 beds for cardiac surgery. The prevalence point was performed on January 28, 2022 at 10 a.m., and the follow-up was carried out until April 19, 2022 at 10 a.m. To assess the the characteristics and resource consumption of patients admitted to the ICU due to Covid-19 according to their vaccination status we also registered we also recorded: Age, Gender, Comorbidities such as Immunosuppression, Asthma, Emphysema/COPD, chronic kidney disease (CKD), and the need for renal replacement therapy (RRT), invasive mechanical ventilation (IMV), tracheostomy, extracorporeal membrane oxygenation (ECMO), the days of IMV and ECMO, the ICU length of stay and in the hospital (HOSP), and the Estimated Health Expenditure.

Results: Twenty-nine patients admitted for COVID-19 were registered, 20 of whom were unvaccinated and 9 vaccinated (4 with ChAdOx1 nCoV-19 from AstraZeneca, 4 with BNT162b2 from Pfizer-BioNTech, and 1 with mRNA-1273 from ModernaTX, Inc). None of those vaccinated with AZ had yet received the 3rd booster dose. Of those vaccinated with Pfizer-BioNTech, there were 2 immunosuppressed patients (a patient with Lupus and a kidney transplant patient). No other patient in the sample had severe immunodeficiency.

The follow-up was carried out until April 19, when 3 patients from the non-vaccinated group were still admitted to the ICU, and up to that moment they still remained on ECMO.

	Unvaccinated (n 20)	Vaccinated (n 9)
Age, median years (min.–max.)	54 (27–75)	63.8 (38–78)
Male gender, n (%)	14 (70%)	7 (77.8%)
Comorbidities:	1 (5%)	7 (77.8%)
Immunosuppression, n (%)	0	2 (22.22%)
Asthma, n (%)	1 (5%)	1 (11.11%)
Emphysema/COPD, n (%)	0	1 (11.11%)
CKD, n (%)	0	3 (33.33%)
RRT, n (%)	4 (20%)	3 (33.33%)
IMV, n (%)	20 (100%)	7 (77.8%)

	Unvaccinated (n 20)	Vaccinated (n 9)
IMV, mean days (SD)	52.8 (23)	36.4 (21)
IMV, sum of days	1,056	255
Tracheostomy, n (%)	17 (85%)	4 (44.4%)
ECMO, n (%)	11 (55%)	1 (11.1%)
ECMO, mean days (SD)	50.5 (23.5)	9
ECMO, sum of days	556	9
UCI stay, mean days (SD)	58.85 (23.6)	34.7 (23.9)
Occupancy UCI beds, sum of days	1,117	312
HOSP stay, mean days (SD)	66.1 (25.1)	50 (28.7)
Occupancy HOSP beds, sum of days	1,322	451
Estimated ICU expenditure	1,840,000 €	670,000 €

Conclusion: Regarding SARS-CoV-2 vaccination status of the critically ill patients admitted to the ICU due to COVID-19, the group of unvaccinated patients, despite being younger and with hardly any comorbidities, consumed more resources (ECMO and occupation of ICU beds) than the group of vaccinated patients.

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1. Estimated health expenditure source: Spanish Ministry of Health, autonomous communities.

Acknowledgements: NA

001158

Departmental Quality Intervention to Improve Documentation of Central Venous Catheter Tip Position on Post Insertion Chest X-rays and to Reduce Central Venous Catheter Tip Malpositioning

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Intensive Care Medicine Experimental 2022, **10(2)**:001158

Introduction: Central venous catheters (CVCs) are omnipresent in Intensive Care and High Dependency Units; it has been estimated that 200,000 CVCs are inserted annually in the UK [1]. They are used for both short- and long-term therapy, have roles in drug and fluid administration, repeated blood sampling, central venous pressure monitoring and in the absence of peripheral veins. CVCs should be positioned in the lower superior vena cava (SVC) or upper right atrium [2]. CVCs are commonly misplaced in the high SVC, low right atrium, innominate vein, internal jugular vein and right ventricle. A considerable issue in the correct positioning of CVC's is the absence of dependable surface landmarks. For this reason, post insertion chest x-ray is recommended as the most pragmatic, reliable method. The risk of complications such as erosion, pericardial tamponade and thrombosis is increased with a poorly positioned catheter tip [3].
Objectives: This project was initiated with the dual goal of (1) improving the documentation of CVC tip position on post insertion chest x-rays and (2) reducing the rate of CVC tip malpositioning. Ultimately promoting patient safety and reducing the potential for harm.
Methods: Baseline data was reviewed from an audit carried out in 2019 and a retrospective case note review from all patients admitted to ITU & HDU over a one-month period. This provided pre-intervention results. For the intervention all medical staff in ITU & HDU were educated on the correct placement of CVC tip and documentation of CVC tip on post insertion chest x-rays, a review checklist stamp was designed to be placed in patient notes following a post insertion chest x-rays, the nursing team was engaged in enforcing stop-checks amongst staff prior to using CVCs, the nurse in charge added this to daily nursing handover and information regarding the intervention was published in the ITU newsletter. Following the intervention, patient notes were prospectively reviewed over a one-month period assessing (1) was the CVC tip documented and (2) was the CVC tip positioned in the correct location.
Results: Pre-intervention, 24% of 41 chests x-rays carried out to confirm CVC tip position had a documented CVC tip position in the patient notes. Post-intervention, preliminary data has illustrated an improvement to 27% of 11 chest x-rays carried out (data collection ongoing). Pre-intervention, 43% of CVC tips were located too high compared to 33% located too high post-intervention.
Conclusion: Our study suggests that the education of medical and nursing staff and the introduction of the stop-check stamps for reviewing CVC tip position have improved the documentation and positioning of CVCs within our ITU and HDU departments. To attain further improvements, we propose an update to the current chest x-ray sticker to include the checklist stamp, the introduction of this new sticker to theatres for completion following CVC insertion in theatre and the inclusion of post insertion chest x-ray position review in the National Safety Standards for Invasive Procedures (NaTSSIPS) forms.

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001197

Development and validation of an early warning model for hospitalized COVID-19 patients: A multi-center retrospective cohort study

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Introduction: Timely identification of deteriorating COVID-19 patients is needed to guide changes in clinical management and admission to intensive care units (ICUs). There is significant concern that widely used early warning scores (EWSs) underestimate illness severity in

COVID-19 patients [1,2] and therefore, we developed an early warning model specifically for COVID-19 patients.
Methods: We collected electronic medical record data to extract predictors and used these to fit a random forest model. To simulate the situation in which the model would have been developed after the first COVID-19 'wave' in the Netherlands and implemented during the second wave, we performed a temporal validation by splitting all included patients into groups admitted before and after August 1, 2020. Furthermore, we propose a method for dynamic model updating to retain the model's predictive performance over time. We evaluated model discrimination and calibration, performed a decision curve analysis, and quantified the importance of predictors using SHapley Additive exPlanations values [3].
Results: We included 3 514 COVID-19 patient admissions from six Dutch hospitals between February 2020 until May 2021, and included a total of 18 predictors for model fitting. The model showed a higher discriminative performance in terms of partial area under the receiver operating characteristic curve (0.82 [0.80 to 0.84]) compared to the National Early Warning Score (0.72 [0.69 to 0.74]) and the Modified Early Warning Score (0.67 [0.65 to 0.69]), a greater net benefit over a range of clinically relevant model thresholds, and good calibration (intercept = 0.03 [− 0.09 to 0.14], slope = 0.79 [0.73 to 0.86]).
Conclusion: This study shows the potential benefit of moving from early warning models for the general inpatient population to models for specific patient groups. The COVID-19-specific early warning model is available online [4] and we encourage others to further validate this model independently.

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001202

Documentation of Microbiology Ward Round Pre and Post CareFlow Implementation on the ICU at Buckinghamshire Healthcare Trust

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Intensive Care Medicine Experimental 2022, **10(2)**:001202

Introduction: Microbiology ward rounds are an integral aspect of the bidaily ward rounds on the ICU and their documentation is crucial to ensure the best possible treatment. CareFlow was founded in 2007 by doctors wanting to improve the efficiency and efficacy of communication between clinical teams regarding hand overs of treatment. The management of severely ill patients is complex and involves the participation of multidisciplinary teams which can become disjointed and fragmented especially when documenting microbiology ward rounds. This system is crucial within the ICU and allows a comprehensive platform that can be updated remotely to alter all aspects of care. This was implemented during COVID to allow for remote interactions between the ICU and microbiology. As this tool has made it easier to document multidisciplinary discussions and agreements, it should portray nearly 100% of daily microbiology ward round in comparison to the previous handwritten proforma used.
Objectives: Evaluate the effectiveness of the implementation of CareFlow on the documentation of the daily microbiology ward rounds on the intensive care unit.
Methods: Although daily microbiology ward rounds take place and form part of the trust's guidelines on critical care management, the advice provided by the microbiology team is not always documented. It is therefore crucial to analyse the effectiveness of measures implemented to improve this. CareFlow is a private online network for documenting care implemented by the Trust. CareFlow allows healthcare professionals to access medical records retrospectively, which were documented, to compare to documentation prior to its implementation. To access the medical records prior to CareFlow implementation records were accessed retrospectively using 'Evolve', an electronic database of records used as well.
Inclusion criteria included detailed mention of a "microbiology ward round" taking place each day regardless of what the patient's treatment was as well as a minimum length of stay of one week excluding admission within the ICU. Exclusion criteria included copying the notes from the day prior, regardless of content, whether they had Covid, length of stay shorter than week.Ten patients from 2016, prior to CareFlow implementation, and patients from 2020, post CareFlow implementation, were selected and 10 days post ICU admission were analysed. The presence of these ward round documentations were processed and analysed.
Results:

Patient	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Total
10719385	0	0	0	1	0	1	0	2
11081344	0	0	0	1	0	1	0	2
10561608	1	0	0	0	0	1	0	2
11028042	0	1	0	0	1	0	0	2
11619378	0	0	0	0	0	0	1	1
30115806	0	0	1	0	0	1	1	3
11073944	0	0	0	1	0	0	0	1
11059575	0	0	0	0	0	0	0	0
10557172	0	0	0	0	0	1	1	2
20190518	0	0	0	0	0	0	0	0

Table 1: Documentation of ward round in 10 patients over a week period pre Careflow.

Patient	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Total
10863326	0	0	0	0	0	0	0	0
10896354	0	1	0	0	0	1	0	2
20054638	0	1	1	1	1	1	0	5
20168660	1	1	1	1	0	0	1	5
11336878	1	1	1	1	0	0	1	5
20248761	0	1	1	0	0	0	0	2
31176990	1	1	1	0	1	1	0	5
31180855	1	0	1	0	0	1	0	3
31180856	0	1	0	0	0	0	0	1
31005246	1	0	1	0	1	0	0	3

Table 2: Documentation of ward round in 10 patients over a week period post CareFlow.

Conclusion: Prior to the implementation of CareFlow, the frequency of documented microbiology ward rounds was extremely low. This could be due to the Covid pandemic and the use of a different Proforma that was used for these patients, as well as the transition of ward rounds and multidisciplinary team interacts being converted to virtual online discussions. The results do show the use of the Careflow tool has a positive influence on the recording of daily ward rounds, but is still not 100% efficacious and utilisation needs further exploration. We commmend: Ensuring staff are proficiently trained in CareFlow, having designated doctors to ensure documentation is in place each day, regular audits to ensure standards of documentation are maintained, and encourage use of tool throughout the department.

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001217

Diaphragm ultrasound exploration to predict of weaning mechanical ventilation

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Introduction: Ultrasound is a commonly used imaging modality for procedures and clinical evaluation in modern intensive care units. Recently, an assessment of diaphragmatic contractile structure and function has been described. Diaphragmatic dysfunction is often identified as a potential cause of weaning failure. However, its contribution to predict weaning issue has not been clearly demonstrated.
Objectives: The aim of our study was to assess the contribution of diaphragmatic ultrasound during spontaneous breathing trial (SBT) in order to predict its outcome and to compare the findings to the rapid breathing index (RSBI) parameter validated to predict the outcome of weaning.
Methods: A prospective study was carried out on ready-to-wean ventilated patients. The function of both left and right hemi-diaphragms was assessed at onset of SBT (T0) and at 30 min (T30) by measurements of diaphragmatic displacement (DD) and thickness (DT) as well as diaphragmatic thickening (DTF). A DT < 20 mm and/or DD < 10 mm and/or DTF < 30% were considered to define Diaphragmatic dysfunction. Univariate analysis was done to detect predictors of weaning failure. Receiver Operating Characteristic (ROC) curves, were analyzed to determine the best thresholds for predicting weaning failure.
Results: Fifty-two patients were included during the study period. SBT was performed in a mean delay of 10 ± 6 days. Eleven patients (21%) failed SBT. Diaphragmatic dysfunction was observed in 52% of patients on ultrasound. Chronic obstructive pulmonary disease, sedations duration and infection by SARS COVII differed significatively in the diaphragmatic dysfunction group (p = 0,024, p = 0,047 and p = 0,004 respectively). Univariate analysis comparing the SBT failure group and the success one showed a significant difference in left DD on T0 (p = 0,037). RSBI did not differ between the two groups. New parameters such as the ratio respiratory rhythm on DD (RR/DD) right and left on T0 were significatively higher in the failure group (p = 0,034 et p = 0,048 respectively).
On multivariate analysis, the ratio RR/DD right on T0 was predictor of weaning issue with Odds ratio 1.056 (confidence interval 95% [1.001–1.113], p = 0.046). A cut-off of RR/DD right at T0 < 37 c/min/cm was found to be a good predictor of successful weaning with a sensitivity of 77% and specificity of 73%, area under the ROC curve 0.757 [0.598–0.916]; p = 0.018.
Conclusion: Diaphragmatic ultrasound is feasible in intensive care unit. Prevalence of diaphragmatic dysfunction on ready to wean patients is high (52%). RSBI was not the best predictor of weaning issue. A ratio RR/DD right at T0 was a good predictor of successful weaning and should be introduced into weaning parameters.

001220

Exploring the ventilatory and functional outcomes for vaccinated and unvaccinated patients admitted to ICU with COVID-19: A single centre observational study from a large London Teaching Trust

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Introduction: During the COVID-19 pandemic, prolonged mechanical ventilation (MV) and functional impairment have been cited as issues contributing to increased ICU and hospital length of stay (LOS)1,2,3. Vaccination uptake in the UK significantly increased during 2021 4, with the aim of reducing disease severity for those contracting the virus.
Objectives: To compare ventilatory and functional outcomes in vaccinated (VAC) and unvaccinated (UVAC) patients admitted to ICU during the third UK COVID-19 wave.
Methods: A retrospective clinical review of patients admitted to ICU with a primary diagnosis of COVID-19 between December 2021 and January 2022 was conducted at a large London NHS Foundation Trust. Electronic clinical notes were screened and the following data extracted: patient demographics, vaccination status, comorbidities, MV duration, sedation duration, ICU LOS, hospital LOS, ICU mobility score (ICUMS) at ICU discharge, ICUMS at hospital discharge and need for oxygen therapy on discharge home. Data was analysed using descriptive statistics and presented as median (range) and percentages.
Results: 56 patients were identified. 30 were excluded due to incidental findings of COVID-19 at ICU admission. 3 patients were excluded due to no record of vaccination status. 23 patients with a primary diagnosis COVID-19 were included in the final analysis.UVAC patients were older with a higher percentage of non-white ethnicity but fewer comorbidities than VAC patients (Table 1).

Table 1—Patient Demographics

	Age	Gender %Male	Ethnicity % White	BMI Median	Comorbity Median	ICU Mortality	Hospital Mortality
Vaccinated n = 10	58.5 (40–74)	50%	60%	26.5	6 (2–9)	2 (20%)	5 (50%)
Unvaccinated n = 13	62 (32–76)	54%	15%	29	4 (0–8)	3 (23%)	4 (31%)

ICU LOS was similar between groups, however a higher percentage of VAC patients required MV during ICU stay (60% vs 39% UVAC). For patients requiring MV, duration of sedation was shorter (6.5 Vs 17 days) with fewer MV days (8 Vs 19) in the VAC group compared to UVAC. The VAC group also had a shorter hospital LOS and no oxygen requirements at hospital discharge compared with the UVAC group (Table 2). No differences were noted between groups in terms of ICUMS at ICU

or hospital discharge. All patients were discharged home with no ongoing rehabilitation needs.

Table 2—Patient outcomes

	ICU LOS (Days)	MV During ICU Stay	Sedation Duration (Days)	Days on Mechanical Ventilation	ICUMS ICU D/c	ICUMS Hosp D/c	Hopsital LOS	Long term Oxygen on D/c
Vaccinated n = 10	8 (1–34)	6 (60%)	6.5 (2–23)	8 (2–32)	5 (3–5)	10	16 (9–96)	0
Unvaccinated n = 13	9 (3–56)	5 (39%)	17 (3–9)	19 (1–35)	5 (2–8)	10 (9–10)	21 (8–56)	2 (15%)

Conclusion: Trends from our data suggest vaccination against COVID-19 appears to reduce disease severity for those requiring MV for COVID-19 pneumonitis. VAC patients had a shorter duration of sedation, MV and hospital LOS than UVAC patients. Despite this, no differences were observed in ICU mortality or functional outcomes at ICU or hospital discharge between groups. Primary admissions to ICU for COVID-19 were markedly reduced during the third UK wave, resulting in the small numbers analysed within this review. Pooling results across organisations would enable further examination of these trends on vaccination status and patient outcomes.

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000909

Pandemic impact in the outcome of management of ischaemic stroke in the emergency department

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Introduction: The COVID-19 pandemic has caused an unprecedented global healthcare crisis. During the year of 2020 and 2021 the healthcare centers were forced to adapt with consequences to the management of another conditions beyond COVID-19. Our notion was that those years were accompanied by a reduction of stroke patients admitted within fibrinolytic period.
Objectives: This study aims to identify the impact of pandemic years in the outcome of patients present in the emergency department within fibrinolytic/thrombectomy period.
Methods: We performed a retrospective study on patients with the diagnostic of ischemic stroke present in emergency department with less than 24 h of evolution between 1 January of 2019 and 31 December of 2021.
Results: Among the 193 patients enrolled, 59% (n = 113) were male. The mean age was 72 (± 13) y.o., with patients in 2019 being younger ($p < 0.05$) than in 2020 and 2021. The year 2020 had the lower rate of admission with only 35 patients ($p < 0.05$) (35–93 interval) for fibrinolysis/thrombectomy. Most patients (62.8%) were submitted to fibrinolytic treatment and 29.6% were transferred to a tertiary hospital for thrombectomy. The average stroke-door time was 184 ± 124 min, being significant shorter in 2020 and 2021 ($p < 0.05$). Due to that difference, the number of patients submitted to fibrinolysis was significantly superior in 2020 (80%; $p < 0.05$) vs 2021 (66%) and 2019 (50%). Remarkably, the year 2020 had the most prolonged door-needle time ($p < 0.05$) with an average 32.3 ± 15.8 min. The NH Stroke Scale (NHSS) was performed in all patients and the mean value was 10 (± 6,9) points ($p > 0.05$ in all years).
Conclusion: Our results show a clear impact of pandemics in the admittance of Stroke patients within fibrinolytic window. We were able to find that the average stroke-door time was shorter in pandemic years (2020–2021), although this study was not designed to evaluate such causes. This short period between stroke and hospital arrival can explain the higher percentage of patients that were submitted to fibrinolytic treatment in 2020–2021.
However, in the first year of the pandemics (2020), not only a lower number of patients arrived within the fibrinolytic/thrombectomy window but also it took longer ($p < 0.05$) to start the fibrinolytic therapy. Those results might have been influenced by the fact that normal routines were disrupted due to COVID-19 pandemics, and it took time to rearrange new routines adapted to the new times. An example is 2021 with the lowest door-needle time. Nevertheless, the outcomes were kept stable during 2019–2021 triennium.
This study confirms what was expected and that COVID-19 pandemics have clearly interfered with generalized healthcare, but also showed that hospitals were able to adapt and surpass difficulties.

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001063

Elective ICU booking for postoperative patients and actual utilization

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Introduction: With the growing population, the surgical volume is perpetually increasing. The planned postoperative utilization of the intensive care unit decreases perioperative mortality. However, the preoperative request for ICU admission is made subjectively. It is often driven by the local policies and depends upon the availability of beds. Some high-risk elective procedures can get delayed or canceled due to the unavailability of the ICU bed. The cost and burden of this practice may impose an additional burden on an already resource-limited setting. The American College of surgeons' national surgical quality improvement (ACS NSQIP) risk calculator estimates the likelihood of postoperative complications. Thus, the increased probability of postoperative complications can guide the physician to book ICU in advance to avoid unplanned ICU admission.
Objectives: (1) To determine the number of preoperative ICU requests generated and their utilization postoperatively after an elective or time-sensitive surgical procedure.
(2) To evaluate the characteristics of the patients undergoing an elective surgical procedure for whom a preoperative ICU admission was requested using the ACS NSQIP risk calculator and its effectiveness as a predictive tool for postoperative ICU admission.
Methods: Study design: A retrospective cohort study
Inclusion criteria:

- Age > 18 years
- All elective non-cardiothoracic surgical procedures

Exclusion criteria:

- Urgent cases
- Emergency case
- In complete medical record

Methodology: All patients who underwent elective surgical procedures from January 2019 till December 2020 were included and their files were reviewed. The patient's demographics, addiction history, comorbidities, surgical specialty, surgical procedure, and the reason behind preoperative ICU request were noted. For the risk assessment, ACS NSQIP risk calculator was used.
Results: During the period, 395 requests were generated for the postoperative ICU admission, however, only 26% (103 patients) ensued in ICU. The patients who did not utilize ICU were from the surgical specialty of neurosurgery followed by obstetrics. General surgery accounted for the most optimum utilization of requests. One possible reason is the usage of ACS NSQIP calculator is part of their practice for every patient.
The result of the NSQIP calculator and the postoperative ICU admission is in process and will be completed by the start of May 2022.
Conclusion: Their number of postoperative ICU bookings was higher in comparison to the actual utilization.
To conclude, the results of NSQIP data are pending and will be completed by the start of May 2022.

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001193

Proxy interview reliability for assessment of preadmission disability and quality of life in elective surgery patient: a nformatics prospective observational study

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Intensive Care Medicine Experimental 2022, **10(2)**:001193

Introduction: Pre-admission assessment of disability or quality of life is a prerequisite for prognosis and individual treatment goals, and in research, for enrolment in a trial or baseline assessment. Patients who are unable to provide information themselves, such as those with critical illnesses, are most likely to have these values obtained through proxies. Evidence of the reliability of these responses in surgical patients, however, is limited.
Objectives: Evaluation of the reliability of disability and quality of life assessment via proxies in elective surgery patients admitted to the normal ward or ICU post-operatively.
Methods: Adult (≥ 18 years of age) patients undergoing elective surgery were included into the trial if they were able to independently answer the questionnaires preoperatively and had a proxy present postoperatively that was also able to answer the questionnaire. The WHO Disability Assessment Schedule 2.0 (WHODAS) was used to assess disability and the five-level version of the EuroQol five-dimensional (EQ-5D-5L) to assess quality of life. Intraclass-correlation coefficient (ICC) (oneway-random, absolute agreement, single rater) as well as Bland-Altman-Plots were used to assess reliability. The influence of the postoperative ward on the difference between patient and proxy responses was assessed via a univariate general linear model.
Results: A total of 204 pairs of patients and proxies were included into the trial of which 102 (50%) were postoperatively admitted to the ICU and 102 (50%) to the normal ward. Patients admitted to the ICU postoperatively were significantly older, had more comorbidities and had a higher share of heart and visceral surgeries (see Table 1).
The ICC showed moderate reliability for the WHODAS 2.0 for all patients (ICC (95% CI): 0.56 (0.46–0.65)) as well as the subgroup admitted to the ICU (ICC (95%CI): 0.52 (0.36–0.65)) and normal ward (ICC 95%CI): 0.58 (0.43–0.69)). The ICC for the EQ5D5L showed moderate reliability only for the normal ward patients (ICC (95%CI): 0.59 (0.44–0.70)) and poor reliability for the whole cohort (ICC (95%CI): 0.41 (0.29–0.52)) as well as the ICU patients (ICC (95%CI): 0.25 (0.05–0.42)). These results were confirmed by the Bland-Altman-Plots showing an insufficient reliability and a systematic bias. Patients rated themselves better as their proxies if they were admitted to the ICU postoperatively (see Figure 1). There was a significant difference between normal ward and ICU patients regarding the difference between patients and proxy ratings for the WHODAS 2.0 (mean (95%CI)—normal ward: − 1.33 (− 4.85–2.19); ICU: − 8.28 (− 11.80 to – 4.75); p = 0.006) and the EQ-5D-5L (mean (95%CI)—normal ward: 0.07 (0.01–0.14); ICU: 0.17 (0.11–0.24); p = 0.028).

Variable	All	Ward	ICU	p-value
n	204	102	102	
Age (years)	69 [59 - 77]	66.5 [58 - 73]	72 [64 - 79]	0.001
Gender				
Male	121 (59)	60 (59)	61 (60)	0.887
Female	83 (41)	42 (41)	41 (40)	
Hospital length of stay (days)	13 [8 - 21]	15 [9 - 23]	11 [7 - 20]	0.145
ICU length of stay (days)	n/a	n/a	3 [1 - 5]	n/a
Number of preexisting conditions	3 [2 - 6]	2 [1 - 4]	6 [3 - 9]	< 0.001
Number of previous surgeries	2 [1 - 3]	2 [1 - 3]	2 [1 - 3]	0.713
Number of preexisting medications	3 [1 - 7]	2 [0 - 3.5]	6 [3 - 8.5]	< 0.001
Operation field				
Orthopedic	1 (1)	1 (1)	0 (0)	< 0.001
Trauma	9 (4)	9 (9)	0 (0)	
Visceral	89 (44)	57 (56)	32 (31)	
Heart	63 (31)	0 (0)	63 (62)	
Thoracic	11 (5)	10 (10)	1 (1)	
Vascular	10 (5)	9 (9)	1 (1)	
Neuro	11 (5)	10 (10)	1 (1)	
Gynecology	7 (3)	4 (4)	3 (3)	
Plastics	1 (1)	1 (1)	0 (0)	
Otorhinolaryngology	2 (1)	1 (1)	1 (1)	
Location of postoperative interview				
ICU	38 (19)	0 (0)	64 (63)	< 0.001
Ward	166 (81)	102 (100)	38 (37)	

Table 1. Baseline characteristics patients. Continuous variables are shown as median [interquartile range]. Categorical variables are shown as count (percentage). Significance level between patients admitted to the ward and ICU was determined with Mann-Whitney U test for continuous variable and Chi-Square test for categorical variables. ICU = Intensive Care Unit

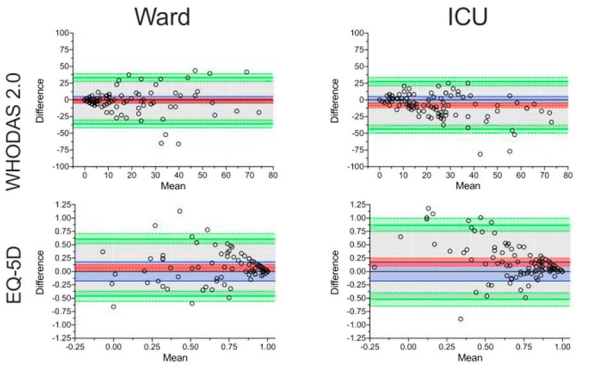

Figure 1. Bland-Altmann plots of WHODAS 2.0 and EQ-5D for normal ward and ICU patients.
The difference between patients and proxies can be seen on the Y-axis while the mean of their score can be seen on the X-axis. The red area indicate the mean (solide line) with the 95% confidence intervall (dashed line) for the entire cohort. The blue area indicates the minimal clinically important difference. The grey area between the solid green lines indicated the limits of agreement. The dashed green lines and the green area indicated the 95% confidence intervall for those limits of agreement.

Conclusion: Proxy assessment of disability and quality of life showed insufficient reliability particularly in ICU patients. There was a systematic bias, i.e. relatives systematically rated worse.

001203

Venous excess ultrasound score in patients with sepsis and cardiorenal syndrome

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Intensive Care Medicine Experimental 2022, **10(2)**:001203

Introduction: Fluid overload and venous congestion are deleterious in critically ill patients with cardiorenal syndrome. There is scarce literature on Venous excess ultrasound score (VEXUS) assessment characteristics in cardiorenal syndromes with hypoxic respiratory failure and sepsis.
Methods: This study was an observational, prospective, single-center study, including the patient with sepsis and heart failure who were transferred to the cardiac care unit (CCU). An intensivist in critical care ultrasound performs serial ultrasound examination till acute kidney injury (AKI) is resolved or the patient is initiated on dialysis. VEXUS comprising inferior vena cava, hepatic vein waveform, and portal vein pulsatility was assessed. The patient with grade 0 and I was allowed to receive boluses of IV fluid on admission. Grade 2 and 3 were observed only with fluid restriction and diuresis till renal replacement therapy if needed.
Staging of venous congestion
VEXUS
Grade 0: IVC grade < III, HD grade 0, PV grade 0
Grade I: IVC grade IV, but normal HV/PV pattern
Grade II: IVC grade IV with mild flow pattern abnormalities in HV/PV
Grade III: IVC grade IV with severe flow pattern abnormalities in HV/PV
Results: Of the 109 patients with suspected sepsis, 33(71%) were selected with renal and cardiac failure. The median patient age was 73 (57–85) years, and 15 of the patients (45.5%) were men. The clinical characteristics of the patients with confirmed cardiorenal syndrome are shown in Table 1.
Mean Left ventricular ejection fraction 46%, tissue nforma Right ventricle S'8.8 cm, right ventricular diameter 3.9 cm, mean pulmonary hypertension 51 mmHg, mean creatinine was 377 ummol/l. Patients with acute kidney injury were 17 (82%). Seventeen patients (51.5%) had VEXUS grade III. Resolution of AKI injury showed a significant correlation with improvement in VEXUS grade (*p-value* 0.005). Renal replacement therapy was needed acutely for VEXUS grade III in six patients (18%) and two patients in VEXUS grade2 (6%); no renal replacement therapy was conducted in grades 0 and 1. Grade 0 and I received fluid for resolution of acute kidney injury. There was a significant association between changes in VEXUS grade and fluid balance (*p-value* 0.04).

Variables	Description
Acute kidney injury	17 (82)
Renal replacement therapy	8 (24)
VEXUS score (%)	
0	2 (6.1)
1.00	7 (21.2)
2.00	7 (21.2)
3.00	17 (51.5)
Respiratory status	
Pulmonary edema with ultrasound chest B lines	21 (64)
Cardiac function	
Left ventricle Ejection fraction%	46.4
Pulmonary artery systolic pressure (PASP) mm Hg	52

Conclusion: In a population with sepsis and cardiorenal disease, the combined grading of IVC, hepatic vein, and portal vein (VEXUS) can help manage fluid and predict the need for renal replacement therapy

001277

SMART ICU: digitalization of an adult intensive care unit

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Intensive Care Medicine Experimental 2022, **10(2)**:001277

Introduction: Introducing nformatics clinical systems in ICU has a drastic change: the clinic graphic is extremely important for doctors and nurses to treat patients, vital information (temperature, breath, arterial pressure, pulse), patient fluid balance, ventilator parameters and lab and other diagnostic information is essential for critical patients' treatment and safety.
Objectives: To develop and implement a computerized clinic system to set up all patient information in one space, to improve critical patient care in a safe way; and also, to avoid paper graphics.
Methods: Develop a departmental platform adjusted to the hospital and ICU need by the provider technical and functional team; helped by hospital nformatics department, and ICU professionals.
All monitoring and nformatic support devices are connected to the platform, which is linked to hospital internet, so is capable to gain information and show clinical results in the same digital tool.
Results: We decided to implement this project by three steps. To start, all ICU boxes were equipped with an nformatics station (clinical computer station, a touch screen, keyboard and mouse).
First step: to connect all monitoring and nformatic support devices, needing professional support to validate the obtained parameters. Our nformatics system brings together all the patients variables and automatically draws a personal graphic.
Second step: develop nursery and medical protocols, clinic history, medical and nursery commentaries, diagnostic and prognostic scales, diagnose list and procedures. All these information was automatically linked to hospital clinical history.
Third step: The most complex phase was the treatment management. It required the integration of the own tool of the hospital pharmacy service, where physicians make the prescriptions and nurses register the administration, so that all this information was mirrored in the ICU service program. Moreover, in our units most of the medication is administered through volumetric perfusion pumps, which were

actually able to connect to the platform, sending real time information of doses, infusion rates and total infused volumes.
All the information reflected in the computerized clinic system become an important way to achieve information to develop studies or predictive models, which before this app was extremely difficult.
Conclusion: The clinic graphic is extremely important for doctors and nurses to treat patients, vital signs, patient fluid balance, ventilator parameters and lab and other diagnostic information is essential for critical patients' treatment and safety. With our platform all this information, treatment and administration of these treatment, is reflected, and much of it automatically, so is an important improvement in safety, efficacy and immediate attention.
All the paper information is now automatically recorded in the platform, so the data is easier to search and use for different studies, protocols or management. This "Smart ICU" is the beginning of medical artificial intelligence.

001315

Mixed-methods exploration of trainee wellbeing in relation to out-of-hours staffing: a pilot study

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Intensive Care Medicine Experimental 2022, **10(2)**:001315

Introduction: There is a growing interest in wellbeing amongst critical care physicians, with emerging data suggesting an impact on patient safety and the provision of a sustainable workforce. A wealth of literature can be found describing innovative solutions to improve sleep, nutrition and mental health; however such measures can appear performative if attention is not equally paid to repairing physician grievances as they arise.
Within our intensive care unit, trainee dissatisfaction was highlighted in relation to distribution of skill-sets amongst clinicians on the out-of-hours rota.
Objectives: A pilot quality improvement project was developed aiming explore the beliefs of trainees around skill-sets required out of hours and implications on trainee wellbeing.
Methods: Structured and unstructured interviews were held with all junior doctors on the unit from 25th March to 25th April. Interviews aimed to understand what trainees felt were required skill-sets overnight, and how comfortable each trainee felt supervising or practising these independently. Ethnographic analysis with complete participation was used for context and theory genesis. Data from each interview was pruned and coded by mixed methods within a week of collection.
Quantitative analysis of the rota aimed to identify whether current staffing met the required skill sets for trainees to feel comfortable out-of-hours.
A summary of recommendations was fed-back at a local meeting of trainees and executive staff. Trainee suggestions were received and incorporated into rota and employment planning.
Results: All trainees were interviewed with the exception of the interviewer themselves. Out of 11 junior doctors surveyed, 4 requested supervision to feel comfortable practising all or some of the required skills. There was no correlation between staff seniority and comfort levels expressed. Required skill-sets ranged from assessments of critically unwell patients, ventilator management, invasive monitoring insertion and central venous access.
There was 100% concordance between the answers provided during interview and the interviewer's predictions, suggesting a shared understanding amongst trainees around comfort levels in performing required skills out-of-hours.
Of the rota gaps identified, there was a higher chance of a trainee who had been requesting more senior supervision to be inadvertently rostered against a locum shift.
Common themes of discussion included consultant approachability and the desire to learn and become independent. Differences in hospital micro-cultures were Referenced as well as knowledge and skills arch over time, referencing the Dunning–Kruger effect and Johari window.
Conclusion: This pilot project uses a consultative management style to explore the effects of rota coordination on trainee wellbeing. It has been applied in an NHS district general hospital setting, carried a low cost-burden and did not require specialist resources.
Competence and performance measures were not used in the study, as the focus was purely to investigate trainee perspectives of their own ability and how this related to wellbeing. Ethnographic methodology was used to reduce performance bias and the use of formal competence measures could have detracted from this. Additional exploration into the correlation between trainee beliefs and validated competency outcomes could contribute to theory genesis in a larger study.
Within the context of a small, single centre pilot project, qualitative data collected offers preliminary evidence regarding the impact of skill-set and availability of supervision out-of-hours on trainee wellbeing.

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001322

Lung and Diaphragmatic Ultrasound as predictors for successful weaning from mechanical ventilation

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Intensive Care Medicine Experimental 2022, **10(2)**:001322

Introduction: Lung and diaphragmatic ultrasound is increasingly being utilized to assess the right time to wean critically ill patients from ventilator assistance. A detailed literature search has not revealed any study from India which evaluated lung and diaphragmatic ultrasound in combination as weaning index. Hence this study is planned to assess their usefulness in predicting weaning outcome in critically ill mechanically ventilated patients.
Objectives: To correlate and compare lung ultrasound score (LUS), diaphragmatic thickening fraction (DTF) and diaphragmatic excursion (DE) in predicting weaning outcome
Methods: A prospective observational study was conducted from July 2020 to January 2021 at Department of Critical Care Medicine, Bharati Vidyapeeth Medical College Hospital, Pune, India. Adult patients who are mechanically ventilated for more than 24 h and are ready to be weaned are enrolled after fulfilling the inclusion criteria. Sample size was calculated assuming a simple weaning of 69% (by ICC statement by Boles et al.). A total of 89 patients were studied in the setting of a multidisciplinary ICU after obtaining a written informed consent from next of their kin.
After the readiness to wean assessment, a spontaneous breathing trial (SBT) was performed in PSV mode PS-8; CPAP-5; FiO_2 40%. Lung and diaphragmatic ultrasound is performed by an intensivist during the SBT using a standardised protocol. If the patient passed the SBT, he was liberated from the ventilator. However if the patient failed the SBT, he was continued on ventilator support and next attempt was tried after 24 h. The number of SBTs required before being completely

weaned and the need for re intubation or reconnection to the ventilator, duration of mechanical ventilation and weaning outcomes are noted. The findings of lung and diaphragm ultrasound viz., lung ultrasound score, diaphragmatic thickness fraction and diaphragmatic excursion were correlated with the weaning outcome, whether successful or failed.

Weaning outcomes are categorized as per the 2007 International Consensus Conference definitions. Simple weaning is weaning and extubation after the first SBT. Failed Weaning (or) weaning failure is categorised by either failure of SBT or difficult weaning or prolonged weaning or extubation failure. After the 1st SBT, the patients are categorized either as simple weaning or failed weaning based on the outcome.

Results: Out of the 89 patients, 47 patients (53%) were weaned and extubated after 1st SBT (simple weaning). Out of the 42 patients (47%) who failed weaning, 27 had failed 1st SBT and 15 had failed extubation (9 patients required reintubation, 1 weaned to NIV, and 5 patients died within 48 h of extubation). Both the groups simple and failed weaning have comparable baseline characteristics of median age, gender, category of patients and source of admission, median duration of illness and severity scores (APACHE II and SOFA) at presentation. However there was a statistically significant difference in the median duration of mechanical ventilated days ($p < 0.001$), duration of ICU stay ($p < 0.01$), duration of hospital stay ($p < 0.05$) and survival at 28 days ($p < 0.001$) with all values being higher in failed weaning group.

POCUS was done at time of 1st SBT for calculating LUS, DTF and DE. The AUROC for predicting weaning outcome showed the cut off values of lung ultrasound score (LUS) of less than 12 (sensitivity 94% and specificity 74%), diaphragmatic thickening fraction (DTF) of more than 22% (sensitivity 85% and specificity 45%) and diaphragmatic excursion (DE) of more than 1.27 cm (sensitivity 74% and specificity 50%) could predict successful weaning at time of SBT.

Conclusion: Patients who had simple weaning had lesser LUS and higher DTF and DE compared to those with failed weaning. LUS has a significantly higher predictive value for successful weaning compared to DTF and DE on logistic regression analysis in our study. The results were similar to earlier studies done in other regions across the globe but had different cut offs probably due to varied cohort. Multi-centric studies with standard methodology will be necessary for obtaining disease specific cutoffs which can reliably predict successful weaning.

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001342

Assessment of EIT-derived regional ventilation distribution and dyspnea in COVID-19 survivors at 1-year follow up

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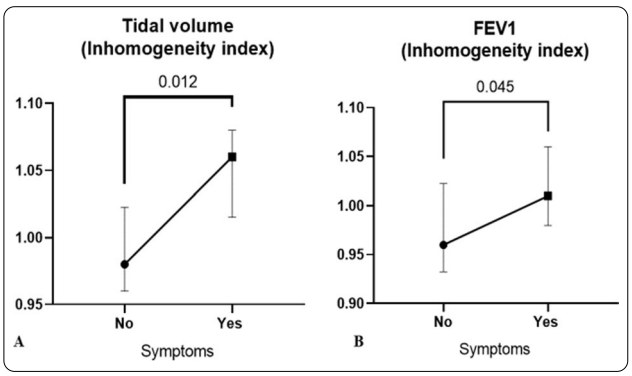
Intensive Care Medicine Experimental 2022, **10(2)**: 001342

Introduction: COVID-19 related pneumonia can result in "new onset dyspnea" [1][2], but its morpho-functional characteristics are still not totally understood by now. Electrical impedance tomography (EIT) could improve the understanding of the long-term lung physiological alterations in patients who experience dyspnea after being hospitalized for COVID-19 pneumonia.

Objectives: To evaluate lung function and ventilation distribution patterns in patients who have been hospitalized for severe COVID-19 pneumonia and to assess their possible role in dyspnea at 1 year after hospital discharge.

Methods: We followed up patients at 12 months from ICU and subintensive care unit admission for COVID-19 pneumonia. A 16-electrodes EIT monitor (Dräger PulmoVista 500, Drägerwerk AG, Germany) was positioned around the chest at the 4th–5th intercostal space before starting the respiratory function assessment and EIT data were recorded during the spirometry. We calculated the coefficient of variation (CV) and the global inhomogeneity index (GI) from EIT images recorded during tidal breathing (TV) and forced spirometry (FEV1, FVC and FIV1), as previously described by Frerichs et al. [3]. Therefore, we classified patients according to the presence or not of new onset dyspnea (mMRC/dyspnea score ≥ 1). Furthermore, we compared pulmonary function and EIT derived data between the two groups (respiratory symptoms yes/no). The Wilcoxon signed-rank test ($\alpha = 0.05$) was used to evaluate if the difference between variables in the two groups were significant.

Results: We enrolled 29 patients with a mean age 64 ± 11 years and a mean BMI of 29 ± 3.3 kg/cm^2. 20/29 (68.9%) were admitted to the ICU during their hospital stay and 7/29 (24%) required endotracheal intubation, 14/29 (48%) NIV/CPAP while 4/29 (14%) were supported with HFNC and 4/29 (14%) with low-flow oxygen. Of these, 13/29 (45%) had an mMRC ≥ 1 at 1 year follow up. No difference was found among the two groups when evaluating the pulmonary function data. Interestingly, we found that patients with dyspnea had higher levels of heterogeneity in regional ventilation distribution, as assessed by EIT, both during quite breathing (GI TV = 0.98 [0.96–1] vs 1.1 [1–1.1], $p = 0.012$, figure 1A), and forced expiration (GI FEV1 = 0.96 [0.94–1] vs 1 [0.98–1.1], $p = 0.045$, figure 1B).



Conclusion: Persistent dyspnea at 1 year after COVID-19 pneumonia is associated to a higher inhomogeneity in lung regional ventilation distribution in both quiet breathing and forced expiration, but preserved respiratory function parameters derived from spirometry.

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Acknowledgements: None.

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001021

Cost-effectiveness analysis in the use of inotropes in acute heart failure

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Intensive Care Medicine Experimental 2022, **10(2)**:001021

Introduction: Acute heart failure (AHF) is defined as the onset or exacerbation of signs and symptoms of heart failure that progress rapidly. In high-income countries, treatment of this disease encompasses around 3% of the total health expenditure, and costs are expected to increase. As health policy-makers endeavor to achieve safety and efficacy, cost-effectiveness of therapies is an important consideration, even more in low-income countries. Based on economic analyzes it may be inferred that levosimendan in some scenarios may be more cost-effective.
Objectives: To evaluate the cost-effectiveness of inotropic agents in patients with AHF admitted to the intensive care unit (ICU) in a mid to low-income country.
Methods: This retrospective observational study included patients aged ≥ 18 years, admitted to the ICU with AHF, and who received inotropic agents. The clinical outcomes were: mortality, mechanical ventilation requirement, dyspnea, and days of stay in the ICU. The cohort was analyzed based on the aforementioned outcomes and, according to the frequency distribution, the effectiveness rates of each pharmacological regimen were calculated. The average cost of patients who died, required mechanical ventilation, or presented dyspnea in relation to the different medications was calculated. Incremental cost-effectiveness ratios were assessed to compare drug regimens. Exchange rate from Colombian peso to US dollar was 1 USD = 3,758 COP.
Results: 21 patients were collected from 2018-to 2019, these patients received norepinephrine (N), levosimendan (L), and/or dobutamine (D). In the mortality outcome, the effectiveness was N: 100%, L: 100%, N + L:75%, D + L:100%, D + N:50%, and the combination of the three drugs 66%. The incremental cost-effectiveness analysis (ICE) to avoid one death using L vs using D + N increases costs by USD 1,085. In the outcome of requiring mechanical ventilation, an increase in the cost of USD 6,205 was evidenced to avoid the use of mechanical ventilation in one patient using L vs N, and an incremental cost of USD 133 in one patient if we used D + L vs L. In the outcome of dyspnea, the effectiveness of 50% was evidenced with D + N and 100% with the combination of the three drugs. The ICE showed that USD 1,350 are needed to prevent dyspnea in a patient if we use the three-drug scheme compared to using D + N. Table 1 shows ICU days for each treatment. The ICE showed that USD 328 is required to avoid one day in the ICU with L vs N. If we compare only using L vs D + L, the CEI resulted in USD 4.8 to avoid one day in the ICU. Using L + N compared to just using N the CEI resulted in USD 54 to avoid one day in the ICU.

Table 1. ICU days

Inotropic Agent	ICU days
L + N	11.5
L + N + D	18
D + L	3
L	12.3
D + N	16.2
N	14

Conclusion: Levosimendan may be more effective as monotherapy and in combination schemes in different outcomes. However, its high cost may be a challenge from a cost-effectiveness standpoint in low- to middle-income countries.

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Acknowledgements: This research received no funding

001273

Effectiveness of a visual tool developed to promote adherence to early mobilization protocol and increase the out-of-bed mobilization rate for adult patients in the intensive care unit: a quality improvement before-and-after study

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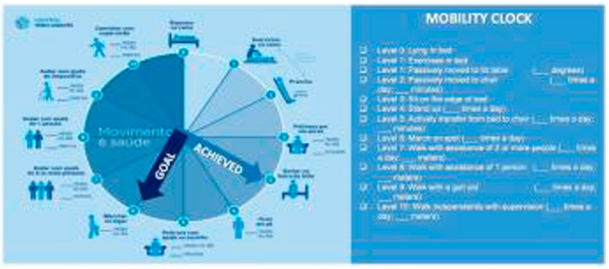
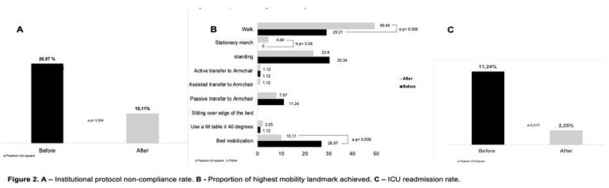
Intensive Care Medicine Experimental 2022, **10(2)**:001273

Introduction: The ABCDE bundle in critical care is recommended to reduce long-term consequences of intensive care unit (ICU) and to promote better outcomes for the patients. Early progressive mobilization, represented as letter "E", despite of had been proposed as a safe strategy in intensive care unit, it is still considered challenging by the inherent ICU barriers and poor adherence to early mobilization protocol. Recently, the letter "F" was incorporated into the bundle, representing the patient's family participation, which can optimize care and patient's recovery. The aim of this study was to evaluate the effectiveness to improve the adherence to the early mobilization protocol after a quality improvement multifaceted strategy which resulted in the development of a specific visual tool, in order to involve in the process beyond the healthcare professionals the patients, and family members.
Methods: A single-center before-after study was conducted using retrospectively data from medical records or hospital electronic databases.
To elaborate the improvement strategy, initially, we performed a summary of the evidence considering out-of-bed mobilization. Posteriorly, we optioned to understand the problem in the perception of the multidisciplinary team to paired it with the data obtained from a meticulous verification of the patient's medical records to elucidate modifiable barriers. The analysis of these activities together verified the importance of improving communication between the characters involved, planning, and individualizing the process considering the specific barriers at the moment, in addition to including the patient and family more actively. Considering these points, a visual tool was developed named as "mobility clock" (Fig. 1) to simultaneously quantifies, informs, and monitors the patient's functional level. This, instead of hours, it displays the different landmarks of mobility based on the ICU mobility scale. An action plan to educate and sensitize the members envolved was designed to promote the use of the tool.



A sample size of 88 patients per period was calculated to verify a reduction by 10% on the non-compliance rate with the institutional early mobilization protocol. Statistical significance was set at 0.05.
Results: After the intervention compared to the previous period was observed a decline in non-compliance with the protocol (10.11% vs. 26.97%, p < 0.004) a higher proportion of patients walking (49.44% vs. 29.21%, p < 0.006) and a decline on ICU readmission rate (2.25% vs. 11.24%; p = 0.017) (Figure 2).



Conclusion: The multifaceted estrategy was effective in increasing adherence to early mobilization protocol and in the out of bed mobilization rate in the adult ICU of a tertiary hospital.

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001316

Assessing recovery from critical illness at a District General Hospital

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Introduction: Critical care survivors are at high risk of a constellation of physical and mental impairments which form the Post-intensive Care Syndrome (PICS). There is no consensus on how best to support survivors. We report our two year experience of providing multi-disciplinary follow up with structured biopsychosocial screening assessments from discharge to three month follow-up.
Methods: Eligible patients discharged from critical care (January 2020–January 2022) underwent physical (Chelsea Critical Care Physical Assessment Tool (CPAx), Grip strength, Incremental Shuttle Walk Test (ISWT) and one minute sit-to-stand test (STS)) and mental (GAD7 for generalised anxiety disorder and PHQ9 for depression) assessments at critical care and hospital discharge and at three month follow up. At the point of hospital discharge survivors were provided with an individualised exercise programme depending on baseline function and acute functional state.
Results: Of 145 survivors, median length of ICU stay was 14 days (IQR 8–22) and hospital stay 27 days (18–42). COVID-19 was the primary diagnosis in 43%. CPAx score increased from 14 (4–31) on critical care discharge to 49 (47–50) at 3 months (P < 0.001). Mean grip strength was 12 kg (10–23) on ICU discharge, 19 kg (12–28) on the ward and 21 kg (15–29) at 3 months (P = 0.02). ISWT increased from 60 m (20–130) to 250 m (90–355) at 3 months (P < 0.001). 1 min STS increased from 12 (8–15) to 20 (14–24) (P < 0.001). Moderate-severe anxiety was reported by 24% on discharge and remained at 23% on follow-up (P = 0.86). Moderate-severe symptoms of depression were reported by 31% at discharge and 25% at 3 months (P = 0.86). None of the outcome measures were significantly different between COVID-19 and the remaining cohort.

	ITU Discharge	Ward Discharge	3 month follow up	P Value
Mean CPAx Score	14 (IQR 4–30)	46 (IQR 43–48)	49 (IQR 47–50)	< 0.001
Mean Grip Strength (kg)	12 (IQR 9–23)	19 (IQR 12–28)	21 (IQR 15–29)	0.02
Median ISWT (metres)		60 (IQR 20–130)	250 (IQR 90–355)	< 0.001
Mean 1 min STS		12 (IQR 8–15)	20 (IQR 14–24)	< 0.001
GAD7 Moderate-Severe (%)		24	23	
PHQ9 Moderate-severe (%)		31	25	

Conclusion: In a cohort of critical care survivors significant improvement in indices of physical function, between ITU and hospital discharge and at 3 months follow-up were observed. Symptoms of anxiety and depression remained emphasising the need for holistic support of this group.

001349

The association between BMI and 90-day mortality among critically ill patients with COVID-19 disease

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Intensive Care Medicine Experimental 2022, **10(2)**:001349

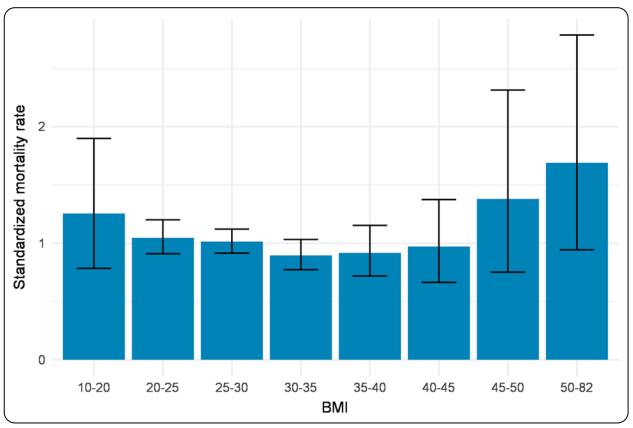
Introduction: Obesity is a risk factor for the development of severe Covid-19 disease [1, 2]. Further, a recent metaanalysis identified that

obesity was an independent risk factor for mortality [3]. Yet, whether obesity is a risk factor for mortality among critically Covid-19 patients is still controversial [4–6]. An obesity paradox has been reported among cohorts of critically ill patients, with underweight and very overweight patients having the highest risks of mortality, and those with mild-moderate obesity having decreased risk when compared to patients of normal weight [7, 8]. A major limitation of previous studies examining the effects of BMI or body weight on survival among Covid-19 patients is the exclusion of underweight subjects or their assignment to a 'normal weight' category.

Objectives: The aim of this study is therefore to examine body mass index (BMI) for its independent association with 90-day mortality among critically ill patients with Covid-19.

Methods: Retrospective, cohort study from the Swedish Intensive Care Registry (SIR) including all patients with confirmed SARS-COV2 infection admitted to ICUs in Sweden from 6 Mar 2020-30 Jun 2021 aged at least 18 years. We examined the effect of BMI on mortality, adjusting for age, sex, SAPS3 score (age excluded), number of comorbidities and timing of ICU admission using multivariable logistic regression.

Results: BMI was registered for 3382 of 6945 patients admitted to ICU because of Covid-19 disease. The 90-day mortality was 28%. After adjusting for confounders, the lowest mortality was seen among those with BMI between 30 and 40. There was a significant interaction between age and BMI (p 0.02).



Conclusion: This study demonstrates the obesity paradox for mortality among critically ill patients with Covid-19. We demonstrate the independent relationship between very low and very high BMI and mortality. Obese patients with a less severe disease may need intensive care due to decreased respiratory reserve. This may explain why a moderate obesity does not lead to an increased mortality. The U-shape and the interaction with age may explain why BMI is found to be a significant predictor in some studies but not in other.

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001352

Psychosocial impact on healthcare professionals due to the COVID-19 pandemic

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Introduction: COVID-19 pandemic has challenged health care professionals both professionally and personally (socially and psychologically). In this study, we evaluate COVID-19 professionals' psychological impact at a third level Spanish Hospital.

Objectives: To analyse personal and professional COVID-19 pandemic impact in Intensive care units healthcare professionals in Spain.

Methods: Epidemiological, transversal, multicentre study executed by a web test from January to April 2021. The COVID-19 impact test included "agree", "disagree" or "don't care" reponses. Participants: ICU doctors and nurses.

Descriptive analysis was expressed as means (standard deviation) for normally distributed quantitative variables, medians (interquartile range) for non-normally distributed quantitative variables, and percentages for qualitative variables. In the univariate analysis chi-square was used for cualitatve variables and T-student for cuantitative variables.

Results: 1500 questionaries, 85% nurses/15% doctors, 81% women, 39 years old (31–47 years) with 5 years of critical patients experience (2 + 14 years). 76% considered COVID-19 pandemic their worse professional moment, 53% were strengthened, 40% improved group work, 58% valued teamwork more highly. 83% felt supported by their colleagues, 52% from their superiors, 34% don't felt social support and 60% don't felt institutional support. 85% were satisfied with the work performed and 84% with teamwork. 20% thought about quiting, 17% needed psicological help ant 5% time off work,

Univariant analysis, with "agree" Reference was:

Worst moment: Doctors 83%, nurses 90% ($p < 0.00$). Institutional support doctors 27%, nurses 17% ($p < 0.00$). Colleagues support: doctors 93%, nurses 98% ($p < 0.00$). Teamwork satisfaction: doctors 91%, nurses 95% ($p > 0.00$). Psychological help: doctors 12%, nurses 18% ($p < 0.05$). Younger people and less experienced considered it as the worst professional moment (39 ± 1 vs 41 ± 9 and 8 ± 8 vs 10 ± 9 years).

Perception: personal improvement and teamwork improvement were well considered in less experienced professionals (8 ± 9 vs 10.53 ± 8 and 10.53 ± 8 vs 10 ± 9 years). Institutional support perception improves with age (43 ± 9 vs 39 ± 10 years); colleagues support better with high experience (8 ± 8 vs 12 ± 9); and social support with age and experience 42 ± 10 vs 37 ± 10 and 10 ± 9 vs 8 ± 8). Quitting job (37.1 ± 9 vs 4 ± 10) and need of psychological help (36 ± 9 vs 40/-10) was higher in young people.

Conclusion: COVD-19 pandemic has had a significative impact in the analysed negative psychosocial aspects, and it was more relevant in nurses, youngers and less experienced.

001362

Inferior vena cava evaluation for fluid responsiveness in intubated patients breathing in pressure support mode: comparison of subcostal and trans-hepatic views

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Introduction: Assessment of the size of the inferior vena cava (IVC) and its change in diameter in response to respiration have been investigated as a tool to screen for severe hypovolemia, predict fluid responsiveness and assess potential intolerance to fluid loading. However, IVC evaluation has been validated in intubated patients ventilated in pressure support mode. On the contrary, the role of IVC assessment in intubated patients in assisted ventilation modality is controversial. Also, IVC visualization from the subcostal (SC) region may not be achievable in many critically ill patients (laparotomy, mediastinal drains, obesity), making the coronal trans-hepatic (TH) approach a possible valid substitute. Moreover, artificial intelligence (AI) software has been implemented in modern ultrasound machines to perform automated real-time calculation, and the use of this software may be clinically helpful.
Methods: We performed a prospective study aimed at comparing the IVC size and its variation according to the respiratory cycle in the two anatomical sites (SC and TH). We nalysed results obtained with both standard M-mode calculation and AI assessment in a population of 23 intensive care unit (ICU) intubated patients during pressure support ventilation. Imaging was obtained by a single experienced operator with *GE Venue Go R2* ultrasound machine model. IVC diameters (min and max) were measured manually by the operator and automatically by the AI. Collapsibility index was measured as (Diameter Max–Min)/Diameter Max. Vital parameters and anthropometric data were also recorded. The Bland–Altman analysis was performed to evaluate the mean bias between measurements and to calculate the limits of agreement (LoA) with confidence interval at 95%.
Results: Of the 23 patients, three patients did not have the TH window (13%). The mean bias with 95% LoA are shown in table 1 and divided according to the method of calculation.

COMPARISON		Measure	VARIABLE	Bias	LoA (lower and upper 95%)	
M-mode SC	M-mode TH	Single	Collapsibility index	1.69%	-18.9	22.2
			IVC Max diameter	0.9 mm	-8.5	10.4
			IVC Min diameter	0.5 mm	-9.3	10.3
AI SC	AI TH	Repeated measures	Collapsibility index	0.8%	-23.6	25.2
			IVC Max diameter	2.0 mm	-5.9	9.9
			IVC Min diameter	1.4 mm	-6.8	9.6

Conclusion: Our investigation has shown that TH and SC visualization of IVC produces results with large LoA on the measured diameters and therefore wide variation in CI. These findings were apparent with both standard M-mode calculation and with assessment performed with the aid of AI, although the mean bias seemed reduced by the use of this new approach. Hence, the two methods of visualization of the IVC are not clinically interchangeable in intubated patients breathing in pressure support mode.

001383

3D electrical impedance tomography (EIT) to measure anterior-posterior distribution of ventilation/perfusion (VQ) ratios in anesthetized pigs

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Intensive Care Medicine Experimental 2022, **10(2)**:001383

Introduction: Efficient gas exchange requires regional matching of ventilation and perfusion (VQ) (1). Electrical impedance tomography (EIT) has been used to study the single-plane (2D) regional distribution of VQ ratios (2–5). A 3D approach to EIT could provide information over a wider area of the lung (6). We describe a method to nalyse the 3D regional distribution of lung VQ mismatch, and to compare its anterior, intermediate, and posterior distribution.
Methods: Ten ventilated (tidal volume 10 ml/kg, RR 15-20, PEEP 5 cmH_2O, FiO_2 1.0) pigs in supine were studied. A 32 electrodes belt in a 2×16-electrode arrangement was used. After instrumentation, EIT data (Swisstom AG, Switzerland) was recorded. Thereafter, 0.2 ml/kg of hypertonic saline 7.5% was injected through a jugular catheter, and EIT data recorded. A 2D pig thorax boundary was extruded into a 3D model using EIDORS (7). Two rows of electrodes were added to the 3D model according to the spacing from the electrodes. A 3D GREIT model was constructed with 3 layers. The posterior layer was centered around the lower plane of electrodes, the anterior layer on the upper electrodes, and central layer in-between, resulting in a $32 \times 32 \times 3$ pixels 3D image. Ventilation and perfusion data were extracted and values lower than 10% of the maximum value were removed. A method for perfusion (5) was adapted to subtract the cardiac phase in 3D by performing the technique on a voxel-by-voxel basis. Manual selection was used to identify the start time of the bolus injection and the location of the heart and lung pixels on the central slice of the 3D image to initialize a gamma fit. To compare ventilation and perfusion impedance images (3) and V/Q ratios were calculated. Layers were divided into ventral and dorsal regions. In this preliminary report, mismatch was identified as a V/Q ratio less than 0.5 or greater than 1.5. Data are reported for each layer and region as a percentage of total mismatch. This is an ongoing report of baseline measurements only. Differences between layers in dorsal and ventral regions nalysed with 2-way ANOVA.
Results: It was possible to reconstruct the 3D distribution of VQ ratios and describe 3 layers in the anterioposterior axis. There were differences in both ventilation and perfusion distribution between layers, however the percentage of mismatch did not differ between layers (Figure 1A). A representative image of ventilation, perfusion and VQ ratio reconstruction is shown in figure 1B for each layer.

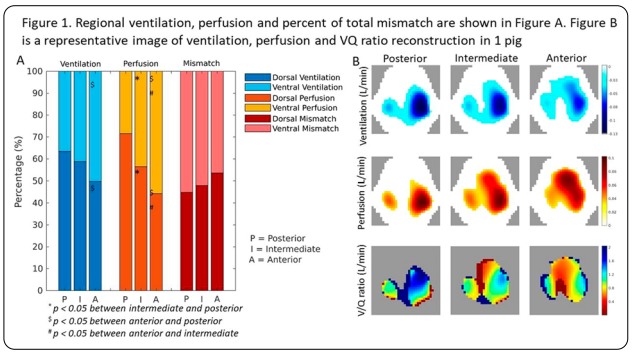

Figure 1. Regional ventilation, perfusion and percent of total mismatch are shown in Figure A. Figure B is a representative image of ventilation, perfusion and VQ ratio reconstruction in 1 pig

Conclusion: Ventilation and perfusion are heterogeneous on the anterioposterior axis. Use of 3D EIT to study VQ ratio distribution might be helpful in pathological and heterogeneous conditions, but further work is required to optimize the technique and compare it with a gold standard.

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Acknowledgements: The authors acknowledge the intramural "Resident Grant" funding at the College of Veterinary Medicine, Cornell University, for providing the funds to perform this study.

001390

Is Gamma (P.1) variant associated with a higher severity in ICU patients with SARS-CoV-2 infection?

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Intensive Care Medicine Experimental 2022, **10(2)**:001390

Introduction: The emergence and rapid spread of SARS-CoV-2 variants have generated alarm worldwide. Several reports have shown that some variants of concern (VOC) can be associated with increased transmissibility [1,2], disease severity [2,3], and a greater probability of admission to the ICU [3].
Most studies about SARS-CoV-2 variants have focused on their epidemiologic impact and the relative risk of being admitted to ICU, but there is scarce information about whether they determine a different clinical evolution after ICU admission.
With the hypothesis that the presence of the Gamma (P.1) variant may play an essential role in the evolution of the patient with severe disease, we decided to study whether Gamma (P.1) lineage was associated with differences in clinical characteristics, severity, and outcomes, compared to ICU patients infected with non-Gamma (P.1) lineage and then the Alpha, Delta and Omicron variants.
Methods: This prospective observational study was carried out at the Clinical Hospital of Pontificia Universidad Católica de Chile in Santiago. The Institutional Ethics Committee approved the study. Patients with laboratory-confirmed SARS-CoV-2 infection admitted to the ICU for invasive mechanical ventilation were consecutively included between March 24, 2021, and Marc 31, 2022. A nasopharyngeal swab (NPS) sample was taken within the first 72 h after ICU admission. Epidemiologic data, clinical characteristics, and outcomes were collected. A search for mutations for Alpha, Gamma, Delta, and Omicron lineages was performed. According to the analysis of variants, patients were grouped as Gamma (P.1) or non-Gamma (non-P.1) lineage, Alpha, Delta, and omicron lineages.
Results: During the study period, 210 critically ill and mechanically ventilated patients with confirmed COVID-19 were consecutively recruited, 122 (58.1%) patients were positive for Gamma (P.1) lineage, 33 (15.7%) had a non-Gamma (non-P.1) lineage and 55 (26.2%) were negative. All patients had a complete follow-up to 30 days. Gamma (P.1) lineage patients became the majority of COVID-19 patients at the end of the study period.
The demographic and clinical characteristics of the patients were similar between the three groups (Table). Regarding the intensity of treatment, there were no differences in use of prone position (64.3% vs. 74.5%, $p=0.25$), for VV-ECMO (9.2% vs. 4.9%, $p=0.41$), or renal replacement therapy 6.3% vs. 9.3%, $p=0.57$), between the Gamma (P.1) lineage and the non-Gamma (non-P.1) lineage groups, respectively.
Conclusion: The main result of this study shows that ventilated patients infected with SARS-CoV-2 Gamma (P.1) exhibited similar clinical course, disease severity, and outcomes compared to those infected with a non-Gamma (non-P.1) SARS-CoV-2 lineage.
Previous studies have shown that dissemination of the Gamma lineage could increase the total number of ICU admissions [3]. However, there is no information about whether this lineage determines a different clinical course or higher mortality for those critically ill patients admitted acutely infected. Our results show that once the patient developed a critical illness due to a SARS-CoV-2 infection, outcomes were similar, regardless of the variant.
It should be noted that the second wave in Chile affected younger people since older people were vaccinated just before its emergence, which may have affected our results. However, there was no difference in the age of patients according to the presence of the Gamma (P.1) lineage.
As mentioned above, our results are only hypothesis-generating but provide vital evidence to help future decision-making on acute patient isolation policies and other issues related to COVID-19 treatment.
In summary, for patients admitted to the ICU requiring mechanical ventilation due to SARS-CoV-2 infection, the Gamma variant (P.1) is not associated with a worse outcome. More extensive studies examining these aspects are required to confirm our findings.

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000256

Evaluation of One-Year Survival and Quality of Life After Intensive Care: A Retrospective 5-Year Study

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Intensive Care Medicine Experimental 2022, **10(2)**:000256

Introduction: The long-term prognosis of the patients with discharged from the Intensive Care Unit (ICU) is of great concern to the patients, their families, health care workers, and health care decision makers.
Objectives: The aim of this study is to examine the one-year survival after discharge, return to working life and ability to do daily work of patients who have been hospitalized in the ICU and then discharged from the hospital.

Methods: This retrospective study was conducted in the Medical ICU. The patients included in the study were patients who were discharged from the hospital after at least 48 h of ICU stay. The information of the patients was obtained from the hospital electronic record system and by contacting the patient or his/her relatives by telephone.
Results: A total of 154 patients were included. The median age was 51 (IQR: 34–68) years and 79 (51%) were male. The most common reasons for ICU admission were acute respiratory failure (18.8%) and sepsis/septic shock (18.2%). The median value for the Charlson comorbidity index was 1 (IQR: 0–2). The median length of ICU stay was 5 (IQR: 4–11) days. One-year mortality was 23.4%. Re-hospitalization in one year was 54.5% and re-admission in the ICU was 20.1%. It was determined that 89.8% of the patients who lived in the first year after discharge performed self-care such as going to the toilet and wearing their own clothes. The rate of patients who did not started working within one year was 63.6%. The median value of the Charlson morbidity index was 2 (IQR: 1–3) in patients with non-survivors within one year, and 0 (IQR: 0–1) in survivors ($P < 0.001$). The median age was 69.50 (IQR: 57–79) in patients with non-survivors within one year, while it was 44 (IQR: 31–65) in survivors ($P < 0.001$).
Conclusion: As a result of this study; It was determined that approximately one-fourth of the patients who were treated in the ICU and were discharged from the hospital died within a year. A total of the 90% patients were able to perform their own self-care while most of the patients had not been started to work within one year. Healthcare workers and heath care authorities should be more carefully about these patient's management.
Keywords: Post-intensive care, Survival, Functional assessment, Mortality, Quality of life

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000117

Development of a novel Early Warning Score for clinical deterioration based on multilevel data

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Intensive Care Medicine Experimental 2022, **10(2)**:000117

Introduction: Early warning scores are widely used to prevent life threatening events in order to improve outcomes. None of them include analytical parameters.
Objectives: To elaborate an score to predict the probability of the deterioration of patients admitted in the ward.
Methods: Observational retrospective research, using the digitalized data of all patients admitted in the ward of Hospital de Galdakao during the year 2019. Deterioration was described as need of critical care unit admission or death.
We analyzed sociodemographic variabilities, comorbidities, previous hospitalizations, vital signs during the hospitalization, analytical parameters and treatments.
A multivariate logistic regression model was used to evaluate the association between all the collected data and deterioration.
A points-based score was developed designating the specific weight of each value included. The risk was categorized in mild, moderate and severe. Statistical significance $p > 0,05$. Software SAS 9.4
Results: 16486 patients were studied, 788 presented an episode of deterioration (4,8%), and 660 died (4% of the total sample, 83.4% of deteriorated patients). 56% of the sample were male, the average age was 67.9 (SD) years, the 76.4% were admitted from the emergency area. The following variables were related to deterioration and included in the score: oxygen saturation (SO_2) $<= 94\% -> = 88\%$ OR 2.3 (IC 1.8–2.9), $SO_2 < 88\%$ OR 12.3 (IC 8.2–18.5); tachycardia, HR > 100 rpm OR 1.9 (IC 1.5–2.4); length of stay between 7–14 days OR 1.6 (IC 1.3–2.1), 15–21 days OR 4.7 (IC 3.3–6.9) or more than 21 days OR 7.7 (IC 5.2–11.5), age 75–85 years OR 1.4 (IC 1.1–1.9) and > 85 years OR 1.9 (IC 1.5–2.6); malignancy OR 2.4 (IC 1.8–3.3) and cerebrovascular disease OR 2.2 (IC 1.5–3.1) at hospital admission; neuroleptic drugs during hospital stay OR 1.8 (IC 1.4–2.3), as well as gastrointestinal prokinetics OR 2.3 (IC 1.5–3.1); hyperkaliemia OR 3.7 (IC 2.3–3.8), decreased prothrombin time OR 2.2 (IC 1.6–2.9), hyperglycemia OR 2.2 (IC 1.6–3.0) and increased levels of creatinine OR 1.9 (IC 1.5–2.6). Predictive value: AUC of 0.8690.
Conclusion: Vital signs, comorbidities, medical treatments and analytical data as oxygen saturation, tachycardia, age, length of stay at hospital, presences of malignancy or cerebrovascular disease, medical treatments as neuroleptic drugs and gastrointestinal pro kinetics, and analytical data as hiperkaliemia, decreased prothrombin time, hyperglicemia and creatinine were related to deterioration. An score that includes all the variables above is presented. The performance of the score was very good.

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Acknowledgements: Health Department of the Basque Government

Health Services Research & Outcome 16

001106

Does D-dimers value at admission predict outcome in severe COVID-19?

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Intensive Care Medicine Experimental 2022, **10(2)**:001106

Introduction: Infection by SARS-Cov2 has a wide clinical range of severity. While the understanding of pathophysiology underlying severe COVID-19 remains poor, thrombotic events in SARS-Cov2 infection have been demonstrated in a significant percentage of severe cases [1]. D-dimer is biomarker for the identification of a thrombotic-state. Several studies have shown altered coagulation in patients with severe COVID-19 [2] and some of them were able to demonstrate its impact on the ICU outcome [3]. Nevertheless, the optimal cutoff D-dimer is not definitely established.
Objectives: This study aims to establish the accuracy of the D-dimer values in predicting the outcome of the patients with ARDS associated to SARS-Cov2.
Methods: All adults ($\geq$ 18 years old), under mechanical ventilation, with COVID-19 (PCR positive) admitted to an ICU from 1st January to 31st December of 2021 were included in the present study. Demographic, clinical, laboratory data from electronic medical records were retrospectively analyzed. The correlation between D-dimer at admission and definitive outcomes in all patients was evaluated and the receiver operating characteristic curve (ROC) was used to determine the accuracy of D-dimer in predicting mortality.
Results: In total, 115 patients were included in this study. The mean age was 67.2 ± 11.3 years. The SAPS II mean value was 34.64 ± 9.99 (survivors) versus 43.77 ± 12.99 (non-survivors) ($p = 0.04$). The in-ICU mortality was 62%. The median admission value of the D-dimer, among the survivors, was 1014 (min. 171–max. 5250) µg/ml versus

1255 (min.254–max. 5250) µg/ml in non-survivors (p = 0,006). The area under the curve of the ROC for D-dimer value determined at ICU admission was 0.597 (95% CI 0.492–0.702, p = 0,082). On Cox proportional hazards regression analysis the odds ratio (OR) was 1.0 (95% CI = 1.0–1.0), when adjusted for age.
Conclusion: D-dimer levels elevation at admission in the ICU in patients with COVID-19 are associated with worst outcome since the median of the D-dimers values at admission were significant different between survivors and non-survivors. However, the accuracy of the D-dimers value was 59,7% (p = 0,082) which was not found to be a significant marker of the prognosis, when adjusted to age. Therefore, in severe COVID19 patients, the D-dimer admission level does not retain a predictive value regarding outcome.

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001244

The impact of interdisciplinarity on training experience and transferability

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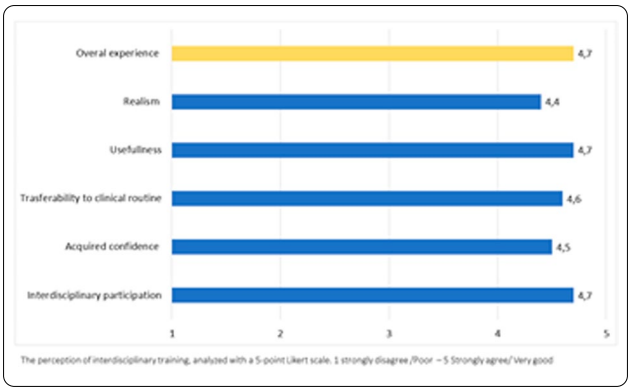
Intensive Care Medicine Experimental 2022, **10(2)**:001244

Introduction: In-hospital emergencies are generally managed by multiple teams. Adding an interdisciplinary approach to the training curriculum of young residents may augment realism and enhance transferability of acquired knowledge to their clinical routine.
Objectives: The aim of this study was to increase learner confidence and clinical impact in the management of common critical care scenarios.
Methods: We organized four 2-h simulation-based training events for residents of the Humanitas Research Hospital. The simulation scenarios focused on clinical emergencies requiring attention from an anesthesiologist or intensivist, in alignment with an interdisciplinary team. Examples included the management of the septic, the dyspneic or the polytrauma patient. After the four 2-h sessions in high fidelity simulation, in which residents of various specialties were mixed to jointly "solve" an unknown clinical case, an electronic survey was distributed. The 10-question survey focused on general satisfaction with the methodology, comprehensive understanding, and transferability to the clinical routine. Responses were measured via the 5-point Likert scale.
Results: 117 residents from eight different disciplines collaborated with twenty-one anesthesiology and intensive care residents to interdisciplinary manage clinical emergencies. The results of the survey revealed a generally high satisfaction with the overall course structure (4.7/5). Specifically, the responders positively appreciate the usefulness (4,7/5), realism (4,4/5) and transferability (4,6/5) to the clinical routine, as an indirect marker of increased confidence (4,5/5) to better manage in-hospital emergencies. The interdisciplinary participation positively impacted the learning experience (4,7/5), with 98% of the residents desired to see more transversal simulation cases integrated in their future training curriculum.



Conclusion: Interdisciplinary training was positively perceived as a tool to transfer acquired skills to the clinical routine. More activities based on simulation should be proposed during the residents training, as augmented transferability may increase quality and safety of patient's care.

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001339

Treatment Escalation Decisions: A retrospective single-centre comparison between two COVID-19 surges

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Intensive Care Medicine Experimental 2022, **10(2)**:001339

Introduction: In the early COVID-19 pandemic, risk prediction tools including the 4C Mortality risk score (4C), the Clinical Frailty Scale (CFS) and age were utilised to determine allocation of Critical Care resources. Decisions on who to admit to Critical Care based solely on clinical scores have received criticism. We explored the influence of these risk prediction tools on treatment escalation decisions by comparing age, CFS and 4C score of patients referred to Critical Care during two surges of the COVID-19 pandemic.
Methods: We retrospectively analysed all referrals to Critical Care at the Royal Liverpool University Hospital during the first (28th March–5th May 2020) and the fifth COVID-19 surge (10th October–21st November 2021). Patients with confirmed or high clinical suspicion of COVID-19 infection were included. Data on age, CFS, C4, escalation status and hospital mortality was collected. We compared three patient subgroups: 1) ward-care as ceiling of treatment, 2) suitable for escalation including mechanical ventilation, but critical care admission not required, and 3) suitable for escalation with admission to Critical Care. Wilcoxon rank and Fisher's exact test were used for cohort comparison.
Results: 203 referrals were analysed: 139 patients (cohort 1) and 64 patients (cohort 2) in the first and fifth surge respectively. There were no significant differences in age, CFS and 4C scores between the two cohorts. 54 (38.8%) patients died during their hospital admission in cohort 1, versus 17 (26.6%) in cohort 2 (p = 0.113). In cohort 1, 55 (39.6%) patients were not suitable for escalation, compared to 19 (29.7%) patients in cohort 2 (p = 0.21). Significantly more females were referred in cohort 2 (45.3% vs. 30.2% in cohort 1, p = 0.041). There were significantly more Critical Care admissions in cohort 2 compared to cohort 1 (44.4% vs. 28.1.%, p = 0.025).
Conclusion: Compared to the first surge, there were less than half the number of referrals to Critical Care in the fifth surge, indicating that fewer patients were expected to require invasive ventilation. 4C, age and CFS did not change significantly between the two surges,

indicating that these risk prediction tools may still influence intensivists' decision-making regarding treatment escalation. Further research is required to confirm these results in larger multi-centre studies.

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Acknowledgements: None to declare

001355

Development and validation of a novel marker of ICU strain—The ICU Activity Index

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Intensive Care Medicine Experimental 2022, **10(2)**:001355

Introduction: The COVID-19 pandemic put unprecented demand on Intensive Care Unit (ICU) resources throughout the world. Patients admitted to ICUs under strain may have worse outcomes than those in ICUs where more resources are available. During 2020 in Melbourne, Australia, The ICU Activity Index was developed as a daily metric to identify sites which might be under strain and the need to transfer patients to another hospital [1]. The relationship between the ICU Activity Index and patient outcomes is unknown.
Objectives: Our aim was to determine whether there was a relationship between in-hospital mortality and the ICU Activity Index (as a marker of overall ICU strain) over the duration of a patient's stay in the ICU.
Methods: Data were extracted for all ICUs contributing to the ANZICS Adult Patient Database and the Critical Health Resources Information System between June 2020 and December 2021. The mean Activity Index for the duration of the patient stay in ICU was calculated by allocating a point for every patient in the ICU with active COVID-19, every patient who required 1:1 critical care nursing, invasive mechanical ventilation, renal replacement therapy or extracorporeal membrane oxygenation, and divided by the total number of open available ICU beds. Information on severity of illness, diagnostic and in-hospital mortality were extracted. Patients admitted for palliative care or organ donation, and readmission episodes to ICU were excluded. Descriptve statistics and mixed effects logistic regression were used to determine the relationship between the Activity Index and outcomes.
Results: Data were available for 254,111 patients admitted to 187 ICUs in Australia and New Zealand. Their mean age was 62 years with 56% men, and 30% receiving mechanical ventilation.
The median (IQR) Activity Index was 0.9 (0.4–1.2) and rose to 1.4 (1.0–1.8) at hospitals in Canberra, Melbourne and Sydney during peak COVID-19 demand from October to December 2021.
Overall in-hospital mortality was 6.8%. After adjusting for baseline severity of illness, frailty, hospital type, size and location, increasing ICU strain indicated by a rising Activity Index, was associated with an increased odds of in-hospital death (adjusted odds ratio 1.37, 95%CI: 1.31–1.48, P < 0.001). This relationship persisted in all subgroups examined and in the absence of COVID-19 demand.
Conclusion: Higher ICU Activity Indices are associated with adverse patient outcomes. The ICU Activity Index may allow quantification and monitoring of ICU strain.

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Acknowledgements: Nil funding

001397

Post Intensive Care Syndrome in COVID-19 ICU survivors: a retrospective cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:001397

Introduction: Up to 12% of patients infected with SARS-CoV-2 require an admission to an intensive care unit (ICU) [1]. Survivors report lasting effects of their ICU stay [2], commonly referred to as "long-COVID". A similar condition, the Post Intensive Care Syndrome (PICS), has been a topic of research for many years.
Objectives: The aim of this study was to investigate whether COVID-19 is an independent risk factors for the development or severity of PICS.
Methods: This retrospective cohort study included critically ill patients (COVID-19 and non-COVID-19) admitted to the post-ICU outpatient clinic at the Department of Anaesthesiology and Operative Intensive Care Medicine (CVK, CCM) at Charité—Universitätsmedizin Berlin. We collected demographic characteristics, severity scores and characteristics of their ICU stay. In the post-ICU outpatient clinic, physical (Timed Up and Go-Test, grip strength), cognitive (MiniCog, Animal-Naming-Test) and psychological (Patient Health Questionnaire-4) tests were performed 90 days after ICU discharge. A PICS was present if at least one test was abnormal [3]. Influencing factors were calculated using a multivariate logistic regression model (PICS yes/no) using COVID (yes/no) and all factors presented in Figure 1. PICS severity was characterised by how many domains were affected and the influence of COVID assessed using linear and logistic regression analysis.
Results: In this study, 95 patients were included (COVID: n = 50; non-COVID: n = 45). Figure 1 shows demographic and clinical characteristics of both groups. 89.5% of all patients had pre-existing conditions. In the multivariant logistic regression, APACHE II at admission and the maximum SOFA score were significantly associated with PICS (OR: 1.1, 95% CI: 1.0–1.2 and OR: 0.8, 95% CI: 0.6–0.9, respectively) while COVID diagnosis was not (OR: 0.3, 95% CI: 0.7–1.4). Figure 2 demonstrates that there was no statistical difference in the PICS severity between COVID and non-COVID patients.

	COVID n = 50	non-COVID n = 45	p - value
Age (y)	59.0 [54.0 - 68.0]	59.0 [42.0 - 74.0]	.650
BMI	29.4 [24.1 - 36.8]	25.1 [22.8 - 26.3]	.001
Charlson-Comobidity-Index	2.0 [1.0 - 4.0]	2.0 [0.0 - 4.0]	.800
APACHE 2, admission	29.0 [24.0 - 35.0]	29.0 [21.0 - 35.0]	.812
SOFA Score, maximum	12.0 [11.0- 13.5]	7.0 [3.0 - 11.0]	.005
ICU length of stay (d)	38.0 [24.5 - 61.5]	22.0 [10.0 - 33.5]	.000
Ventilation duration (d)	32.3 [15.0 - 51.1]	9.4 [2.2 - 20.8]	.000
ECMO, nr. of patients	17 (34.0)	6 (13.3)	.016
Dialysis, nr. of patients	14 (28.0)	11 (24.4)	.651

Values presented as median [Interquartile range] or number (%)

Figure 1. Demographic and clinical characteristics of the patients.

	COVID n = 50	non-COVID n = 45	p - value
PICS	34 (69.4)	27 (60.0)	.341
PICS severity			.598
PICS, 3 domains	4 (8.2)	2 (4.4)	
PICS, 2 domains	10 (20.4)	11 (24.4)	
PICS, 1 domain	20 (40.8)	14 (31.1)	

Values presented as number (%)

Figure 2. Frequency of Post Intensive Care Syndrome (PICS) and its severity by affected domains tested by Pearson's chi-squared test.

Conclusion: COVID-19 was not associated with the development or the severity of PICS.

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001417

Clinical outcomes and characteristics of critically ill patients hospitalized for COVID-19 in a leading hospital in Colombia: A comparison between the third wave and the Omicron wave

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Intensive Care Medicine Experimental 2022, **10(2)**:001417

Introduction: Different variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been identified and producing outbreaks all over the world. Each country was affected in a different way depending on its public policies, risk mitigation measures and vaccination stage. On November 2021, a SARS-CoV-2 variant of concern, Omicron, was identified in South Africa as responsible for a fourth wave of COVID-19, which struck Colombia a few weeks later, despite advances in the national vaccination program. It is essential to understand the characteristics of critically ill patients in the third (Delta variant) and fourth (Omicron) waves, severity and comorbidities, case-mix, resource use and outcomes, because it allows not only a better understanding of the disease, but also of organizational processes that allow greater response capacity in pandemic and regular times.
Objectives: To describe the clinical outcomes, characteristics of critically ill Covid-19 patients in a leading hospital in Colombia, during the two lasted waves, highlighting aspects of case-mix, comorbidities, resource use and outcomes as well as different trends in the delivery of care.
Methods: We assessed ICU patients of a leading hospital recognized for being a hospital with a high level of complexity. All patients had a positive SARS-CoV-2 test result. We compared the third wave (Jun to August 2021) with the last (Omicron) wave (December 2021 to February 2022) in terms of case-mix, resource use, severity scores and comorbidities, and outcomes. Standard descriptive statistics were used.
Results: Our data indicated a total of 454 Covid-19 ICU admissions in the third wave and 145 in the Omicron wave. The mean age increased from 55,59 to 69,59 years in the Omicron wave, with more than 70% of patients older than 65 years old. Patients with a frailty index (MFI) greater than 3 corresponded to 6,98% of patients admitted to the ICU during the third wave, reaching 30,7% more recently. The mean hospital length of stay decreased from 15 to 9 days. We also could see the increase in the Sequential Organ Failure Assessment (SOFA) from 3,7 to 5,32 and in the Simplified acute physiology score 3—SAPS3 (54×60). We also could see the increase in the use of non-invasive ventilation and vasopressors over the last months. Of the 45 patients who had some major immunosuppression factor (organ transplantation, chemotherapy, or malignant hematological diseases), 64.5% died. Data also showed information of ICU performance during the pandemic. We could observe a decreased Standardized Mortality Ratio from 1,74 in the third wave to 1,2 in the omicron wave.
Conclusion: Different characteristics and outcomes were found among critically ill patients in the third wave of Covid-19 and the Omicron wave. Differences found in case-mix can be partly explained by the advance in the vaccination national program over the months, which may result in the fact that more elderly, frail, and immunosuppressed patients prevailed in the latest wave. Despite having more severe patients (with higher SAPS3 and SOFA), the crude mortality rate remained the same. However, there was a significant decrease in standardized mortality rates. This improvement in global performance may be due to some factors, as learning during the first waves, less collapse of the health system and advances in vaccination coverage.

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001429

Long stay in the intensive care unit: Epidemiological and evolutive characteristics and factors associated with mortality

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Intensive Care Medicine Experimental 2022, **10(2)**:001429

Introduction: Despite scientific and technological progress in intensive care units allowing the resolution of serious clinical situations that were previously fatal, some patients are faced to a prolonged stay because of their initial seriousness or because of the morbidities endured in resuscitation environment. Studying the characteristics of these patients would make it possible to identify them early and better control their outcome.
Objectives: To study the epidemiological and evolutive characteristics of patients with long stay in the intensive care unit and the factors associated with mortality in this population
Methods: This is a retrospective study carried out in our anesthesia and intensive care unit. Were included patients hospitalized for a period longer than 14 days between January 2019 and December 2021.
Results: 138 patients were eligible for the study. They represent 18.9% of all hospitalizations during the study period. The sex ratio was 2. The mean age was 46.6 years-old $\pm$ 19.89 with extremes of 1 to 84 years.

The average length of stay was 39.84 days ± 31.71 with extremes of 15 to 191 days. The average duration of mechanical ventilation was 27.24 days ± 22.21. Hypertension and diabetes topped the list of comorbidities with respective percentages of 34.1% and 29.7%. The reasons for admission are dominated by neuropathies and myasthenia in 27.5% of cases, traumatology in 17.4%, intracranial hemorrhage in 15.9%, epilepsy in 10.1% and postoperative care in 10.1%. Morbidities during the stay in intensive care are dominated by ventilator-acquired pneumonia in 85.5% of cases, septic shock in 44.2%, transfusion in 23.2%, catheter-related infection in 18.1%, urinary tract infection in 17.4%, ARDS in 16.7%, pulmonary embolism in 13.8% and the use of renal replacement therapy in 10.8%. Mortality in the study population was 54.3%. The statistical study,as shown in table 1, highlighted the following as factors associated with mortality with a significant difference: advanced age, ASA 2 and 3 status, history of hypertension, diabetes and stroke, reasons for admission such as cerebral ischemia, occurrence of ARDS and septic shock and high APACHE 3 score.

Table 1: Factors associated with mortality

		Deceased (75)	Survivors (63)	p
Age (years)		52.03 ± 19.99	40.16 ± 17.87	**0.000**
ASA	ASA 1	36%(27)	66.66%(42)	**0.001**
	ASA 2	46.66%(35)	26.98%(17)	
	ASA 3	17.33%(13)	6.34%(4)	
Comorbidities	Hypertension	44%	22.22%	**0.006**
	Diabetes	41.33%	15.87%	**0.001**
	Stroke	17.33%	4.76%	**0.019**
Cause of hospitalization	Traumatology	8%	28.57%	0.001
	Cerebral ischemia	14.66%	3.17%	**0.019**
	Septic shock	65.33%	19.04%	**0.000**
	ARDS	24%	7.93%	**0.01**
Duration of mechanical ventilation (days)		28.41 ± 23.98	25.84 ± 19.99	0.5
Length of stay (days)		36.64 ± 29.18	43.65 ± 34.23	0.197
APACHE III score		40.61 ± 25.57	32.27 ± 18.02	**0.031**

Conclusion: This is a particular population at high risk of mortality. If the long stay is unavoidable, the early identification could improve the prognosis and shedule followu-up care.

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001436

Post-ICU Mortality: Knowing our population can help us improve?

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Intensive Care Medicine Experimental 2022, **10(2)**:001436

Introduction: Discharge after critical illness is a complex task. Considerations must be given to patient characteristics, the impact of the disease, the sequelae after Intensive Care Unit (ICU) stay, but also to the location and level of care required after discharge. Knowledge about those at risk of death and complications after ICU stay is still a challenge and not well established in literature.
Objectives: Characterize the patients who died after ICU discharge and identify risk factors for early mortality (< 30 days post-ICU stay).
Methods: Retrospective analysis of ICU survivors who died in the hospital after discharge from the Intensive Care Department of a University Hospital in Portugal, between 1st of January 2019 and 31st of December 2021. Collected data included: demographic characteristics, comorbidities, illness severity and therapeutic intervention (TISS) scores, type of admission, organ support, complications in ICU and status, vital signs and laboratory findings at discharge. Post-ICU nosocomial infection was also recorded.
Results: One hundred fifty-three patients were analyzed, 66% males, with a mean age of 70 ± 14 years and a median clinical frailty scale (CFS) of 4. The mean Charlson Comorbidity Index was 6 ± 2 and the most frequent comorbidities were diabetes mellitus (37,6%) and active cancer in the last 5 years (23,5%). The median ICU stay was 5 (3–12) days. Acute Physiologic and Chronic Health Evaluation (APACHE) II and Simplified Acute Physiology Score (SAPS) II corrected mortality were 35,5% and 22,96%, respectively. 29% of patients were mechanically ventilated (median of 7 day) and 12% have done renal replacement therapy (median of 16 days). As ICU complications, delirium (26%) and nosocomial infection (19,9%) stand out as the most frequent. On discharged day, mean TISS was 30 ± 7 and median Sequential Organ Failure Assessment (SOFA) score was 3 (2–5). In the ward, nosocomial infection was documented in 56,9% of the patients. In univariate analysis, no physiologic variables showed significant association with early mortality, opposite to previous CFS ($p = 0.041$) and post-ICU nosocomial infection ($p = 0.031$).
Conclusion: Early mortality showed a significant association with variables that cannot be modified by the intervention of an intensivist. The question that arises is whether the inclusion of the clinical frailty scale in the initial assessment could result in a decrease of ICU admissions of patients who do not benefit from this level of care.

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001440

The myocardial performance index is a more robust assessment of the septic heart than traditional measures

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INTRODUCTION: Reversible ventricular impairment within 7–10 days from the onset of sepsis occurs from myocyte exposure to inflammatory cytokines, however the exact mechanism for septic cardiomyopathy (SCM) remains unknown1. Increased filling pressures are characteristic as a result of myocardial oedema but echocardiography is limited in its assessment2; ejection fraction is load-dependent and reflects the coupling between LV contractility and afterload3. New measures are therefore needed which reflect myocardial performance in critical illness. Strain, both left ventricular global longitudinal (LVGLS) and right ventricular free wall (RVFWS) are considered less-load dependent and may be imperfect gold standards, limited by the

requirement for good views but have limited data to support their use critical illness4.

Objectives: To determine parameters which may be used to assess ventricular performance in critically ill patients with septic shock by comparison with LVGLS and RVFWS.

Methods: A retrospective analysis of 26 patients with septic shock in whom a transthoracic echocardiogram was undertaken achieving the British Society of Echocardiography minimum dataset5, LVGLS and RVFWS. The myocardial performance index (MPI) was calculated using tissue doppler velocities of the right and left lateral walls6. Demographic and biomarker data were also measured. Groups were defined by median values for LVGLS and RVFWS.

Results: Patients with impaired LV performance assessed by global longitudinal strain demonstrated impaired LV MPI (0.57(0.43–0.71) v 0.39(0.26–0.45), $p < 0.05$) and higher levels of syndecan 758(385–4155) µg/L v 227(196–304) µg/L $p < 0.05$) than those with preserved GLS. Ejection fraction (50.7(31–60)% v 62(48–71)%, $p = 0.11$), troponin-C (212(138–954) ng/L v 1249(194–2668) ng/L, $p = 0.23$) and BNP (12747(1727–23932) ng/L v 15699(3804–25000) ng/L, $p = 0.75$) were not significantly different between groups.

Patients with impaired RVFWS had greater IVC diameters (2.6(2.3–2.8) cm v (2.17(1.7–2.2) cm, $p < 0.05$), reduced tricuspid annular plane systolic excursion (TAPSE) (0.91(0.65–0.99) cm vs (1.53(1.28–1.7) cm, $p < 0.001$) and elevated BNP values (14406(6177–34982) ng/L v 4713(1835–8098), $p < 0.05$) ng/L, Myocardial performance index of the right heart failed to meet significance (0.36(0.22–0.45) v 0.23(0.17–0.31), $p = 0.07$).

Conclusion: The myocardial performance index of the left ventricle demonstrates promise as a echocardiographic parameter in the assessment of SCM and reflects the more difficult to assess LVGLS. Biomarkers were not predictive of left ventricular performance, but BNP values were higher in those with impaired right ventricular performance. This study suggests several surrogate markers which could be adopted to reflect ventricular impairment in critical illness and be used for the future study of SCM.

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001368

Focussed echocardiography in Critical Care – the use of Artificial Intelligence to bridge the Advanced/Expert gap on the ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:001368

Introduction: The use of ultrasound including echocardiography has become ubiquitous in modern critical care practice. Rather than comprehensive examinations, multiple professional societies have advocated focussed transthoracic echocardiography (fTTE) as a core skill for intensivists. Such fTTE examinations tend to prioritise qualitative (rather than quantitative) assessments of the cardiac function and anatomy. More advanced examinations/calculations eg. speckle tracking and strain analysis are often inaccessible to the average intensive care unit for a variety of personnel and logistically reasons.

In other areas of healthcare, the use of Artificial Intelligence and machine learning in image interpretation is gaining momentum. The AI-based software LViVo™ from DiA Imaging Analysis has automated tools to assess both left and right ventricles. The additional information provided includes end-diastolic/systolic area, strain analysis, ejection fraction etc. (Table 1). Most, if not all, of these parameters do not form part of the fTTE competencies.

LV parameters	RV Parameters
End systolic/diastolic area, Stroke volume, Ejection fraction, Global Longitudinal strain, Segmental and Global LV Strain	Fractional area change, End systolic/diastolic area, Free wall strain, TAPSE

Objectives: To assess the feasibility of Artificial Intelligence in the critically ill patients, its value in training as well as a guide to the quality of image obtained in fTTE.

Methods: A retrospective analysis of images obtained from critically ill patients in a tertiary centre who underwent comprehensive TTE examination by specialist operator (highest national TTE qualification). AI-based technology LViVo™ from DiA Imaging Analysis was used to analyse the images obtained.

Results: A total of 50 patients underwent comprehensive TTE examination with 178 study windows obtained. In all patients, some form of apical and/or parasternal windows were obtained to allow for images of sufficient quality to allow for more advanced calculations such as left ventricular outflow tract VTi, EDV/ESV and EF by the expert operator.

The software was able to run a full analysis of 26/50 (52%) and 32/50 (64%) of images for the left and right ventricle respectively, providing parameters shown in table 1. The main reason for inability to perform analysis was poor image quality.

For both ventricles, the software package was able to calculate and provide measures of global longitudinal strain which would otherwise be unobtainable with our established echocardiography analysis package.

Conclusion: The use of fTTE in critical care is becoming well established and all practitioners at this level are trained to obtain the standard apical, parasternal and subcostal windows. There is then an obvious gap in capabilities at an individual and departmental level to achieve more advanced echocardiography skillsets/measurements. Our study has shown that the use of AI technology can play a role in bridging this skill gap.

In addition, given that these AI-powered analyses are often automated and objective, they replace subjective manual or visual analysis and provide a degree of image quality assurance. The additional parameters obtained could then be used to guide patient care.

The main limitation of the study was that it was performed by highly skilled operator. It would be reasonable to assume that less skilled operators might not achieve similar results and hence the ability to interpret and perform the manual assessments on this group of patients might be lower. Secondly, this was a retrospective analysis and images were not obtained with the capabilities/limitations of the software in mind.

Our results show that in critically ill patients, suboptimal images in fTTE windows are not uncommon. It is however feasible to employ AI-based software to help clinicians gain more information from the images obtained in order to improve patient care. Such software will obviously not replace the expert echocardiographer but could potentially help bridge this gap which exists in a considerable number of ICUs. Further work is needed.

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Infection 1

000225

Gender differences in Self-reported Adverse events of patients visiting the emergency department after mRNA COVID-19 vaccination: A retrospective multicenter study

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Intensive Care Medicine Experimental 2022, **10(2)**:000225

Introduction: Previous studies reported a possible association between COVID-19 mRNA vaccination and the risk of myocarditis/pericarditis in young adults male. However, few survey studies on adverse events (AEs) following administration of COVID -19 vaccines found that females reported AEs more frequently than males.
Therefore, we investigated gender differences in self-reported AEs of patients visiting the emergency department after mRNA COVID-19 vaccination
Methods: The patients of AEs after mRNA COVID-19 vaccination COVID-19 vaccination who visited EDs between March 2021 and September 2021 were selected in three EDs. The clinical data and outcomes of these patients were collected by retrospective reviewing medical records.
Results: Among 2487 patients, 881 (35.4%) were male. The number of patients in their 20 s was the highest (36.2% of males, 27.6% of females) ($P < 0.001$). More patients visited the ED for adverse reactions following the first vaccine dose (70.5% vs. 29.5%). Chief complaints were chest pain/discomfort (43.7%), headache (7.6%), allergic response (7.6%) and fever (7.4). Males presented with more chest pain/discomfort than females (51.3% vs. 39.6%) (P < 0.001) A total of 2355 (94.7%) patients were discharged from the ED, and 128 (5.1%) were admitted to the hospital. The admission rate was higher in males than in females (6.7% vs. 4.3%) (p = 003). In admitted patients, infectious disease accounted for the highest rate of admission at 64 (50.0%).
Conclusion: This study shows that most patients regardless gender were discharged from the ED with non-life threatening AEs. However, emergency physicians should take care to differentiate serious AEs in male patients visiting the ED with AEs after mRNA COVID-19 vaccination.

000132

Candida auris in critically ill patients: the experience of a small cohort of patients in a Hellenic Intensive care Unit

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Introduction: Candida auris (C.A.), a newly isolated fungus, presents a global health challenge due to issues related to its identification, ability to transmit and difficulty to treat and eradicate.
Objectives: To record and analyze the clinical characteristics, treatment and outcome of patients with established colonization with or without infection caused by C.A. in a critical care setting. We also investigated the possibility of decolonization as an infection control strategy.
Methods: Retrospective single cohort study from January 2022 and for a 2 month period. Patients' samples were identified via both colony coloring and Vitek2 system. Susceptibility was tested via standard broth microdilution method. After isolation all patients were receiving daily baths with a mixture of tricloxan 0,2% and boric acid 5% in order to facilitate decolonization. Swabs from skin folds were tested on a weekly basis. Pearson correlation was computed to assess linear relationship between variables. 28-day mortality after the diagnosis of C.A. colonization/infection was recorded.
Results: Twelve post-COVID ICU patients (9 males 3 females) with documented colonization with C.A. with or without infection were enrolled. All infectious strains were sensitive to echinocandins and amphoterecin B but resistant to fluconazole. Among patients enrolled, only 2 presented C.A. bloodstream infection (BSI) which did not affect mortality (p = .418). Image 1 presents the body sites from which C.A. was isolated. Table 1 tabulates clinical characteristics of the population enrolled. 6 patients were treated successfully with an echinocandin (BSI, catheter tip, pleural fluid). Significant negative correlation was found between SOFA score at C.A. isolation and survival (r = − .77; p = .003). Mortality at day 28 was 25%. Decolonization after 1 month was feasible in 6 patients (66.7%).

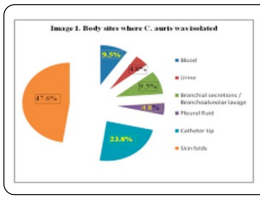

Table 1. Clinical characteristics of patients with colonization / infection with C. Auris (C.A.)

	Mean value	SD
Age (years)	63.42	9.46
Duration of ICU stay prior to colonization (Days)	45.50	45.41
APACHE II on admission	16.33	7.24
SOFA score on admission	6.92	3.48
CHARLSON comorbidity index	2.75	1.86
SOFA score at isolation of C.A.	3.08	2.81
Number of catheters	4.00	0.60
Candida Score	1.83	1.47
Number of sites of C.A. colonization	1.67	0.78

Conclusion: In our cohort of ICU patients C. auris colonization was not associated with increased mortality, probably due to the fact that strains were susceptible to antifungal drugs. SOFA score at the time of yeast isolation correlated with mortality. Our results showed that the implementation of decolonization measures can be effective. Further studies are required in order to elucidate clinical outcomes of infections caused by this newly emerging yeast.

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000180

The impact of haematologyc comorbidity in patients with SARS-CoV-2 infection admitted in the ICU

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Introduction: Patients infected by SARS-CoV-2 who are admitted in the ICU have been shown to carry a high mortality rate, especially in

some risk groups. Some previous comorbidities may pose ICU patients at higher risk of mortality, but the low incidence requires its evaluation trough large series.
Objectives: To evaluate the incidence and the prognosis of patients with previous haematologic malignancy who were admitted in ICU due to SARS-CoV-2 infection.
Methods: An analysis of a cohort study conducted in several ICUs, including ventilated and non-ventilated COVID-19 adult patients between February 6 and December 31, 2021. Continuous variables are reported as number and percentages and categorical variables as median and interquartile range. Primary outcome was all-cause ICU mortality. Comparison was performed using Chi-squared test or Fisher's exact when indicated. Multivariate analysis was performed to detect independent variables associated with mortality. Statistical significance was considered as $p \leq 0.05$.
Results: 5600 adult patients were admitted in the 174 participating ICUs. 70.1% were male, with mean age of 61.6 years old (SD 12.1), APACHE II score of (median) 13 (IQR 10; 17) and SOFA score (median) of 4 (IQR 3; 7) at admission. The most frequent comorbidities were hyperthension 45.6%), obesity (36.8%), diabetes (22.9%), COPD (7.1%), asthma (6.3%), ischemic cardiopathy (6.3%), whereas hematologic malignancy (HM) was present in 3.1% of patients. In the overall population 76.1% required mechanical ventilation (MV), whereas it rose to 84% in patients with HM. In the multivariate analysis, risk factors associated with mortality were age (OR = 12.4; $p < 0.001$), SOFA score (OR = 5.8; $p < 0.001$), MV (OR = 4.8 $p < 0.001$), APACHE II score (OR = 3.9; $p < 0.001$), chronic renal failure (OR = 3.9; $p < 0.001$), immunodepression (OR = 3.5; $p < 0.001$), ischemic cardiopathy (OR = 3.3; $p < 0.001$), and haematologic malignancy (OR = 3; $p = 0.003$). Overall mortality was 29%, and 34.4% in those with MV. Patients with HM showed a mortality rate of 45.9%, and it rose to 50.3% in those requiring MV ($p = 0.007$).
Conclusion: Patients with haematologic malignancies represented a low number of ICU admissions due to SARS-CoV-2 infection. Our results suggest that patients with haematologic malignancies who were mechanically ventilated are in high risk of mortality.

000196

Factors related to the Serious Adverse Events in Patients Visiting the Emergency Department after COVID-19 vaccination

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Introduction: As the number of COVID-19 vaccinations has increased, the number of patients visiting the emergency department (ED) complaining of adverse events (AEs) has also increased. However, studies on AEs in the general population are still insufficient.
Methods: This study was conducted on patients aged 19 or older with AEs that occurred within 28 days after COVID-19 vaccination from March to September 2021. The general characteristics of patients, types of vaccines, types of AEs, types of ED examinations and treatment results from three EDs were examined through retrospective medical records. Serious adverse events (AEs) were defined as any untoward medical events that led to hospital admission.
Results: 3,572 patients visited the ED with AEs within 28 days of COVID-19 vaccination, 69.2% was administered with mRNA vaccines, and the median (IQR) age was 48 (31–63) years. 70.5% in mRNA group and 80.5% in ChAdOx1 group visited the ED after the first dose. In chief complaints, chest pain/discomfort (43.7%) and dyspnea (6.7%) were more in mRNA group, while, fever (15.8%) and headache (14.2%) were more in ChAdOx1 group. Most of patients (93.9%) were discharged from the ED. There was no difference in final diagnosis between admitted patients in both groups, and infectious disease accounted for 49.1% in admitted patients. In multivariate analysis, age $\geq$ 70 years, days from vaccination to ED visit $\geq$ 8 days, fever and dyspnea as chief complaints were higher independent risk factors for serious AEs (OR 27.94, OR 2.55, OR 1.95 and OR 2.18: $p < 0.001$, $p < 0.001$, $p = 0.003$ and $p = 0.003$, respectively).
Conclusion: Most patients who visited the ED with AEs after vaccination were discharged from the ED regardless of the type of vaccine. Emergency physicians need to differentiate serious AEs and consider factors that may require admission in the ED.

000300

Risk factors for mortality of Enterobacter Cloacae associated pneumonia in the critically ill: a 10-year retrospective cohort analysis

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Introduction: *Enterobacter* infections can lead to high mortality. Lungs as portal of entry, in particular, adversely influenced mortality. No study has evaluated *Enterobacter cloacae* associated pneumonia in the critically ill in the past decade.
Objectives: We aim at identifying the predictors for mortality in pneumonia associated with *E. cloacae* and studying the pattern of antibiotic resistance of *E. cloacae* isolates in respiratory specimens.
Methods: All adult patients admitted to the ICU of a regional hospital in Hong Kong during the 10-year period from July 2011 to June 2021 were screened. Patients with *E. cloacae* associated pneumonia were included. Demographics, clinical features, microbiological characteristics, and outcomes were analyzed.
Results: Among 112 patients with *E. cloacae* associated pneumonia, 76 of them (78%) survived at Day 30. Both 30-day survivors and non-survivors required intensive care for about 5 days (5.3 days vs 5.4 days $p = 0.77$). After discharge from the ICU the survivors had prolonged hospital stay (47.0 days vs 19.2 days $p < 0.001$). Carbapenem resistance was more common in *Enterobacter* isolates yielded from non-survivors (19.4% vs 1.3% $p = 0.001$). Multivariate analysis showed that carbapenem resistance and APACHE IV score are independent predictors of 30-day morality. Patients with carbapenem resistant *E. cloacae* (CR-ECL) had a four-fold increase in 30-day mortality ($p = 0.001$).
Conclusion: Carbapenem resistant *E. cloacae* pneumonia result in high mortality. Empirical antibiotic choice remains a difficult clinical decision for intensivists in the presence of antibiotic stewardship. The local prevalence of ESBL- carrying species and the presence of patient's risk factors for CR-ECL are important considerations.

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Acknowledgements: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

000343

Experience of Secondary Bacteraemia with Tocilizumab Among COVID-19 Patients Admitted to a Teaching Hospital Critical Care unit in the North East of England, UK

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Intensive Care Medicine Experimental 2022, **10(2)**:000343

Introduction: IL-6 inhibition is a recognised treatment for COVID-19 pneumonitis. The Coronavirus causes pathological hyper-activation of the immune system with associated elevated inflammatory cytokines. This potentially causes rapid deterioration and increased mortality risk.[1] Tocilizumab, an IL-6 inhibitor aims to suppress this abnormal cytokine storm syndrome.[2] However, associated inherent risks of secondary infections and impact on patient outcomes remain unclear.
Objectives: To determine if critically ill COVID-19 patients receiving Tocilizumab had greater predisposition to develop secondary infections leading to prolonged ICU stay.
To assess reliability of inflammatory markers in superadded infections.
Methods: Retrospective analysis of our tertiary centre COVID-19 ICU patients who received Tocilizumab between 8/1/21 and 24/2/21. Demographics, BMI, co-morbidities and illness severity scores (APACHE II and ICNARC) were collected. Severity scores, length of stay and mortality were compared with patients who had not received Tocilizumab. Corresponding positive microbiology cultures for Tocilizumab patients were extracted. Inflammatory markers, C-Reactive Protein (CRP) and Procalcitonin (PCT), both pre- and post-Tocilizumab were noted. Unpaired t-test with statistical significance $p < 0.05$ was used to compare Tocilizumab and non-Tocilizumab groups.
Results: Of 156 COVID-19 patients admitted to ICU, 37 received Tocilizumab and 119 given standard care including dexamethasone. 56.8% of Tocilizumab patients were males, with average age of 53 years and BMI 33.8. 51.3% patients required mechanical ventilation for a mean 8.5 days.
APACHE II and ICNARC Scores were 14 and 17.1 respectively with no statistical difference between both cohorts.
Tocilizumab patients had an extended ICU stay by an average of 7 days (18.7 days vs. 11.6 days, p-value 0.04) with no mortality benefits (32.4% Tocilizumab vs. 34.5% non-Tocilizumab, p-value 0.82).
Excluding contaminants, 10 positive blood cultures ($n = 5$) were recorded on average 9.1 days into admission. 4 patients (10.8%) had non-Staphylococcal bacteraemia – *Escherichia coli*, *Corynebacterium striatum*, *Anthrobacter* sp., *Enterococcus avium*, *Morganelaa morganii*, *Providencia stuartii*, *Pseudomonas aeruginosa* and 1 *Staphylococcus aureus* bacteraemia.
Their mean age was 61.2 years and only 1 patient survived. Average CRP was lower at 126.0 IU compared to 149.8 IU on admission though higher for mean PCT at 0.54 IU and 0.31 IU respectively.
Conclusion: Tocilizumab was associated with a comparably longer critical care stay without demonstrable survival benefit. Mean age of patients who developed secondary infections was around 8 years higher than the average age of the Tocilizumab cohort, suggesting possible vulnerability amongst elderly. Suppressed CRP levels post-Tocilizumab and a corresponding marginal rise in PCT, made them unreliable markers of infection.
Clinicians must have a high index of suspicion for secondary infections when prescribing Tocilizumab treatment for ICU COVID-19 patients.

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000362

Ten years application of Selective digestive decontamination in a mixed ICU: impact on nosocomial multi-resistant infection, antibiotic consumption and colistin- and tobramicyn colonization

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Intensive Care Medicine Experimental 2022, **10(2)**:000362

Introduction: Selective digestive decontamination (SDD) have been associated with reduced mortality and lower ICU-acquired infection (NI) rates However, long-term effects of SDD in areas where multidrug-resistant Gram-negative bacteria are endemic is of great interest.
Objectives: To prospectively evaluate the impact of SDD application on nosocomial muli-resistant (MR) infections (NI) antibiotic consumption and colonization rates, after 10 years in a mixed ICU.
Methods: This study was conducted in a 30-bed-medical-surgical ICU. All consecutive patients admitted to the ICU from October 1, 2011 to September 30, 2021 expected to require tracheal intubation > 48 h were given SDD (SDD study group) with a 4-day course of intravenous cefotaxime, plus enteral colistin, tobramycin, nystatin in an oropharyngeal paste and in a digestive solution. Oropharyngeal and rectal swabs were obtained on admission and once weekly. We used ENVIN NI criteria. We compared all patients admitted to ICU with ICU NI from October 1, 2010 to September 30, 2011 (non-SDD group) to the SDD study group. A univariate and a multivariate logistic regression analysis were performed. For each one of the NI the incidences per 1000 days of exposure in each cohort and the corresponding relative risks were obtained using the Poisson regression. Statistical significance was $p \leq 0.05$.We analyzed colistin- and tobramycin-resistant colonization and also antibiotic consumption as Defined antibiotics Daily Doses (DDD)/100 ICU days.
Results: Results are shown in Tables 1, 2 and 3. A total of 9715 patients were collected, 692 of them whose received SDD developed NI.Patients with SDD had significantly less Extended Spectrum Beta-lactamase (ESBL), Gram Negative Bacteria Multirresistant (GNB-MR) and *Acinetobacter spp* infections. We had also a significant reduction in ventilator associated pneumonias (VAP), urinary, other secondary bacteremias and multiresistant (MR) NI rates, in SDD group versus non SDD. There was no infection by *Clostridium difficile*. Colistin- resistant colonization was 18,6% and tobramycin-resistant colonization was 26,8% of samples. There was a decrease on the DDD/100 ICU stays after SDD.

Table 1. Characteristics of the patients: overall and according to *SDD* group

	Overall N = 802	No SDD N = 110	SDD N = 692	*p*-value
Age, years	61.2 ± 14.6	59.5 ± 15.8	61.5 ± 14.4	0.197
APACHE II score	21.0 ± 7.8	21.2 ± 7.7	21.0 ± 7.8	0.752
Sex male	525 (67.6)	74 (67.3)	451 (67.6)	0.943
Trauma patients	88 (11.0)	17 (15.4)	71 (10.3)	0.107
Coronary artery disease patients	166 (20.7)	19 (17.3)	147 (21.3)	0.336
Emergency surgery	194 (24.2)	34 (30.9)	160 (23.2)	0.079
Immunosuppression	92 (11.5)	8 (7.3)	84 (12.2)	0.136
Neutropenia	30 (3.8)	3 (2.7)	27 (3.9)	0.787
Immunodepression	6 (0.8)	3 (2.7)	3 (0.4)	0.037
Parenteral nutrition	179 (22.4)	26 (23.6)	153 (22.1)	0.727
Malnutrition	295 (36.8)	34 (30.9)	261 (37.8)	0.166
Diabetes mellitus	74 (9.2)	12 (11.0)	62 (9.0)	0.492
Diabetes mellitus	251 (31.3)	34 (30.9)	217 (31.4)	0.925
COPD	127 (15.8)	9 (8.2)	118 (17.1)	0.018
Renal failure	163 (20.3)	40 (36.4)	123 (17.8)	< .001
Cirrhosis	40 (5.0)	6 (5.5)	34 (4.9)	0.792
Neoplasm	72 (9.0)	10 (9.1)	62 (9.0)	0.964
VAP	296 (36.9)	59 (53.6)	237 (34.2)	< .001
CRB	291 (36.4)	26 (23.6)	265 (38.4)	0.003
Secondary bacteremia	203 (25.4)	31 (28.2)	172 (25.0)	0.472
Urinary infection	211 (26.3)	29 (26.4)	182 (26.3)	0.996
ATB 48 hours before admission	215 (27.7)	28 (25.4)	187 (28.1)	0.563
Death	275 (34.3)	36 (32.7)	239 (34.5)	0.710
Acinetobacter baumannii	20 (2.5)	13 (11.8)	7 (1.0)	< .001
MRSA	16 (2.0)	4 (3.6)	12 (1.7)	0.257
ESBL	190 (23.7)	38 (34.5)	152 (22.0)	0.004
MR Pseudomonas	64 (8.0)	10 (9.1)	54 (7.8)	0.65
MR GNB	39 (4.9)	12 (10.9)	27 (3.9)	0.002
Admission				0.35
Medical	579 (72.3)	79 (71.8)	500 (72.4)	
Scheduled surgery	101 (12.6)	10 (9.1)	91 (13.2)	
Emergency surgery	117 (14.6)	21 (19.1)	96 (13.9)	
Inflammatory response:				0.865
Non sepsis	27 (3.4)	2 (1.8)	25 (3.6)	
Sepsis	174 (21.7)	23 (20.9)	151 (21.8)	
Septic shock	601 (74.9)	85 (77.3)	516 (74.6)	
ICU days	33 (19.8 ; 52)	28 (16 ; 44.8)	34 (20 ; 54)	0.006

Data are means SD and frequencies (%) RRT: Renal replacement therapy; VAP: ventilator associated pneumonia;CRB: Catheter related bacteremia; COPD: chronic obstructive pulmonary disease; MRSA: methicillin resistant Sthaphyloccocus aureus; ESBL: extended spectrum belalactamase; MR: multiresistant; GNB: gram negative bacteria

Table 2. Multivariate logistic regression for regimen of *SDD* (yes/not)

	p-value	BIC	Odd-Ratio (95% CI)
VAP	< .001	617.4	0.480 (0.314,0.733)
Renal failure	< .001	621.1	0.393 (0.250,0.620)
Acinetobacter infections	< .001	628.3	0.098 (0.037,0.260)

SDD: Selective Digestive Decontamination; VAP: ventilator associated pneumonia

Table 3. Incidences per 1,000 days of exposures (Poisson regression with overdispersion)

		SDD			Relative Risk
		No	Yes	*p*-value	(95% CI)
VAP/MV	VAP/1000 days of MV	10.31	3.88	< 0.001	0.376 (0.286 - 0.495)
Urinary infections	Infections/1000 days of catheter	3.79	2.35	0.010	0.620 (0.430 - 0.893)
Bacteremia related to catheter	Bacteremia/1000 days of CVC	3.59	3.55	0.960	0.990 (0.663 - 1.478)
Secondary bacteremia	Bacteremia./1000 ICU days	4.69	1.95	< 0.001	0.416 (0.299 - 0.579)
Multiresistant germs	Multiresistant germs/1000 ICU days	9.59	2.64	< 0.001	0.276 (0.217 – 0.351)

SDD: Selective Digestive Decontamination; VAP: ventilator associated pneumonia; MV: mechanical ventilation.

Conclusion: After ten years application of SDD a significant reduction of infections by ESBL, GNB-MR and *Acinetobacter,* were observed. A significant decrease of VAP, secondary bacteremias, urinary and MRNI rates were also shown. An antibiotic consumption reduction was found after SDD. Low rates of colistin and tobramycin-resistant colonization bacteria were observed.

000369

Outcome of vaccination in the evolution of critical illness due to covid 19

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Intensive Care Medicine Experimental 2022, **10(2)**:000369

Introduction: the main element in the fight against SARS-CoV-2 pandemic has been the development of vaccines against this virus. During the fifth wave that took place last summer, there has been a change in the number and the demographics of the critically ill, probably due to the start of widespread vaccination.
Objectives: To determine vaccination effects in the outcome of patients with critical illness due to COVID-19.
Methods: A Prospective observational study which includes patients admitted to Toledo's Universitary Hospital ICU due to COVID-19 during the fifth wave, between July 2th and September 8th of 2021; this period is defined by the Spanish Health Ministry as the time interval in which the cumulative incidence at 14 days exceeds 150 cases/100.000 habitants. Patients were classified as unvaccinated, partially vaccinated, and fully vaccinated. Demographic and severity variables, and results of the entire cohort were reviewed. Categorical variables were expressed as statistical frequency and percentages and were compared using a χ^2 and Fisher's exact test; continuous variables were expressed as medians and interquartile range (IQR) and were compared using Kruskal–Wallis test. A two-sided level of significance of 5% was used. Data analysis was performed using STATA version 13 ® (StataCorp LCC).
Results: During the study period, 76 patients were admitted to the ICU for SARS-CoV-2 pneumonia; of which 50 (65.8%) were not vaccinated, 11 (14.5%) were partially vaccinated and 15 (19.7%) had a complete vaccination schedule. Among the vaccinated, the vaccine was Comirnaty® (BioNTech/pfizer) in 53.9% (14), Spikevax® (Moderna) in 3.9% (1), Vaxzevria® (AstraZeneca) in 23.1% (6) and COVID -19 Vaccine Janssen® (Janssen) in 19.2% (5). Median age was 51.5 (35.8–60) years in unvaccinated, 62 (44-67) years in partially vaccinated, and 57 (49–68) years in fully vaccinated ($p = 0.045$) (Table 1); in under-55-years group, there were no deceases in those who had any vaccine dose ($p = 0.720$). Unvaccinated patients had less oncohematological disease history (6%) compared to partially vaccinated (45%) and fully vaccinated (13%), ($p = 0.005$). There were no significant statistical differences in complications, length of stay or mortality in ICU between the study groups (Table 2).
Conclusion: During the fifth wave, unvaccinated patients constituted the majority of admissions in ICU, and were younger and had less concohematological disease than the vaccinated ones. Complications, mortality and length of stay in ICU, there were no significant statistical differences between the study groups. The sample size of the study was main limitation, therefore more future studies will be necessary.
Acknowledgements: ICU Department of the Hospital General Universitario de Toledo.

000414

Utility of the biofire-filmarray respiratory panel in the antibiotic treatment of patients with VAP and tracheobronchitis

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Intensive Care Medicine Experimental 2022, **10(2)**:000414

Introduction: Ventilator-associated pneumonia (VAP) is common in hospitalized patient populations in which standard methods frequently fail to identify the infectious etiology due to the polymicrobial nature of respiratory specimens and intrinsic characteristics of these patients. The potential severity of these infections, combined with the inability to clearly identify the causative pathogen, results in the administration of empiric antibiotic agents. The potential for antibiotic titration based on the NP panel result, including discontinuation or de-escalation, resulting in an average saving of antibiotic treatment days, has been revealed.
Objectives: To analyze the usefulness of the Biofire-Filmarray respiratory panel in bronchoaspirate sample to guide the antibiotic treatment in patients diagnosed with pneumonia associated with mechanical ventilation or tracheobronchitis
Methods: A retrospective descriptive study is developed where are analyzed the PCR respiratory panel undergone on bronchoalveolar lavage and aspirates samples of patients diagnosed of VAM and/or tracheobronchitis. The samples were included in the battery of microbiological tests available at the HCV Critical Care Unit in Zamora. Study period January 2020 to December 2021. Demographic data, severity scales, days of MV and tracheostomy, antibiotic treatment received, isolated microorganisms, modifications made based on the results of the respiratory panel in general and by groups of antibiotics are analyzed.
Results: The severity scales at admission showed an APACHE median of 16.5 with a SD ± 8.08 and a SAPS II of 40 with a SD ± 17.33. Of the total sample, the median number of IMV days was 31 days ± 15.54 SD, there were a total of 3 failed extubations, and 53% of the sample ended with tracheotomy. Intra-ICU mortality was 50% of the sample.
A total of 40 bacterial PCRs were performed, of which 62% were negative and the remaining 38% positive. Alonge the days in UCI a 28% turned positive. Of the entire sample the most frequent microorganism was *Pseudomonas aeruginosa* (18%), followed by *S. aureus* (10%), tied with 5% for *K. aerogenes* and *E. cloacae* complex; Isolates of *E. coli* and *H. influenzae* were also found in 2.6%, respectively.
Of the total PCR collected, in 64% of the cases modifications were made based on the results obtained. The most frequent reason was for directed treatment (43%), followed by early suspension and maintenance of empirical antibiotics in 27.5% and 23% respectively. Starting empirical antibiotic therapy was avoided in 5%.
By group of antibiotics, analyzing the carbapenemases administered, we found that in 22% of cases the drug was discontinued early, and in 55% it was well directed. The other group studied was that of oxazolidinones, specifically Linezolid, where the percentage of early suspension was 54.5%.
Conclusion: Analyzing the results we can conclude that the respiratory panel has a great impact in directing or early suspension of antibiotic treatment in the 70.5% of the cases. Futhermore, we maintain empirical treatment in 20% of cases because it was well directed. Whereas Linezolid was the antibiotic with the highest percentage of early suspension, carbapenemases were also suspended (22%) although maintenance was more frequent because of well-directed antibiotic therapy.

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Infection 2

000415

Impact of the COVID-19 pandemic on the incidence of multidrug-resistant bacterial bloodstream infections and change in colonization patterns in a tertiary intensive care unit in Hungary

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Intensive Care Medicine Experimental 2022, **10(2)**:000415

Introduction: Multidrug resistant (MDR) bacteria are responsible for significant mortality and morbidity worldwide particularly among critically ill patients. Host, pathogen and healthcare factors determine clinical outcomes. Recent data shows that COVID-19 pandemic had a profound impact on the frequency and pattern of MDR bacteria in intensive care units.
Objectives: We aimed to evaluate the dynamism of change in the burden of colonising (surveillance sample) and invasive (blood culture) MDR bacteria in an intensive care unit of a tertiary teaching hospital in Hungary, which had a central role in the COVID-19 pandemic.
Methods: We performed a retrospective analysis of prospectively collected microbiological data (surveillance samples and blood cultures) of critically ill patients grouped in sequential cohort as pre-pandemic period (PP), pandemic period non-COVID patients, (PNC) and pandemic period COVID patients (PC). MDR bacteria were defined according to the European Society of Clinical Microbiology and Infectious Diseases definition guideline. We focused on the four most common MDR bacteria: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococcus faecium* (VRE), carbapenem resistant *Pseudomonas* spp (CRP) and multiresistant *Acinetobacter* spp. (MRA). Surveillance samples were collected twice weekly from throat, tracheal aspirate and perineal region, whereas blood samples were taken in the clinical context of invasive infection according to the local protocol.

Frequency of positive surveillance samples were assessed according to patient groups and compared using chi-square test. Rates of bloodstream infections were calculated per 1000 patient days.
Results: In total, 24,229 samples (20,927 surveillance and 3302 blood culture samples) from 2380 patients were analysed and divided into three cohorts (PP 10197/1000, PNC: 8678/1003 PC 5354/377 samples/patients, respectively). A significant increase in resistance rate has been seen in the PC cohort regarding MRSA, MRA and VRE, but not CRP, where a decline was observed (Table 1). Similarly, there has been a significant increase in bacteraemias in the PC cohort involving all of the four MDR bacteria. An increase in bloodstream infections has also been seen in the PNC cohort in MRSA, MRA and VRE, but not in CRP (Table 2).
Table 1. Resistance rates (%) in surveillance samples

	Pre-pandemic cohort (PP) 2018–2019	Pandemic non-COVID-19 cohort (PNC) 2020–2021	Pandemic COVID-19 cohort(PC) 2020–2021
MRSA	9.1	12.5	23.2
MRA	44.2	28.3	70.8
VRE	43.3	45.7	83.8
CRP	36.4	27.4	30.2

Table 2. Bloodstream infections (/1000 patient days)

	PP	PNC	PC
MRSA	0.56	0.71	1.69
MRA	0.73	1.32	7.62
VRE	0.24	0.61	2.82
CRP	1.05	0.71	3.95

Conclusion: In this single centre sequential cohort analysis of microbiological data of critically ill patients before and during COVID-19 pandemic with and without COVID-19 disease, we found a numerical increase in the rate of MRSA, VRE and MRA as colonizing pathogens and bloodstream infections in COVID-19 infected patients. A decrease in resistance rate of CRP has been observed in the study period with a moderate increase of bloodstream infections in the COVID-19 cohort. These observations show the changing spectra of MDR bacteria in ICU, which is affected by the pandemic, and highlight the crucial role of infection prevention & control as well as antibiotic stewardship programs in this setting.

000417

Incidence of multiresistant microorganisms and relationship with broad-spectrum antimicrobial therapy in patients with SARS-COV2 infection admitted to the ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000417

Introduction: The start of the SARS-CoV2 pandemic has changed the way (and sometimes even the place) of work of intensivists, forcing us to adapt to a routine with personal protective equipment, and depriving us of continued contact and exploration of patients, which is so necessary in our profession. The uncertainty in the management of patients with COVID-19 and the appearance in them of an acquired immunodeficiency due to the use of immunosuppressive drugs, has led to the use of more broad-spectrum antimicrobials, and this in turn has led to the appearance (perhaps most frequent) of multiresistant microorganisms (MRM) in our patients.
Objectives: The main objective is to analyze the use of broad-spectrum antimicrobials in patients admitted to the ICU with COVID 19, and its relationship with the appearance of MRM. The number of antimicrobials used, the number of broad-spectrum antimicrobials, and the appearance of multiresistance are analyzed.
Methods: This is a retrospective descriptive study. Data were extracted from the 670 patients admitted to our Intensive Care Unit (with a polyvalent profile), belonging to a tertiary care hospital. The data was collected from the start of the SARS-CoV2 pandemic until November 2021. The variables analyzed were: presence of MMR (in the form of infection or colonization), number of broad-spectrum antimicrobials used, days of stay in the ICU, days of invasive mechanical ventilation, previous comorbidities of the patients (diabetes mellitus, arterial hypertension, disease chronic obstructive pulmonary disease (COPD), ischemic heart disease, obesity, obstructive sleep apnea (OSA) and dyslipidemia), and severity scales (APACHE II).
Results: The mean age of the patients analyzed was 59 years (± 13.12). The mean stay in the ICU was 19.74 days (± 22.8), and the mean hospital stay was 32.34 days (± 31.8). Of the patients admitted to the ICU, 83.4% required mechanical ventilation. The mean value of the APACHE II scale was 10.74 (± 4.9). 72.4% of all patients died. Of the patients who presented infection or colonization by MMR, 47.85% died. A rate of 756.34 days of antimicrobials was observed for every 1000 days of stay. 3.6% of the patients did not receive any antimicrobial during their ICU stay, while 77.5% of the total received 5 or more antimicrobials. 4.9% of the patients who received antimicrobial therapy did not receive any broad-spectrum antimicrobial, while 90.7% of this group of patients received 5 or more broad-spectrum. Of the total number of patients, MMR appeared in 20%, in the form of infection (17.9%) or colonization (82.1%). Of the patients who received two or more broad-spectrum antimicrobials, 39.2% presented MMR, and only in 1.5% of the cases, the appearance of multiresistant was associated in patients who had only been administered one broad-spectrum antimicrobial. In the patients in whom no broad-spectrum antimicrobial was used, no appearance of multiresistance was observed. Among the types of MMR, the most frequent were ESBL enterobacteria (65.78% of all patients with MMR), followed by multi-resistant gram-negative bacilli (14.35%), producers of metallo-beta-lactamases (11%) and multi-resistant Pseudomonas (7). %). Methicillin-resistant S. aureus (MRSA) was isolated in 1.87%.
Conclusion: It is well known that the appearance of MMR in Intensive Care Units is due to the combination of multiple factors: selective antibiotic pressure, compromise of the patient's immune system, increased exposure time to antimicrobials in more severe patients, increased care pressure and the nurse/patient ratio… Undoubtedly, the adequate use of antimicrobials with the help of the Antibiotic Use Optimization Programs, the active search for patients colonized by MMR and the experience that is being acquired in the treatment of critically ill patients due to severe SARS-CoV2 infection, will be elements to take into account to try to improve these figures in coming years.

000433

The Phenotype of Covid-19 Respiratory Failure in Thai Patients: A Single-Center Retrospective Study

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Intensive Care Medicine Experimental 2022, **10(2)**:000433

Introduction: Clinical heterogeneity was observed among COVID-19 patients with acute respiratory distress syndrome (CARDS). The heterogeneity of disease was contributed to different clinical progression, responses to treatment, and mortality.
Objectives: We aim to study the phenotype and associated mortality of COVID-19 respiratory failure in Thai patients.
Methods: We conducted a single-center, retrospective observational study. The data were collected in CARDS who received an invasive mechanical ventilator in ICU. Patient-related data were collected at

admission before the onset of respiratory failure. The main features include demographics data, SOFA score, laboratory, CXR severity score, treatment during hospitalization, and the following data at the onset of respiratory failure during invasive mechanical ventilator. We also collected patients' status at 28-day, in-hospital complications, and ventilator-free days at 28-day after intubation. The latent profile analysis was performed to identify distinct phenotypes. After identifying phenotypes, characteristics and clinical outcomes were compared between phenotypes. The primary outcome was the phenotype and associated mortality of COVID-19 respiratory. Secondary outcomes include characteristics of phenotype, ventilator-free days, response to treatment, and complications in each phenotype.

Results: A total of 80 patients with CARDS met inclusion criteria and underwent latent profile analysis. From the best fitting model, we can divide the study cohort into 2 classes by using 3 variables (CRP, LDH, and NLR). In class 2, we found that SpO2 was lower than in class 1 (mean [SD] SpO_2, 86[12] vs 94[7] %; $p < .01$). Moreover, class 2 had a higher mean [SD] SOFA score (3 [1] vs 2 [1]; $p = .01$), the median of D-dimer (917 [IQR 521–1847] vs 532 [IQR 358–933] ng/mlFEU; $p < .01$), and CXR severity scores (10 [IQR 8–10] vs 3[IQR 1–6]; $p < .01$). Class 2 showed a significant reduction in inflammatory markers and CXR severity scores. There was no significant difference between class 2 and class 1 in mortality and ventilator-free day.

Conclusion: The COVID-19 ARDS could be categorized into two classes. Both classes had different characteristics and treatment responses in terms of biomarkers but no difference in mortality and ventilator-free day.

000456

Characteristics of invasive fungal infection and its relationship with the appearance of multiresistant microorganisms in patients admitted for SARS-CoV2 pneumonia in the ICU

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Introduction: The SARS-CoV2 pandemic has led to a change in the profile of patients admitted to Intensive Care Units during 2020.
The conjunction in these patients of high severity and complexity, the more frequent use of broad-spectrum antimicrobials, and the addition of immunosuppressive drugs in the treatment (apart from other factors intrinsically present in ICU patients, such as venous catheters or parenteral nutrition), may have led to a high incidence of fungal infection in these patients.
Objectives: The main objective is to determine the frequency of invasive fungal infection (IFI) in patients admitted to our unit with SARS-CoV2 pneumonia. In addition, the relationship of these infections with the appearance of multiresistant microorganisms (MRM) and the use of broad-spectrum antimicrobials was studied. Secondary variables were analyzed: days of mechanical ventilation, severity at admission defined by the APACHE II scale, mortality associated with previous comorbidities.
IFI was defined as the appearance of invasive candidiasis (candidemia or infection with multi-organ involvement), and invasive aspergillosis (API).
Methods: This is a retrospective descriptive study. Data were extracted from the 670 patients admitted to our Intensive Care Unit (multipurpose profile), belonging to a tertiary care hospital, since the start of the COVID-19 pandemic.
The variables analyzed were: age, days of stay in the ICU, APACHE II, need for invasive mechanical ventilation, death data, and the relationship of IFI with the use of broad-spectrum antimicrobials and with the appearance of multi-resistant microorganisms (MRM).
Results: The mean age of the patients was 59 years ($\pm$13.12), the mean ICU stay was 19 days ($\pm$22.79), and the mean hospital stay was 32.34 days ($\pm$31.80). The mean severity score, measured by the APACHE II scale, was 11 $\pm$ 5. Invasive mechanical ventilation was required in 75.7% of the patients. 27.6% of all admitted patients died.
In our series of patients, fungal colonization appeared in 31.4%, with IFI presenting in 20.9% of the total. Among the patients who presented IFI, 75.6% did so in the form of candidemia, and 24.4% in the form of API. Of the total number of patients, 0.6% presented concomitant candidemia and invasive pulmonary aspergillosis. Of the total number of patients with IFI, 12% also had MRM infection. All patients who presented IFI were under broad-spectrum antimicrobial treatment (at least 2 or more of them).
The comorbidities most frequently associated with the presence of IFI were arterial hypertension and obesity. Among the patients who presented invasive fungal infection, the mean stay was 35.75 days $\pm$ 23.18, the mean APACHE II score was 13 $\pm$ 6. All patients with IFI received invasive mechanical ventilation, and in this group, mortality was 62.63%.
Conclusion: Invasive fungal infection is a serious problem in Intensive Care Units, which mainly determines an increase in the days of stay in the ICU. In our series, we observed that the severity of the patients, measured by the APACHE II score, did not differ significantly between the patients who developed IFI compared to those who did not.
During the SARS-CoV2 pandemic, a slightly higher incidence of IFI was identified in our unit than had been described in the same period in previous years, which may be due to longer stays, use of broad-spectrum antimicrobials, immunosuppressive drugs… In critically ill patients admitted to Intensive Care Units, early identification of IFI is complex, but it is essential to start treatment as soon as possible, being a variable that has been associated with a better prognosis and greater survival.
Undoubtedly, the treatment of patients with fungal infection in the context of severe SARS-CoV2 infection is a challenge that will continue to require our dedication to face it successfully.

000487

Clinical profile of first vaccinated patients admitted in ICU

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Introduction: Vaccination has undoubtedly meant a before and after in the activity of the ICUs, noting a drastic decrease in ICU admissions. This has meant a change in the clinical profile of the patient who was previously admitted to the ICU due to severe SARS CoV2 pneumonia.
Objectives: The objective of the study is to describe the characteristics of the first patients with a complete vaccination regimen admitted to the ICU.
Methods: Multicenter descriptive study performed in seven intensive care units (ICU) from Andalusian, in the south of Spain. Consecutive critically ill patients with confirmed SARS-CoV2 pneumonia despite have received complete vaccination admitted in ICU were included. Time of study was 2 months in post vaccination COVID time.
Variables analyzed were demographic characteristics and comorbidities. Descriptive statistical analysis was applied using absolute frequencies for qualitative variables and mean with standard deviation (SD) when appropriate.
Results: 35 patients were included during the time of study, most of them were admitted in ICU three weeks after receiving the last dose of vaccine. 11 (31,4%) were admitted in ICU between the first 21 days after vaccine administration. 26 patients (74,28%) had a known

immunocompromised state. Table 1 shows clinical characteristics of patients.

Demographic characteristics 35 vaccinated patients	
Age (years)	**64 (44–84)**
Gender: Male/Female	28 (80%)/7 (20%)
Comorbidities	
Any comorbidity	33 (94,28%)
Hypertension/Heart disease/Respiratory disease/COPD	21 (60%)/9(25,7%)/11 (31,4%)/3(8,6%)
Chronic kidney disease	7 (20%)
Immunosuppression (malignancy, transplantation status, or receipt of immunosuppressive treatment)	10 (28,57%)
Haematological disease	6 (17,1%)
Neurologic disease	2 (5,7%)
Cirrhosis	3 (8,6%)

Conclusion: Most vaccinated patients admitted to the ICU had some comorbidity, an more than third of patients had previous respiratory disease.
Covid 19 post vaccination time shows a new profile of patients with SARS-CoV2 in ICU: immunocompromised patients, the most effective diagnostic and therapeutic strategies must be discussed.

000500

Invasive pulmonary aspergillosis in patients with severe COVID-19 pneumonia

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Intensive Care Medicine Experimental 2022, **10(2)**:000500

Introduction: Patients with severe COVID-19 pneumonia (SCN) are at risk of secondary infections, including COVID-19 Associated Pulmonary Aspergillosis (CAPA).
Objectives: CAPA analysis in patients with SCN admitted to our ICU.
Methods: A retrospective descriptive analysis of CAPA in patients with SCN admitted to our ICU from March 14, 2020 to June 25, 2021. The diagnosis of CAPA was made according to the 2020 ECMM/ISHAM consensus criteria (1). Its incidence, time of appearance respect to ICU admission, diagnosis, Aspergillus species that produces it, treatment and mortality are analyzed.
Results: During the study period, 203 patients were admitted to our ICU with SCN, of whom 157 (77.34%) required invasive mechanical ventilation (IMV), with CAPA diagnosed in 27/157 (17.2%). No case was diagnosed in patients without IMV. The mean time from ICU admission to infection was 9 days (95% CI 7.6–10.4). Fiberoptic bronchoscopy (FBC) was performed on 12/27 (44.44%), with positive BAL in 11 (40.74%) [6/11 culture (54.55%) and 9/11 (81.82%) galactomannan (GM)], not being able to obtain BAL in one patient, resulting in this positive BAS. In the 15 patients in whom FBC was not performed, 12/27 (44.44%) were diagnosed by BAS culture (one of them also with positive blood GM) and in 3 (11.11%) the only diagnostic test positive was GM in serum. In 18 (66.66%) the Aspergillus species was identified: in 9 (50%) *A. fumigatus* was isolated, in 3 (16.67%) *A. terreus*, in 2 (18.18%) *A. niger* and in 4 (22.22%) *A. fumigatus* with *A. terreus*. Received antifungal treatment 26 patients (96.3%); this was started empirically in 17 (65.38%) and directed (by microbiology or GM) in 9 (34.62%). The time from the suspicion of infection to the start of the antifungal treatment was 2.65 days (95% CI 1.22–4.08), starting in the first 24 h in 16 patients (61.54%). Received isavuconazole 17 (65.38%) patients, liposomal amphotericin B 14 (53.85%), voriconazole 8 (30.77%) and anidulafungin 2 (7.7%), receiving combined treatment 13 patients (50%), being the most common combination isavuconazole with liposomal amphotericin B [9 (34.62%)]. Fourteen patients (51.85%) died, all in the ICU, including the one who did not receive treatment.
Conclusion: In our ICU, the incidence of CAPA in patients with SCN who required IMV was 17.2%. The time from admission to the ICU to infection was 9 days (95% CI 7.6–10.4). Received antifungal treatment 26 patients (96.3%), starting this empirically in 65.38%. Mortality was 51.85%.

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000515

Candida infection and antifungal prophylaxis in patients receiving mechanical circulatory support and veno-arterial extra-corporeal membrane oxygenation

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Intensive Care Medicine Experimental 2022, **10(2)**:000515

Introduction: Candida infection is a cause of mortality and morbidity among the most unwell patients in intensive care but the evidence of benefit of antifungal prophylaxis is limited. International guidelines recommend the use of antifungal prophylaxis in high risk mechanical circulatory support (MCS) patients but it is unclear if these apply to patients supported with veno-arterial extracorporeal membrane oxygenation (VA-ECMO).
Objectives: We sought to compare the rate of clinically significant fungal infection among patients receiving VA-ECMO versus another form of MCS.
Methods: A retrospective analysis of all patients receiving MCS or VA-ECMO in a single specialised centre in the UK over a 5 year period. Clinically significant infection was defined as Candida species isolated from blood culture or a site of significance (superficial or tracheal swabs excluded) within 0 and 8 weeks of initiation of support. Use of antifungal prophylaxis, type of MCS (right, left or bi-ventricular assist device), and survival was recorded. Byars method was used to determine confidence intervals for the rate of fungal infection per implantation, and mid-P exact method was used to compare rates.
Results: Over a 5 year period, 173 patients received MCS and 204 patients received VA-ECMO. The rate of Candida infection among MCS patients was 2.3% infections per implantation (1.6–2.7%, 95% confidence interval), with 75% of infected patients having received antifungal prophylaxis (as per institutional guidelines). The rate of Candida infection per VA-ECMO implant was 4.9% (4.0–5.3%), with 20% of these infected patients having received antifungal prophylaxis. The rate ratio was 2.12 (95% confidence interval: 0.68–7.8). Mortality for patients with fungal infection was 89% for VA-ECMO and 25% for other types of support.
Conclusion: Within our cohort, there is a higher rate of clinically significant Candida infection in patients receiving VA-ECMO when compared to patients receiving MCS. To conclusively determine the benefit of antifungal prophylaxis in patients receiving VA-ECMO, a prospective trial is indicated. Although patients requiring MCS have different characteristics and clinical trajectories to those requiring VA-ECMO, our results suggest that antifungal prophylaxis may be indicated in specific groups of patients receiving VA-ECMO.

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000526

Risk Factors associated with *Candida auris* candidaemia: Observational study from a Tertiary Care Indian Intensive Care Unit (ICU)

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Intensive Care Medicine Experimental 2022, **10(2)**:000526

Introduction: Infection caused by *Candida auris* has emerged as a vital challenge in the treatment of critically ill patients in India. The major concerns are outbreak potential, multi-drug resistance and associated high mortality. The present study is an observational trial on finding the risk factors associated with Candida Auris infection.
Objectives: Risk factors for developement of *Candida auris* in Critically ill patients.
Methods: The study is ongoing. Its an prospective observational study conducted in a tertiary care hospital in India. We have collected data from 1st January 2020 till 31st July 2021. Patients who were admitted to ICU and stayed for atleast 48 h were included in this trial. The control group was a population from the same period who did not grow *Candida auris* in blood and case was the group which grew candida auris from blood. The rest were excluded from analysis. The clinical data of candidaemia cases due to *C. auris* and other Candida species were compared to determine significant risk factors associated with *C. auris* infection.
Results: Total 1456 patients were screened. 28 grew *Candida auris* from blood culture and 68 grew other candida species from blood culture. The risk factor significantly associted with development of *Candida auris* bacteremia was severity of ill defined by APACHE II which was median 27.50 (24.00–31.00) in *Candida auris* group vs 22.00 (18.00–28.00) in control group (p value < 0.01). The other risk factor significantly higher in *Candida auris* was length of stay 4.00 (2.00–8.00) days in control group while 9.00 (3.00–21.00) in *Candia auris* group (p value < 0.01).
Conclusion: APACHE II and Length of stay were significantly higher risk factors for development of Cadida auris infection in critically ill opatients in Indian population.

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Acknowledgements: No Grants

000531

International Survey on Antibiotic Dosing and Monitoring in Adult Intensive Care Units

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Introduction: The last international survey of antibiotic dosing and monitoring in intensive care units was conducted in 2015 (ADMIN-ICU), (1) and since this time, the literature describing alternative antibiotic dosing strategies has grown and therapeutic drug monitoring and dosing software are now considered more readily available to clinicians. (2–4) Therefore, an up-to-date survey that describes contemporary practice is justified.
Objectives: The aim of this study was to survey a large cross-section of clinicians working in ICUs worldwide to describe contemporary practices in dosing, administration and monitoring of commonly prescribed antibiotics. Additionally, we aimed to compare our findings to both the ADMIN-ICU results and contemporary guidelines and literature.
Methods: An online survey inclusive of clinical vignettes was developed and distributed internationally to obtain information on contemporary practices used in the dosing, administration and monitoring of vancomycin, piperacillin/tazobactam, meropenem and aminoglycosides for critically ill patients.
Results: A total of 538 respondents from 409 hospitals in 45 countries completed the survey, with 60% doctors and 27% pharmacists. Most respondents had access to antibiotic dosing guidelines and 48% had access to guidelines for therapeutic drug monitoring. Vancomycin loading doses were used by 86% of respondents at a median (IQR) dose of 25 (19–25) mg/kg for intermittent dosing. In a 200 kg obese patient scenario, the median (IQR) loading dose administered was 12.5 (10–15) mg/kg. Piperacillin/tazobactam and meropenem were most frequently administered as an extended infusion (42% and 51% respectively). Aminoglycosides were most often administered as a once daily infusion (85%) over 30–60 min, with gentamicin the preferred aminoglycoside (47%). Gentamicin was generally dosed according to actual body weight at a median (IQR) dose of 5 (4–7) mg/kg. Therapeutic drug monitoring was used by 90%, 81%, 46%, and 43% of respondents for vancomycin, aminoglycosides, piperacillin/tazobactam and meropenem respectively. Respondents most often targeted a trough above the minimum inhibitory concentration for beta-lactams, a peak target for aminoglycosides, and trough target of 15–20 mg/L for vancomycin to guide therapy.
Conclusion: Overall, we observed large variation in practice, however our results generally aligned with contemporary evidence and guidelines. (5–7) We observed numerous changes in practice over the last 8-years, including increased loading dose use, and a notable increase in beta-lactam therapeutic drug monitoring and administration of prolonged infusions.

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Acknowledgements: Jason Roberts would like to recognize funding from the Australian National Health and Medical Research Council for a Centre of Research Excellence (APP2007007) and a Practitioner Fellowship (APP2009736). Paul Williams would like to recognize Clinician Researcher Fellowship funding from Sunshine Coast Hospital and Health Service Study Education Research Trust Fund (SERTF) and Wishlist.

000537

COVID-19 vaccine effectiveness against mortality and invasive mechanical ventilation requirement in Tamaulipas, Mexico: Regression Discontinuity Design Study

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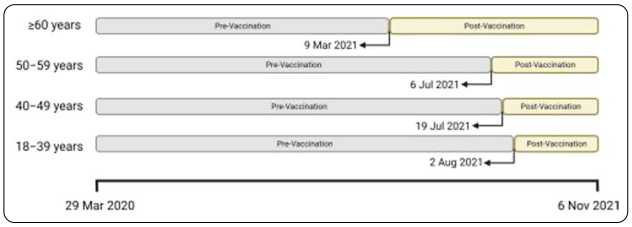
Intensive Care Medicine Experimental 2022, **10(2)**:000537

Introduction: Vaccination against COVID-19 has been one of the most important strategies to diminish the impact of the pandemic, with important reductions in COVID-19 mortality and infection rates (1), while also allowing less stringent non-pharmacological interventions to prevent contagion (i.e., less lockdowns) that allow economic and social activities (2). In Mexico, COVID-19 vaccination has been delivered to priority groups. Healthcare personnel were the first to be vaccinated, followed by age-stratified groups. Due to the particularities of Mexico and its health system, vaccination has the potential to have a greater impact to limit the impact on the pandemic than non-pharmacological population interventions alone (3).
Objectives: To evaluate effectiveness of a state-wide COVID-19 vaccination program in Tamaulipas, Mexico against mortality and invasive mechanical ventilation (IMV) requirement.
Methods: In this retrospective observational study, a regression discontinuity design was applied to evaluate effectiveness of the state-wide COVID-19 vaccination program in Tamaulipas, Mexico against adverse outcomes in hospitalized patients. Adult patients captured by the COVID-19 Epidemiological Surveillance System who were hospitalized for suspected COVID-19 and tested positive for SARS-CoV-2 between 29 March 2020 and 6 November 2021 were included. Exclusion criteria were pregnant women and patients < 18 years since the earlier had varying vaccination periods in Tamaulipas, whereas vaccination for children and adolescents against COVID-19 was not available in Tamaulipas throughout the study period. Patients who tested positive for SARS-CoV-2 ≥ 14 days after the last day of the vaccination week when the vaccination scheme was completed were included in the post-vaccination period (Figure 1). The pre- and post-vaccination periods were the main exposures.



The evaluated outcomes were 30-day mortality and IMV. Cox regression models were built to evaluate 30-day mortality and logistic regression models, for IMV. All models were adjusted for age, sex, comorbidities, and time from symptom onset to hospitalization.
Results: Patients included for analysis (n = 12376) had a mean age of 58.2 (SD:15.9) years and 56.4% (n = 6976) were women. The most frequent comorbidities were hypertension (45.5%), diabetes (39.6%), and obesity (24.9%). Median time from symptom onset to hospitalization was 5.6 (SD:4.1) days. ICU admission occurred in 635 (5.1%) patients, 971 (7.8%) required IMV, and 46% (n = 5694) died. According to exposure groups, 2903 (23.5%) were included in the post-vaccination period and 9473 (76.5%) tested positive in the pre-vaccination period. Intubation (8.5%, n = 808 vs 5.6%, n = 163) and mortality (46.6%, n = 4416 vs 44%, n = 1278) rates were higher in the pre-vaccination period. After adjusting for confounders, patients in the post-vaccination period had a lower risk of 30-day mortality (aHR = 0.80, 95%CI: 0.75–0.86, p < 0.0001) and IMV (aOR = 0.64, 95%CI: 0.54–0.76, p < 0.0001).
Conclusion: The COVID-19 vaccination program in Tamaulipas, Mexico likely reduced 30-day mortality rates and IMV requirement in patients requiring hospitalization.

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Infection 3

000540

Changes in the healthcare profile of COVID patients throughout the pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000540

Introduction: Since the beginning of the SARS-19 virus pandemic, variants of the same have appeared and have changed the epidemiology of the infection. Our objective was to analyze whether these

changes have been reflected in the profile of our patients and the healthcare pressure in the ICU.
Methods: Observational study without intervention. Analysis of patients included in the COVID registry of our Unit. Our admission criteria were restrictive in the first wave but from the second wave they remain unchanged until now (Pprotocol includes dexamethasone, LMWH and in cases with elevated IL-6, Tozilizumab. Patients or their close signed the IC for inclusion in this registry. Data are shown as mean (SD), median (interquartile range) or n(%). We performed a univariate analysis using U-Mann Whitney, Kruskal-wallis and Chi-square tests.
Results: We registered 448 patients. Fifty five (12.3%) patients did not suffer from COVID disease but had to be isolated for a PCR test positive to the virus. During the first 5 waves, the percentage of these cases was 8.34% but in the 6th it increased to 29.23%. For the analysis of the results we will only include those patients who were admitted for COVID disease.
Mean number of admissions per wave was 1.02 cases/day in the 1st, 0.62 in the 2nd, 1.15 in the 3rd, 0.38 in the 4th, 0.91 in the 5th and 0.59 in the 6th (n = 41, 137, 79, 86, 102 and 77 respectively).
Percentage of unvaccinated patients was 74.1% (82.42 in the 5th wave and 60.87 in the 6th wave). Mean age decreased progressively but increased again in the 6th wave (1st: 62.4 + − 14.7 years; 2nd: 62.8 + − 13.5; 3rd: 61.7 + − 10.5; 4th: 55.8 + − 14.6; 5th: 51.4 + − 15.3 and 6th: 60.5 + − 13.5; $p < 0.05$) as well as the percentage of immunocompromised patients (17.1% in the 6th, all of them with a complete vaccination registered).
Need for MV remained stable until the 6th wave, when decreased discreetly (95.2% in 1st, 60% in 2nd, 60.44% in 3rd, 48.48% in 4th, 58.7% in 5th and 51.2% in 6th; $p < 0.05$) and the need for tracheostomy fell from 57.7% in the 1st, to 23.5% in the 6th ($p < 0.05$).
Mean stay was 13.6 + − 11.6 days with progressive decrease (18.4 + − 15.2 in 1st to 10.7 + − 7.8 in 6th wave, p 0.03).
Mortality, overall (Figure 1) and in patients with MV (Figure 2) also decreased but did not reach statistical significance.
Conclusion: The successive appearance of SARS-19 variants have meant a change in the healthcare profile, maintaining a high admission rate in the ICU but with a decrease in severity and mortality, and an increase in the percentage of immunocompromised patients and, above all, unvaccinated or with an incomplete vaccination schedule. A significant increase in patients admitted to the ICU that require isolation without COVID disease can explain in part why this decrease in severity has not been reflected in a decrease in the healthcare pressure in the ICU.

000548

Analisys of intra-ICU infections in a tertiary hospital and the effect of COVID-19 on them

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Intensive Care Medicine Experimental 2022, **10(2)**:000548

Introduction: COVID-19 pandemia had changed dramatically the way to work in our ICUs, making impossible to commit to all the bundles for the prevention of intra-ICU infections. This fact had affect to the infection rates.
Objectives: Analyze main intra-ICU infection rates in our ICU, the location and microorganism, and how they have changed in relation to rates before COVID-19 pandemia.
Methods: Prospective, descriptive study, carried out in the ICU of Santa Ana Hospital in Motril in 2019 and 2021. Demographics, severity index SAPS II and APACHE II, and different intra-UCI infections rates were collected.
Results: 576 patients admitted to the ICU at least for 24 h were recruited: 28,65% required mechanical ventilation, 60,67% urinary catheter, 42,13% central venous catheter and 2,25% parenteral nutrition. 56,18% of the patients recived antibiotic in ICU and 14,04% had recived ATB before admission. 1,12% were immunodeficient and 0,56% had neutropenia. Including secondary bacteriemia due to other focus infection, in 2021 the rate of intraUCI infection was 21,42 infections per 1000 days of ICU stay, in front of 3,95 in 2019. According to location the rates were: 23,04 ventilator-associted pneumonia (VAP) per 1000 days of MV in 2021 in front of 3,16 in 2019; 4,94 bacteriemia per 1000 days of CVC in 2021 against 1,68 in 2019 and 8,65 urinary infections per 1000 days of urinary catheter against 1,84% in 2019.
In both periods Pseudomona aeruginosa was the most frequent isolated microorganism, with more antimicrobial resistance in 2021 extended admissions. In addition in 2021, S. epidermidis was de second microorganism isolated in VAP (14,29%). In relation to Catheter-Related Bloodstream Infection (CRBI) in 2021 P.aeruginosa was the most frequent isolated microorganism (33%), the second was S. epidermidis (33%) and the third was *C. albicans* (16,67%) in front of 2019 when only gram negative bacilli were isolated. Finally, in relation to urinary infections, *Candida albicans* was the most frequent isolated microorganism (33%), followed by *Enteroccocus faecalis* (11,11%) and E. coli (11,11%). This fact means a change regarding to 2019, when *P. aeruginosa* caused 100% of them.
Conclusion: Coronavirus pandemic has had an important effect on intralCU infections rates probably due to prevention bundles has not carried out because of the new working conditions. In addition pandemic has had effect on the location of the infection and microbiology because of high number of patients with mechanical ventilation and immunosuppressive treatments.

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1. 2021 ENVIN-HELICS registry.
Acknowledgements: All colleagues of ICU medicine.

000553

Empirical antifungal treatment in patients with severe COVID-19 pneumonia

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Intensive Care Medicine Experimental 2022, **10(2)**:000553

Introduction: The appearance of COVID-19 Associated Pulmonary Aspergillosis (CAPA) and the mortality associated with it, together with the delay in getting the results of diagnostic tests, has led us to start early empirical antifungal treatment in case of suspicion of pneumonia associated with mechanical ventilation (PAMV) and the possibility of being CAPA, just as we do with antibiotics, assuming that in CAPA the delay in starting treatment would lead to an increase mortality as in bacterial infection.
Objectives: To analyze the early empirically antifungal treatment administered to patients with severe COVID-19 pneumonia (SCN) admitted to our ICU who require invasive mechanical ventilation (IMV) and in those with suspected PAMV, the mortality of patients diagnosed with CAPA who received empiric antifungal treatment (EAT) and targeted antifungal treatment (TAT), and the use of antifungals in patients not diagnosed with CAPA.
Methods: A retrospective descriptive study of patients admitted to our ICU from March 14, 2020 to June 25, 2021 for SCN who required IMV. EAT is analyzed, and in the case of patients with CAPA, the type of treatment they received and mortality. TAT is considered the one that is established after a positive microbiology or galactomannan result. The patient management was carried out according to the criteria of the medical doctor responsible for the patient.
Results: During the study period, 157 patients with SCN who required IMV were admitted to our ICU, of which 27 (17.2%) were diagnosed with CAPA during their admission and 57 (36.31%) received EAT; of these, 16/57 (28%) were diagnosed with CAPA. Patients with CAPA who received EAT (16/27 (59.26%)) had a mortality of 37.5%, with a mean time from the suspected infection to the start of treatment of 0.87 days (CI 95% 0,14–1,6); 10 (62.5%) received isavuconazole (ISV) and 6 (37.5%) voriconazole (VOR), associating liposomal amphotericin B (ABL) after diagnosis in 8 and 2 patients respectively. Nine patients with CAPA received TAT (9/27, 33.33%), of whom 7 died (77.78%), with

a mean time of beginning treatment of 5.67 days (95% CI 2,68–8,66); 6 (66.66%) received ISV and 2 (22.22%) VOR, associated with ABL after diagnosis in 2 and 1 patient respectively. Of the 41/57 (72%) patients treated with EAT without a diagnosis of CAPA, 15/41 (36.59%) had the antifungal discontinued due to therapeutic de-escalation, 13/41 (31.7%) were discharged from ICU with antifungal treatment, 9/41 (21.95%) died during treatment and 4 (9.76%) completed the treatment cycle. Thirty (73.17%) received ISV, 18 (43.9%) VOR, and 3 (7.32%) ABL.
Conclusion: Fifty-seven (36.31%) of patients admitted to our ICU with SCN who required IMV and in whom VAP was suspected received early EAT, of which 16 (28%) were diagnosed with CAPA, with a mean time from the suspected infection to the start of antifungal treatment of 0.87 days (95% CI 0,14–1,6) and 37.5% mortality. The most used antifungal treatment was isavuconazol (70%).

000569

Ventilator-associated pneumonia (VAP): Influence of COVID-19 pandemia on microbiology and antibiotic use

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Intensive Care Medicine Experimental 2022, **10(2)**:000569

Introduction: COVID-19 pandemia had changed the rates of intraUCI infections with an importante increase of them. We have observed a change in the most prevalent microorganism and an increase in multirresistant microorganism and this fact had affected to antibiotic use.
Objectives: To describe clinical and microbiological patterns of ventilator-associated pneumonia in our ICU, the used antibiotherapy and its appropiacy, and to analyze how they have changed regarding to the period before pandemia.
Methods: Prospective, descriptive study, carried out with ENVIN-HELICS registry dataof patients admitted to the ICU. Data of 2020–2021 were compared with the period of 2014 to 2019. Demographics, severity index SAPS II and APCHE II at admission, different intra-UCI infections rates and characteristics of ventilator-associated pneumonia were analyzed.
Results: 330 patients wich required mechanical ventilation were recruited. 24 ventilator-associated pneumonia were documented. Before 2019 the most frequent clinical sign was a new pulmonary infiltrate, whereas in 2021 the most frequent was the spreading of a new one. In a 70% the diagnosis was made by bronchial aspiration in both periods, with a rare use of bronchoalveolar lavage. The most isolated microorganism before 2019 was *E. coli* (25%) close to *P. aeruginosa* (25%), followed by MRSA and *S. pneumoniae*. In 2021 50% of ventilator-associated pneumonia was caused by *P. aeruginosa*, followed by *S. epidermidis* (14%) y S. marcescens y MSSA. Antibiotic resistance levels were higher in the period 2020–2021. In both periods 85% of the patients with VAP received antibiotics and it was considered appropriate in 80% of them in the period before 2019, facing to 46,67% in 2020–2021.
Conclusion: The incursion of COVID-19 pandemia in our ICU has mean a change relating to ventilator-associated pneumonia. Clinical presentation, diagnosis methods, microbiology and antibiotherapy have changed on account of new situation of our clinical practice.

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000578

Continuous Infusion Regimens of Vancomycin in Critically Ill Obese Patients

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Introduction: Despite the development of new agents with activity against Gram-positive bacteria, vancomycin remains one of the primary antibiotics for critically ill septic patients. Because of altered antimicrobial pharmacokinetics during critical illness, continuous infusions and higher than standard drug regimens have been proposed in this setting. Obese patients may have altered vancomycin pharmacokinetics that may result in improper dosing or inadequate drug concentrations. Whether this protocol is adequate also in obese patients remains poorly studied.
Objectives: To assess vancomycin concentrations in obese critically ill patients when a new regimen of continuous infusion (CI) was used.
Methods: We included all adult obese (Body Mass Index, BMI > 30 kg/m^2) patients admitted to a mixed intensive care unit (ICU) between January 2015 and December 2021, who were treated with a new vancomycin CI regimen consisting of a loading dose of 35 mg/kg of real body weight given as a 4-h infusion, followed by a daily CI dose adapted to creatinine clearance, as estimated by the Cockcroft-Gault formula. Urinary creatinine clearance (UCrCL) was also calculated, whenever possible, on 24-h urine analysis. Protocol compliance was therefore calculated based on the differences between the theoretical (i.e. according to the protocol) and received vancomycin daily regimen. Vancomycin concentrations were measured at 24 h and 48 h; concentrations between 20 to 30 mg/L were considered adequate.
Results: A total of 145 patients (67% male) were included. Median age, weight, BMI and UCrCL were 56 [IQR 44–67] years, 100 [90–112] kgs, 33.9 [33.1–37.4] kg/m^2 and 48 [8–109] mL/min, respectively. Vancomycin concentrations at 24 h were 25 [20–31] mg/L; concentrations were adequate in 52% (75/145) of patients, insufficient in 21% (31/145) and excessive in 27% (39/145). At 48 h (n = 116) and after dose adjustment, 85% of patients had adequate drug levels (98/116). Protocol compliance was observed in 73 patients (50%); the proportion of patients with adequate vancomycin concentrations was similar between those with or without protocol compliance (41/73, 56% vs. 34/72, 47%; p = 0.30).
Conclusion: In obese critically ill patients, this CI vancomycin regimen resulted in target drug concentrations at 24 h in 52% of patients. Further comparison with non-obese critically ill patients with similar characteristics is necessary.

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000603

Dynamic assessment of tissue oxygenation during a vascular occlusion test with Near-Infrared Spectroscopy (NIRS) in severe SARS-COV-2 infection

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Intensive Care Medicine Experimental 2022, **10(2)**:000603

Introduction: Endothelial damage has been postulated to contribute to the development of organ dysfunction and failure in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (1). Nevertheless, the impact of SARS-CoV-2 infection on tissue oxygenation and microvascular reactivity is poorly understood (2).
Objectives: To investigate dynamic tissue oxygen saturation (StO_2) changes and microvascular reactivity during a vascular occlusion test (VOT) with near-infrared spectroscopy (NIRS) in COVID-19 patients admitted to the intensive care unit (ICU).
Methods: Cross-sectional single-center exploratory study. Twenty adult patients with confirmed SARS-CoV-2 infection admitted to the ICU within 24 h were prospectively included in this study. A control group comprised of forty patients included in recently published study aiming to evaluate peripheral perfusion in ICU (non-COVID-19) patients was implemented (2). NIRS-derived parameters were assessed using the InSpectra StO_2 Tissue Oxygenation Monitor (model 650; Hutchinson Technology, Hutchinson, MN, USA) with a 15-mm probe over the thenar eminence. A VOT was performed using a conventional sphygmomanometer cuff inflation to 30 mmHg above systolic blood pressure for 3 min and, after that, the occluded cuff was rapidly deflated to 0 mmHg (3). Descending slope (%/minute), ascending slope (%/minute), maximum value of StO_2 (StO_2max), recovery time (s), and the area under the curve of reactive hyperemia were determined.
Results: The median (IQR) age of included patients was 58 (46–69) years. Patients with COVID-19 presented higher SAPS III score [50 (46–53) vs. 45 (30–53), $p = 0.04$] and less frequently received vasopressors [20.0% vs. 52.5%; $p = 0.03$] compared with control patients. Patients with SARS-CoV-2 infection showed higher StO2 min [60 (49–79) vs. 54 (48–58) %; $p = 0.04$] and lower descending slope [5.7 (3.4–8.8) vs. 8.1 (6.4-9.7) %/minute; $p < 0.01$] compared with ICU patients without COVID-19. Basal StO_2 [80 (74–90) vs. 82 (76–86) %; $p = 0.89$], StO_2 max [(91 (83–95) vs. 90 (84–94) %; $p = 0.86$], ascending slope [2.0 (1.1–2.9) vs. 2.2 (1.5–3.3) %/minute; $p = 0.43$], recovery time [14.5 (12.0–22.0) vs. 21.5 (14.3–28.3) s; $p = 0.13$] and hyperemia area [10.3 (5.8–13.0) vs. 8.6 (4.0–14.3); $p = 0.55$] did not differ between COVID-19 and control groups, respectively.
Conclusion: Severe COVID-19 patients exhibited a lower rate of oxygen extraction by peripheral tissues than non-COVID-19 critically ill patients, which may represent an adaptive mechanism to hypoxemia. This hypothesis needs to be further investigated.

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Acknowledgements: None.

000609

Evolution of antibiotic use in critical care unit throughout the SARS-COV2 pandemic. Data from the ENVIN-HELICS registry

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Intensive Care Medicine Experimental 2022, **10(2)**:000609

Introduction: Multi-resistant bacteria and the availability of antibiotics have been a public health problem for years. We have experienced how the COVID-19 pandemic has been a real challenge for healthcare and we have analyzed the exponential increase in the use of antibiotics and the increase in multi-resistant bacteria in this context.
Methods: Data from the 2019 to 2021 ENVIN-HELICS database was used, which is a multicentric, prospective, voluntary registry. The studied periods were: April–June 2019; March–May 2020; September–December 2020; April–June 2021. The results are descriptive and shown as percentages or mean value.
Results: A total of 64.803 patients were studied. Arranged by date, the percentage of patients with antibiotics in each period was 64%, 92%, 68% and 67%. The number of antibiotics per patient with antibiotics were 2.15, 5.18, 2.66 and 2.5. Community acquired infection was the main cause for the antibiotic use in 2019 (30%) switched to in ICU acquired infection since the 2020, representing 35% of the indications in 2021. In all the studied periods most of the antibiotic treatment was empirical (77%, 73%, 71%, 71%), showing similar results concerning the appropriateness of the treatment: in 2021, 34,09% of the indications were considered adequate, 15,71% not adequate and in 42,21% of the indications the cultures were negative, with similar results the other studied periods. The most frequently used antibiotics in changed between the studied periods, being amoxicillin–clavulanic acid (10.9%), piperacillin–tazobactam (9.7%) and meropenem (9.6%) in 2019; ceftriaxone (12.4%), azithromycin (11.15%) and hydroxychloroquine (10.7%) in 2020-CoVID period; meropenem (10.4%), ceftriaxone (9.6%) and piperacillin-tazobactam (9.7%) in the second 2020 period; meropenem (11.7%), piperacillin-tazobactam (9.4%) and linezolid (9.26%) in 2021. Piperacillin-tazobactam, meropenem and linezolid were the most used antibiotics in ICU-acquired and/or in-hospital acquired infection during all the studied periods. The most used antifungals were fluconazole, anidulafungin, voriconazole, caspofungin and amphotericin B.
Conclusion: Rates of antibiotic use have increased during the pandemic, mostly due to ICU-acquired infection. In addition, the percentage of empirical treatment is lower, and the spectrum is reduced less frequently. It has also been observed that the choice of antibiotics has changed and that new antibiotics are used more.
Acknowledgements: Spanish Agency of Medicines and Medical Devices (Ministry of Health). File number: 2021/48603/001.

000612

Study on mortality in patients with pneumonia sars -cov-2 and respiratory coinfection with other microorganisms

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Intensive Care Medicine Experimental 2022, **10(2)**:000612

Introduction: The last year, one of the most frequent causes of admission to our ICU has been SARS-CoV-2 pneumonia. In most patients, this microorganism has been the only cause of pneumonia, but in some cases, concomitant infections have been detected that could influence the mortality of these patients.
Objectives: To investigate whether mortality was increased in patients with SARS-CoV-2 pneumonia associated with respiratory coinfection by other microorganisms.
Methods: Patients admitted to the ICU for covid-19 for six months (March 1, 2021–August 31, 2021) were included; mortality was compared in patients with and without respiratory coinfection. The search for coinfection was performed by PCR of pneumotropic virus in nasopharyngeal exudate, culture of sputum or bronchial aspirate on admission, serology of atypical bacteria, and antigenuria of pneumococcus and Legionella.
Results: 268 patients were included; in 27 of which (10.07%) coinfection was detected. The most frequent causative microorganisms were

atypical bacteria, with positive serology found in 17 of the 27 patients: 13 *Chlamydophila pneumoniae*, 2 *Mycoplasma pneumoniae*, 2 *Coxiella burnetti*. The other isolates were: positive *Streptococcus pneumoniae* antigenuria in 4 patients, isolation of other bacteria in broncoaspirate or brochoalveolar lavage at admission in 3 patients of *Mycobacterium lentiflavum*, *Haemophilus influenzae* and *Pseudomonas aeruginosa*; or *Aspergillus fumigatus*, found in 3 patients. Mortality in patients with coinfection was 18.5% and in patients without coinfection 18.25%.
Conclusion: Patients admitted to the ICU for SARS-CoV-2 pneumonia and presenting co-infection with other microorganisms did not present higher mortality than patients admitted with pneumonia only due to SARS-CoV-2, probably due to early diagnosis and the establishment of a specific treatment.

000624

Characteristics of severe SARS COV 2 pneumonia patients during pandemic wave 5 vaccinated vs unvaccinated population: are there differences?

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Introduction: The impact of coronavirus disease during the first waves of the pandemic has driven research development towards prevention by proposing a safe and effective vaccine to mitigate severe disease, reduce morbidity and mortality and decrease the demand for health care. Thus, during the 5th wave of the pandemic, we began to observe that several of the patients admitted to intensive care units for SARS Cov 2 pneumonia already had a partial or complete vaccination schedule, so it is very interesting to analyse the characteristics of these patients, the evolution of the disease and morbidity and mortality in order to contribute to establishing/clarifying the predisposing or protective factors of severe disease in the vaccinated population.
Objectives: To determine and compare the morbidity and mortality of severe patients with SARS-CoV-2 pneumonia vaccinated vs unvaccinated patients admitted to the ICU during the 5th wave of the pandemic.
Methods: Retrospective descriptive observational study of patients admitted to the ICU with a diagnosis of SARS-CoV-2 pneumonia vaccinated vs unvaccinated patients during the period June to December 2021. Demographic variables, severity scales, mean ICU stay, complications and mortality were analysed. Results are expressed as mean (95% CI).
Results: 24 patients were analysed. 46% of patients had 1 or 2 doses of SARS Cov 2 vaccine and the remaining 54% had not received any vaccine. Of those vaccinated, 9% had 3 doses of Spikevax (Moderna), 36% had 2 doses of BioNTech (Pfizer), 27% had 2 doses of Vaxveria (Astrazeneca) and the remaining 28% had received 1 dose from Pfizer, 1 from Astrazeneca and 1 from Jansen. Of the vaccinated patients the mean age was 63.27 years (57.49–69) and 81% were male. The unvaccinated had a mean age of 55.8 years (45.96–65.63) and 53.8% of the cases were female. Mean severity scores were for the vaccinated Apache 14.27 (10.5–18.04), SOFA 3.63 (2,637–4,623) and for the unvaccinated Apache 15.16 (11,296–19,024), SOFA 3.58 (2,663–4,497). All patients had an associated diagnosis of ARDS on admission and 72% of those vaccinated required IMV and of these, prone therapy was performed in 36% of the cases. Of the non-vaccinated 53% were ventilated invasively and all of them received prone therapy. The mean number of days of IMV was 6.81 (0.61–13.00) in the vaccinated and 8.23 (1.65–14.80) in the unvaccinated. A T-test was performed to compare means with a CI of − 10.57–7.73 with $p = 0.75$. The mean number of days of ICU stay in vaccinated patients was 11.81 (4.24–19.37) and in unvaccinated patients 12.61 (6.74–18.47) with a comparative t-test (CI − 10.68–9.18) with $p = 0.8695$. The overall complication rate was 20% in vaccinated versus 33% in unvaccinated. The most frequent complication was the development of VAPV in 36% of the sample, 8% vaccinated and 28% unvaccinated; other complications were pneumothorax in 8% of the total with a similar distribution in the two groups. The unvaccinated also had bleeding episodes (8%) and UTI (8%). The reintubation rate was 4% in all unvaccinated patients. Non-vaccinated patients received a mean of 13.46 days of corticosteroid therapy (95% CI 10.24–16.61) compared to 9.27 days (95% CI 6.22–12.31) for vaccinated patients. Intra-ICU mortality was 9% in vaccinated and 23% in non-vaccinated with a Fischer's Exact Test with a value of $p > 0.05$.
Conclusion: Vaccinated patients who develop severe disease present morbidity data similar to those described in non-vaccinated patients, however it appears that complications and mortality observed in vaccinated patients is lower than that reported in case series of non-vaccinated patients. Although the severity scales on admission were similar in the two groups, the difference in sex and age of vaccinated and unvaccinated patients may have influenced the clinical course of the disease. In this sample there are no statistically significant differences to ensure that unvaccinated patients have higher morbidity and mortality than vaccinated patients.

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Infection 4

000636

May the biofire filmarray respiratory panel in patients with pneumonia due to SARS COV2 suppose a change in antibiotic management?

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Intensive Care Medicine Experimental 2022, **10(2)**:000636

Introduction: Patients with COVID pneumonia have posed a challenge for effective treatment of the primary infection and its complications. VAP in patients with COVID has been difficult to diagnose due to the use of empiric antibiotics, immunosuppressive therapy and the low yield of microbiological samples to guide antibiotic treatment. It is

these circumstances that have seen a likely positive impact on the use of the BioFire FilmArray Pneumonia Panel.
Objectives: Analyze the impact of carrying out the Biofire-Filmarray respiratory panel in patients with SARS-COV2 pneumonia and to assess changes in antibiotic treatment according to the microbiological results obtained
Methods: Retrospective descriptive study. It was collected a sample of 47 patients diagnosed with SARS-COV2 pneumonia who underwent the Biofire-Filmarray respiratory panel in bronchoalveolar aspirate an bronchoalveolar lavage between March 2020 and May 2021 during the pandemic period. Demographic data, severity scales, ICU stay, antibiotic treatment, days of treatment, detected microorganisms and associated complications were analyzed.
Results: The results for severity scores were APACHE 14.24 (7.64–20.84), SAPSII 33.9 (25.27–53.83) and SOFA 5 (3.77–8.43). Average stay in ICU was 16.5 days and days of invasive mechanical ventilation 11.42 ± 8 days. A 10.63% of the patients did not receive antibiotic treatment. Of the 89.36% who did receive it, the respiratory panel underwent was useful in 80% of cases by reducing days of prophylactic (first wave) or empirical antibiotic treatment. In patients in whom the results did not lead to a reduction in spectrum or suppression of antibiotic treatment, the cause was poor clinical evolution due to bacterial superinfection in other locations. Were found catheter-related bacteremia, Stenotrophomonas maltophila infection and pulmonary aspergillosis. In relation to microbiological isolates in order of frequency were *Pseudomonas aureginosa* in 12.76%, *Haemophilus influenzae* and *Staphylococcus aureus* in 8.5% and *Klebsiella aerogenes* 4.2%. Less frequent were *Enterobacter cloacae, Streptococcus pneumonia* and *Streptococcus pyogenes* and *S. agalactiae*.
Conclusion: The performance of the Biofire-Filmarray in BAS or BAL in our group of patients represented a great impact in antibiotic management. It meant a reduction in the days of treatment in patients with prophylactic antibiotic therapy, reducing the use of unnecessary treatment and thus reducing possible future resistance. It can be concluded that it is a useful test in 80% of the sample. The cases where its negative result has not motivated a reduction and/or suppression of antibiotic therapy, was due to poor clinical evolution, infections of another location or fungal infection

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000639

Increasing SARS-CoV-2 antibody levels in a normal human immunoglobulin preparation for intravenous use

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Introduction: The use of large pools of plasma from healthy donor for the production of intravenous immunoglobulin (IVIG) preparations ensures a consistent content of antibodies specific for a wide spectrum of pathogens. Such antibodies prevent serious infections in patients with primary and secondary immunodeficiencies.
Objectives: We determined and characterized antibodies to SARS-CoV-2 as an emergent novel pathogen.
Methods: Consecutive batches of an IVIG preparation (IntratectTM) and experimental IgG preparations from convalescent and vaccinated donors are analyzed. Binding activities against different pathogens are measured using modified commercial and in-house ELISA systems. A quantitative in-house ELISA based on the S protein (Wuhan strain) is used to determine the anti-SARS-CoV-2 IgG activity. Antibodies to SARS-CoV-2 variants as well as different other respiratory pathogen antigens is determined with a kit systems from Meso Scale Diagnostic.
Results: All tested IVIG batches contained consistent levels of antibodies directed against common bacteria, viruses and fungi.
Pre-pandemic IVIG batches showed no detectable anti-SARS-CoV-2 activity. In recent batches this activity rose to a level comparable to a hyperimmunoglobulin produced from convalescent plasma or vaccinated donors. In parallel the reactivity with MERS and anti-SARS-CoV-1 but not with other corona or influenza viruses increased.
The reactivity of the present antibodies against other virus variants (alpha, beta, gamma, delta) was similar. They also bound the Omikron variant, albeit weaker.
Conclusion: Within two years after the onset of the pandemic the SARS-CoV-2 antibody level in an IVIG preparation reach high levels. Because antibody titers correlate with virus neutralization this may be beneficial for patients with primary and secondary immunodeficiencies. Since clinical trials with individual hyperimmune plasma donations have demonstrated successful prophylaxis and therapy of mild disease, an IVIG preparation may be beneficial for the treatment of certain patient populations.

000650

Prognosis of SARS-COV-2 associated ARDS in the setting of the intensive care unit. The role of NETs

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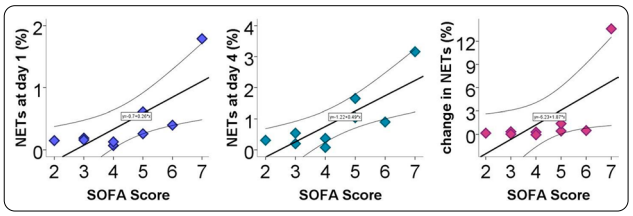
Introduction: SARS-COV-2 infection is closely related to life-threatening acute respiratory distress syndrome (ARDS) requiring mechanical ventilation. Recent data suggest a role for neutrophil extracellular traps (NETs) in SARS-COV-2 infection-related lung injury, ARDS development and outcome. Thus, little is known on their prognostic role in SARS-COV-2 related ARDS patients requiring mechanical ventilation in the intensive care unit setting.
Objectives: We investigate the variation of plasma levels of NET markers measured shorty after ICU admission and their association to well-known markers of prognosis in the ICU setting.
Methods: This is a prospective study enrolling patients with SARS-COV-2 related ARDS syndrome requiring mechanical ventilation. Blood was collected at ICU admission and after 4 days, in ethylenediaminetetraacetic acid (EDTA) tubes for flow cytometry and processed within 3 h of collection. Neutrophil surface NETs markers were determined by flow cytometry by gating of neutrophils (Anti-Hu CD15 PE, Exbio Praha a.s. (Vestec, CR), stained for surface citrullinated histone (anti-histone H3 antibody, H3 cit, Thermo Fisher Scientific, Rockford, IL) and myeloperoxidase MPO FITC, Exbio Praha a.s. (Vestec,CR).
Results: We report preliminary data of an ongoing study. In total, 9 patients [mean age 57.11 ± 4.33 years, 3 (33%) women] were included in the analysis. Analysis revealed increase of circulating NETs serum levels in days 1 and 4 after ICU admission (2.21 ± 1.96 vs 4.07 ± 3.33, $p = 0.015$). There was a strong positive correlation of NETs serum

levels at both days 1 and 4 as well as of its change, with prognosis, as expressed by SOFA score (r = 0.709, p = 0.032, r = 0.751, p = 0.02 and r = 0.776, p = 0.014 respectively (Image).



Conclusion: Our results reinforce the hypothesis that NETosis is an attractive prognostic marker in intubated ICU patients with COVID-19. Further studies are needed to support the hypothesis.

000653

Assessing predictors of Intensive Care Unit (ICU) outcome in vaccinated vs non-vaccinated COVID-19 propensity score matched patients using MCMC sampling

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Intensive Care Medicine Experimental 2022, **10(2)**:000653

Introduction: National uptake of vaccinations in the UK COVID-19 vaccination programme has increased rapidly since 8/12/20. By April 2022, approximately 91.2% of the UK population had received a first dose of the vaccine [1]. Understanding the survival benefits of COVID-19 vaccination on critical care patients and assessing risk factors for survival may benefit the management of critically unwell COVID-19 patients.
Objectives: Using propensity score matching, we assessed risk factors for overall outcome in vaccinated and non-vaccinated patients admitted to our intensive care unit (ICU) with COVID-19 in a UK district general hospital.
Methods: Deidentified data was collected for 275 patients admitted with COVID-19 to East Surrey Hospital ICU between 25/3/2020 and 25/3/2022. All patients aged 18 years or older with a diagnosis of COVID-19 and a record of at least one vaccination at the time of admission were included. We generated a control group of unvaccinated patients using propensity score matching for age and gender. A positive outcome was defined as discharge from ICU and negative outcome was defined as death whilst in ICU. Multivariate analysis was performed using Monte Carlo Markov Chain (MCMC) logistic regression to assess factors likely to affect patient outcome. These included age, sex, numbers of days between being admitted to hospital and admission to ICU alongside various biomarkers from [BB1] the first 24 h of admission (highest heart rate, highest glucose, highest lactate, highest creatinine, lowest blood pH). Analysis was performed using R (version 4.1.3, Austria, Vienna).
Results: After the initiation of the COVID-19 vaccination programme, 165 patients were admitted to our ICU, of which only 24 (14.5%) patients were identified as having received at least one dose of the vaccination at the time of admission. Average (SD) age in both groups were 59.5 (12.9) years. Both groups had 16 male and 8 female patients. MCMC logistic regression mean parameter estimates and 95% credible intervals demonstrated that outcome was significantly affected by age, vaccination status, number of days between admission to hospital and ICU, and highest heart rate in the first 24 h of admission [BB1]. These estimates suggest that younger patients, being vaccinated, fewer days between hospital and ICU admission, and lower heart rates are associated with improved survival.
Conclusion: Our findings suggest that vaccination against COVID-19 increases the chances of survival in patients admitted to critical care with COVID-19, as confirmed in other large studies [2]. To the best of our knowledge, this is the first study that uses propensity score matching, which aims to aggregate multiple confounding factors into a single dimension [3]. Limitations include small sample size and use of only two covariates for propensity scoring. However, we believe that analysis of larger multicentre datasets using propensity score matching may provide more accurate predictions of treatment response.

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000657

Incidence of COVID-19-associated pulmonary aspergillosis and its significance in mechanically ventilated patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000657

Introduction: Since COVID-19 pandemic outbreak, acute respiratory distress syndrome (ARDS) has emerged as an important disease that predisposes patients to secondary pulmonary aspergillosis
Objectives: To describe the main clinical characteristics of intubated patients with acute respiratory failure due to COVID-19 pneumonia and *Aspergillus* spp isolation and to examine the significance og the later in the course of the disease.
Methods: This is an observational, single center study enrolling intubated patients with confirmed COVID 19 pneumonia, hospitalized in the ICU setting from 1st of March 2020 to 30th of September 2021. Routine respiratory samples were performed at admission and every 7 days and were used for the isolation of *Aspergillus* spp in all patients (galactomannan and cultures). All patients with confirmed *Aspergillus* spp isolation were included.
Results: During the study period, 469 patients (175, 37.3% females, mean age 64.0 ± 14.6 years), with confirmed COVID-19 pneumonia were treated with invasive mechanical ventilation. Out of them, 42 (9%) (20, 47.6% females) were diagnosed with *Aspergillus* spp isolation in their respiratory samples after a median of 6 (4-8) days from ICU admission. At the time of aspergillus isolation 29 (69%) patients have been treated for COVID-19 disease with corticosteroids while 24 (57.1%) patients received antifungal treatment. The more frequent treatment was itraconazole [20 (47.6%) patients]. Procalcitonin and C-reactive protein serum levels were 1.15 (0.9–8.5) and 11.0 (10.2–23.5) respectively. Patients with confirmed Aspergillus spp isolation were younger (59.3 ± 21.3 vs 64.5 ± 13.7 years, p 0.028), had more prolonged stay in the yard before their ICU admission and the initiation of invasive mechanical ventilation (24.7 ± 14.4 vs 14.7 ± 11.3 days, p < 0.0001) as well as total ICU stay (18.6 ± 13.7 vs 14.7 ± 11.3 days, p 0.043). Interestingly, although younger, patients with Aspergillus spp isolation had similar ICU survival compared to the control group (26% vs 22%, p 0.561). Cox regression analysis revealed age as the only prognosticator of mortality in our cohort (HR 0.965 CI 0.953-0.978, p < 0.0001).

Conclusion: *Aspergillosis* spp. isolation may be a relatively frequent finding in COVID-19 pneumonia ICU patients receiving invasive mechanical ventilation. In our study population, patients with *Aspergillus* spp. isolation, although younger, had similar prognosis compared to controls, fact probably indicating the severity and the unfavorable effect of Aspergillus infection in the course of COVID-19 pneumonia.

000662

Prognosis in solid cancer patients with sepsis admitted to a tertiary ICU: The Vall d'Hebron Intensive Care Department/ Vall d'Hebron Institute of Oncology (VHIO) cohort

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Intensive Care Medicine Experimental 2022, **10(2)**:000662

Introduction: Sepsis is one of the leading causes of Intensive Care Unit (ICU) admission in cancer patients. Despite continuous improvement in the prognosis of cancer patients with sepsis during the last decades, a significant number are still dying because of sepsis, so a better understanding of this disease in this particular group of patients is needed.
Objectives: Our aim was to describe the cohort of patients with solid organ cancer admitted to a tertiary hospital ICU with the diagnosis of sepsis and analyze factors associated with mortality.
Methods: Ten-year (2010–2019) retrospective study, including adult patients with solid organ cancer and sepsis who required ICU admission. Sepsis was defined according to Sepsis-3 criteria. Septic shock was defined as sepsis and need for vasoactive drugs. Chi-Square, Fisher's test, T test, U Mann-Whitney and Cox´s regression were employed as appropriate. Quantitative variables are reported as median (IQR) and categorical as frequency (%).
Results: Two hundred and thirty-eight patients were included, 90 (38%) during the 2010–2014 period and 148 (62%) during the 2015–2019 period. One hundred and forty-eight (62%) were male with a median age of 64 (55–72) years. Lung cancer was present in 58 (24%), followed by colon 43(18%), bladder 19 (8%), ovary 14 (6%), and breast 12(5%). One hundred and five (44%) had metastatic disease. Septic shock was present in 187 (79%). Thirty-five (15%) were neutropenic. SOFA score at day 1 was 7 (5–9). One hundred and thirty-three (56%) required invasive mechanical ventilation (IMV), 187 (79%) vasopressors (VP), and 27 (11%) renal replacement therapy (RRT). The most common sources of infection were respiratory 109 (46%), digestive 86 (36%) and the urinary tract 28 (12%). A causative pathogen was isolated in 170 (71%); 74 (31%) gram-negative bacilli, 27 (11%) gram-positive cocci, 51 (21%) polymicrobial, 10 (4%) virus and 8 (3%) fungal. *E. coli*; 54 (23%) and *Pseudomonas* spp; 24 (10%) were the most frequent microorganisms isolated. Bloodstream infection was present in 75 (32%). One hundred and sixty-two (68%) were discharged to the Oncology ward and 140 (59%) were discharged home, 46 out of 90 (51%) during the 2010–2014 period and 94 out of 148 (64%) during the 2015–2019 period. One year after hospital discharge 89 (32%) patients were alive. Differences between hospital survivors and non-survivors are detailed in Table 1. Patients with sepsis of respiratory origin (OR 3.4, 95% IC (1.5–7.8), requiring IMV (OR 4.1, 95% IC (1.6–10.4), with a SOFA score on day 1 higher than 9 (OR 3.25, 95% IC (1.2–8.4) or without decrease of their SOFA score at day 5 (OR 4.9, 95% IC (2.1–11.3) had higher in-hospital mortality after multivariate analysis.
Table 1. Characteristics of in-hospital survivors and non-survivors

Variable	Survivors (n = 140)	Non-survivors (n = 98)	p value
Age (years)	64 (55–73)	65 (56–72)	0.970
Gender (male)	88 (63%)	60 (61%)	0.798
Lung Cancer	25 (18%)	33 (34%)	0.005
Metastatic disease	56 (40%)	49 (50%)	0.126
Neutropenia	22 (16%)	13 (13%)	0.6
IMV	60 (43%)	73 (75%)	< 0.001
VP	107 (76%)	80 (82%)	0.336
RRT	10 (7%)	17 (17%)	0.015
SOFA > 9 (day1)	22 (16%)	35 (36%)	< 0.001
No decrease in SOFA			
Day 3	34 (29%)	39 (51%)	0.002
Day 5	15 (17%)	32 (51%)	< 0.001
Respiratory infection	49 (35%)	60 (62%)	< 0.001

Conclusion: ICU admission of cancer patients with sepsis is growing while mortality is decreasing. Despite this fact, a significant number of cancer patients die during the first year after ICU discharge. In-hospital mortality does not depend on oncologic disease but on organ failure and need for organ support. Respiratory source was also associated with mortality.

000680

Delta vs Omicron SARS CoV2 Variants in critically ill patients

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Introduction: During SARS CoV2 pandemic, the delta variant quickly displaced the pre-existing variants, demonstrating greater transmission capacity and increased severity. However, in November 2021, during the sixth wave of the pandemic in Spain, the appearance of omicron and its rapid spread caused some uncertainty about how it could affect a much more contagious variant.
Objectives: The objective of the study was to know the variant that predominated in severe cases of SARS-CoV2 pneumonia that need ICU admission during the sixth pandemic wave in Spain and to analyze clinical profile of these patients.
Methods: Retrospective, observational study in a community hospital with an 19-beds ICU. Patients admitted to the hospital for respiratory infection by SARS CoV2 were included, differentiating according to the severity those admitted to the ICU and in the hospitalization ward. Clinical and laboratory test were collected.
Time of study was from November 2021 to January 2022. For variant screening, Allplex variant kits I and II (Seegene) and subsequent analysis by PCR-RT in the CFX96 (Bio-Rad) system were used. The delta variant was defined by the L452T mutation. The omniron variant by mutations N501Y, del69-70 and K417N. Statistical analysis: Data were analyzed by SPSS 18 and quantitative variables were expressed as a mean ± standard deviation.
Results: 82 patients were included, 39 (47.6%) with delta variant and 43 (52.4%) with omicron. 17 patients required admission to the ICU (20.73%), delta variant was the the predominant one, 70.6% of ICU admissions.
Omicron predominated in hospitalization ward, 58.5%. The percentage of unvaccinated patients with Delta variant infection was 45.9% (17), with omicron only 13.5% (5). 28.9% (11) of delta cases occurred in patients without comorbidities, mainly in unvaccinated patients, while omicron mainly affected patients with comorbidities (97.3%) [OR

14.667, 95% CI 1.783–120.618; P = 0.002]. 52.6% (20) of patients with delta had values > 3 on the WHO maximum severity scale compared to 29.7% (11) in omicron (OR 0.381, 95% CI 0.147–0.985; P = 0.044). Patients with delta more frequently required ICU admission [28.9% (11) vs. 2.7% (1); OR 0.068, 95% CI 0.008–0.561; P = 0.002)]. The table shows the differences between the different variants in patients admitted to the ICU.

Severe SARS COV 2 Pneumonia	Delta variant n:12	Omicron Variant n: 5
Age (years)	62,7 ± 8,6	56 ± 16
Vaccinated (%)	33,3%	60%
Comorbidity (%)	58,3%	80%
Leucocite count /Linf count	7978 ± 5175/634,2 ± 218	10,946 ± 6921/729,8 ± 336,8
LDH U/L/ Ferritin ng/ml	492,2 ± 297,5/1877,9 ± 1742	431 ± 231,87/1108 ± 843,24

Conclusion: The Omicron variant of SARS CoV2 was less likely to result in severe disease and ICU admission.
The Delta variant was related with unvaccinated patients who need ICU admission despite abcense of comorbidity.

000682

The metabolomic and lipidomic response to severe SARS-COV-2 infection: prospective observational study

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Intensive Care Medicine Experimental 2022, **10(2)**:000682

Introduction: Quantitative analysis of serum metabolomic and lipidomic response to severe SARS-COV-2 infection may help to identify patients at risk of respiratory failure, multiple organ dysfunction (MOD) and mortality.
Objectives: To describe differences in plasma metabolomic and lipidomic profiles from patients with severe coronavirus disease (COVID-19) and respiratory failure requiring invasive mechanical ventilation. Additionally, we explored the differential metabolite signatures between healthy controls and severe COVID-19, and in patients with or without sepsis, use of vasopressors, tracheostomy, or death.
Methods: Prospective observational study using a multiplatform fingerprinting analysis of plasma samples from 32 severe confirmed SARS-COV-2 infected adult patients and 10 healthy controls. A single plasma sample was collected from healthy controls and from severe COVID-19 patients requiring invasive mechanical ventilatory support during the first 24 h after admission to the intensive care unit (ICU). Metabolites with a fold-change > 0.25, variable importance in projection (VIP) score > 1 and p-value < 0.05 were selected for further analysis.
Results: A total of 388, 376, 1426, 766 and 822 molecular features were obtained by GM-LC/MS–QTOF(+), GM–LC/MS–QTOF(−), GM-HILIC-LC/MS-QTOF(−), GL–LC/MS–QTOF(+) and GL–LC/MS–QTOF(−), respectively. For all analytical platforms, PCA and OPLS discriminative analysis showed clustering of healthy controls and severe COVID-19 patients, and between severe COVID-19 patients requiring invasive mechanical ventilation. Patients that required invasive mechanical ventilation had altered expression in the glycerophospholipid (p = 0.002), porphyrin and chlorophyll (p = 0.02), linoleic acid (p = 0.03), and steroid biosynthesis (0.003) metabolic pathways. In such patients, metabolite-metabolite interaction network analysis documented significant functional enrichment for biosynthesis of unsaturated fatty acids (p < 0.0001), arachidonic acid (p = 0.02) and amino sugar and nucleotide sugar metabolism (p = 0.02). Pathways involved in sepsis development and mortality included fatty acid metabolism and steroid hormone biosynthesis. No significant difference in metabolite profiling was found for the need of vasopressors nor tracheostomy.
Conclusion: In our sample, patients with severe COVID-19 at increased risk of requiring invasive respiratory support, sepsis and death showed alterations in lipid and porphyrin metabolism and steroid biosynthesis pathways.

000685

Haematologic malignancies patients admitted in a polyvalent intensive care medicine unit: a 5-year review

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Intensive Care Medicine Experimental 2022, **10(2)**:000685

Introduction: Patients with haematologic malignancies (HM) have certain characteristics that make them a special population, mainly when they are admitted to the intensive care unit (ICU).1 The development of new treatments enhanced the survival rate of these patients, which combined with the general aging of the population, led to an increasing number of older patients with HM admitted in the ICU.2 Despite the improvement in supportive care and prognosis over the years, due to the immunocompromised status and complications related to the treatment of these patients, a dim prognosis is still observed. High ICU mortality rates have been described (54%, increasing up to 76% when submitted to mechanical ventilation).3
Objectives: The aim of this study is to analyse the characteristics of the population with HM admitted at our ICU.
Methods: Retrospective study of patients admitted in a polyvalent ICU between 1st January of 2016 and 31st December of 2020. Data were collected through the review of the electronic patient file: sex, age, length of ICU and hospital stay, severity scores at 24 h (APACHE II, SAPS II, SAPS 3), SOFA score and mortality rate.
Results: Fifty-one patients with HM were admitted at our ICU: 61% (n = 31) were males and the mean age was 70.7 ± 1.4 years. The most common HM at presentation was multiple myeloma with a prevalence of 31% (n = 16), followed by low-grade non-Hodgkin lymphoma with 23% (n = 12), high-grade non-Hodgkin lymphoma with 18% (n = 9), myelodysplastic syndromes and myeloproliferative disorders each one with 8% (n = 4) and acute leukaemia and chronic leukaemia each one with 6% (n = 3). The most prevalent diagnosis at admission was septic shock (35%, n = 18), followed by sepsis and acute heart failure, each one with a prevalence of 16% (n = 8). The median ICU length of stay was 3 days (IQR = 6) and the hospital length of stay 11 days (IQR = 18). Fifty-one percent (n = 26) of the patients were on vasopressors, 37% (n = 19) under non-invasive mechanical ventilation, 25% (n = 13) under invasive mechanical ventilation and 16% (n = 8) on renal replacement therapy. Regarding the severity scores, APACHE II was 21.3 ± 1.1, SAPS II 50.3 ± 2.4, SAPS 3 75 ± 2.6, SOFA at admission 6.6 ± 0.6 and at discharge 4 (IQR = 6). ICU mortality rate was 24% (n = 12) and hospital mortality rate was 35% (n = 18). In patients admitted with septic shock the ICU mortality rate was 50% (n = 9). Comparing the different categories of HM, no statistically significant

difference was found regarding age, ICU and hospital length of stay, severity scores and mortality.
Conclusion: Patients with HM represent an elderly population, with high severity conditions and the infectious pathologies represent the most common diagnosis at admission. Despite representing 1.6% of the admissions at our ICU, these patients have higher mortality when compared to the general population, although inferior to that described in the literature. The category of HM didn't have an impact on analysed ICU related variables.

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000697

Epidemiology and risk factors for bacteremia of critically ill COVID-19 patients in isolated ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000697

Introduction: The incidence of in-hospital bacteremia is known to increase in critically ill patients with COVID-19 infection who were admitted in intensive care unit (ICU). We aimed to analyze the epidemiology and risk factors of bacteremia in critically ill COVID-19 patients admitted to an isolated intensive care unit (ICU).
Methods: The medical records of 134 patients (male 67, female 67) diagnosed with critically ill COVID-19 from September 2021 to January 2022 were retrospectively analyzed. Patients were admitted to an ICU exclusively for COVID-19 patients at a 1,000-bed tertiary hospital in Incheon, Korea, and all health care workers working in the ICU wore level D or higher personal protective equipment.
Results: Of 134 patients, 32 patients (23.9%) developed 61 episodes of bacteremia. Of all the 61 pathogens, 55.7% (n = 34) were gram negative organisms, 40.1% (n = 25) were gram positive organisms. The most common organisms were *Acinetobacter baumannii*, followed by Coagulase-negative Staphylococci and *Providencia stuartii*. Bacteremia was associated with high-body mass index (BMI), uncontrolled hypoxia in admission, longer ICU length of stay, increased inflammatory serum markers, invasive mechanical ventilator, high-flow nasal cannula, central line insertion, and ECMO treatment (all variable's $P < 0.05$). Interestingly, use of steroids was not associated with bacteremia, but use of tocilizumab showed a significant difference between group with and without bacteremia (bacteremia vs. non-bacteremia: 38% *vs.* 13%, $P = 0.004$). In multivariate regression analysis, higher-BMI (1-unit increase in BMI: OR = 1.22, $P = 0.048$), central line use (if use of central line: odds ratio [OR] = 122.61, $P < 0.001$), and tocilizumab (if use of tocilizumab: OR = 8.35, P = 0.026) were more likely to occur bacteremia. The in-hospital mortality was 38.1% (51/134) and patients with bacteremia were significantly higher mortality than those without bacteremia (bacteremia *vs.* non-bacteremia: 71.9% *vs.* 27.5%, $P < 0.001$).
Conclusion: Bacteremia was highly associated with mortality in patients with critically ill COVID-19. Our study shows that higher BMI, use of central line and tocilizumab were risk factors for bacteremia with critically ill COVID-19 patients.

Infection 6

000701

The association between baseline kidney function and ICU mortality in critically ill patients with carbapenem resistant *Acinetobacter baumannii* pneumonia

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Intensive Care Medicine Experimental 2022, **10(2)**:000701

Introduction: Carbapenem-resistant *Acinetobacter baumannii* (CRAB) pneumonia is a serious worldwide problem because of the high rate of treatment failure and intensive care unit (ICU) mortality. Because baseline kidney function may influence drug selection for CRAB pneumonia, this may affect ICU mortality in critically ill patients with CRAB pneumonia.
Objectives: The aim of this study was to investigate the association baseline kidney function and ICU mortality in critically ill patients with CRAB pneumonia.
Methods: This study was a multicenter retrospective observational study conducted at 13 university-affiliated hospitals of Republic of Korea from September 2017 to September 2019. Baseline kidney function was classified into stage 1 to stage 5, based on the estimated glomerular filtration rate at admission.
Results: A total of 568 patients with CRAB pneumonia were included in this study. The mean age was 71 years, and 364 (64.1%) were male. The APACHE II score and Charlson comorbidity index at admission were 21 and 5, respectively. The sequential organ failure assessment score at the diagnosis of CRAB pneumonia were 8. In this study, the mean ICU stay was 34 days and 256 patients (42.4%) died during ICU admission. Multivariate Cox proportional hazards analysis showed that impaired baseline kidney function (hazard ratio, 1.15; 95% confidence interval, 1.012–1.306; $p = 0.032$) was a significant, independent predictor of ICU mortality. Kaplan-Meier analysis using log rank test showed that patients with impaired kidney function had significantly shorter survival than patients with normal kidney function ($p = 0.042$).
Conclusion: In critically ill patients with CRAB pneumonia, impaired baseline kidney function was associated with ICU mortality. For CRAB pneumonia patients with impaired kidney function at admission, greater attention should be paid to the possibility of high ICU mortality.

000709

Management of invasive fungal diseases: the physicians' perspective

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Intensive Care Medicine Experimental 2022, **10(2)**:000709

Introduction: Invasive fungal diseases (IFDs) are associated with high morbidity and mortality. Management of IFDs depends on physicians perceptions about the IFDs diagnosis and treatment.
Objectives: The aim was to investigate the physicians perceptions and adherence to guidelines for IFDs management.
Methods: In September 2021, electronic questionnaires were sent to physicians in hematology, intensive care units (ICUs), respiratory and infectious disease departments of 18 tertiary hospitals in China. The questionnaires included: invasive candidiasis (IC), invasive aspergillosis (IA), cryptococcosis, and rare mycosis. The full score was 100 points. Guideline concordant option: 1 point; guideline discordant option: no deduction.
Results: Responses from 294 physicians were analyzed. The total score was 72.0 ± 12.21. The guideline concordance of ICU physicians (66.8 ± 14.49) was lower than those of infectious disease (77.1 ± 10.10), hematology (73.2 ± 11.07), and respiratory (72.4 ± 10.24) department. Guideline concordance of all physicians for rare mycosis, IA, and cryptococcosis were higher than that for IC. Moreover, guideline concordance of ICUs physicians for IA and IC was lower than other three departments (Table 1). For IA part, 62.9% of physicians recommended bronchoalveolar lavage fluid-galactomannan assay for non-agranulocytosis patients. However, only 44.6% of physicians recommended serum galactomannan assay for agranulocytosis patients. For patients with hematological malignancies whose persistent fever after chemotherapy and failed to antibiotics therapy for 4 days, when CT revealed halo sign/air crescent sign/cavity/wedge consolidation, 84.7% of physicians agreed that diagnosis-driven therapy should be initiated. However, when CT showed ground glass opacities/tree-in-bud opacities/nodule/exudative shadow, only 37.1% of physicians agreed to start diagnosis-driven therapy. For IC part, 64.3% of physicians disagreed with the guidelines and perceived that current antifungal therapy should be maintained for patients with candidiasis-induced septic shock when blood culture turned negative following initial treatment with echinocandins.

Table 1 Score

Index	Full score	Score (N = 294)	Hematology department (N = 97)	Respiratory department (N = 67)	Infectious disease department (N = 52)	ICUs (N = 78)
IC	19	11.1 ± 2.7	10.5 ± 2.45	10.9 ± 2.56	12.8 ± 2.53ab	10.9 ± 2.86c
IA	57	43.0 ± 7.77	44.9 ± 7.03	42.8 ± 6.46	45.6 ± 6.45	39.2 ± 9.01abc
Cryptococcosis	11	8.1 ± 2.0	7.8 ± 1.90	8.6 ± 1.67a	8.8 ± 1.52a	7.4 ± 2.26bc
Rare mycosis	13	9.8 ± 2.3	10.0 ± 2.23	10.1 ± 2.17	9.9 ± 2.13	9.3 ± 2.66
Total	100	72.0 ± 12.21	73.2 ± 11.07	72.4 ± 10.24	77.1 ± 10.10	66.8 ± 14.49abc

Values are mean ± standard deviation. a, b, c: P value for comparison with hematology (a), respiratory (b), or infectious disease department (c) is < 0.05.
Conclusion: There was a certain difference between physicians perceptions and existing guidelines for IFDs management; further research is needed to explore the reasons for the difference. The physicians in different departments may need specific training.

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Acknowledgements: Pfizer fund QI (No.67183713)

000712

A retrospective, single centre audit investigating timely attainment of therapeutic voriconazole levels in a tertiary adult ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000712

Introduction: Invasive fungal infections (IFIs) are common in the critically ill, with 0.3–19% attributable to *Aspergillus spp* (1). Severe infection with influenza or COVID-19 has been associated with Invasive Pulmonary Aspergillosis (IPA) and carries an appreciable morbidity and mortality (2,3). Voriconazole, a triazole antifungal, is first-line therapy for confirmed or suspected IPA. Critical illness induces numerous pathophysiological changes resulting in significant alterations in drug pharmacokinetics and pharmacodynamics (PK-PD), which can affect drug clearance resulting in lower plasma levels and therapeutic failure or toxicity contributing to organ dysfunction (4). Additionally, extracorporeal therapies, such as extracorporeal membrane oxygenation (ECMO) can impact drug handling (5).
Objectives: Due to frequent concerns relating to timely therapeutic level attainment in critically ill patients, we sought to audit our critical care antifungal guideline to check compliance and investigate suitability of current dosing regimen. The following standards were assessed.

1. Loading dose prescribed as per guideline (6 mg/kg twice daily for 2 doses)
2. Maintenance dose prescribed as per guideline (4 mg/kg twice daily)
3. Initial trough voriconazole serum levels (VSLs) taken appropriately, pre 5th or 6th dose, to allow attainment of steady state
4. Therapeutic VSLs achieved within 7 days of starting voriconazole

Methods: Adult critical care patients administered intravenous voriconazole from April 2019 to September 2021 were included in our study. Patients were excluded if initiated on oral voriconazole therapy, voriconazole treatment prior to ICU admission or received < 12 h of voriconazole. Pharmacy records were used to identify patient's supplied with voriconazole injection for infusion. Electronic Health and Medicines Administration Records were used to extract data using a predefined audit tool. VSL of 1.5–5 mg/L was deemed therapeutic. Doses were calculated as mg/kg based on total body weight.
Results: A total of 62 patients were eligible for inclusion. 13 patients were excluded; inaccessible medical records (n = 1), initiated on oral therapy (n = 7), received < 12 h of voriconazole (n = 4), voriconazole treatment prior to ICU admission (n = 1). A total of 53 treatment courses were observed. Following a loading dose, 4 were ceased; interacting drug (n = 1), prolonged QTc (n = 1), drug shortage (n = 1), microbiology advice (n = 1). VSLs were taken for 37 treatment courses and measured by an external provider with an average time of 2.9 days to receive result.

Standard	Results
Loading dose of voriconazole prescribed as per guideline (6 mg/kg twice daily for 2 doses)	58% (n = 53)
Maintenance dose prescribed as per guideline (4 mg/kg twice daily)	69% (n = 49)

Standard	Results
Initial trough voriconazole serum levels (VSLs) taken appropriately, pre 5th or 6th dose, to allow attainment of steady state	46% (n = 37)
Therapeutic voriconazole serum level achieved within 7 days of starting voriconazole	46% (n = 37) Sub-therapeutic = 43% Supra-therapeutic = 11%

Conclusion: Therapeutic levels was achieved in 46% of patients by day 7 of therapy, with moderate guideline compliance for loading and maintenance dosing. No correlation was observed between different weight descriptors and target level attainment. Voriconazole PK-PD is affected by multiple factors, leading to significant variation in drug exposure. Additionally, non-linear kinetics adds to dosing complexity. Onsite VSL monitoring is advised to facilitate timely access to levels and guide therapy to prevent patient harm from therapeutic failure or toxicity. Further analysis of the data is required to identify reasons for guideline non-compliance, and attempt to identify risk factors for non-target attainment.

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000713

Convalescent plasma therapy with high titers of neutralizing antibodies to reduce 28-day mortality in patients with COVID-19-induced acute respiratory failure requiring mechanical ventilation (MV): results of the multicenter randomized CONFIDENT trial

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Intensive Care Medicine Experimental 2022, **10(2)**:000713

Introduction: Passive immunization with plasma collected from convalescent patients has been widely used to treat COVID-19. Few trials used plasma with documented high titers of neutralizing antibodies and minimal data are available from patients submitted to MV. Our hypothesis was that passive immunization with plasma collected from patients having contracted COVID-19 and developed high titers of neutralizing antibodies—in addition to standard of care—may reduce mortality when administered early in patients treated with MV for severe respiratory failure due to SARS-CoV-2 pneumonia.
Methods: We randomly assigned adult patients with critical Covid-19 pneumonia requiring MV for less than 5 days in a 1:1 ratio to receive either convalescent plasma with a neutralizing antibodies titer at least 1/320 or standard of care. Randomization was stratified by the time from tracheal intubation to inclusion (less or more than 48 h). The primary outcome was day-28 mortality. 17 investigating centers. Plasmas were delivered by the Belgian Red Cross. Number of patients to include for a 40% expected mortality in controls and 13.5% crude reduction: n = 500. Interim analysis every 100 patients. The rules to recommend trial interruption by the independent committee (DSMB) have been predefined and published. Only the DSMB had access to the results of the interim analyses. The protocol has been published (1).
Results: At the time of abstract submission, 475 patients (95%) have been included, 72% in strata < 48 h and 28% between 48 h and 5 days. Median [IQR]: age = 64 [55–71] years, BMI = 30 [26–35] kg/m^2, APACHE 2 = 13 [9–18] points, CRP = 120 [56–190] mg/L, time from hospital admission = 5 [2–7] days. Use of hydroxychloroquine = 0.2%, remdesivir = 6.7%, anti-IL-6 = 3.5%, steroids = 95.0%. Day 28 mortality = 39%. Use of ECMO = 20%, vasopressors = 80%, RRT = 15%. No adverse event was directly attributed to the plasma. The DSMB have analyzed the results after 100, 200, 300 et 400 patients and recommended to complete the trial at each step. Patients' enrolment was stopped on April 13, 2022 because of the absence of new cases for more than one moths, likely due to the lower virulence of the Omicron variant. The database will be closed by June 2022 allowing definite results presentation.
Conclusion: This trial is the only one to test convalescent plasma which high titer of neutralizing antibodies against SARS-CoV-2 is documented in a population of COVID patients requiring MV. The day 28 and 90 outcomes of the entire population will be presented at the Congress.

000732

Prediction of the location of infectious droplets and aerosols with computational fluid dynamics in the rooms of ICU patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000732

Introduction: SARS-CoV 2 is likely transmitted between humans through direct contact and/or infectious droplets and aerosols. Droplets are defined as particles over 5 µL and aerosols as particles less than 5 µL diameter. Our aim was to estimate the location of the particles within a real intensive care room when hosting a patient with COVID-19 and assess the presence of SARS-CoV-2 in these particules.

Methods: We used the architectural features of several individual rooms of our Intensive Care department, the prescribed and measured heating, ventilation, and air-conditioning characteristics.
We modeled the air flow and droplet dynamics using Computational Fluid Dynamics. Unsteady RANS, three-dimensional numerical simulations used a k-w SST turbulence model with heat transfer and buoyancy for natural convection. The computational domain included the room ventilation system with piping and vents, air leakage from the doors, and the main objects in the rooms. Air and surface samples for SARS-CoV-2 PCR were guided by the simulation.
Results: The measured HVAC characteristics in terms of air flow were different than the prescribed one. Simulations showed that droplets were mostly present on the workbenches and on the floor in front of the door, and that aerosols flew vertically towards the ceiling, stayed in suspension or followed the leakage around the doors. SARS-CoV-2 was searched in the rooms of 9 patients treated with high flow oxygen and nasal Ct between 17 and 31. PCR was positive in 10/25 (40%) surface and 3/15 (20%) air samples where it was expected by simulation, and in 1/5 (20%) surface and 0/12 air samples where it was not expected. Positive surfaces were air-extract units, the floor in front of the door and the nurse workbench. Positive air samples were over the patient's head and in front of the door outside the room. Additional samples are underway to increase the prediction of the computational model.
Conclusion: In our institution, the observed HVAC characteristics are different from the prescribed ones. Taking the actual characteristics of the rooms into account and using a numeric 3-D simulation model, the use of a computational model accurately predicts locations where SARS-Cov-2 particles can be found.

000767

Complication of Central Venous Catheters usage—retrospective study in a Portuguese Intensive Care Unit

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Intensive Care Medicine Experimental 2022, **10(2)**:000767

Introduction: Central Venous Catheters (CVC) are increasingly used in the intensive care unit (ICU) set and are not without risk.1–7 Complications such as pneumothorax, vascular injury, infection and misplacement can occur and are responsible for significant morbimortality and consumption of healthcare resources.1–7
Objectives: The authors aimed to identify and characterize the occurrence of CVC-related complications in a portuguese ICU.
Methods: The authors performed a retrospective cohort study, between June and December 2021. Patients (aged $\geq$ 18 years) admitted to a 28 bed ICU that had a CVC placed during their ICU stay were included. CVC used for renal replacement therapy were excluded. Data collected: gender, date of birth, length of ICU stay (LOS), admission diagnostic, APACHE, SAPS II, use of ultrasound guidance and radiographic control following CVC placement, number of CVC lumens, anatomical CVC placement location, and coagulopathy (INR > 1.5). Data was analyzed with a statistical significance of 0.05.
Results: A total of 391 patients had a CVC placed during their ICU stay, of whom 268 were included. The median age was 62 (IQR 52–70) years, 60.1% were male and most additions were for a medical condition (68.7%). The median ICU LOS was 8 (IQR 3–15) days. Our population had a median APACHE score of 20 (IQR 13–26) and SAPSII of 43 (IQR 30–56). During the study period, 333 CVC were placed and the right subclavian vein was the preferred location (33.4%, n = 111). During the ICU stay, the median time of catheterization was 7 (IQR 4–12) days. One of the main reasons for CVC removal was the suspicion of a CVC-related infection (12.9%, n = 32). Medical records concerning use of ultrasound guided CVC placement was available in only 23 catheterization. Of those, 69.6% (n = 16) were guided. Thorax radiographic control up to 24 h after placement was performed in 96.1% (n = 317) of the patients. Complications occurred in 4% (n = 16) of all procedures. Pneumothorax was the most frequent immediate complication (71,4%; n = 5). CVC-related bloodstream infection was identified in 6 CVC with Stahylococcus epidermidis as the most frequently isolated agent (n = 3). In situ inflammatory signs without CVC-related bloodstream infection were observed in 3 patients (18.8%) and 1 patient (6.3%) had a deep vein thrombosis at the catheter site. The duration of the CVC implantation as a cause for CVC-related bloodstream infection was statistical significant (p = 0.001). Multivariable analysis did not identify any risk factors for the complications analyzed.
Conclusion: The literature describes CVC associated complication rates between 15 and 33%7. During the study period, the incidence of CVC-related complications in our study was lower. Despite all the preventive measures, bloodstream infection is still a frequent complication. Most often, infection occurs with skin agents such as Staphylococcus aureus and S. epidermidis2 as in our study. The local infection group has started to address this issue with the implementation of new protocols and staff education. This study conclusion may have been limited due to incomplete clinical records about the procedure, something to improve in the future.

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000789

COVID 19 mortality and corticosteroid – does dose matters?

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Intensive Care Medicine Experimental 2022, **10(2)**:000789

Introduction: SARS-CoV-2 is a single stranded RNA beta coronavirus. Controlling the immune host response to SARS-CoV-2 has been considered key in the fight against the COVID-19. The Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial demonstrated that dexamethasone reduced mortality in patients with COVID-19. However, the impact that corticosteroids have on the development of secondary infection in critically ill patients with COVID-19 remains unknown.
Objectives: To understand if the dose of corticosteroid is associated with secondary infection. To understand if there is an

association between corticosteroid dose and mortality at ICU and at 6 months.
Methods: We conducted an observational retrospective study on patients admitted in our ICU due to SARS-CoV-2 pneumonia in a tertiary referral hospital, between September 1st 2020 and March 31st 2021, corresponding to the second wave of the pandemic. All patients were mechanically ventilated and treated with corticosteroids. We collected demographics data; type and dose of corticosteroids; mortality in the ICU and at 6 months; and bacteria isolation. Secondary infection was considered in those with both clinical infection criteria and the presence of bacterial isolation. Patients were divided into three groups: A—standard RECOVERY dose group—dexamethasone 6 mg/day; B—high-dose group—methylprednisolone < 500 mg/day; and C—very high-dose group—methylprednisolone ≥ 500 mg/day. The data was analyzed using the SPSS® v. 25.0. The significance level used was 0,05.
Results: A total of 149 patients were enrolled: 108 (72.5%) males, with median age of 66 years (P25 = 57.0, P75 = 70.5). Median ICU length of stay (LOS) was 7 days (P25 = 3.5, P75 = 12.5). In 63 (42.3%) secondary infection was present. A total of 47 (31.5%) died during ICU stay. After discharge, a total of 10 (6.7%) patients died within the first 6 months. Group A had 103 patients (69%), while group B had 21 (14.1%) and group C had 25 (17.8%). Group B had a 66.7% prevalence of secondary infection, which was significantly ($p < 0.05$) higher compared with that found in the group A (28.2%) or C (36.0%). Considering the whole sample, survival at ICU was not associated with corticoid dose ($p = .580$). Survival at ICU was 68.0% for group A, 61.9% for group B and 76.0% for group C. At 6 months no survival differences were found between groups (log-rank test, $p = .832$).
Conclusion: In our sample, secondary infection was found in 42.3% patients and was higher in group B (66.7% vs 28.2% and 36.0% group A and C, respectively). Although some series demonstrate that secondary infection may be associated with the corticosteroid dose, our results may be biased and limited by sample size. The overall mortality in our study group was elevated (31.5%) in concordance with literature. Despite different prevalence of secondary infections between groups, we did not found differences in terms of survival, either during hospitalization or at 6 months ($p = .580$ and $p = .832$, respectively).

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000826

Continuation versus De-escalation of Broad Spectrum Antibiotic Therapy in Critically ill COIVD -19 patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000826

Introduction: Antibiotic de-escalation is a stewardship initiative that aims to reduce exposure to antimicrobials, thus limiting their unwanted effect, including antimicrobial resistance. Many guidelines advocated the daily assessment of de-escalation among septic patients. During the COVID-19 pandemic, many studies determined a higher rate of antibiotic utilization. Many initiatives proposed limiting antibiotics in COVID-19 patients. National Institute of Health (NIH) guidelines recommend against antibacterial therapy in moderate to severe COVID-19 unless clinical evidence of infection or secondary infection is suspected. Data on the de-escalation of antimicrobials in COVID-19 patients in a critical care setting is limited.
Objectives: To compare the mortality and presence of super-infection in the de-escalation versus continuation of antimicrobials in COVID-19 patients in the critical care unit, in the setting of a high prevalence of multi-drug resistant pathogens.
Methods: A single-center retrospective study included adult critically ill COVID-19 patients admitted between January 01, 2019, and August 31, 2021, and started on broad-spectrum antibiotics. Only patients started on antipseudomonal carbapenem or ceftazidime–avibactam were included. The study excluded those who received the broad-spectrum antibiotics for less than 48 h, ICU discharge, or death within 48 h of ICU admission. The primary outcome is ICU mortality. Secondary outcomes include super-infection, ICU and hospital length of stay, ICU readmission rate, and hospital mortality.
Results: The study included 73 patients with a mean age of 61.0 ± 19.4, and de-escalation was performed in 10 (13.6%) patients. In the de-escalation group, 8/10 (80%) of cultures were positive. Among the ten patients in the de-escalated group (13.6%), four (5.5%) required re-escalation of treatment. Meropenem was the most used antibiotic among 66 (90.4%) patients. Concurrent antibiotic use was found in ten (13.7%) patients, mainly fluoroquinolones 5 (6.8%) and aminoglycosides 4 (5.5%) among our patients.). The culture was positive in 35 (47.9%) of our patients. The most common reported microorganism was *Pseudomonas aeruginosa* in 7 (9.6%) cultures. The most commonly seen resistance patterns were extended-spectrum beta-lactamases and carbapenem-resistant Pseudomonas among 5 (14.3%) and 2 (5.7%) cultures, respectively. ICU mortality was not statistically different between groups (60% vs. 41.3%, P = 0.317) in de-escalation and continuation of therapy, respectively. Super-infections were similar between groups and only occurred in 4 (5.4%) patients. Hospital mortality, length of stay, and ICU readmission rates did not differ significantly between groups.
Conclusion: During the era of COVID-19, in critical care units with a high prevalence of multi-drug resistance, carbapenems were only de-escalated in a small percentage of high disease severity score patients and microbiological confirmation, with similar mortality to the patients in the continuation group. Although statistically non-significant, patients who continued broad-spectrum antibiotics had more frequent bacterial and fungal superinfections than those in the de-escalation group. Future studies are needed to improve rapid diagnostics in critical care units.

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000829

Clinical features and outcomes of patients with pancreatic cancer requiring medical ICU admission: a retrospective multicenter study

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Intensive Care Medicine Experimental 2022, **10(2)**:000826

Introduction: Pancreatic cancer is the sixth leading cause of solid malignancy in France, with increasing incidence and low survival probability. About 5–10% of cancer patients will require intensive care unit (ICU) admission in the two-year following diagnosis. However, there is no data regarding clinical features and outcomes of pancreatic cancer patients admitted to the ICU. Primary aim was to describe the reasons for ICU admission. Secondary aim was to identify factors associated with ICU mortality.
Methods: Retrospective multicenter cohort study in five French ICUs from January 2009 to January 2020. All consecutive patients with proved pancreatic cancer admitted to the ICU were screened for inclusion. Patients with a recent surgery were excluded (< 4 weeks). Logistic regression multivariate analysis was performed on ICU mortality.
Results: Two hundred and sixty-nine patients were included (161 (60%) males, 65 [57–73] median [interquartile interval] years old, simplified acute physiology score 2 (SAPS 2) 39 [29–55]). Tumors were mainly adenocarcinoma (90%) in cephalic location (70%). Time between diagnosis and ICU admission was 8 [1–17] months. At ICU admission, most of the cancer were metastatic (57%) and the disease was responsive/stable, newly diagnosed or progressive in 32%, 25% and 43% of cases respectively. Prior to ICU admissions 74% of patients received chemotherapy, 24% surgery and 13% radiotherapy.
By frequencies, reasons for ICU admission were sepsis/septic shock (32%) followed by gastrointestinal bleeding (28%), acute respiratory failure (16%), metabolic disorder (12%) and miscellaneous (12%). Among the 87 patients admitted with sepsis/septic shock, a biliary tract infection was identified in 45 (52%) patients. Biliary tract infection was more frequently observed in tumors with cephalic location than their counterparts (61% vs. 24%, $p = 0.003$). During the ICU stay, mechanical ventilation and vasopressors were required in 101 (38%) and 95 (35%) patients.
ICU mortality rate was 26% 95% confidence interval [20%;31%]. Using multivariate analysis, performance status 3–4 (OR 3.58), cancer status (responsive/stable -ref-, newly diagnosed OR 3.28, progressive OR 5.99), mechanical ventilation (OR 8.03), vasopressors (OR 4.19), SAPS 2 (OR 1.69) and pH (OR 0.02) were independently associated with ICU mortality.
Conclusion: The reasons for ICU admissions of pancreatic cancer patients seem to substantially differ from that observed in previous work on solid cancer (acute respiratory failure). ICU mortality seems roughly similar to that observed also in previous works on solid cancer and is strongly influenced by performance status, disease status and organs failure at ICU admission.

Infection 7

000839

Prevalence and outcome of Covid-19-Associated Pulmonary Aspergillosis in critically ill patients admitted to Intensive Care Unit

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Introduction: COVID-19-associated pulmonary aspergillosis (CAPA) remains a challenging diagnosis in the critically ill patient. Consensus definitions have been recently published based on mycological criteria, clinical characteristics and imaging findings, to help physicians in daily clinical practice regarding diagnosis and management of CAPA, and also on the grounds of clinical research.
Objectives: Aim of this study is to assess the prevalence of invasive pulmonary aspergillosis (IPA) in mechanically ventilated Covid-19 patients and its impact on mortality.
Methods: A retrospective study was conducted in a Covid-19 ICU of a Greek tertiary hospital, from October 2020 until February 2022 (17 months). Patients were diagnosed with CAPA, using the 2020 European Confederation of Medical Mycology/International Society for Human and Animal Mycology (ECCM/ISHAM) definitions. The baseline characteristics and outcome of the patients diagnosed with CAPA were recorded, and compared with those from patients without CAPA, admitted to the ICU with severe Covid-19 pneumonia. We used Welch's t-test to compare continuous variables due to unequal sample sizes, and chi-squared test for categorical variables. Binomial logistic regression was used to evaluate possible independent risk factors associated with CAPA diagnosis and mortality.
Results: During the study period, 384 patients (37% female) with PCR-confirmed SARS-CoV-2 infection were admitted to the ICU due to severe COVID-19 acute respiratory distress syndrome (ARDS). The mean age of all Covid-19 patients was 65.4 ± 13.2 (21-92). Seventeen patients ($n = 17$), 41% female, were diagnosed with CAPA, with a prevalence of 4,4%. The mean age of CAPA patients was 75.3 ± 11 (52–89) years, significantly higher than the mean age of non-CAPA cases, which was 65 ± 13.1, ($p = 0.001$). The median time from ICU admission to CAPA diagnosis was 6 days (0–15), and the mean ICU length of stay (LOS) of CAPA patients was 23.7 ± 22.4 (5–98) days, not significantly higher than the mean ICU LOS of non-CAPA patients, which was 16.4 ± 14.8 (0–156), ($p = 0.2$). All CAPA patients required mechanical ventilation. Median APACHE II score on admission was 13 and median Charlson comorbidity index was 4. Regarding comorbidities, 3/17 patients had chronic pulmonary disease (18%), 5/17 cardiovascular disease (29%), 6/17 diabetes type II (35%), 13/17 (76%) hypertension. All CAPA patients (100%) received dexamethasone for at least ten days. Only one (6%) received tocilizumab. Two of them (12%) required renal replacement therapy.
Direct microscopy of either bronchoscopic lavage or non-bronchoscopic lavage (NBL) was positive for branching hyphae in all CAPA patients. *Aspergillus* culture was positive in 16 out of 17 patients (94%). The distribution of *Aspergillus* species was as following: 6 (35%) *Aspergillus fumigatus*; 2 (12%) *A. terreus*; 5 (29%) *A. niger*; 2 (12%) *A. flavus*; 1 (6%) *A. flavus* + *A.niger.* Serum galactomannan (GM) was positive in one patient (6%), with index 0.98. Respiratory GM was positive in one patient, with index 5.5. *Aspergillus* PCR was not available. Twelve patients (71%) received voriconazole for treatment, 3 patients (18%) received liposomal amphotericin, one patient was treated with isavuconazole, while one patient did not get any treatment.
Overall ICU mortality of Covid-19 patients for the aforementioned period was 39% (150/384), while in the group of CAPA patients, mortality was 58.8% (10/17 patients), and in the group of non-CAPA patients mortality was 38.1%, ($p = 0.06$). In multivariate analysis, age was the only independent risk factor associated both with CAPA diagnosis

(OR: 1.09, 95%CI: 1.03–1.15, p = 0.002), and mortality (OR:1.07, 95%CI: 1.05–1.09, p < 0.001).
Conclusion: In relation to other studies, we observed a relatively low CAPA prevalence (4.4%) with a high mortality (58.8%), compared to the mortality observed in non-CAPA patients (38.1%), although the difference was not statistically significant at p < 0.05. In our cohort, CAPA patients were significantly older with relatively longer ICU stay. As timely diagnosis and prompt antifungal treatment are crucial, systematic testing for pulmonary aspergillosis in suspected cases of critically ill Covid-19 patients is needed.

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Acknowledgements: None

000843

Self-Reported Penicillin Allergy is Associated with Improved Survival in Critical Care

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Intensive Care Medicine Experimental 2022, **10(2)**:000843

Introduction: Self-reported penicillin allergy (SRPA) is far more common than true immune-mediated penicillin allergy. Approximately 10% of the population self-report a penicillin allergy (1–3), however it is estimated that fewer than 5% of these are true allergies (2–4). Many SRPA symptoms, such as rash or gastrointestinal disturbance, can be explained by other non-immune mediated reactions and there is a concern that self-reported penicillin denies patients antibiotics therapy that may severely impact on outcomes. Despite this a recent French study demonstrated lower mortality in SRPA (5). We performed an audit to assess the impact of SRPA in our ICU.
Objectives: To compare hospital mortality in patients with and without SRPA admitted to the Intensive Care Unit (ICU) in our institution.
Methods: We extracted age, sex, SOFA Score, admission demographics, antibiotic administrations and SRPA status from electronic patient records. We defined an antibiotic day as any calendar day on which an antibiotic was administered. A new antibiotic course was defined as antibiotics started after a period of 48 h without no antibacterial agents. Administration routes of intrathecal or topical antibiotics and chlorhexidine mouthwashes were excluded.
The primary outcome was hospital mortality. Secondary outcomes included ICU mortality, number of ICU courses and length of antibiotic treatment in days.
Results: There were 35,481 patients with complete data admitted to ICU during the defined study period. SRPA patients were older (mean 58.3 SRPA vs 56.8 non-SPRA, p < 0.001) and more likely to be female (52.2% SRPA, 37.3% non-SRPA, p < 0.001). The median time from Hospital Admission to ICU admission was longer in the SRPA group (0.70 days IQR 0.23–1.73 vs non-SRPA 0.67 days IQR 0.18–1.45 p < 0.001).
The unadjusted ICU mortality was 10.2% in SRPA and 11.4% in non-SRPA (p = 0.022). The difference persisted in a model adjusting for age, sex and admission SOFA score (no-SRPA OR 1.266 (95% CI 1.126 ± 1.423 p < 0.001)) and Cox Regression analysis of mortality at 28-days (p < 0.01). Adding the number of antibiotic days in ICU as an interaction or the number of courses did not account for the SRPA advantage (p = 0.558 and p = 0.391), neither did treatment with meropenem (p = 0.236). Hospital Mortality in ICU survivors was not different between SRPA and non-SRPA groups (p = 0.959).
Conclusion: Within the single-centre study of admissions to ICU, SRPA patients were more likely to older and female and was associated with lower ICU mortality despite delayed ICU admission. The additional use of meropenem did not account for our findings nor did the number of antibiotic courses or the number of antibiotic days.

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000864

Usefulness of periodic surveillance cultures to identify colonization and infection by multi-resistant saor to reduce the empirical consumption of linezolid in a polyvalent ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000864

Introduction: A total of 2,657 patients admitted consecutively between April 1, 2014 and November 30, 2021 in the polyvalent ICU of a 2nd level University Hospital were analyzed, after excluding 335 admissions with a SARS-Cov2 diagnosis from the study. Following the recommendations of the Zero Resistance Project (Envin-Helics), surveillance cultures (nasal, pharyngeal, rectal, and bronchial aspirate) were performed on admission and weekly in all patients.
Objectives: To evaluate the usefulness of periodic surveillance cultures to identify patients with colonization vs infection by SAOR and the avoidable consumption of linezolid in a polyvalent ICU of a 2nd level hospital.
Methods: The following were analysed: demographic variables, results of surveillance cultures, criteria and source of infection, prescription of linezolid (indication, empiric vs. directed administration, administration time).
Statistical analysis: qualitative variables in number and %, quantitative variables mean ± SD vs median + IQR according to the Kolgomorov Smirnov test. Analysis of sensitivity, specificity and predictive values. Software: SPSS25.
Results: Surveillance and clinical cultures of 2,657 admissions (non-SARS Cov2) over a 90-month period (Apr2014–Nov2021) were analyzed. 335 patients with SAOR isolation were identified in at least one surveillance sample and/or one clinical sample (obtained due to clinical suspicion of infection: fever, elevated reactants, sepsis and compatible focus), with an incidence rate = 4.00 isolations/1000 days of ICU stay.
55 cases (83.3%) were colonizations, 11 (16.7%) were infections: 4 (36.4%) pneumonias, 1 catheter bacteremia, 1 endocarditis, 1 orthopedic infection, 1 abdominal, 1 soft tissue, 1 urine. 50 of the isolates (75.8%) were positive in the screening performed on admission to the ICU and 16 (24.2%) were intra-ICU acquisition.
Surveillance screenings at admission and periodic were reported by the laboratory in 3 [3–4] days. Surveillance samples obtained prior to or simultaneously with the infectious process had a negative predictive value of 99.5%.

In the subsample made up of 920 non-SARS Cov2 admissions between January 1, 2019 and November 21, 2021, a total of 463 empirical linezolid treatments were analyzed to cover a respiratory focus, without subsequent microbiological confirmation of a susceptible microorganism: the duration was 4 (2–7) days, adding 815 defined daily doses/1000 stays. It was calculated that a protocol aimed at not starting or stopping linezolid treatment early in the absence of isolation of SAOR in surveillance cultures would have led to a minimum saving of 427 DDD/1000 stays.
Conclusion: Periodic surveillance cultures have a negative predictive value of 99% to rule out SAOR infection in non-SARS Cov2 critical patients. Its use to avoid or early suspend empiric linezolid allows a significant reduction in the consumption of linezolid in the ICU.

000935

Impact of obesity in 5167 critically ill patients with COVID-19

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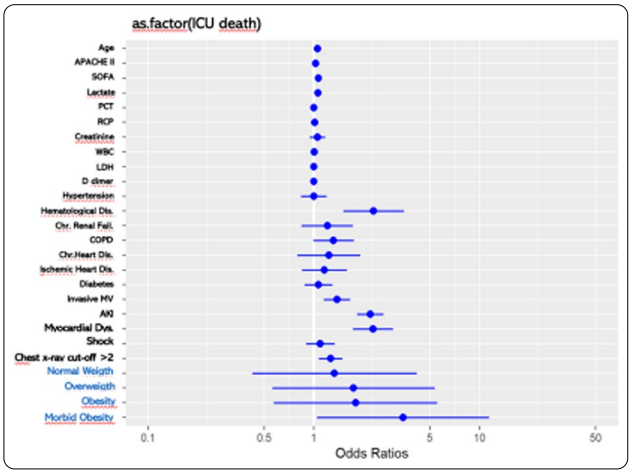
Intensive Care Medicine Experimental 2022, **10(2)**:000935

Introduction: The coronavirus disease 2019 (COVID19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has a wide range of symptoms from none to severe respiratory failure with diffuse lung damage and death. Given these diverse effects, understanding the risks for developing the most severe manifestations is particularly important. (1)
In Spain, it is estimated that in 2019 one in 4 men and one in 5 women suffered from obesity, defined as a body mass index (BMI) $\geq$ 30 kg/m^2 (2). Obesity and BMI has been shown to be associated with adverse outcomes in viral infections such as influenza (3). As reported, BMI may play an important role in COVID-19; however, this still remains unclear.
Objectives: To assess the impact of obesity on ICU mortality in critically ill patients with COVID-19.
Methods: Observational, multicenter, retrospective and pre-planned study in critically ill patients with COVID-19 admitted to 67 ICUs (2/20–3/21). The data was obtained from the COVID-19/SEMICYUC database. Only adults with COVID-19 confirmed by (RT-PCR) were included. Demographic characteristics, comorbidities, clinical and laboratory parameters and treatment received were recorded. Follow-up was until death or discharge from the ICU. Patients were classified according to BMI as: A) Obese (O) BMI > 30 and B) non-obese (NO) for univariate comparisons between groups and 1) Underweight (UW): BMI < 19; 2) Normal weight (NW): BMI 19–25; 3) Overweight (OW): BMI > 25–29.9; 4) Obesity (OB): BMI 30–40 and 5) Morbid obesity (MO): BMI > 40 for multivariate analysis. Differences were evaluated using Chi square, U Mann–Whitney or Wilcoxon, as appropriate. The impact of obesity on mortality was performed through binary logistic regression (LR). For the internal validation of the model, the population was randomly divided into a training group (80%) and a validation group (20%). Model performance was assessed using accuracy and AUC ROC. $p < 0.05$ was considered statistically significant.
Results: A total of 5167 patients were included, 1668 (32.3%) were OB, 244 (4.7%) MO, 2347 (45.4%) with OW, 871 (16.9%) with NW and 37 (0.7%) in UW. The O were younger (61 vs 65 years, $p < 0.05$), with a higher incidence of hypertension (53.6% vs 41.6%, $p < 0.05$), diabetes (29.4% vs 19.4%, $p < 0.05$), asthma (7.5% vs 5.7%, $p < 0.05$) and chronic heart failure (4.1% vs 3%, $p < 0.04$) compared to NO. No differences were observed in severity (APACHE II 13 vs 13 and SOFA 4 vs 4), need for mechanical ventilation (43% vs 41%, $p = 0.19$) and ICU mortality (29.4% vs 28.6%, $p = 0.58$) between O vs NO. Only MO (OR = 3.4, 95% CI 1.1–13.0) was independently associated with ICU mortality in the multivariate analysis (Figure). The model was adequate (Hosmer–Lemeshow $p = 0.12$) with an accuracy of 75% and AUC of 0.78 (95% CI 0.76–0.81).



Conclusion: The presence of obesity was not associated with higher mortality in the ICU, except in morbid obesity.

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Acknowledgements: None.

000953

Effects of high dose intravenous vitamin C in critically ill COVID-19 patients. A retrospective propensity matched before-after study

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Intensive Care Medicine Experimental 2022, **10(2)**:000953

Introduction: Vitamin C has been reported to have a potential signal of benefit for critically ill COVID-19 patients.
Objectives: This study aimed to investigate the effect of high dose of intravenous vitamin C (HDIVC) on clinical course and outcomes in critically ill COVID-19 patients.
Methods: We performed retrospective propensity matched before-after study, in which we compared the clinical course and outcomes of critically ill COVID-19 patients treated with a HDIVC protocol (intravenous injection of vitamin C 22.5 g on the first day of admission, followed by 12 g per day for 3 days) with a control group treated without HDIVC protocol. Patients in control group were treated between January and March 2021 and patients in HDIVC group—between April and June 2021.
Results: The HDIVC and control groups each comprised of 57 and 55 patients. Compared to the control group, there was no difference in duration of invasive mechanical ventilation and ICU mortality. However, HDIVC resulted in a higher survival rate on day 4 (last day of protocol) ($p < 0.05$). During the 4-day treatment period, patients in the HDIVC group had a significantly higher pH on day 2 (7.41(7.37–7.46) vs 7.36(7.30–7.42), $p = 0.006$) and on day 3 (7.44(7.37–7.49) vs 7.37(7.27–7.42), $p < 0.001$), with no differences in $PaCO_2$, comparing with the control group.

Conclusion: HDIVC may be beneficial in the treatment of critically ill COVID-19 patients, which may be related to its improvements in the metabolic state (pH) and in survival rate during HDIVC protocol. Further randomized controlled trials are required to augment these findings.

000986

Prognostic feasibility of determining NLR in addressing the issue of surgical treatment of patients with intestinal obstruction

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Intensive Care Medicine Experimental 2022, **10(2)**:000986

Introduction: Intestinal obstruction (IO) is a clinical symptom complex characterized by the cessation or impairment of the passage of contents through the intestine, caused by various reasons [1,2]. IO is one of the major indications requiring emergency abdominal surgery, and it has a high morbidity and mortality rate when not treated properly [3].
The neutrophil-to-lymphocyte ratio (NLR) is known to be a valuable diagnostic marker in decisions about surgical procedures in urgent cases. It has also been reported that NLR can be used as an independent marker of septic shock and sepsis when a patient is admitted to an intensive care unit [4,5].
Objectives: Research of the ratio of NLR as a cheap and easily calculated marker in the surgical treatment of patients with intestinal obstruction (IO).
Methods: The study included 135 patients hospitalized with IO. The patients were divided into two groups: first group—patients who were operated on with intestinal obstruction and second group—patients who received conservative therapy.
Demographic data, such as age and gender, and CBC parameters, such as neutrophil, lymphocyte, WBC, CRP, and NLR values, of the hospitalized patients were statistically evaluated to determine whether there was any difference between the groups.
Results: The results obtained at the initial blood count were compared between patients who were operated on ($n=67$) and conservative therapy ($n=68$). No statistically significant difference in WBC counts was found between first and second group ($p=0.237$). The mean CRP levels were 62.59 ± 70.91 mg/L in the first group and 58.54 ± 68.89 mg/L in the second group. There was no statistically significant difference between the groups in terms of CRP levels ($p=0.67$). The mean NLR values were 9.03 ± 2.89 in the first group, and 8.21 ± 5.60 in the second. Thus, the NLR values were higher in the first group, and there was a statistically significant difference between the groups ($p=0.023$)
Conclusion: As in previous studies examining other criteria for inflammation, we found that high NLR values were statistically significant in favor of the surgical treatment group when determining the need for surgery in cases of intestinal obstruction. The data obtained in our study demonstrate that NLR measurement contributes to early surgical decision-making in patients with intestinal obstruction during their initial hospitalization in the surgical department.

000992

Inadequate Voriconazole And Isavuconazole Serum Concentrations In Critically Ill Patients On Mechanical Ventilation

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Intensive Care Medicine Experimental 2022, **10(2)**:000992

Introduction: Invasive aspergillosis is an increasingly frequent infection in our environment due to the increase in oncological therapies, biological/corticoid treatments or viral infections, such as influenza virus or SARS-CoV-2, among others.
Objectives: To describe trough serum levels of voriconazole and isavuconazole monitored to determine therapeutic range vs toxic effects, in a cohort of critically ill patients with diagnosis or high suspicion of invasive aspergillosis on mechanical ventilation and MODS.
Methods: Descriptive observational study about serum levels of patients treated with voriconazole who received two doses of 6 mg/kg on the first day and maintenance dose 4 mg/kg/12 h from second day, along with patients on CRRT treated with isavuconazole who receiving 200 mg/8 h the first two days and 200 mg/24 h from the third day.
Serum trough levels were measured using the HPLC method at steady state, considering 1.5–5.5 mg/L as the therapeutic range for voriconazole and 2–5 mg/L for isavuconazole. Renal or hepatic dysfunction were considered as SOFA scale ≥ 1 point.
The following variables were collected: APACHE II, SOFA scale at sample extraction, pre-treatment renal and hepatic function and extraction day *(Table* 1*)*.

TABLE 1: Summary of the characteristics and results obtained.

LEVELS	APACHE II	SOFA	% AKD	% ALD
THERAPEUTIC RANGE	17.5	9	33%	33%
SUBTHERAPEUTIC	11	8	0%	37.5%
SUPRATHERAPEUTIC	23	9	12.5%	50%

*AKF: acute kidney dysfunction *ALF: acute liver dysfunction

Results: Total of 25 determinations of VORICONAZOLE were carried out in 14 patients. Only 36% of them were in the therapeutic range but not 64% of cases (50% in subtherapeutic range and 50% supratherapeutic).
In case of **levels in therapeutic range**, 11% of patients had renal or hepatic dysfunction prior to treatment, evolving to 33% in each case during treatment. The same dose was maintained.
In case of **levels in subtherapeutic range** (average 0.65 mgL, $SD \pm 0.33$), 12.5% had liver dysfunction prior to treatment and 37.5% developed it during treatment. However, no patient presented or developed renal dysfunction. Doses were increased according to levels obtained.
In case of **levels in supratherapeutic range** (average 8.4 mg/L, $SD \pm 2.66$), none of patients presented hepatic or renal dysfunction prior to treatment, but 50% developed hepatic dysfunction and 12.5% renal dysfunction. Doses were decreased according to levels obtained.
Despite current ISAVUCONZOLE levels consideration as an unobservable variable, as part of our study we collected determination of levels, obtaining an subtherapeutic range in 67% of cases (1.28 and 1.5 mg/L).
Conclusion: The result of our observation highlights the importance of monitoring serum levels of voriconazole, since it allows dose adjustment, according to range of determination, to achieve an effective treatment and avoid toxicity derived from overdose, which in our sample means development of liver dysfunction in 50% of patients.
In case of isavuconazole, preliminary result of our study is interesting since it could call into question the current premise of not requiring monitoring of its levels. However, we do not have enough data to draw conclusions and future studies are necessary in this regard.

001003

Impact of corticotherapy and administration of corticosteroids in the 6th wave of covid: superinfection and mortality

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Intensive Care Medicine Experimental 2022, **10(2)**:001003

Introduction: The worldwide pandemic caused by SARS-COV-2 infection has urged us to establish new treatments. Since Coronavirus

disease is characterized by dysregulated hyperimmune response, a potential tool in the treatment of it has been corticosteroids and immunomodulators.
Objectives: We aim to compare if there is an increased in the rate of nosocomial superinfections (respiratory infections related to mechanical ventilation, catheter-related bacteremia, device-associated urinary tract infection) in patients with respiratory distress syndrome caused by SARS-CoV-2 treated with corticosteroids at high dose (> 1 mg/kg/day of methylprednisolone) and/or immunomodulators (monoclonal antibody tocilizumab; JAK2 inhibitor baricitinib) as well as their association with mortality.
Methods: Longitudinal retrospective observational study, based on a consecutive series of cases treated in the Intensive Care Medicine Service of the Virgen de las Nieves University Hospital in Granada (Spain,) on a cohort of 83 patients with SARS-CoV-2 infection diagnosed between September 20 from 2021 to February 20, 2022. The treatment received is classified in high-dose corticosteroids (> 1 mg/kg/day of methylprednisolone); immunomodulators (tocilizumab, baricitinib); combination of both or none. We evaluate the presence of superinfection in these patients by classifying it in respiratory infections, catheter-related bacteremia and device-associated urinary tract infection. Finally we compared mortality in the different treatment groups.
Results: 83 patients were included in the study, among them, 8 patients (9.8%) were treated with high dose of corticosteroids; 5 (6%) received immunomodulators; 23 patients (27.7%) were treated with a combination of both and 47 (56.5%) didn't have neither of both. Surinfection happened in 31.3% of patients, the most prevalent focus was respiratory infections (14.7%); 8.5% of patients had urinary tract infection and bacteremia was the rarest infection suffered by 7.3%. There was a statistically significant relationship in the incidence of superinfection in the group of patients treated with tocilizumab, high doses of corticosteroids or a combination of both ($p < 0.05$). There was no statistically significant relationship with treatment with baricitinib alone or in combination with corticosteroids.
With regard to mortality, no statistically significant differences have been found in the group of patients treated with these drugs (either in monotherapy or in combination), with respect to those who did not receive these treatments.
Conclusion: We have found an increased risk of infection in patients treated with corticosteroids, tocilizumab or both, not with baricitinib or its combination with corticosteroids. There is no difference in the mortality of patients treated with these drugs compared to those not treated with them

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001008

Analysis of the impact of the vaccination against COVID-19 in patients admitted to the ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:001008

Introduction: COVID-19 infection has represented a significant health impact. The development of vaccines has been one of the main advances in the fight against it. Following the introduction of the vaccine, patients who had received the vaccine have been added to the usual patients admitted to the ICU for COVID-19. Although it appears that patients who have received the vaccine have a lower risk of developing serious disease we do not know what the evolution may be once they are admitted to the ICU.
Objectives: The objective of this study is to evaluate the effects of vaccination on the evolution of patients with SARS-CoV-2 infection admitted to the ICU. We assess the need for respiratory support: high-flow cannulas (HNOs), invasive mechanical ventilation, or both in vaccinated and unvaccinated patients as well as their association with mortality.
Methods: Longitudinal retrospective observational study based on a consecutive series of cases treated in the Intensive Care Medicine Service of the Virgen de las Nieves University Hospital in Granada (Spain) about a cohort of 83 patients with SARS-CoV-2 infection diagnosed between September 20, 2021 and February 20, 2022 by PCR in which the vaccination status was evaluated by classifying in complete vaccination (two doses) and unvaccinated/incomplete vaccination (1 dose).
Within each group, the need for respiratory support is studied: high-flow cannulas, invasive mechanical ventilation or both and its association with mortality during hospital admission.
Results: During this period, a total of 83 patients were admitted to the ICU, of which 53 patients (63.9%) had received a complete vaccination schedule; 30 patients (36.1%) had not been vaccinated and had done so with a single vaccine. Regarding the type of respiratory support received, 27 patients (32.5%) received only support with High Flow Nasal Cannula Oxygen Therapy (ONAF); 15 patients (18.1%) received only Invasive Mechanical Ventilation (IMV); 25 patients (30.1%) received ONAF + IMV and 13 patients (15.7%) received conventional oxygen therapy or no support. Received a complete vaccine schedule is not associated with having received ONAF without IMV with $p = 0.0628$.
In terms of mortality, 22 patients (26.5%) died during hospital admission with a statistically significant association between the complete regimen and greater survival ($p < 0.05$).
Conclusion: Complete vaccine is not associated with reduced need for invasive mechanical ventilation in patients admitted to the ICU for SARS-CoV-2 infection, however, patients with two doses of vaccine have lower mortality compared to unvaccinated or vaccinated patients with incomplete regimens

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Acknowledgements: none.

001030

Control of the outbreak of invasive pulmonary aspergillosis associated with COVID-19 (CAPA) through a program of measures

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Intensive Care Medicine Experimental 2022, **10(2)**:001030

Introduction: Invasive pulmonary aspergillosis associated with COVID-19 (CAPA) is a serious complication of critically ill patients. There is a strong relationship between the incidence of invasive aspergillosis and environmental contamination by aspergillus.
Objectives: In the COVID-ICU of the Ramón y Cajal Hospital (Madrid) with 24 beds, we detected an outbreak of CAPA in April 2021, coinciding with hospital remodeling works.Our primary objective is to verify the efficacy of a CAPA-control protocol with environmental detection measures, active search for CAPA, and antifungal prophylaxis.
Methods: CAPA criteria according to ECMM/ISHAM consensus definition CAPA-control protocol consisted of:
-Prophylaxis with inhaled amphotericin B lipid complex (ABLC), 50 mg every 48 h (Aerogen®) to all patients on mechanical ventilation.
-Active search for CAPA by fiberoptic brochoscopy;
-Fungal culture and galactomannan in bronchoalveolar lavage if there was suspicion of co-infection or intra-ICU infection.
-Weekly measurement of environmental aspergillus and surfaces.
-Cleaning and isolation measures if environmental aspergillus/surfaces > 10 5UFC/m^3.
Efficacy definition: Detection of environmental aspergillus < 10 CFU/m^3 and < 10% incidence of CAPA.
Results: We recorded two CAPA outbreaks applying the CAPA-control protocol.
First in April-2021; 11 CAPA patients in 3 weeks, incidence of 22.4% (11/49), aspergillus > 10 environmental CFU/m3. Outbreak control on 10-May-21. After starting prophylaxis with ABCL, the incidence of CAPA decreased to 0, even with persistence of aspergillus > 10 CFU/m^3. Withdrawal measures July-21 due to low incidence and absence of environmental contamination.
Second outbreak in August-2021; incidence 18.5% (5/27) and aspergillus > 10CFU5. Once again, protocol efficacy after starting prophylaxis, even with persistence of environmental contamination.
Conclusion: A protocol of measures that includes antifungal prophylaxis with inhaled ABCL was effective in controlling the CAPA outbreak in the context of environmental contamination of aspergillus.

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Infection 8

001047

Lung necropsy of covid-19 patients: correlation between microbiological analysis of respiratory secretions and postmortem sample culture

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Introduction: One of the main causes of mortality in COVID19 patients was bacterial superinfection. It is important to know how many of the deceased had some microorganism in the postmortem study that was not present in the previous respiratory secretion culture, in order to evaluate the antibiotic therapy administered.
Objectives: Our objectives are to evaluate the correlation between the microorganisms isolated in the respiratory secretions of patients during their stay in the ICU with their presence or not in the autopsy study of the lung paremchyma, in order to determine in this way the convenience of broad-spectrum antibiotic therapy.
Methods: We have collected lung samples from 43 deceased patients diagnosed with COVID19 (fine needle puncture) who were sent to microbiology and compared them with the last sample analyzed from the same patient while he was admitted to the ICU. The antibiotics administered at the time of exitus are evaluated with respect to the microorganism isolated postmortem. Likewise, analytical data such as PCT, CRP, ferritin, leukocytes and lymphocytes are collected at the time of admission to the ICU and at Exitus.
Results: Approximately 40% of premortem samples are negative, the most commonly isolated microorganism has been Candida, followed by *E. coli* and Pseudomonas. In contrast, more than 50% of post-mortem samples are negative. HSV was not diagnosed or treated in any patient during ICU admission, although it was positive in more than 15% of postmortem samples. Procalcitotin on admission was normal in more than 75% of cases. 35% had leukocytosis at admission, another 35% leukopenia. Only in two cases were multiresistant microorganisms isolated at necropsy. 95% of the patients had antibiotic therapy at the time of death, of which 2 out of 3 were empirical, with carbapenems generally used in more than 95% of the patients at the time of death (and more specifically meropenem).
Conclusion: In general, there are no significant microbiological isolates in postmortem samples compared to premortem samples. The data point to an overuse of carbapenems with negative cultures. No differences seem to be observed in terms of microbiological isolates in the biopsy between patients who received immunomodulatory therapy vs COVID19 compared to those who did not receive it, although more precise studies would be needed to confirm this.

001036

After ICU admission… Vaccine or no vaccine?

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Intensive Care Medicine Experimental 2022, **10(2)**:001036

Introduction: The reluctance to receive COVID-19 vaccine is a significant growing public health concern forits terrible consequences. Currently we have evidence on the beneficial impact of having a full-vaccination for SARS-CoV-2. We present the results of the patients admitted to the ICU duringthe period of time in which the population had availability to the vaccine, their decision andsubsequent conduct.
Methods: We screened and recorded all consecutive patients admitted to the Intensive Care Departmentin a polyvalent Intensive Care Unit, diagnosed with SARS-CoV-2 pneumonia, from May 1 st, 2021, to June 6 th, 2021. At this time, more than 23 million vaccines had been administered in Spain.
48.9% of the population had received at least one dose. Among the age group, 50–59 years, 85.7% had been vaccinated. Being higher than 90% in older groups. The period of timeselected is the necessary for the discharged patients to have had the opportunity to bevaccinated after admission, given that they had to wait six months from the initial diagnosis ofSARS COV2 pneumonia.
We collect, sex, SOFA, APACHE II, SAPS II, mean age, mechanicalventilation, ICU stay, mortality and subsequent vaccination.
Results: 30 patients were admitted to our ICU. Among the admitted patients, 76.5% (23) were men, with mean age of 55.4, 66.6% (20/30) of these underwent mechanical ventilation, with a meanICU stay of 10 days. Most of these patients (83%) were not vaccinated. 68%

requiredmechanical ventilation compared to 60% of the vaccinated patients.
The overall mortality ofthe sample was 13.3% (4/30), 20% (1/5) in vaccinated patients and 12% (3/25) in unvaccinated.Of the 22 survivors in the unvaccinated population who were discharged from the ICU.
All ofthem were educated about the benefits of the vaccine, the possibility of having minimized theseverity of their infection and preventing their relatives and themselves from undergoingthrough this situation.
After this, 100% of the patients who were unvaccinated at first arecurrently fully vaccinated.
Conclusion: Our patients, who required admission to the ICU, intubated and underwent mechanicalventilation, decided to being vaccinated aftermath. The scientific literature published supports the paramount importance of vaccination. Ourpatients, after having suffered the consequences of the disease to the greatest degree, rectifies their decision of not being vaccinated.

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001048

Antimicrobial use and nosocomial infection incidence in critically ill patients during the first COVID-19 wave—results from the ESICM UNITE COVID study

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Intensive Care Medicine Experimental 2022, **10(2)**:001048

Introduction: During the first COVID-19 wave, treatment guidelines advised early use of antimicrobial therapy as a high risk of bacterial co-infection was expected based on earlier experience with influenza. During the first COVID-19 wave however, clinical experience suggested that co-infection at admission was lower and nosocomial infection during ICU stay higher than anticipated [1].
Objectives: To describe the antimicrobial use and nosocomial infections in critically ill patients during the first COVID-19 wave.
Methods: Sub-analysis of the ESICM UNITE-COVID study, a multicentre, international, point prevalence study, including adult patients with confirmed COVID-19 diagnosis under intensivists care on the day with the highest number of patients under intensivist care during wave one (defined as the 15th of February until the 15th of May 2020). Data collected included co-infection at ICU admission, nosocomial infection (operationally defined as an infection developing after ICU admission and during ICU stay) and antibiotic use, including antibiotics used as well as antibiotic free days at day 30. Statistical analysis was performed using R Statistical Software. Categorical variables are expressed as frequencies (percentages), continuous variables are described with medians with interquartile range [25th to 75th percentile]. Differences in categorical variables were assessed with chi-squared tests. Statistical significance was defined as $p < 0.05$.
Results: 4,994 patients from 280 hospitals in 46 countries were included in this study. 15% of patients were diagnosed with a bacterial pulmonary co-infection on admission with a slightly higher prevalence in patients intubated at admission (7.74% vs 7.18%, $p = 0.04$). 85% of all included patients were prescribed antimicrobials within 24 h after ICU admission with a median of 2 [1–3] antimicrobials per patient. Antimicrobials used included azithromycin (34.4% of patients), ceftriaxone (34.2%), piperacillin–tazobactam (20.3%), meropenem (12.4%), co-amoxiclav (12.3%) and clarithromycin (9.67%).
During ICU stay 56.7% of patients developed a nosocomial infection, with a median of 2 [1–2] infection sites per infected patient. Most nosocomial infected patients experienced a bacterial pulmonary infection (77.0%), non-catheter related bacteraemia (26.1%), urinary tract infection (21.1%) or central line associated infection (20.7%). 24.5% of nosocomial infected patients were infected with a multi drug resistant organism, the most common being ESBL (4.1%), MRSA (2.5%), Acinetobacter (2.3%) and MDR pseudomonas aeruginosa (2.3%). The median number of days alive without antimicrobials at day 30 since admission was 7 [0–17].
Conclusion: Although bacterial pulmonary co-infection at admission was low, antimicrobial use within 24 h of admission was high. Nosocomial infection rate was high and infection with an MDRO was common, resulting in few antimicrobial free days.

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Acknowledgements:
1. ACM is supported by a Clinician Scientist Fellowship from the Medical Research Council (MR/V006118/1).
2. JDW is is a Senior Clinical Investigator funded by the Research Foundation Flanders (FWO, Ref. 1881020N)

001051

Can selective decontamination of the digestive tract (SDD) reduce ventilator-associated pneumonia (VAP) in critically ill COVID-19 setting?

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Intensive Care Medicine Experimental 2022, **10(2)**:001051

Introduction: The effectiveness of selective decontamination of the digestive tract (SDD) in preventing of ventilator-associated pneumonia (VAP) in critically ill patients is controversial. We investigated if SDD prevents VAP in COVID-19 setting. VAP bundles were routinely applied in all invasive ventilated patients and from the third wave SDD were used.
Methods: We retrospectively analysed 321 invasive mechanical ventilated COVID-19 patients consecutively admitted to the intensive care (ICU) from February 2020 to December 2021. Our study is a pre-post study in which 63 (19.6%) patients who received SDD were compared with 258 who did not.
Results: VAP occurred in about 35% of patients with no differences in both groups (p = 0.638), no difference was also found with regard to early and late ones. VAP were mainly caused by gram negative microorganism (68.8%) both without differences between the two groups (p = 0.690). SDD group showed a reduction of pseudomonas aeruginosa (10.0 vs 28.9%) and klebsiella spp (15.0 vs 21.1%) and an increase of other entobacterales (35.0 vs 17.8%), although without statistically differences. Moreover, SDD group showed a reduction of multidrug-resistant pathogens (20.0 vs 45.6%, p = 0.036).

	No SDD (n = 258)	SDD (n = 63)	p value
VAP (n, %)	90 (34,9)	20 (31,7)	0,638
VAP Gram-stained micro-organisms			0,690
VAP Gram-positive micro-organisms (n, %)	28 (30,4)	7 (35,0)	
VAP Gram-negative microorganisms (n, %)	64 (69,6)	13 (65,0)	

	No SDD (n = 258)	SDD (n = 63)	p value
VAP Microorganisms species (n, %)			0,408
S. aureus	24 (26,7)	6 (30,0)	
Pseudomonas aeruginosa	26 (28,9)	2 (10,0)	
Klebsiella spp	19 (21,1)	3 (15,0)	
Other entobacterales	16 (17,8)	7 (35,0)	
Other	5 (5,6)	2 (10,0)	
VAP MDR (n, %)	41 (45,6)	4 (20,0)	0,036

Conclusion: In COVID-19 ICU patients SDD did not seem to be useful in preventing VAP, although it did seem to modify the microbiological flora.

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Acknowledgements: Modena COVID19 Working Group

001053

Changes in etiology of nosocomial infections during COVID-19 pandemics and antibiotic stewardship

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Introduction: Changes in bacterial flora of nosocomial infections during covid-19 pandemic evolution has not been extensively reported. Furthermore, a low rate of bacterial coinfection in patients with covid-19 has been reported and empirical antibiotic stewardship recommended.
Objectives: Main objective of this study is to evaluate changes in bacterial flora of nosocomial infections in critically ill patients with covid-19 during different waves of the pandemic. Second objective is to evaluate the implementation of an empirical antibiotic stewardship program during this period.
Methods: Retrospective observational single center study of adults with covid-19 admitted to an Intensive Care Unit of a University Hospital from March 2020 to June 2021. Patients were distributed in four pandemic waves depending on the date of admission. Etiology of bacteremias and the first episode of clinically suspected nosocomial respiratory infection were analyzed. Empirical antibiotic stewardship program was implemented during the pandemic course.
Results: Of 671 patients studied (mean age 62,7 years old/68,7% male), 256 microorganisms were isolated from respiratory cultures and 231 from blood cultures. Distribution of microorganisms isolated in respiratory and blood samples during the different pandemic waves is detailed in tables 1 and 2. During the first two waves Enterobacteriaceae sp were predominant in respiratory infections versus methicillin sensitive Staphylococcus aureus (MSSA) which prevailed in the fourth one (table 1). Coagulase negative Staphyococcus (CNS) were most prevalent microorganisms isolated in blood cultures while high rate enterococcus bacteremia at the beginning dropped significantly later.

In the first wave, 96% of the patients received empirical antibiotic therapy (92% combination therapy) compared with the 25,9% during thwe foruth wave (27% combination therapy) (p < 0,05) (table 3).

Table 1. Microorganisms responsible for the first episode of respiratory infection.

	Wave 1	Wave 2	Wave 3	Wave 4	P
Non-Fermentative Gram Negative Bacilli	29,2	28,1	29	16,9	> 0,2
Enterobacteriaceae	37,5	44,8	34	18	< 0,05
MSSA	4,2	12,5	22	41,6	< 0,05
Aspergillus sp	12,5	10,4	1,7	7,8	0,19

Table 2. Microorganisms isolated in blood cultures during the pandemia.

	Wave 1	Wave 2	Wave 3	Wave 4	P
E. faecalis	33,3	10,3	11,9	9,1	0,018
E. faecium	6,7	9,2	11,9	3,6	> 0,2
CNS	50	48,3	30,5	45,5	0,085
MSSA	0	2,3	3,3	12,7	0,018
Enterobacteriaceae	0	11,5	6,8	9,1	> 0,2
Candida	0	6,9	6,8	0	0,13

Table 3	WAVE 1 N = 61	WAVE 2 N = 229	WAVE 3 N = 193	WAVE 4 N = 188
Empiric antibiotics(%)/Combination therapy (%)	96,7/92	79,5/77*	51,8/63*	25,9/27*
Ceftriaxone (%)	92	82	79,8	81,3
Azitromicine (%)	95	79,3	59,6	25
Levofloxacine (%)	3,4	1,1	6	6,26
Piperaciline/Tazobactam (%)	0	5,2	9	6,25

Conclusion: A change in bacterial etiology of nosocomial infections has been documented during the course of the pandemic. Implementation of antibiotic stewardship program resulted in a reduction of antibiotic consumption which is probably, in part, the explanation of the changes in the etiology of nosocomial infections.

001062

Impact and occurrence of herpes virus infection and pulmonary aspergillosis in mechanically ventilated COVID-19 patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001062

Introduction: Pulmonary superinfections with Herpesviridae (1) and Aspergillus species (2) are common in patients with severe COVID-19 pneumonia, but there is little data about the epidemiology and impact of these superinfections in patients with severe COVID-19 pneumonia.
Objectives: The aim of this study was to review the virology and fungal results in patients with COVID-19 on mechanical ventilation who underwent diagnostic bronchial lavage (BL) to identify possible risk factors and the impact on clinical outcome.
Methods: In this retrospective observational study, data were collected from the electronic records of mechanically ventilated patients in the ICU of Deventer Hospital in 2020 and 2021 with COVID-19 pneumonia

(wild type, alpha and delta variants), undergoing BL. Blood and respiratory samples, treatment given, and clinical outcome were analysed.
Results: Of 160 mechanically ventilated COVID-19 patients admitted to our ICU, 61 underwent BL, all because of clinical deterioration. Of these, 18 had COVID-19 associated pulmonary aspergillosis (CAPA), 7 had infection with herpes virus (5 HSV and 2 CMV), 9 had herpes virus infection (8 HSV and 1 CMV) and CAPA combined, and 27 had no viral or fungal superinfection (Table 1). These superinfections were treated with antiviral and antifungal medication as indicated. High dose corticosteroid treatment was not given to CAPA patients. When patients with only herpes virus infection were compared with only CAPA, viral infection was diagnosed later in the course of mechanical ventilation (median of 14 days vs. 8 days, $p=0.014$). Patients with viral infection spent more time on mechanical ventilation and in the ICU (median 47 vs 18.5 days, $p=0.015$ and 74 vs 24, $p=0.021$ respectively). Neither pretreatment with dexamethasone or tocilizumab, nor any of the other baseline and laboratory parameters showed a significant association with viral infection or CAPA in logistic regression analysis or ANOVA. There was a significant difference in the duration of ICU stay: CAPA 24 (15.5–53.0) days, viral 74 (34–88) days, combined superinfection 29.9 (24.3–34.9) and no superinfection 24 (14–40) ($p=0.010$). There was no significant difference in mortality between the groups.

	Total (n=61)	CAPA (n=18)	herpes infection (n=7)	CAPA and herpes (n=9)	No CAPA/herpes infection (n=27)	*p*-value
Baseline parameters						
Sex (man)	45 (73,8)	15 (83.3)	4 (57.1)	5 (55.6)	21(77.8)	0.306
Age, *years*	67 (63-72)	66 (61.5)	65 (64-72)	66 (57-74)	69 (64-72)	0.900
Dexamethasone	52 (85,2)	16 (88.9)	6 (85.7)	9 (100)	21 (77.8)	0.400
Tocilizumab	29 (57)	7 (38.9)	5 (71.4)	5 (55.2)	12 (44.4)	0.479
BMI,	27.9(25.6-33.4)	29.3 (25.8-33.6)	25.3 (25-29.4)	29.9 (24.3-34.9)	27.7 (25.0-32.0)	0.754
Laboratory findings						
White blood cell count, */nl*	13.3(8.7-20.4)	13.6 (8.8-20.7)	17.3 (7.1-23.5)	12.2(10.3-21.3)	12.1(7.4-20.4)	0.887
CRP, *mlf*	68 (17.5-217.5)	55.5 (21.0-155)	70 (41-244)	83 (3-183)	133(13-237)	0.725
P/F-ratio, *kPa*	19.9 (14.3-22.6)	19.6 (14-23.5)	14.7 (13.9-21.2)	16.6 (13.7-21.1)	20.4(15.2-23.0)	0.456
Lymphocytes, */nl*	1.0 (0.7-1.5)	0.9 (0.6-1.3)	1.4(0.7-2.1)	0.8(0.3-1.4)	1.2(0.7-1.6)	0.552
Treatment						
Antifungal,	27 (26.2)	18 (100)	0 (0)	9 (100)	0 (0)	0.000
Antiviral	16 (15.5)	0 (0)	7 (100)	9 (100)	0 (0)	0.000
Corticosteroids	11 (10.7)	0 (0)	2 (28.6)	2 (22.2)	7 (25.9)	0.125
Outcome parameters						
Death in ICU	29 (47,5)	10 (55.6)	1 (14.3)	5 (55.6)	13 (48.1)	0.283
Renal replacement therapy	18 (29)	4 (22.2)	2 (28.6)	4 (44.4)	8 (29.6)	0.699
Prone position ventilation	24(39)	7 (38.9)	2 (28.6)	2 (22.2)	13 (48.1)	0.508
Duration of ventilation, *days*	24 (14.5-44)	18.5 (13-38.5)	47(31-59)	25 (9.5-45.5)	24 (14-40)	0.099
Duration of ICU stay, *days*	28 (17-49.5)	24 (15.5-53.0)	74 (34-88)	29.9 (24.3-34.9)	24 (14-40)	0.010
Duration of ventilation after BL, *days*	15 (6-28)	11 (4.6-28.5)	34 (16-36)	17 (6-23)	15 (7-24)	0.296
Ventilator days to BL, *days*	9 (5-13.5)	8 (2-12.3)	14 (11-30)	10 (6.5-13.5)	9 (4-15)	0.154
Ventilator free days at day 60 after BL, *days*	35.5(26-45.8)[1]	39.5 (23.3-52.8)[2]	26 (23.5-34.3)[3]	37 (22.5-44)[4]	39 (30.8-49.8)[5]	0.322

Table 1. Data are presented as median (IQR: interquartiles); count (%). P values comparing all the groups are tested by the one-way ANOVA(continuous variables) or chi-square (categorical variables). [1](n=32), [2](n=8), [3](n=6), [4](n=4), [5](n=14). *Abbreviations:* BMI body mass index, ICU intensive care unit, CAPA Covid-19 Associated Pulmonary Aspergillosis, BL bronchial lavage.

Conclusion: In mechanically ventilated patients with COVID-19 undergoing BL because of clinical deterioration, the incidence of infection with herpes virus was 14.8%, and the incidence of CAPA was 44.3%. Herpes infections occurred later in the course of disease than CAPA, and was associated with longer duration of mechanical ventilation and ICU stay.

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001083

Bacterial co-infection on admission is associated with increased mortality in critically-ill COVID-19 patients. A single-center retrospective study

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Intensive Care Medicine Experimental 2022, **10(2)**:001083

Introduction: The incidence of bacterial co-infection during ICU stay in COVID-19 mechanically ventilated patients is very high; usually attributed to ventilator-associated pneumonia (VAP) and often involving multi-drug resistant microbial pathogens. Interestingly, although bacterial co-infection in non-intubated COVID-19 patients is rather uncommon, nevertheless most COVID-19 hospitalized patients receive antibiotics for a possible bacterial co-infection. Besides, the incidence of bacterial co-infection in mechanically ventilated patients at the time of ICU admission remains understudied together with the possible effect of bacterial co-infection at the final patient's outcome.
Objectives: To record the incidence of bacterial pneumonia co-infection in COVID-19 mechanically ventilated patients at the time of their ICU admission and investigate if there is any association with patient outcome.
Methods: We have performed a retrospective study from 03/2020 to 12/2021 including all consecutive mechanically ventilated patients admitted to our COVID-19 ICU who had a bronchial secretions sample taken on ICU admission. Patients' demographics, co-morbidity including Charlson Comorbidity Index (CCI), ICU length of stay, bloodstream infection occurrence, ventilator-free days, and 28-day mortality were recorded for each patient. Two patient groups, i.e., with and without a positive bronchial secretion culture on admission were formed and a statistical analysis was performed.
Results: Altogether 188 patients were screened with 153/188 (81.3%) having a bronchial secretions culture on ICU admission. Of them, 13.07% (20/153) had a positive bronchial secretions culture with a pathogen causing pneumonia: 6 patients grew *Acinetobacter* spp., 4 *Pseudomonas* spp, 3 *Staphylococcus aureus*, 2 *Klebsiella* spp., 2 *Stenotrophomonas* spp., 1 *Serratia* spp., 1 *Enterobacter* spp. and 1 unspecified gram-negative rod. Twenty-eight day survival was low in patients with a positive culture (28.5%), though not statistically different, probably due to small sample number, when compared to patients without a positive culture (45%). There was no statistically significant difference among two groups in terms of mean age (69 ± 11.6 vs 67.5 ± 11.5, $p=0.56$), comorbidity, such as type II diabetes, cancer, autoimmune diseases, cirrhosis, chronic kidney disease, and CCI. Interestingly, patients with a positive culture had a significant increase in the 7-day mortality (33.3% vs 6.06%, $p=0.005$)
Conclusion: In our study, the presence of bacterial co-infection on admission was associated with increased mortality in critically ill COVID-19 patients occurring usually early at the course of hospitalization.

001085

The incidence of bacteremia in COVID-19 vs non-COVID-19 critically ill patients and its association with patients' outcome. A single-center retrospective study

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Intensive Care Medicine Experimental 2022, **10(2)**:001085

Introduction: Since the onset of the COVID-19 pandemic, several reports of increased incidence of bacteremia in critically ill COVID-19 patients have been published. It has been also suggested that the presence of bacteremia increases mortality in this group of patients.
Objectives: To investigate the incidence of bacteremia in our COVID-19 Intensive Care Unit (ICU) patients and compare their characteristics and outcome with non-COVID-19 critically ill patients hospitalized in our non-COVID-19 ICU.
Methods: We have performed a retrospective single-center study including all consecutively critically ill mechanically ventilated patients admitted from 03/2020 to 11/2021 to our COVID-19 ICU and all

consecutively critically ill mechanically ventilated patients for more than 48 h from 08.2020 to 01.2021 and from 03.2021 to 08.2021 admitted to our non-COVID-19 ICU. Patients' demographics, comorbidity including Charlson Comorbidity Index (CCI), blood culture results, ICU length of stay (LOS), ventilator-free days, and 28-day mortality were recorded for each patient. Two patient groups, i.e., COVID-19 and non-COVID-19 patients were compared in terms of characteristics and outcome.
Results: Altogether 340 patients, 183 COVID-19 and 157 non-COVID-19, were included in our study (mean age 66.3 ± 14.3 years). Between the two patient groups there was no difference in age, sex and incidence of autoimmune disease, chronic kidney disease and liver cirrhosis. COVID-19 patients had a lower CCI score (84% had a score of < 5 compared to 68.8%, p = 0.004), a higher incidence of type II diabetes (29.5% vs 17.8%, p = 0.021) and a lower incidence of cancer (6.6% vs 15.9%, p = 0.008). COVID-19 patients during their ICU stay had also a higher incidence of bacteremia (65% vs 37.6%, p = 0.0001) and candidemia (8.2% vs 1.3%, p = 0.0001). In addition, COVID-19 patients had a significantly lower 28-day survival (41% vs 60.5%, p = 0.0001).
Conclusion: In our study, COVID-19 mechanically ventilated patients when compared to non-COVID-19 patients had a higher risk for bacteremia and mortality. COVID-19-associated immune dysfunction and COVID-19 specific medical management could be major contributing factors. More studies are required to investigate this further.

001089

The incidence of enterococcal bacteremia in COVID-19 critically ill patients and its association with patients' outcome. A single-center retrospective study

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Intensive Care Medicine Experimental 2022, **10(2)**:001089

Introduction: Since the onset of the COVID-19 pandemic there have been increasing reports of *Enterococcus* spp. bacteremia in both non-critically and critically ill COVID-19 patients. The outcome of critically ill COVID-19 patients with enterococcal bacteremia remains still understudied
Objectives: To record the incidence of bloodborne enterococcal infections in our COVID-19 Intensive Care Unit (ICU) and assess their effect on patients' outcome.
Methods: We have performed a retrospective single-center study from 03/2020 to 11/2021 including all consecutively critically ill mechanically ventilated PCR SARS-COV-2 positive patients. Patients' demographics, comorbidity including Charlson Comorbidity Index, blood culture results, ICU length of stay (LOS), ventilator-free days, and 28-day mortality were recorded for each patient. Two patient groups, i.e., with and without episode of enterococcal bacteremia (Group A and Group B respectively), were compared.
Results: Altogether 183 patients were included in our study and 53/183 (29%) had an episode of enterococcal bacteremia (Group A). There was no difference between the two patient groups in terms of age (67.1 ± 11.8 vs 67.7 ± 11.9, p = 0.728, for Group A and Group B respectively) or prevalence of co-morbidities. Patients with enterococcal bacteremia had a longer median ICU LOS (24 days, min 0 and max 144 days, vs 15 days, min 1 and max 74 days, p = 0.001), a higher incidence of gram-negative bacteremia (67.9% vs 43.9%, p = 0.009) and a trend for higher 28-day mortality (50.1% vs 36.9%); the latter just failed to reach statistical significance (p = 0.08) probably because of the small study patient sample.
Conclusion: In our study, enterococcal bacteremia seems to be common in COVID-19 critically ill patients. Presence of enterococcal bacteremia appears to be associated with a higher incidence of gram-negative bacteremias as well as increased ICU LOS and mortality. Larger multicenter studies are required to investigate this further.

001114

Characteristics of vaccinated patients hospitalized with severe COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**:001114

Introduction: Until today, no treatment against COVID-19 had proven its effectiveness. On the other hand, vaccination against COVID-19 does not fully protect against severe forms of disease. Despite that many studies showed that vaccinated individuals have a significantly reduced risk of serious illness, some hospitalizations and deaths have been reported in this population.
Objectives: This study aimed to examine severe COVID-19 infection in SARS-CoV-2-vaccinated patients who needed ICU hospitalization and to identify factors associated with poor outcomes in comparison with unvaccinated patients.
Methods: This was a retrospective observational study of SARS-CoV-2-vaccinated patients admitted at the intensive care unit of regional hospital of Zaghouan, Tunisia between the start of the national vaccination strategy on March 2021, to March 2022. The vaccines most commonly administered was Pfizer, followed by Moderna, Astra-Zeneca, and Janssen. We defined patient's complete vaccination as symptom onset 15 days after the second dose of a vaccine (or a single Janssen dose), and partial vaccination as the administration of only the first dose or symptom onset within 15 days after the second dose (or a single dose of Janssen). The vaccine administration date was obtained from patient or their caregivers.
The comparison of vaccinated patients (G1) was made with unvaccinated patients (G2) admitted to intensive care unit during the same period.
Results: During the study period, 210 patients were enrolled, 190 patients were unvaccinated. Among the 20 vaccinated patients: 11 were fully vaccinated and 9 were partially vaccinated.
Median age was 62 [32–83] years in G1, and 52 [20–80] in G2. Gender ratio was 1.5 in G1 and 1.04 in G2. Patients in G1, had more comorbidities: diabetes (45% vs 14.7%;p = 0.003), chronic respiratory illness (35% vs 12.6%;p = 0.027), hypertension (50% vs 20.5%;p = 0.012) and ischemic heart disease (5% vs 2.1%;p = 0.002). At admission, the 2 groups had comparable respiratory exchange (PaO_2/FiO_2 = 105.7 ± 45 mmHg in G1 and 124 ± 67.6 mmHg in G2;p = 0.3), and laboratory findings. There was no significant difference between Median SAPS II and APACHE II scores. However, there was a significant difference in CHARLSON and Mortality 4C scores (2.5 [0–7] in G1 vs 1 [0–8] in G2;p < 103 and 10 [1–16] in G1 vs 7 [1–50] in G2;p = 0.04) respectively. Less extensive CT pulmonary involvement was seen in G1 (62 ± 20% vs 70 ± 16%; p = 0.02). Patients received the same therapeutic management. Length of ICU stay was similar in two groups (8.8 ± 6 day [2–24] vs 8 ± 6.2 day [1–39]). No significant differences were observed in need to invasive mechanical ventilation (35% vs 42.1%; p = 0.7) and mortality (35% vs 42%; p = 0.54).
Conclusion: Compared with unvaccinated COVID-19 patients, those vaccinated and hospitalized in ICU were older with more comorbidity. No differences in prognosis parameters were noted.

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One Year On: An Analysis of Physiological and Meteorological Factors on the Mortality of patients admitted to ICU with SARS-CoV-2 between March 2020 and February 2021

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Intensive Care Medicine Experimental 2022, **10(2)**:001115

Introduction: The SARS-CoV-2 pandemic led to unmitigated pressures on global healthcare resources, particularly in intensive care.1, 2 Both physiological3,4 and environmental variables5, 6, 7 have been known to influence patient mortality, however, there are no References in the literature which combine environmental factors with physiological factors in identifying mortality risk in patients admitted to ICU with SARS-CoV-2.
Objectives: In this study, we aim to provide an effective clinical tool combining physiological patient factors in addition to environmental variables to predict the probability of death in UK patients admitted to ICU with SARS-CoV-2. The authors hope this model can identify trends predicting mortality, thus advising further treatment and secondary prevention strategy.
Methods: 1180 datasets were collected from three individual hospitals in Birmingham, United Kingdom between 01/03/20 and 28/02/21; this comprised all patients admitted to the relevant ICUs during this timeframe. These three hospitals consisted of two district general hospitals and one tertiary referral centre, collectively forming part of a large academic teaching trust. A number of environmental and physiological variables were tested for correlation with patient mortality at hospital discharge. A binary logistic regression model of statistically significant variables was used, and adjusted with Ridge and Lasso regularisation. Key binary logistic regression model assumptions were appraised using multicollinearity, linear relationship and outlier testing.
Results: The final predictors utilised for this model include age, body mass index (BMI), Rockwood frailty score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Intensive Care National Audit & Research Centre (ICNARC) model physiology score, temperature, humidity and wind speed. Model validation was performed using a confusion matrix on 30% of the original dataset. The receiver operating characteristic (ROC) curve generated had an area under the curve (AUC) of 0.76, demonstrating good predictive abilities for this model.
Conclusion: Prediction models to accurately determine the risk of individuals experiencing poor outcomes would assist healthcare professionals in triaging patients when allocating limited medical resources. The authors hope this model can identify trends predicting mortality, thus advising further treatment and secondary prevention strategy.

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Acknowledgements: The authors have no conflicts of interest or funding sources to disclose.

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Clinical characteristics and outcome of *Candida auris* bloodstream infections during an outbreak

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Intensive Care Medicine Experimental 2022, **10(2)**:001131

Introduction: *Candida auris* is a recognized emerging, often multidrug resistant pathogen, associated with difficult-to treat infections, intensive care unit (ICU) outbreaks and high mortality (1).
Objectives: We aimed to describe the characteristics and outcomes of *C. auris* bloodstream infections (BSIs), occurring during an ongoing outbreak in our ICU.
Methods: Since the identification of an index case of *C. auris* BSI in our 55-bed, tertiary, academic ICU, on June 4th, 2021, a surveillance system has been set up and an ongoing outbreak was declared. All admitted patients underwent weekly axilla-groin swabs and tested for *C. auris* by matrix assisted laser desorption/ionization- time-of-flight (MALDI-TOF). This is a retrospective analysis of all subsequent *C. auris* BSIs. Recording is ongoing and preliminary data up to January 16th, 2022 (date of surveillance halt due to a new COVID-19 surge), including clinical characteristics at BSI diagnosis, treatment and 28-day survival are presented. Antifungal susceptibility testing was performed by broth microdilution technique and interpretation was based on the tentative FDA breakpoints for echinocandins, fluconazole and amphotericin B and on the tentative epidemiological cutoff values (2). Treatment failure was defined as *C. auris* fungemia or death within 28 days after 5 days of appropriate antifungal treatment.
Results: Among 812 ICU patients with 8031 patient-days, a total of 141 patients were found colonized by *C. auris*. Of those, 12 (8.5%) were diagnosed with *C. auris* BSI, a median of 20 (13–34) days after ICU admission and 11 (2–20) days after first colonization. Baseline characteristics are presented in Table 1. Central venous catheters (CVCs) present at the time of BSI were removed immediately in all cases but 2, where they were removed 48 h later. Treatment was considered appropriate in 10 (83.3%) cases and was administered within 2 (1–2) days from positive blood culture. Echinocandins were used in 7 (58.3%) cases (6 with anidulafungin and 1 with caspofungin), while 3 (25%) received liposomal amphotericin B. *C. auris* strains were resistant to caspofungin (Minimum Inhibitory Concentration-MIC = 2–>8 mg/l) in 4 (33.3%) cases, to amphotericin B (MIC = 2 mg/l) in 1 (8.3%) case and to fluconazole (MIC = 32–256 mg/l) in 11 (92%) while all isolates were wild-type to triazoles. Treatment failure was observed in 6 (60%) cases. By day 28, 8 (66.7%) patients had died, including all 3 (30%) patients with recurrent BSI. No difference was observed between echinocandins and amphotericin B in terms of mortality [HR 0.902 (0.164–4.973);p:906].

Patient characteristics at diagnosis	Total (N = 12)
Age, median (Q1–Q3)	70 (65–77)
Sex (male), n (%)	7 (58.3)
Charlson Comorbidity Index, median (Q1–Q3)	4.5 (3–7)
SOFA score, median (Q1–Q3)	10 (6–14)
COVID-19 diagnosis, n (%)	4 (33.3)
Prior corticosteroid intake, n (%)	7 (58.3)
Prior continuous renal replacement therapy, n (%)	6 (50.0)
Prior total parenteral nutrition, n (%)	1 (8.3)
Prior antibiotic treatment (antibiotic-days), median (Q1–Q3)	69 (47–113)
Presence of a central venous catheter, n (%)	12 (100)
Organ support, n (%)	
Mechanical ventilation	11 (91.7)
Vasopressor use	8 (66.7)
Continuous renal replacement therapy	4 (33.3)

Conclusion: *C. auris* BSI occurred early after colonization, among high-risk patients, and carried substantial 28-day mortality, despite appropriate treatment and prompt CVC removal.

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001209

Assessment of current practice for ß-Lactam therapeutic drug monitoring in French ICUs in 2021: A nationwide cross-sectional survey

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Intensive Care Medicine Experimental 2022, **10(2)**:001209

Introduction: Current guidelines and literature support the use of therapeutic drug monitoring (TDM) to optimise ß-Lactam treatment in adult intensive care unit (ICU) patients. Nevertheless, data are scarce regarding therapeutic drug monitoring use in routine practice. Additionally, the limited literature primarily concerns hyper-specialised centres and comes from Australia.
Objectives: To describe the current practice of ß-Lactam monitoring in French ICUs.
Methods: A nationwide cross-sectional survey was conducted from February to July 2021 utilising an online questionnaire that was sent as an email link to ICU specialists (one questionnaire per ICU).
Results: Overall, 119 of 221 (53.8%) French ICUs participated. Eighty-seven (75%) respondents reported having access to ß-Lactam TDM including 52 (59.8%) with on-site access. ß-Lactam concentrations were available in 24 h to 48 h and after 48 h for 36 (41.4%) and 26 (29.9%) respondents, respectively. The majority of respondents ($n = 61$, 70.1%) reported not knowing whether the ß-Lactam concentrations in the TDM results were expressed as free or total fractions of the ß-Lactam concentrations. The 100% free concentration of the ß-Lactams above the minimal inhibitory concentration was the most frequent pharmacokinetic and pharmacodynamic target used ($n = 62$, 73.0%).
Conclusion: Despite improved access to ß-Lactam TDM in French ICUs, TDM interpretation and the time required to receive results still require to be improved. This survey also highlights the mismatch between guidelines and routine practice.

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Acknowledgements: We thank all the intensivists who answered to the survey

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Incidence and impact on outcomes of ventilator-associated pneumonia in COVID-19 patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001237

Introduction: Ventilator-associated pneumonia (VAP) is recognized as being the most frequent secondary infection in critically ill patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia [1]. There is a potential to improve management by characterizing the clinical disease course further.
Objectives: The aim of this work was to extend current knowledge of incidence and impact on outcomes of VAP in coronavirus disease 2019 (COVID-19) patients.
Methods: A prospective, observational study was conducted during the first and second waves of the COVID-19 pandemic at the Department of Anaesthesiology and Intensive Therapy, Semmelweis University, Hungary. Cases of VAP were identified according to the European Centre for Disease Prevention and Control diagnostic criteria. VAP was characterized by incidence, implicated pathogens and resistance patterns. A Cox proportional hazard model was used to evaluate the clinical variables associated with the duration of mechanical ventilation.
Results: A total of 140 patients were eligible. The median age of the represented population was 66 (interquartile range [IQR] 57–73) years, and 98 (70.0%) were male. The median Acute Physiology and Chronic Health Evaluation II (APACHE II) score was 26 (IQR 19–29). Among all the patients, 61 (43.6%) developed at least one episode of VAP. The incidence density was 37.9 VAP episodes/1000 ventilator-days, which was twice as high as in our non-COVID-19 population [2]. Fifteen (10.7%) patients experienced multiple episodes. The median time until the onset of VAP was 10 days (IQR 7–13 days). The nurse-to-patient ratio was 1:3 and remained constant over time. The most common pathogen was *Pseudomonas aeruginosa*, represented in 50% of lower respiratory tract samples, followed by *Acinetobacter baumannii* (44.5%) and *Staphylococcus aureus* (14.4%). Remarkably, 50.8% of *Pseudomonas aeruginosa* and 99.0% of *Acinetobacter baumannii* strains were multidrug-resistant. *Aspergillus species* were isolated in 9.7% of the samples. The Cox proportional hazard model indicated a decreased risk for extubation in those developing VAP (hazard ratio 0.34 [95% confidence interval 0.14–0.83] $p = 0.02$) and in those with low initial PaO_2/FiO_2 ratio (hazard ratio 0.33 [95% confidence interval 0.13–0.83] $p = 0.02$), independently from age, sex, APACHE II score, obesity, Charlson comorbidity index and clinical frailty scale. We observed a significantly longer duration of mechanical ventilation (16 [IQR 11–27] days, $p = 0.001$) and longer ICU length of stay (18 [IQR 12–27] days, $p = 0.001$) in those developing VAP.
Conclusion: Our study supports the previous observations that the incidence of VAP is high in mechanically ventilated COVID-19 patients. Noteworthy, difficult-to-treat pathogens are particularly prevalent. VAP and low initial PaO_2/FiO_2 ratio was associated with longer duration of mechanical ventilation.

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Risk factors for ventilator-associated pneumonia due to multidrug-resistant *Acinetobacter baumannii*

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Intensive Care Medicine Experimental 2022, **10(2)**:001242

Introduction: Over the recent decades, *Acinetobacter baumannii (A. baumannii)* has become one of the most prevalent pathogens of ventilator-associated pneumonia (VAP), associated with a high and constantly rising antibiotic resistance and increased mortality rates.
Objectives: The aim of this study was to identify risk factors for VAP due to multidrug-resistnat (MDR) *A. baumannii*.
Methods: A retrospective cohort study of patients treated in ICU for VAP due to multidrug-resistant Gram-negative bacteria (GNB*)* over a 3-year period was carried out.
Results: One hundred eighty two cases of monobacterial VAP due to MDR GNB were analysed: 105 (57.7%) due to MDR *A. baumannii* and 77 (44.2%) due to other GNB (*K. pneumoniae*, *P. aeruginosa*, and *E. coli*).
Univariate analysis revealed statistical signifficant differences between cases of VAP due to MDR *A. baumannii* and other MDR GNB respectively in rates of SOFA score respiratory > 2 on ICU admission (76/105 (72.4%) vs 42/77 (54.5%), $p = 0.013$), sepsis on VAP diagnosis (93/105 (88.6%) vs 60/77 (77.9%), $p = 0.052$, treatment with carbapenems (37/105 (35.2%) vs 9/77 (11.7%), $p < 0.001$) and treatment with ≥ 2 clases of antibiotics (82/105 (78.1%) vs 45/77 (58.4%), $p = 0.004$) in preceding 90 days before VAP onset, admission for surgical reason (38/105 (36.2%) vs 43/77 (55.8%), $p = 0.008$), surgery in preceding 2 weeks before VAP onset (45/105 (42.9%) vs 55/77 (71.4%), $p < 0.001$), SOFA score neurological > 2 both on ICU admission (15/105 (14.3%) vs 21/77 (27.3%), $p = 0.030$) and on diagnosis day (12/105 (11.4%) vs 22/77 (28.6%), $p = 0.003$), as well.
Multivariate analysis's (binary logistic regression, enter method) revealed the treatment with carbapenems in preceding 90 days before VAP onset (OR 2.965, 95% CI 1.234–7.073) was independent risk factor for VAP due to MDR *A. baumamnnii*. The surgery in preceding 2 weeks before VAP onset (OR 0.321, 95% CI 0.162–0.634) and SOFA score neurological > 2 on diagnosis (OR 0.362, 95% CI 0.154–0.854) were found to be risk factors for VAP due to other MDR GNB but *A. baumannii.*
Conclusion: Carbapenems use before VAP onset increases the risk for VAP due to MDR *A. baumannii*, but surgery and impaired consciousness—for VAP due to other MDR GNB (*K. pneumoniae*, *P. aeruginosa*, and *E. coli*).

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Effect of corticosteroids on mortality and clinical cure in community-acquired pneumonia: A systematic review, meta-analysis, and meta-regression of randomized control trials

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Introduction: Community-acquired bacterial pneumonia is a leading cause of hospitalization, with a significant risk of mortality and morbidity (1). Apart from antimicrobial therapy, there are no routinely used therapeutic strategies associated with improvements in illness mortality, severity, or hospital stay. Corticosteroids may be a beneficial adjunct in the treatment of bacterial pneumonia.
Objectives: To evaluate the clinical benefits of adjuvant corticosteroid therapy in the management of bacterial CAP amongst patients requiring hospitalization?
Methods: PubMed, Cochrane Library and Embase were systematically searched to identify all randomized control trials (RCTs) assessing the use of adjunctive systemic corticosteroid therapy compared to standard care alone for the treatment of CAP. A systematic review, meta-analysis, and trial sequential analysis (TSA) were performed. The primary outcome was all-cause mortality. Secondary outcomes included disease progression (need for intensive care unit admission or mechanical ventilation), treatment failure, readmission, and adverse events. Data are presented as relative risk (confidence intervals), p-value, and heterogeneity (*I2*).
Results: Fifteen trials met the eligibility criteria, including 3,279 patients. All-cause mortality [15 studies including 3279 patients; RR = 0·79 (95% CI, 0·59–106); $p = 0·12$; *I2* 20%] (*Figure* 1), treatment failure [6 studies (2093 patients); RR = 0·78 (95% CI, 0·37–1·67); $p = 0·52$; *I2* 68%], and the incidence of total adverse events [5 studies (1870 patients); RR = 1·16 (95% CI, 0·96-1·39); $p = 0·12$; *I2* 59%] were similar between patients receiving corticosteroids and patients assigned to the control group. The need for ICU admission [6 studies (2619

patients); RR = 0·66 (95% CI, 0·45–0·97); p = 0·04; *I2* 0%] and mechanical ventilation [8 studies (1457 patients); RR = 0·51 (95% CI, 0·33–0·77); p = 0·001; *I2* 0%] was lower among patients receiving corticosteroids compared to standard care. However, corticosteroid use was associated with higher rates of hospital readmission [4 studies (2350 patients); RR = 1·30 (95% CI, 1·08–1·56); p = 0·007; *I2* 0%].
Conclusion: Corticosteroid therapy is associated with a lower incidence of progression to ICU admission and mechanical ventilation among patients hospitalized with CAP. There was no association between corticosteroid therapy and mortality, treatment failure, or adverse events.

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001314

Infections in transplanted patients in a Portuguese university ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:001314

Introduction: The main problems in solid organ transplant recipients are rejection and infection. The new immunosuppressive regimens have lowered the risk of rejection; however, infections continue to be one of the most important determinants for morbidity and mortality in these patients. [1] Severe infections are among the most common causes of death in immunocompromised patients admitted to the intensive care unit (ICU). The diagnosis and treatment of these infections have evolved in the last decade. [2]
Objectives: We aim to assess the rate of severe infections in this population, admitted on our ICU.
Methods: Monocentric, descriptive observational study. Demographics variables and the prevalence of infection (bloodstream, urinary and respiratory) in our ICU from 1st January to 31st December 2021 were registered. We describe the results of microbiological data (blood, urine and respiratory secretions) along with the resistance phenotypes.
Results: A total of 35 organ solid transplanted patients were admitted on our ICU during 2021, from which 7 had a confirmed infection. The average age was 54,9 (range from 38 to 67) with a median SAPS II of 45 ± 15, and median SOFA of 10 ± 3. Of these, 5 were admitted due to septic shock and 2 were admitted on the immediate post hepatic transplant and developed an infection during their stay at the ICU. The most common infection was pneumonia (n = 6), with 3 patients with critical respiratory disfunction and need to start mechanical ventilation. On admission, there were 2 cases of skin infection due to multisensible *Staphylococcus aureus*, and 3 cases of pneumonia, one due to a carbapenemase producing *Klebsiella pneumoniae* and the other a *Stenotrophomonas maltophilia*; on one case wasn't possible to isolate an agent. On nosocomial infection, the 2 patients admitted post operative of hepatic transplant both had pulmonary infection with presentation in septic shock. The isolated microorganisms were in one of the cases a *Serratia marsensis*, and on the other case a multiple isolation of *Aspergillus fumigatus* and *Pseudomonas aeruginosa* ESBL. The other nosocomial infection occurred in one of the patients admitted for septic shock, and it was a complication of the central venous access with a bacteriaemia due to *Candida parapsilosis*. The mechanisms of resistance in each microbiological isolation were determined.
Conclusion: The key clinical elements to improve the outcome of critically ill solid organ transplant recipients depend on the knowledge of geographic epidemiology, hospital microbial ecology, aggressive diagnostic strategy and search for source control, rapid initiation of antimicrobials and minimization of iatrogenic immunosuppression.

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Acknowledgements: None

001319

How ICU admission influences outcomes of patients with solid malignancies after ICU?

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Intensive Care Medicine Experimental 2022, **10(2)**:001319

Introduction: Prognosis in patients with solid malignancies (SM) has improved due to advances in oncologic treatment and supportive care. However, data about outcomes in critically ill cancer patients after intensive care unit (ICU) discharge is scarce.
Objectives: To assess the impact of ICU admission on patients with SM in terms of deterioration on functional status, cancer treatment discontinuation and mortality at 1, 3 and 6 months (m) after ICU admission.

Methods: Retrospective single-centre study including adult patients with SM requiring unplanned ICU admission in a University Hospital in Barcelona during 2019. Clinical and laboratory data were collected and compared.
Results: Ninety-seven patients with a mean age of 63.8 years and 54% male were included. Lung was the most frequent cancer (22.6%), followed by colorectal (16.4%) and breast (12.3%). Almost 80% presented metastatic disease and 75% were receiving active oncologic treatment, being chemotherapy the most frequent modality (51%). Cancer was diagnosed during hospital admission in 12.5%. Performance status (PS) distribution before ICU admission was 74% 0–1, 25% 2 and 1% 3–4. The main cause of ICU admission was respiratory failure (38%), followed by septic shock (36%). Median (IQR) APACHE II and SOFA scores at admission were 13 (8) and 4 (5), respectively. Mechanical ventilation was required in 13% of patients. Median (P25–75) ICU and hospital length of stay was 4 (2–6) and 25 (11–34) days. ICU and hospital mortality was 9.4% and 24%, respectively. Half of the patients diagnosed of cancer during admission died in the hospital. Overall mortality at 1, 3 and 6 m was 1.5%, 37.1% and 56.7%, respectively. Median overall survival was different between patients with and without metastatic disease (5 m vs 14 m, $p < 0.05$). In the univariate analysis, presence of liver metastasis and cachexia (defined as hypoalbuminemia < 32 g/dL or CRP > 0.5 mg/dL the prior month) were correlated with higher 1-m (9 vs 29.4% and 3 vs 22.5%, respectively) and 3-m (25.3% vs 61.7% and 14.7 vs 50%, respectively) mortality ($p < 0.05$). Adequacy of therapeutic effort was decided during hospitalisation in 31% of cases. At hospital discharge, median PS score (2.7) was lower compared to admission ($p < 0.05$). Eleven percent of the patients were transferred to a socio-sanitary centre and 40% needed hospital readmission at least once in the following 6 m (11.3% in the ICU). Cancer treatment was discontinued in 37% of patients, modified or dose-reduced in 56.7% and a new line was started in 20%.
Conclusion: Critically ill patients with SM present a significative deterioration on their functional status and high rates of definitive discontinuation or changes in cancer treatment, hospital readmission and mild-term mortality. Cachexia and liver metastasis are risk factors for mild-term mortality. A better understanding of clinical prognostic factors would help to develop proper ICU admission criteria for SM patients.

001357

Decision-making on appropriate antibiotic therapy duration in the Intensive Care Unit: direct observations of multidisciplinary meetings

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Intensive Care Medicine Experimental 2022, **10(2)**:001357

Introduction: In the intensive care unit (ICU), antibiotic therapy is commonly prescribed longer than recommended in guidelines [1–4]. Understanding key drivers of prescribing behaviour is crucial to generate meaningful interventions to bridge this evidence-to-practice gap [5].
Objectives: This study aimed to describe the decision-making process regarding duration of antibiotic therapy during ICU multidisciplinary meetings (MDM) and to observe strategies used by healthcare workers from different specialities to contribute to this decision-making process.
Methods: A multicentre qualitative study was conducted involving direct observations of antibiotic decision-making during MDMs at ICUs of 4 Dutch hospitals. Data collection consisted of field notes and audio recordings. The MDMs were observed at three different levels: (1) procedural, (2) interaction and (3) content level [6, 7]. Text fragments were perceived as relevant when they focused on decision-making with regards to the duration of antibiotic therapy. See Figure 1 for an overview of the decision-making process. For all relevant participants we described their role in the antibiotic decision-making process and we focused on the arguments and strategies provided by each healthcare professional to contribute to the decision-making process.

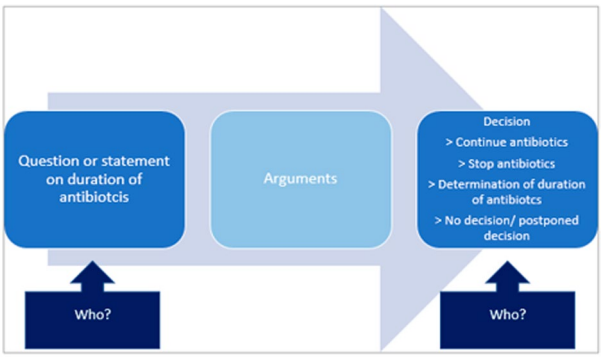

Figure 1: Antibiotic therapy duration decision-making process

Results: Sixty MDMs where observed, of which 121 relevant text fragments were analysed. In 37.2% of the cases, the exact therapy duration with prospective stop date was determined, in 24.8% it was decided to stop antibiotics and in 9.9% antibiotics where continued without a specific end-date. In 9.1% no decision was made (i.e. postponed), while in 7.4% the decision was unclear. The final decision was most often made by intensivist (35.5%), followed by the microbiologist (22.3%), but rarely by junior ICU residents (4.1%) or referring physicians (0.8%). In 28.9%, multiple professionals equally participated in the decision process ("shared decision-making"). There was a wide variation in the level of participation of healthcare professionals in the discussions on antibiotic duration ranging from "active" to "absent" (Figure 2). Finally, arguments related to clinical status of the patient, culture results, (lack of) source control and related to the content of guidelines were mostly used in the decision-making process on antibiotic therapy duration. Bargaining, repetition of their message and showing commitment to shared decision-making were the most common strategies used by professionals.

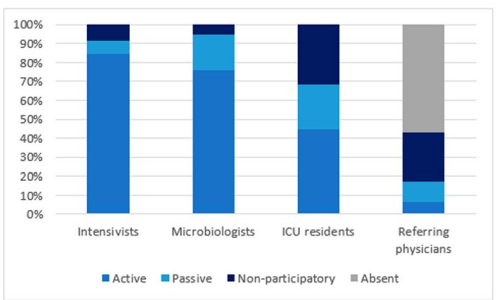

Figure 2: Roles of physicians of different specialties in decision-making regarding antibiotic therapy duration

Conclusion: Only in one third of ICU patients the decision to either stop or continue antibiotic therapy is the result of a shared-decision making process. Healthcare professionals involved in antibiotic decision-making use a variety of arguments and apply different strategies and communication skills to convince their colleagues to either stop or continue antibiotic therapy. Antimicrobial stewards involved in ICUs

should be aware of these elements to optimally understand and influence ICU antibiotic prescribing.

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Acknowledgements: This work was supported in part by a research grant from the Investigator Initiated Studies Program of Merck Sharp & Dohme [grant number 58288].

001377

Effect of adequacy of antibiotic therapy for hospital-acquired bacteraemia on patient prognosis: a causal inference approach using data from the Eurobact2 study

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Intensive Care Medicine Experimental 2022, **10(2)**:001377

Introduction: Hospital-acquired bloodstream infections (HA-BSI) in intensive care unit (ICU) are frequent life-threatening events in ICU patients.

Objectives: To determine the effect of early adequate antibiotic therapy on 28-day mortality in patients followed at least 3 days after the HA-BSI onset

Methods: We used individual data from a prospective observational multicentre intercontinental cohort study (EUROBACT II). We included for analyses adult patient with a HA-BSI treated in the ICU. We excluded patients with less than 3 days of follow-up after the HA-BSI and with no time-to-treatment adequacy in hours. Effect on outcome was estimated using a causal inference approach based on the inverse probability of treatment weighting (IPTW) and a Directed Acyclic Graph (DAG) selected in the literature with the help of experts (AT, JFT, NB, FB) to identify confounding factors. Independent patients-related variables considered according to the DAG were age, sex, time between hospitalization and HA-BSI, pathogen, comorbidities and immunosuppression, source of infection and SOFA score at HA-BSI onset. ICU-related variables were university hospital, number of ICU beds, infectious diseases (ID) specialists or microbiologists consultants available, 24/7, clinical pharmacists consultants available upon request 24/7, and senior ICU physician on site 24/7.

Survival analyses were performed with weighted frailty Cox proportional-hazard model. The time-to-treatment adequacy was treated as a binary variable (adequacy at 24 h). Times to adequacy at 48 h and 72 h were tested in secondary analyses.

Results: From the 2,600 patients of the study, 2,146 patients were included from 301 centres in 38 countries. 1,677 (78.1%) patients acquired their BSI in the ICU. 28-day mortality was 338 (30.9%) in the adequate treated patients and 393 (37.3%) in non-adequate treated patients, p = 0.0018. Adequacy to treatment at 24 h was more frequently obtained young patients, immunosuppressed, with septic shock, in case of HA-BSI of abdominal origin, due to Gram-negative microorganism and Gram-negative and positive germ were more sensitive to treatment. Inadequacy was more frequent for BSI due to intravascular catheter or primary source and in case of fungemia. Considering all measured confounders, and country effect using a weighted frailty Cox model, the adequacy of antimicrobial therapy was not significantly associated with 28-day survival (HR 0.91, 95%CI 0.78–1.05, p = 0.19).

	Adequate treatment H24 n=1093	Inadequate treatment H24 n=1053	p
Age	63 [50 ; 72]	65 [54 ; 74]	0.0044
Male gender	702 (64.2)	669 (63.5)	0.7379
Comorbidities	825 (75.5)	776 (73.7)	0.3420
Immunosuppression	225 (20.6)	181 (17.2)	0.0446
ICU-Acquired BSI	809 (74)	868 (82.4)	<.0001
Vasopressors HA-BSI onset	644 (58.9)	506 (48.1)	<.0001
SOFA score at HA-BSI onset	8 [5 ; 11]	8 [5 ; 11]	0.5690
Gram Positive	375 (34.3)	361 (34.3)	0.9898
Gram Negative	707 (64.7)	608 (57.7)	0.0010
Fungus	47 (4.3)	138 (13.1)	<.0001
Anaerobes	30 (2.7)	22 (2.1)	0.3235
28-day death	338 (30.9)	393 (37.3)	0.0018

Results remained similar if time to adequacy is < 48 h (HR = 0.94; 95%CI [0.81;1.09]) and < 72 h (HR = 0.84 95%CI [0.73; 0.97]).

Limitations: (1) Our statistical techniques could be limited by unmeasured confounders; (2) Given patients' selection, the impact of adequacy on the first 72 h mortality was not evaluated.

Conclusion: Using a carefully adjusted model considering all measured confounders, adequacy of antimicrobial therapy within 24 h in patients followed at least 3 days after a HA-BSI was not significantly associated decreased in 28-day mortality. Further work is ongoing to determine in which patients' subgroups the adequacy is instrumental for prognosis.

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Acknowledgements: ESICM research grant; ESCMID research grant; Norva-Dahlia foundation grant; Redcliffe hospital research grant

Infection 10

001379

Impact of Remdesivir and Systemic corticosteroids in COVID19 patients: a ccurrede cohort comparative study

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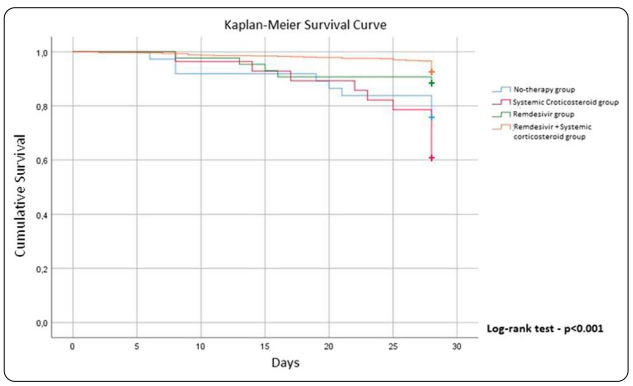
Intensive Care Medicine Experimental 2022, **10(2)**:001379

Introduction: The SARS-CoV-2 pandemic has motivated the evaluation of several therapeutic agents as treatment for the coronavirus disease 19 (Covid-19). Remdesivir and systemic corticosteroids (SC) have been the central hallmarks of those proposed therapies. However, considering the emergence of conflicting data regarding their efficacy, in the past two years, a reliable impact evaluation on survivability is still required.
Objectives: We aimed to evaluate the impact of remdesivir and systemic corticosteroid therapies in hospital 28-day mortality rate of COVID-19 patients.
Methods: A ccurrede retrospective cohort study was performed in 5 hospitals in Portugal and Brazil. All adult patients with hospital admission with SARS-CoV-2 pneumonia were eligible for this study. COVID19 was diagnosed using clinical and radiologic criteria with a SARS-CoV-2 positive RT-PCR test. The chi-square test was used for categorical variables and Kruskal–Wallis and logistic regression were used on continuous variables for statistical assessment of outcomes between groups. Kaplan–Meier survival curve and log-rank test were also obtained.
Results: 814 patients (mean age 65 years, 64,5% males) were eligible for the analysis. Remdesivir and SC presented 28-day mortality reducing effect when considered individually (mortality risk of remdesivir-treated patients OR 0.19, CI (0.11–0.34), $p < 0.001$; mortality risk of SC-treated patients OR 0.45, CI (0.24–0.85), $p = 0.013$). This significant protective ccurred of SC therapy was, however, lost when considered a multiple linear regression model with both therapies, even when adjusted for gender, age, and SOFA score at admission (mortality risk of remdesivir-treated patients OR 0.18, CI (0.09–0.36), $p < 0.001$; mortality risk of SC-treated patients OR 1.12, CI (0.5–2.49), $p = 0.776$). Furthermore, no significant difference was found in the 28-day mortality rate of severe patients (SOFA score at admission > 6) treated with SC ($p = 0.118$) or in SC-treated patients already being treated with remdesivir ($p = 0.331$). On the other hand, Remdesivir had a significant statistical reducing effect on mortality of patients already being treated with SC ($p = 0.0001$). Log-rank test of Kaplan–Meier survival curves were also different between no-therapy group ($n = 37$), remdesivir-treated group ($n = 43$), SC-treated group ($n = 28$) and remdesivir + SC-treated group ($n = 706$) ($p < 0.001$) (Figure 1)



Conclusion: Remdesivir and SC therapies appear to have a significant mortality-reducing effect. However, SC therapy does not appear to have a significant impact in severe COVID19 patients or in those already treated with remdesivir.

001381
The relationship between the usage of broad-spectrum antimicrobials for more than 72 h and the detection of multidrug-resistant bacteria in Japanese intensive care units: a ccurrede retrospective cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:001381

Introduction: Large ccurrede studies reporting on the association between the duration of broad-spectrum antimicrobial administration and the detection of multidrug-resistant (MDR) bacteria in the intensive care unit (ICU) are scarce. We evaluated the impact of broad-spectrum antimicrobial therapy for more than 72 h on the detection of MDR bacteria using the data from Japanese patients enrolled in the DIANA study.
Methods: We ccurred the data of ICU patients in the DIANA study (a ccurrede international observational cohort study) from Japan. Patients who received empirical antimicrobials were divided into a broad-spectrum antimicrobial group of those who were treated with broad-spectrum antimicrobials for at least 72 h, and a narrow-spectrum antimicrobial group of those who were treated with narrow-spectrum antimicrobials. Differences in patient characteristics, background of infectious diseases and empirical antimicrobial administration, and outcomes between the two groups were compared using the chi-square tests (Monte Carlo method) for categorical variables and the Mann–Whitney U-test for continuous variables. We also conducted a logistic regression analysis to investigate the factors associated with the detection of new MDR bacteria.
Results: A total of 254 patients from 31 Japanese ICUs were included in the analysis, of whom 159 (62.6%) were included in the broad-spectrum antimicrobial group and 95 (37.4%) were included in the narrow-spectrum antimicrobial group. The detection of new MDR bacteria was significantly higher in the broad-spectrum antimicrobial group (11.9% vs. 4.2%, $p = 0.042$). Logistic regression showed that broad-spectrum antimicrobial continuation for more than 72 h (OR [odds ratio] 3.09, $p = 0.047$) and cerebrovascular comorbidity on ICU admission (OR 2.91, $p = 0.041$) were associated with the detection of new MDR bacteria.
Conclusion: Among Japanese ICU patients treated with empirical antimicrobials, broad-spectrum antimicrobial usage for more than 72 h was associated with the increased detection of new MDR bacteria. Antimicrobial stewardship programs in ICUs should discourage the prolonged use of empirical broad-spectrum antimicrobial therapy.

001386
Ceftazidime-avibactam resistance in *Klebsiella pneumoniae* superinfection in COVID-19 versus non-COVID-19 patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001386

Introduction: During the recent pandemic, given the high demand in Intensive Care Units (ICUs), antimicrobial stewardship was at times put on hold, with an increase in empirical broad-spectrum antibiotics prescriptions. Limitations in the available antibiotic options increase this threat and its burden, transforming known pathogens involved in superinfections in the ICU, like *Klebsiella pneumoniae*, into real challenges. During these times, outbreaks of *Klebsiella pneumoniae* resistance to the novel β-lactam-β-lactamase inhibitor combination, ceftazidime-avibactam, were observed.
Objectives: The main objective was to evaluate the ceftazidime-avibactam susceptibility profile of *Klebsiella pneumoniae* in the setting

of superinfections in COVID-19 patients compared to non-COVID-19 patients. Our secondary objective was to identify the differences in length of stay and mortality between COVID-19 patients and non-COVID-19 patients with *Klebsiella pneumoniae* superinfection.
Methods: We conducted an observational, retrospective study which included 98 patients diagnosed with bronchopneumonia admitted to the ICU in the Clinical Emergency Hospital of Bucharest between March 2020 and April 2021. 34 patients met the inclusion criteria, developing *Klebsiella pneumoniae*superinfection, and were divided in two subgroups: subgroup A-patients with a Real Time Polymerase Chain Reaction (RT PCR) test positive for SARS CoV-2 and subgroup B-patients with non-COVID-19 bronchopneumonia.
Results: We compared the distribution frequency of sensitivity and resistance for ceftazidime/avibactam using Chi-Square. *Klebsiella pneumoniae* causing superinfection in COVID-19 patients proved to be more resistant to ceftazidime-avibactam than in non-COVID-19 patients ($p = 0.0008$). Median survival was 30 days for subgroup B and 14 days for subgroup A ($p = 0,0180$, Kaplan–Meyer test). Median ICU length of stay was 23 days in subgroup A and 14 days in subgroup B ($p = 0.05$, Mann–Whitey).
Conclusion: In conclusion, *Klebsiella pneumoniae* causing superinfection in COVID-19 patients had a higher resistance to ceftazidime-avibactam than in non-COVID-19 patients. Further studies in order to establish the mechanism behind this resistance are needed. Moreover, the length of ICU stay and the mortality were higher in the COVID-19 subgroup.

001388

Epidemiology of candidemia and fluconazole resistance in an ICU before and during the COVID-19 pandemic era

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Intensive Care Medicine Experimental 2022, **10(2)**:001388

Introduction: Secondary infections, both bacterial and fungal, have been increasingly reported in patients with coronavirus disease-2019 (COVID-19); however, data regarding bloodstream infections due to *Candida* species in comparison with non-COVID-19 patient population are limited.
Objectives: The objectives of this study was to investigate the incidence of candidemia and factors for *Candida* species distribution and fluconazole resistance among patients admitted to the intensive care unit (ICU) during the COVID-19 pandemic compared to two pre-pandemic periods.
Methods: All patients, consecutively admitted to the COVID-ICU because of acute respiratory failure from March 2020 through October 2021, who developed candidemia were included. Patients' data were collected by retrospective chart review. The incidence of candidemia, the isolated *Candida* species and the fluconazole resistance were compared with two, pre COVID-19 pandemic, periods: from 2005 to 2008 and from 2012 to 2015.
Results: During the COVID-19 study period, the incidence of candidemia was 10.2%, significantly higher compared with 3.2% and 4.2% in the two pre-pandemic periods, respectively. The proportion of non-*albicans Candida* species increased (from 60.6% to 62.3% and 75.8%, respectively) with a predominance of *C. parapsilosis.* A marked increase in fluconazole resistance (from 31% to 37.7% and 48.4%, respectively) was observed. Regarding the total patient population with candidemia ($n = 205$), ICU length of stay before candidemia was positively associated (OR 1.03; CI: 1.01–1.06, $p = 0.003$) whereas presence of shock on candidemia onset was inversely associated (OR 0.23; CI: 0.07–0.64, $p = 0.006$) with isolation of fluconazole-resistant species.
Conclusion: In conclusion, a substantial increase in the incidence of candidemia, in non-*albicans Candida* species, and in fluconazole resistance was found in patients admitted to the ICU due to COVID-19, compared to pre-pandemic periods. For the whole cohort of patients with candidemia, isolation of fluconazole-resistant pathogens was independently associated with prolonged ICU length of stay and inversely associated with presence of shock on candidemia onset.

001389

Hyperbilirubinemia and hyperamylasemia in COVID-19 critically ill patients: A single-center retrospective study on their prevalence and patient outcome

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Intensive Care Medicine Experimental 2022, **10(2)**:001389

Introduction: Early in the beginning of the COVID-19 pandemic it was noticed that SARS-CoV-2 infection causes a disease that affects not only the respiratory system, but also other organ systems. As far as the liver and the pancreas are concerned there have been several reports presenting cases of liver disease or pancreatitis suggesting a possible causal relationship.
Objectives: To identify the prevalence of hyperbilirubinemia and hyperamylasemia in COVID-19 critically ill patients and to assess whether there is any association with patients' outcome.
Methods: We have performed a retrospective single-center study including all consecutively critically ill mechanically ventilated PCR SARS-COV-2 positive patients admitted from 03/2020 to 11/2021 to our COVID-19 Intensive Care Unit (ICU). Patients' demographics, comorbidity including Charlson Comorbidity Index, blood culture results, ICU length of stay, and ICU mortality were recorded for each patient. In addition, total Bilirubin (TBIL), Alanine Transaminase (ALT), Alkaline Phosphatase (ALP) and amylase (AMS) blood values on day of ICU admission were also recorded and maximum values during the first 10 days of ICU admission and maximum values and day of maximum value during ICU stay were also identified. Two patient groups, i.e., survivors and non-survivors were compared for differences in TBIL, ALT, ALP, and AMS values.
Results: Altogether 183 patients were included in our study. At some point during their ICU hospitalization 45.4% (83/183) had TBIL > 2 mg/dl and 77.6% (142/183) and 27.9% (51/183) had an ALT and an ALP value higher than twice the upper normal limit (UNL) respectively. Amylase was raised during the ICU hospitalization in 65.6% (120/183) of our patients, while 13.7% (25/183) had a raised AMS already on ICU admission. A significant AMS raise ($> 3 \times$ UNL) was noted in 16.9% (31/183) of our patient sample. Among these, there were 3 cases of imaging-confirmed acute pancreatitis; 11 patients had a raised AMS while suffering Multiple Organ Dysfunction Syndrome, and the rest had a transient AMS elevation of no clinical significance. All three patients with acute pancreatitis died in ICU. Mann–Whitney U-test analysis showed a significant higher maximum TBIL value in the non-survivor group (2.4 vs 1.5, $p = 0.0001$) but no difference between survivors and non-survivors regarding AMS value.
Conclusion: In our study, deranged TBIL, ALT, ALP, and AMS values are common among ICU COVID-19 patients and higher TBIL values were associated with higher mortality. Whether there is a causal relationship between COVID-19 disease and hepatic or pancreatic injury remains to be addressed in future studies.

001395

Device-associated Infections in an Adult Intensive Care Unit during pandemic in Colombia: an unexpected increase in uncommon organisms

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Intensive Care Medicine Experimental 2022, **10(2)**:001395

Introduction: Healthcare-associated infections (HAI) are one of the most common complications in hospitalized patients. They constitute a threat to patients and healthcare providers and are considered a public health issue (1) constituting a preventable cause of morbidity and mortality among ICU patients, particularly in low- middle-income countries, with 3–20 times higher infection rates than high-income countries (2). Global efforts have been directed towards decreasing the burden of healthcare-associated infections, and until the COVID pandemic, a significant improvement was made. (3) During the first year of the coronavirus disease 2019 (COVID-19), despite a major focus on standard prevention practices like hand hygiene and contact precautions, a significant increase in HAI was demonstrated worldwide. When compared to the year 2019, HAI in 2020 reached an increase of 47% in Central line-associated bloodstream infection (CLABSI), around 19% in Catheter-associated urinary tract infections (CAUTI), and 44.8% in Ventilator-associated events (VAE) across hospitals in the US (3), while on low- and middle-income countries this increase was reported to be as high as 85% for CLABSI (4).
Mortality rates simultaneously increased during the COVID-19 pandemic in both COVID and non-COVID patients. Several factors have been related to this phenomenon, including longer hospital lengths of stay, collapse of the healthcare system, numerous comorbidities, increase in resource use as vasopressors, mechanical ventilation and hemodialysis; All these factors can partially explain the reduced focus on routine HAI prevention activities (2–4).
Objectives: To describe the epidemiology of device-associated infections (CLABSI, CAUTI, VAE) in an adult Intensive Care Unit of the Hospital Universitario Santa Fe de Bogotá (HUFSFB) from 2018-to 2021.
Methods: We conducted a retrospective, descriptive study of device-associated nosocomial infections in an adult ICU of HUFSFB, from 2018 to 2021. The adult ICU had three non-COVID ICUs and 2 COVID ICUs since the COVID pandemic in 2020. Mortality was evaluated as the primary outcome. Descriptive standard statistics were performed.
Results: Five hundred fifty patients admitted to the ICU during the four-year study presented a device-associated nosocomial infection. Table 1 lists the characteristics of the study patients. Most of the patients were hospitalized in the COVID ICUs (404/550), 73,4%, meaning most infections took place in the two years of the pandemic (2020–2021). Additionally, males were more commonly represented than females (74,18%), and 54.5% of patients were between 60 and 79 years old. Of the 550 patients included, 103 presented concomitant infections for a total of 633 events. 47 cases were recorded for the years 2018–2019 corresponding to the "Pre-COVID'" period and 585 during the pandemic in the years 2020–2021. Microbiological confirmation was obtained in 510 cases. CLABSI was the main HAI in both periods (46.8% vs 42.9%). *K. pneumoniae* was the main microorganism responsible for the 3 HCAIs described, followed by other gram-negative fermenting bacilli and *S. aureus* predominantly sensitive to oxacillin (SAMS); in the years prior to the pandemic, no HCAIs due to this germ had been recorded. Fungi were responsible for 5.1% of HAIs in the COVID period and 4.2% prior to the pandemic, with the appearance of new Candida species other than *C. albicans*, such as *C. glabrata*, *C. tropicalis* and *C. auris*. In this study 39,81% of patients died due to nosocomial infection in the ICU (Table 1). Of the 210 deaths in the two years of the pandemic, 90,4% ccurred in the COVID ICUs. In the pre pandemic period (2018–2019) only 9 deaths related to HAI were reported.
Conclusion: As seen in other countries, device-associated infections in this hospital immensely increased during the pandemic. CLABSI remained the most common HAI through the study period and the incidence of uncommon microorganisms was higher. This rise was greater than expected, and may contribute to higher mortality rates. This study provides information to the scarce data about this topic in Latin America, and could be the starting point for future research and improvement in organizational processes.

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001413

The COVID-19 era: impact of antibiotic therapy

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Intensive Care Medicine Experimental 2022, **10(2)**:001413

Introduction: Amidst a pandemic that has taken more than one million lives, antibiotic stewardship was partially neglected, leading to new problems: antibiotic overuse and consecutively the development of antibiotic resistance. In COVID-19 patients admitted to the hospital, the rate of microbiologically confirmed bacterial or fungal infections is rather low 1, 2, nonetheless, most of them received empirical broad-spectrum antibiotics, a double-edged sword, which will leave its mark in the post pandemic period.
Objectives: Our primary goal was to assess the impact of antibiotic therapy on 28-day survival rate in critical COVID-19 patients admitted to the Intensive Care Unit (ICU). Our secondary aim was to identify the correlation between immunomodulatory, antiviral and corticosteroid therapy and the 28-day survival rate in the same study group.
Methods: We performed an observational, retrospective study which included 100 critical COVID-19 patients admitted to the ICU between March 2020 and March 2021. Inclusion criteria: 1. Real Time Polymerase Chain Reaction positive test for SARS CoV-2; 2. Severe form of COVID-19 with subsequent mechanical ventilation. Exclusion criteria: 1. Age under 18 years old.
Results: The mean age was 66 years (SD = 14.7), 32% were female, 68% were male. The mean hospital stay was 10.19 days (SD = 8.2). Receiving antibiotic therapy had a hazard ratio of death of 0.98, but it wasn't statistically significant. When studying the classes of antibiotics, we concluded that only the macrolides had a positive impact on survival (HR = 0.5, p = 0.04), but no other class had statistically significant impact on survival. The critical COVID-19 patients that received antiviral therapy had a higher hazard ratio of death (HR = 1,97; p = 0.02), while the immunomodulatory therapy had no statistically significant

impact. Corticosteroid therapy was associated with a death hazard ratio of 0.84 ($p < 0.0001$).
Conclusion: Antibiotic therapy is useful in selected critical COVID-19 patients, but its use should be carefully assessed to avoid creating a new problem with deleterious consequences, a return to the pre-antibiotic era. Macrolides and corticotherapy had a statistically significant impact on 28-day survival rate, according to our findings.

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001439

Immune characteristics of COVID-19 patients developing secondary invective events

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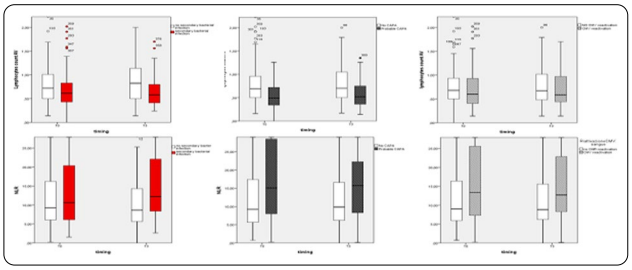
Intensive Care Medicine Experimental 2022, **10(2)**:001439

Introduction: Since the beginning of the SARS-CoV-2 pandemic, it has been clear that the host immune response plays a central role in determining the manifestations and severity of this disease. Immune function derangements are mirrored by the high prevalence of secondary infective events, that appears to be an important determinant of patients' outcome (1).
Objectives: The purpose of this study is to observe which immunological structure correlate with the development of secondary bacterial infections, community acquired pulmonary aspergillosis (CAPA) and cytomegalovirus (CMV) reactivations in critically-ill patients suffering from COVID-19 pneumonia.
Methods: We performed an observational retrospective study analysing a registry specifically conceived to collect information on immune system's functionality in patients undergoing COVID-19 pneumonia. Data from patient of polyvalent intensive care unit of the University Hospital of Modena with diagnosis of SARS-CoV-2 related pneumonia from February to December 2020 were analysed. Patients under 18 years, patients with an end of life decision or too sick to benefit were excluded. The examined population was splitted in tertiles of WBC, lymphocytes, neutrophils-on-lymphocytes ratio (NLR), IgG and IgM titers at baseline and at day 3 from ICU admission. The incidence of each of the above-described infective complications were compared among the tertiles of each variable.
Results: 203 patients were included in the analysis. Median age was 63 (IQR 56–71), 20.2% were females, median SAPS II score at admission was 33 (IQR 28–40) and SOFA score was in median 4 (IQR 3–5), 166 patients (81.8%) had at least one comorbidity; more frequent were hypertension (50.7%), obesity (40.9%) and diabetes (22.7%). Overall 30-days survival was 72.9% (148 patients). Median length of stay in ICU was 8 days (IQR 8–15) and Hospital length of stay 20 days (IQR 12–35).
79 patients (38,9%) developed a secondary bacterial infection, 45 (23,2%) developed a CMV reactivation while 29 (14,4%) had a probable community acquired pulmonary aspergillosis (CAPA). Secondary infection and CMV reactivation had a significant impact on patient's survival. Rates of secondary infective complications according to tertiles of distributions of the examined immunological variables are summarized in Table 1. Lymphocytes counts and NLR distribution ad baseline and at day 3 among patients who developed secondary infective complications are represented in Figure 1.



	Secondary bacterial infection				CAPA				CMV reactivation			
	Tertile				Tertile				Tertile			
	1	2	3	Sig.	1	2	3	Sig.	1	2	3	Sig.
T0 WBC	25 (36.8%)	31 (45,6%)	23 (34,3%)	0,368	10 (14,7%)	9 (13,2%)	10 (15,4%)	0,937	8 (12,3%)	18 (26,9%)	19 (30,6%)	0,034
T3 WBC	28 (43,9%)	22 (34,9%)	28 (44,4%)	0,479	10 (15,6%)	10 (10,9%)	9 (14,8%)	0,984	14 (22,6%)	12 (19,7%)	19 (32,2%)	0,251
T0 lymphocytes	29 (37,2%)	30 (48,2%)	19 (29,2%)	0,076	15 (22,1%)	10 (16,1%)	4 (6,2%)	0,037	19 (29,2%)	11 (18,3%)	13 (21,0%)	0,315
T3 lymphocytes	26 (40,6%)	25 (50%)	13 (26,0%)	0,019	13 (25,5%)	8 (16,0%)	4 (8,2%)	0,066	16 (31,4%)	14 (28,0%)	10 (20,8%)	0,484
T0 NLR	23 (35.9%)	21 (32.8%)	31 (48.4%)	0,159	6 (9,4%)	7 (11,1%)	14 (21,9%)	0,089	10 (16,1%)	13 (21,7%)	19 (30,6%)	0,151
T3 NLR	11 (21.2%)	25 (49.0%)	28 (54.9%)	0,001	5 (9,6%)	7 (14,0%)	13 (26,0%)	0,070	8 (15,4%)	13 (26,5%)	19 (38,0%)	0,035
T0 IgG	18 (42.9%)	12 (28,6%)	14 (34,1%)	0,385	11 (26,8%)	3 (7,1%)	6 (14,6%)	0,049	10 (24,4%)	9 (23,1%)	8 (20,0%)	0,889
T3 IgG	22 (59,5%)	12 (34,3%)	18 (51,4%)	0,094	8 (22,2%)	6 (17,1%)	5 (14,3%)	0,677	12 (33,3%)	7 (20,6%)	8 (22,9%)	0,425
T0 IgM	15 (34,1%)	16 (38,1%)	13 (32,5%)	0,868	8 (19,0%)	7 (16,7%)	5 (12,5%)	0,718	10 (23,8%)	160(25,6%)	7 (17,9%)	0,696
T3 IgM	19 (51,4%)	17 (48,5%)	16 (45,7%)	0,892	10 (27,8%)	4 (11,4%)	5 (14,3%)	0,158	11 (30,6%)	12 (34,3%)	4 (11,8%)	0,072

Conclusion: In critically ill patients with COVID-19 pneumonia lymphocyte count and neutrophil-to-lymphocyte ratio at baseline and at day 3 from ICU admission show a trend toward an impact on the development of all the examined secondary invective complications. Leucocyte count, IgG and IgM titers do not seem to affect the risk of secondary infective complications.

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Acknowledgements: None.

001448

Bloodstream infections caused by multidrug or pandrug-resistant *Acinetobacter baumannii* in critically ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001448

Introduction: Bloodstream infections (BSI) caused by *A. baumannii* have been increasingly recorded among critically ill patients. Resistance of *A. baumannii* strains to commonly used antibiotics is increasing as well, rendering the treatment of those infections rather challenging and permissing few therapeutic options.
Objectives: To retrospectively record the incidence, clinical characteristics, treatment and outcome of BSI caused by multidrug or pandrug—resistant (PDR) *A. baumannii* in critically ill patients.

Methods: The study was performed at a 45-bed polyvalent intensive care unit (ICU). All the mechanically ventilated patients with BSI caused by PDR A. *baumannii*, from January 2020 until March 2022 were enrolled in the study. Concentrations (MICs) were determined by the broth microdilution method, as indicated by the CLSI. APACHE-II and SOFA score on ICU admission were used to define disease severity. Patients' demographics, clinical characteristics, treatment and outcomes in 10 days were recorded. Clinical success was defined by a lessening of the signs and symptoms of infection, while microbiologic success was considered, as the eradication of the pathogen from cultures.
Results: 15 patients (mean age ± SD = 58 ± 15 yrs, 9 males/6 females) with BSI caused by *A. baumannii* were enrolled in the study. Among them, 10 patients were hospitalized due to COVID-19 pneumonia. APACHE-II score in ICU admission was 14 ± 7, while SOFA score was 8 ± 3. Central line associated bloodstream infection (CLABSI) was observed in 6 (40%) pts, and primary bacteremia in 9 (60%) pt. Colonization of bronchial secretions with *A. baumanni* was observed in all patients. Mean length of stay of enrolled patients in the ICU, prior to infection, was 5 ± 15 days. 14 (93%) pts had received broad spectrum antibiotics prior to infection due to *A. baumannii.* All COVID-19 patients were treated with dexamethasone 6 mg for 10 days. PDR *A. baumanii* was the cause of BSI in 9 patients (60%) while *MDR A. baumanii* was observed in 6 patients (40%). MDR strains were sensitive to colistin and amikacin. Combination treatment with colistin, high dose ampicillin/sulbactam (A/S), rifampicin, amicacin, or tigecycline and broad spectrum antibiotics (meropenem or ceftazidim/avibactam), for 14 ± 4 days. Clinical and microbiological success was observed in 10 (66%) of patients. ICU mortality in 10 days of infection was 20%, significantly associated with SOFA score ($p < 0.05$). Mean length of stay in ICU after infection was 15 ± 17 days.
Conclusion: Incidence of MDR and PDR-*A. baumannii* strains has increased in critical care settings, especially in COVID-19 era. Antibiotic combinations might offer a therapeutic benefit, as a result of possible synergistic effect, despite the recorded resistance to separate antibiotics. Further studies are required in order to define the therapeutic options of these life-threatening infections.

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Acknowledgements: None.

Feeding, Rehabilitation, Endocrinology & Metabolism 1

000029

Hemoadsorption therapy for critically ill patients with acute liver dysfunction

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Intensive Care Medicine Experimental 2022, **10(2)**:000029

Introduction: Critically ill patients admitted to the ICU have been shown to be at risk of developing acute liver dysfunction usually as part of multiorgan failure sequelae [1]. Theoretically, clearing the blood from toxic liver related metabolites and cytokines could prevent further organ damage [2]. Despite the increasing use of hemoadsorption for this purpose evidence of its efficacy is lacking.
Objectives: To perform a systematic review on the use of hemoadsorption (HA) for critical illness associated acute liver dysfunction, in order to appraise the level of evidence for its efficacy, and to formulate hypotheses to guide future clinical trials.
Methods: We performed a systematic literature search on Pubmed, Embase, Scopus, CENTRAL, and Web of Science (PROSPERO registration: CRD42022286213). The target population was patients with acute liver dysfunction or failure associated with critical illness and treated with HA. Our primary outcomes were the change in liver function parameters during HA and mortality. The data was analyzed using SPSS 26 software (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Paired t-test was used for comparison, $p < 0.05$ was considered to be statistically significant.
Results: Our search yielded 26 eligible publications between 2011 and 2022, which reported the use of hemoadsorption for a total 309 patients. Of those, 23 are case presentations (number of patients, n = 81), 2 are retrospective observational studies (n = 109) and 1 registry analysis (n = 109). All patients presented with liver dysfunction related to acute critical illness and have been treated with HA: CytoSorb (19 datasets, n = 218), Coupled Plasma Filtration Adsorption (4, n = 88), oXiris (2, n = 2), CytoSorb + oXiris (1, n = 1). Data pooled from individual case reports (n = 8) revealed a tendency of improved liver function (pre- vs. post-treatment mean differences and standard deviations of total bilirubin: − 3.82 ± 5.87 mg/dL; ALT: − 174 ± 272.83 U/L; AST: − 337.53 ± 395.85 U/L) and reduction of vasopressor need (mean difference of − 0.33 ± 0.45 mcg/kg/min). We also managed to pool data on 160 patients from studies with multiple patients (n = 5) which showed significant reduction in total bilirubin levels after HA (Figure 1.).

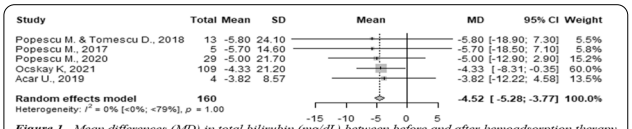

Figure 1. Mean differences (MD) in total bilirubin (mg/dL) between before and after hemoadsorption therapy.

Mortality was 38.5% in the observational studies, and the registry analysis reports 9.2% mortality at the end of HA therapy, along with 56.9% hospital mortality.
Conclusion: Use of HA for critically ill patients with acute liver dysfunction or failure seems to be safe and yield a trend towards improved liver function after HA, but quality of data is insufficient. Our results render the need of adequately designed clinical trials with the above mentioned parameters as main outcomes.

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000043

Thyroid dysfunction in critically ill patients with COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**:000043

Introduction: Previous studies have reported abnormal serum levels of thyroid hormones in various acute pathological conditions (1) including acute respiratory distress syndrome (2), and recently Coronavirus disease 2019 (COVID-19) (3).
Objectives: To investigate the thyroid function in critically ill patients with COVID-19, in order to evaluate the prognostic value of thyroid hormones in this clinical setting.
Methods: We retrospectively studied 60 patients with COVID-19 admitted in the ICU. Collected data included demographic, clinical and laboratory variables measured upon admission and on day 3. According to our local protocols, thyroid function in these patients was assessed by the measurement of plasma levels of free triiodothyronine (fT3), free thyroxine (fT4), and thyroid stimulating hormone (TSH).

Results: Sixty patients (66.7% male) were included in the study. The patients' mean age was 69 ± 11.8 years. Plasma fT3, fT4 and TSH levels measured on admission were abnormal in 40%, 5% and 53% of the patients respectively. Only plasma TSH levels measured on day 3 correlated negatively with acute physiology and chronic health evaluation II score (r = -0.321, P < 0.05) and plasma troponin levels (r = − 0.328, P < 0.05). In patients who died, fT3 levels measured on admission were significantly lower (1,3 ± 0,3 ng/dL, n = 21) than that in patients who were discharged from the ICU (1.53 ± 0.4 ng/dL, n = 39, P < 0.05). Likewise TSH levels on day 3 were significant higher in survivors (1.1 ± 1 µIU/mL, n = 39) than in patients that died in the ICU (0.32 ± 0.3 µIU/mL, n = 21, P < 0.05). Accordingly, in univariate logistic regression analysis, plasma fT3 on admission and TSH levels on day 3 were associated with an increased possibility of survival (table 1). Multivariate analysis revealed TSH on day 3 as an independent predictor of survival (table 2).

Table 1 Univariate logistic regression analysis for the association between thyroid hormones and survival

	OR (95% CI)	P value
fT3 (Admission)	7.985 (1.07–59.57)	**0.043**
fT4 (Admission)	2.209 (0.150–32.603)	0.564
TSH (Admission)	1.166 (0.445–3.053)	0.754
fT3 (Day 3)	1.128 (0.210–6.063)	0.888
fT4 (Day 3)	1.287 (0.154–10.764)	0.816
TSH (Day 3)	21.069 (2.524–175.848)	**0.005**

Conclusion: Our preliminary data suggest that not only thyroid function abnormalities are common in ICU patients with COVID-19, and they may also serve as prognostic markers in this population.

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000169

Energy expenditure of intensive care patients with COVID-19—The difference between indirect calorimetry and rapid estimating prediction formula

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Intensive Care Medicine Experimental 2022, **10(2)**:000169

Introduction: Nutrition therapy guidelines recommend indirect calorimetry (IC) as the gold standard to measure patients' energy expenditure (EE), because the estimated EE is often inaccurate in critically ill patients, even more so with COVID-19. We aimed to compare the difference between measured and estimated EE in intensive care unit (ICU) patients with COVID-19 and to determine the predictive factors of the difference.
Objectives: Comparison of energy expenditure between indirect calorimetry and the rapid estimation formula in COVID-19 ICU patients.
Methods: All ICU patients with COVID-19 who had an IC measurement during their stay were included. We estimated EE at ICU admission using the prediction formula of 25 kcal/kg body weight (BW). The ideal BW (body mass index (BMI) = 22.5 kg/m^2) was used if the BMI was > 25 kg/m^2. After stabilization of the patient, IC measurement was performed in the post-acute phase, from day 7 of admission if possible. The measured and estimated EE were compared by a paired t-test. A multivariate linear regression model tested whether the difference between measured and estimated EE was influenced by body temperature (°C), obesity status, age in decades and sex.
Results: EE was measured with IC in 46 patients. The mean age was 67 (± SD 10) years, 82% were male, and 40% were obese. The mean temperature (°C) during measurement was 37 (± SD 0.7) °C. The mean measured EE was significantly different from mean estimated EE (1893 ± 383 kcal vs. 1687 ± 213 kcal; p < 0.001). The multivariate linear regression model (Table 1) shows that obesity increases the difference between measured and estimated EE further by 215.2 kcal (p-value = 0.032). For each additional degree Celsius, this difference also increases by 187.6 kcal (p-value = 0.007). Age and sex had no significant influence on the difference between estimated and measured EE in the model.
Table 1:

Difference between measured and estimated EE	Coefficient (95% confidence interval)	p-value
Temperature (°C)	187.6 (54.2; 321.0)	0.007
Obesity (BMI > 30 kg/m^2)	215.2 (19.0; 411.4)	0.032
Age (in decades)	− 25.4 (− 120.2; 69.3)	0.591
Sex (women)	96.9 (− 153.4; 347.3)	0.439

Conclusion: Energy expenditure measured with indirect calorimetry in COVID-19 ICU patients is significantly higher than that estimated by the prediction formula. Temperature elevation and obesity increase the differences between measured and estimated EE. These results confirm the recommendation that nutritional therapy in the intensive care should be guided by indirect calorimetry, especially in obese patients.

000174

The Effect of Renal Function on The Clinical Outcomes and Management of Diabetic Ketoacidosis (DKA)

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Intensive Care Medicine Experimental 2022, **10(2)**:000174

Introduction: The global prevalence of diabetes mellitus (DM) has been rising rapidly over the past years (1). DKA is characterized by a triad of hyperglycemia, ketonemia or ketonuria, and acidosis (2). Patients with impaired renal function encounter a delay in insulin clearance, complicating the adjustment of insulin dosing and increasing the risk of hypoglycemic events (3, 4).
Objectives: To evaluate the effect of renal function on the safety and efficacy of insulin use in the management of DKA patients.
Methods: We performed a single-center, retrospective study at King Abdulaziz Medical City, a tertiary academic institution in Riyadh, Saudi Arabia. Patients who received continuous insulin infusion between January 1st, 2016, and December 31st, 2021, were identified using a hospital reporting system. Patients included if they were ≥ 18 years old, admitted to the ICU, received insulin via continuous infusion for ≥ 1-h, documented diagnosis of DKA, and an anion gap of ≥ 16 at ICU admission. Patients were categorized into normal kidney function (Control group) and patients with impaired renal function. Renal impairment was defined as an eGFR of ≤ 60 ml/min.
Results: We included 196 patients in our analysis. The median eGFR of patients with normal kidney function was 62 (45.5–82.5) mL/min/1.73 m^2 compared to 25 (20–41) mL/min/1.73m^2 for patients

with impaired renal function. The median of time to close the anion gap at 12-h among patients with impaired kidney function was 5.65 (4.8–14) hours as opposed to 16 (11.5–29) hours among patients with kidney function (HR 3.644, 95% CI 2.251–5.901, p-value = < 0.001). The time to close the anion gap was significantly shorter among patients with normal kidney function who received an insulin bolus dose with a median of 16 (13.63–32) compared to 20 (11–32) for patients with impaired kidney function who received an insulin bolus (HR 0.3591, 95% CI 0.166–0.6869, p-value = 0.0042). Type 1 diabetic patients with normal kidney function had a significantly shorter time to close the anion gap in contrast to type 1 diabetic patients with impaired kidney function. The median was 17 (12.88–32.4) vs. 19 (12–32) (HR 5.586, 95% CI 3.344–9.69, p-value = < 0.0001) among patients with normal and impaired kidney function, respectively. Hypoglycemia event rates were low in our study. Only four patients with normal kidney function had a documented hypoglycemia event contrasted to six patients with impaired kidney function (OR 2.506, % CI 0.6805–7.896, p-value = < 0.1904).

Conclusion: Patients with impaired kidney function had a shorter time to close the anion gap at 12-h compared to patients with normal kidney function. The administration of insulin bolus dose and being diagnosed with DM type 1 resulted in a shorter time to close the gap among patients with normal kidney function. Hypoglycemia event rates were similar in our study. More studies are needed to confirm our findings.

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000190

Effects of enteral supplement of Vitamin D in critically ill patients with vitamin D deficiency

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Intensive Care Medicine Experimental 2022, **10(2)**:000190

Introduction: The incidence of vitamin D deficiency in critically ill patients is high. Vitamin D deficiency is associated with infection, wound healing, coagulation, and mortality in different populations of critically ill patients (1). Only Stoss therapy is able to increase the 25-hydroxyvitamin D (25(OH)D) level to normal range.

Objectives: This study aimed to investigate the effects of enteral supplement of vitamin D in critically ill patients with vitamin D deficiency.

Methods: This multicenter and prospective study was approved by the Research Ethics Committee (Approval number: 201902073MIPA) and registered on the ClinicalTrials.gov (ID: NCT04292873). Participants with a blood calcifediol concentration less than 20 ng/mL and normal enteral function were enrolled and randomly divided to group Control (no vitamin D supplement) and group Vitamin D (enteral supplement of 569,600 IU vitamin D). The vitamin D level was measured at several specific time points. Patients' diagnosis, vital signs, laboratory data, 30-day survival, and 90-day survival were recorded.

Results: In the enrolled 46 patients, the baseline vitamin D level was 15.7 (12.1–18.2) ng/mL in group Vitamin D and 13.1 (11.4–17.3) ng/mL in group Control. The vitamin D level on day 7 was 34.5 (24.7–58.5) ng/mL in group Vitamin D (25 peoples) and 13.9 (11.8–17.1) ng/mL in group Control (14 peoples). This difference lasts up to 28 days [40.3 (19.5–50.2) vs. 13.1 (8.5–17.5) ng/mL, P = 0.014]. Differences in vitamin D concentrations on day 42 were not statistically significant because fewer patients completed blood draws on day 42. The vitamin D level at other time points was presented in Table 1. The Acute Physiology and Chronic Health Evaluation II score was higher in patients with vitamin D levels < 30 ng/mL than in patients with vitamin D levels ≥ 60 ng/mL (group [19 (17–21) vs. 13 (11–17), p < 0.05]).

Tables:

Table 1 Vitamin D level at each time point

(ng/ml)	Baseline	Day 7	Day 14	Day 28	Day 42
Vitamin D group	13.1 (11.4–17.3)	13.9 (11.8–17.1)	13.4 (10.9–18)	13.1 (8.5–17.5)	15.5 (10.5–18.6)
Control group	15.7 (12.1–18.2)	34.5 (24.7–58.5)	37.3 (24.6–61.6)	40.3 (19.5–50.2)	29.6 (19.1–39.7)
P values	0.584	< 0.001	< 0.001	0.014	0.200

Conclusion: Stoss therapy can increase the vitamin D level to the normal range in critically ill patients. After 569,600 IU of vitamin D supplementation, the median vitamin D concentration increased from 15.7 ng/mL to 34.5 ng/mL, but there was large inter-individual variability (from − 2.4 to 112.4 ng/mL). Further study are required to adjust the dosage of stoss therapy for each individualized patients.

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000261

A self-made teaching kit for practice in using Corgrip bridles to secure enteral feeding tubes

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Intensive Care Medicine Experimental 2022, **10(2)**:000261

Introduction: Preventing the accidental dislodging of nasogastric (NG) feeding tubes is important for critical care outcomes. From patients reviewed in Queen's Medical Centre (QMC), two thirds of our ICU/HDU patients have NG tubes and roughly half of those tubes were secured using a Corgrip Bridle. The use of bridles compared to adhesive stickers has been associated with better clinical outcomes despite the risk of nasal mucosa damage (Lynch et al., 2018). Junior doctors in QMC previously had no formal teaching in inserting bridles.

Objectives: Improve junior doctor confidence and technique in inserting NG tube bridles.

Reduce the overall amount of negative incidents associated with feeding tubes: Unintentionally Removed NG Tubes (URT) and pressure sores.

Methods: A teaching session focussed on practicing bridle insertion on a prosthetic nose was developed and delivered to all junior doctors being inducted into working in critical care at QMC after 1st December 2021. The kit was assembled by cutting two nostril holes in a silicone nose with a scalpel and putting a safety pin in the string of the bridle to keep it re-usable. This keeps costs low.

The status of the NG tubes of all critical care patients were regularly assessed to review how many were bridled and the technique used (N = 109). The record of reported negative incidents relating to unintentionally removed tubes (URT) and pressure sores from NG tubes was also reviewed over a four month period before teaching was started (1st December'21) and four months after.

Doctors were asked to rate their confidence in the skill before and after the teaching on a scale of 1 to 10. Doctors who had not received bridle training were also asked to rate their confidence when they started working in Critical Care and their current confidence.

Results: Average confidence for junior doctors (out of 10). Number in brackets is one standard deviation.
Without teaching:
2.3 (± 1.8), increasing to 6.4 (± 3.0) at current time.
With teaching:
4.5 (± 2.8) before teaching increasing to 7.9 (± 1.0) afterwards.
Proportion of NG tubes bridled
In October'21 (without teaching): 59%
In January'22 (after teaching) 73%
Rates of bridles tied too tightly (< 1 cm gap) rose from 0 to 14% after teaching.
Incidents before teaching (August–November '21):
URT: 40—(6 Bridled, 28 Unbridled, 6 Unknown/Miscellaneous)
Pressure Sores: 17—(7 Bridled, 6 Unbridled, 4 Unknown/Miscellaneous)
Incidents after teaching (December'21–March'22):
URT: 31—(6 Bridled, 16 Unbridled, 9 Unknown/Miscellaneous)
Pressure Sores: 13 (5 Bridled, 4 Unbridled, 4 Unknown/Miscellaneous)
P = 0.36 for URTs and P = 0.72 for pressure sores
Conclusion: Confidence in the skill for doctors who hadn't received teaching increased over time, but teaching offered a greater confidence in doctors from day 1 of the job. The teaching session correlated with more NG tubes being bridled although more were bridled too tightly. Despite this, the introduction of bridle teaching and the resultant increase in rates of bridled NG tubes resulted in reduced recorded events of URTs and pressure sores, though P is significantly > 0.05 and further data is required.

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000398

Prone ventilation for respiratory failure in critically ill COVID-19 patients is associated with increased insulin requirements: a multicentre study

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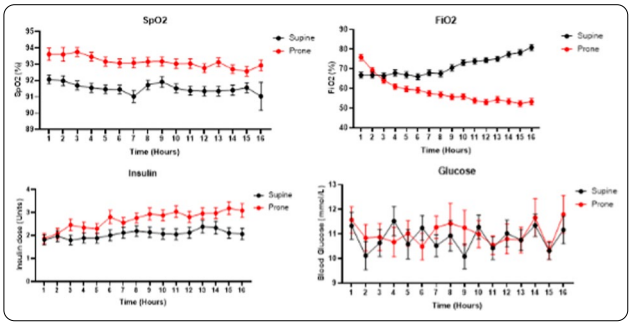
Introduction: We have previously shown that the severity of respiratory failure in COVID-19 pneumonitis is strongly associated with insulin resistance. However, it is unclear if this is driven by hypoxaemia or by other features of critical illness. Studies in healthy humans have suggested that experimental hypoxia increases insulin resistance, but it is unclear how relevant these findings are to the context of critical illness. Understanding how relative hypoxia effects systemic glucose metabolism can provide insight into the metabolic consequences of oxygen therapy and permissive hypoxaemia. Here we use insulin requirements for treatment of stress hyperglycaemia before and during prone ventilation to test the hypothesis that hypoxia regulates insulin sensitivity in patients with severe COVID-19 pneumonitis.
Methods: We performed a retrospective multisite observational study of mechanically ventilated patients who underwent first episode prone positioning for acute hypoxaemic respiratory failure due to COVID-19 pneumonitis between March 2020 and February 2021. Hourly measurements of oxygenation, blood glucose and insulin dose among other co-variates were extracted from electronic medical records. As patients were typically proned for 16 h, we compared the first 16 h of prone ventilation (Prone) to the preceding 16 h of supine ventilation (Supine).



Results: 119 patients from three centres met inclusion criteria and were included in our analysis. As expected, proning was associated with a significant improvement in oxygenation (mean SpO_2, Supine: 91.6 ± 2.0%, Prone: 93.2 ± 2.3%, p < 0.001), reduction in FiO_2 (mean FiO_2, Supine: 71.3 ± 11.2%, Prone: 58.5 ± 13.0%, p < 0.001) and improved SpO2: FiO_2 (mean S:F, Supine: 132 ± 24, Prone: 170 ± 39, p < 0.001). Proning was associated with an increase in insulin requirements during the study period (mean insulin requirement, Supine: 32.9 ± 36.2 units, Prone: 43.0 ± 34.5 units, p = 0.002). This difference was not explained by differing intensities of treatment during the prone and supine periods as blood glucose was unchanged by proning (mean blood glucose, Supine: 10.8 ± 3.1 mmol/L, Prone: 11.0 ± 3.6 mmol/L, p = 0.32). Differences in insulin requirements were not due to nutritional intake as, in a subset of the cohort with detailed dietetic data (N = 71), enteral feed tolerance was significantly reduced by proning (median (Q1, Q3) discarded feed, Supine: 1.5 mls (0.0, 66.5), Prone: 12.0 mls (12, 200), p = 0.001).
Conclusion: Our data demonstrate that proning is associated with an increase in insulin requirements. Contrary to our initial hypothesis, these findings are consistent with a beneficial effect of hypoxaemia on insulin sensitivity in critical illness. However, proning is a complex intervention which has effects independent of oxygenation. As such, we propose that the effects of hypoxaemia on systemic glucose metabolism in critical illness should be investigated in mechanistic, randomised controlled trials.
Acknowledgements: SL is supported by a Clinical Ph.D. Fellowship from the Wellcome Trust.

000416

Cirrhosis is independently associated with mortality in Acute Respiratory Distress Syndrome

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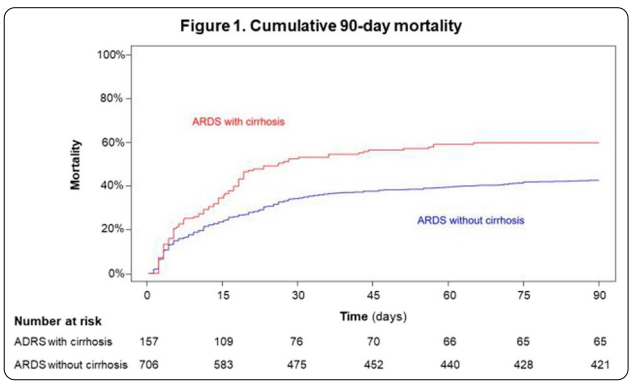
Introduction: Studies have shown that cirrhotic patients in Intensive Care Unit (ICU) under mechanical ventilation have worse outcomes than non-cirrhotic patients. But few studies have focused on outcomes of cirrhotic patients with Acute Respiratory Distress Syndrome (ARDS).
Objectives: Our study aimed to assess the 90-day mortality of cirrhotic patients with ARDS, in comparison to non-cirrhotic patients with ARDS.
Methods: We conducted a retrospective analysis of 863 patients with ARDS (157 cirrhotic patients and 706 non-cirrhotic patients) admitted in a 20-beds ICU from 2003 to 2021. ARDS severity was assessed according to the Berlin definition. The primary endpoint was mortality

at day-90 from the admission in ICU, survival was calculated using the Kaplan–Meier method. We used a Cox-proportional hazard model to determine whether cirrhosis was independently associated with mortality after adjustment for age, Simplified Acute Physiology Score II (SAPS II) and the PaFi at day one of the ARDS onset. To assess discrepancies in ventilation parameters, we compared the Positive End Expiratory Pressure (PEEP) and expiratory tidal volume (Vt) at day one of the ARDS onset. We obtained approval from the Montpellier University Hospital ethics committee (agreement number: 198711).
Results: In the 863 patients, the overall 90-day mortality was of 43.6% (377/863). Analysis of the survival curves showed that 90-day mortality was significantly higher in cirrhotic patients than in non-cirrhotic patients (59.5% vs 40.4%, $p < 0.001$ by the log-rank test, Figure 1.).



After adjusting for age, SAPS II and PaFi at day one using a Cox proportional hazard model, cirrhosis was independently associated with 90-day mortality (adjusted Hazard Ratio 1.72, 95% Confidence Interval [1.35, 2.21], $p < 0.001$). Among the 863 included patients, 33% had mild ARDS, 48% had moderate ARDS and 19% had severe ARDS based on the PaFi at day one, with no significant difference between cirrhotic and non-cirrhotic patients ($p = 0.14$). Ventilation parameters were not statistically different between cirrhotic patients and non-cirrhotic patients. The median PEEP used was 10 cmH_2O [Interquartile Range (IQR) 8–12], with no difference between cirrhotic patients and non-cirrhotic patients ($p = 0.52$). The median Vt set was of 6.3 ml/kg of Predicted Body Weight [IQR 5.9–7.0] ($p = 0.94$).
Conclusion: Cirrhosis is independently associated with mortality in ARDS patients. Cirrhotic and non-cirrhotic patients receive the same ventilation settings, even if cirrhotic patients have often been excluded from prospective trials.

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000429
Acute Decompensations of Urea Cycle Disorders: How are we doing?
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Intensive Care Medicine Experimental 2022, **10(2)**:000429

Introduction: Urea cycle disorders (UCDs) are rare inherited metabolic diseases due to deficiency of an enzyme, transporter or cofactor involved in the degradation of ammonia through the urea cycle. Acute hyperammonemic encephalopathy (HE) is the main life-threatening complication and requires prompt recognition and treatment to prevent brain swelling, structural damage and death. Decompensations of UCDs remain a clinical challenge for intensivists, however, there's a lack of data regarding epidemiological characteristics and outcomes in adults admitted to Intensive Care Unit (ICU).
Objectives: The study aims to assess epidemiological characteristics, treatment and outcome of adults who required ICU admission due to decompensated UCDs.
Methods: Retrospective observational cohort study of all admissions to ICU of adults with decompensated UCDs in a referral center for metabolic diseases (January 2010–September 2021).
Results: A total of 19 admissions were included in the study, all the patients were women, with a mean age of 34 years old (18–39 years). Acute decompensations were more frequent in UCD due to Ornithine Transcarbamylase Deficiency (n = 12) and Argininosuccinic Acid Synthetase Deficiency (n = 7). The leading triggers included non-compliance with diet or pharmacological treatment (n = 7), infectious diseases (n = 4) and drug intoxication (n = 2), however some decompensations (n = 6) occurred without an identified cause. Altered mental status caused by HE was the main clinical presentation, with decreased Glasgow Coma Scale and elevated ammonia levels. Acute management included a multidisciplinary team: a metabolic specialist, an intensivist and a nutritionist. All patients stopped exogenous protein intake during the first 24–48 h followed by a dietary adjustment. Ammonia scavenger agents were the first line therapy, with one agent (Sodium benzoate, n = 6) or a combination of two different agents (Sodium benzoate and phenylacetate, n = 13). One patient required renal replacement therapy (RRT) to achieve a quick reduction of ammonia levels after ammonia scavengers failure. A liver transplant was performed on another patient due to recurrent hyperammonemia refractory to medical therapy. One patient required invasive mechanical ventilation due to coma and another one non-invasive ventilation due to hypercapnic respiratory failure. The median length of ICU stay was 4 days (2–22 days). There are no deaths to report in this study and all the patients were discharged from the hospital without neurological damage.
Conclusion: Acute HE in UCDs is a neurological emergency since prognosis is strongly influenced by the duration of coma and the extent of ammonia elevation. Admission to intensive care allows close monitoring of clinical course after ammonia scavengers and early initiation of support treatments such as RRT. Although recognition and prompt treatment are crucial, referral to a tertiary center with a metabolic specialist is also one of the major determinants of a favourable outcome for these patients.

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000450
Protein intake in intensive care patients with COVID-19—Comparison before and after optimization of a simplified nutrition protocol
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Intensive Care Medicine Experimental 2022, **10(2)**:000450

Introduction: Organisational challenges of the first wave of COVID-19 pandemic led us to develop a practical and simplified nutrition protocol (SNP1) for COVID-19 patients in the ICU (1). After the first wave,

SNP1 was further optimised to a second simplified protocol SNP2, with the aim of improving the coverage of protein target, using specific protein-enriched nutrition products. In this study, we compared protein intake between SNP1 and SNP2.
Objectives: Comparison of protein intake with simplified nutrition protocols (SNP1 vs. SNP2) in COVID-19 ICU patients.
Methods: All COVID-19 patients admitted in the ICU from April 6, 2021 to March 10, 2022 with a length of stay of ≥ 4 days were included. SNP1 was used until October 19, 2021 and SNP2 from October 20, 2021. For both SNP1 and SNP2, the energy target was calculated as 25 kcal/kg body weight (BW) and the protein target as 1.3 g/kg BW/day. The ideal BW (body mass index (BMI) = 22.5 kg/m^2) was used instead if the BMI was > 25 kg/m^2. Descriptive data are presented as median with interquartile range (p25–p75). Wilcoxon Mann–Whitney Rank Sum Test was used to compare protein intake between patients treated using SNP1 and SNP2.
Results: Of the 141 patients included, 34 were treated according to SNP1 and 107 with SNP2. Overall, the mean age was 67 (58–74) years, 50 (35%) patients had overweight and 53 (37%) had obesity. For patients with SNP1, the mean APACHEII score was 25.5 (18–29) and mortality was 20%, and for SNP2 it was 23 (14–29) and 38%, respectively. Non-invasive mechanical ventilation was performed in 38% of patients with SNP1 versus 77% with SNP2. The median number of fasting days represented 6.3 (3.7–9.1) % of the ICU stay for SNP1 and 7.1 (4.0–10.0) % for SNP2. Percentage of days below protein target according to prescription were significantly lower in patients with SNP2 (33.3 (10.0–80.0) versus 59.6 (33.3–90); p-value = 0.01). Prescribed and actual protein intakes are presented in Table 1.
Table 1:

	SNP1	SNP2	p-value
Prescribed protein intake			
• Protein (g/d)	67.4 (60.0–75.4)	74.8 (59.8–84.8)	0.09
• Protein/kg BW	1.0 (0.9–1.1)	1.1 (0.9–1.4)	0.06
Actual protein intake			
• Protein (g/d)	52.4 (44.7–63.4)	51.8 (35.1–63.5)	0.16
• Protein/kg BW	0.8 (0.7–0.9)	0.8 (0.5–0.9)	0.17

Conclusion: The adapted SNP2 nutrition protocol allowed better prescription of protein intake in COVID-19 ICU patients, but actual protein intake was not increased. This is probably due to a higher rate of fasting days in SNP2 patients, with more continuous non-invasive ventilation and higher aspiration risk. Optimisation of nutrition through supplemental parenteral nutrition should be considered early in this special group of intensive care patients

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Feeding, Rehabilitation, Endocrinology & Metabolism 2 + Trauma & Emergency Medicine 3

001191 Hypoxic liver injury in critically ill nonagenarians—clinical characteristics and outcome

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Intensive Care Medicine Experimental 2022, **10(2)**:001191

Introduction: Hypoxic liver injury (HLI) is a frequent and life-threatening complication during critical illness occurring in up to 10% of critically ill patients. Age was previously identified as risk factor of occurrence of HLI. To date, the incidence of HLI and its clinical implications on outcome in very old (≥ 90 years) critically ill patients is unknown
Objectives: Investigate the incidence, clinical characteristics and outcome of HLI in critically ill patients ≥ 90 years
Methods: Retrospective analysis of all consecutive critically ill patients ≥ 90 years admitted to the Department of Intensive Care Medicine of the Medical University Centre Hamburg-Eppendorf (Hamburg, Germany) during an 11-year period. Clinical and laboratory course were analyzed from all patients. HLI was defined according to established criteria as elevation of aminotransferase levels (> 20-fold Upper Limit of Normal). Occurrence, clinical characteristics and outcome were assessed and compared between patients with and without HLI
Results: In total, 1065 critically ill patients ≥ 90 years were included. The median age of the patients in the total cohort was 92.3 (IQR 91.0–94.1) years, 32% (n = 342) were male. During the intensive care unit (ICU) stay, 3% (n = 35) of patients developed HLI. The main cause of HLI was cardiogenic shock (51%, n = 18), septic shock (23%, n = 8), cardiac arrest (20%, n = 7) and other causes (6%, n = 2). The cause of admission to the ICU was medical (HLI: 49% vs. No-HLI: 34%, p = 0.066), surgical—planned (HLI: 9% vs. No-HLI: 38%, p < 0.001) and surgical—unplanned/emergency (HLI: 43% vs. No-HLI: 28%, p = 0.055). The median Charlson comorbidity index (CCI) was 2 (1–3) points in patients with and 1 (0–2) in patients without HLI (p = 0.001). Frequent comorbidities were arterial hypertension (HLI: 71% vs. No-HLI: 70%, p = 0.487), chronic kidney disease (HLI: 46% vs. No-HLI: 22%, p = 0.001) and congestive heart disease (HLI: 31% vs. No-HLI: 22%, p = 0.200). Patients with HLI presented with higher disease severity by SAPS II (HLI: 55 vs. No-HLI: 36 points p < 0.001). Patients with HLI compared to without HLI were mechanically ventilated (HLI: 66% vs. No-HLI: 34%, p < 0.001), required vasopressor therapy (HLI: 91% vs. No-HLI: 40%, p < 0.001), renal replacement therapy (HLI: 20% vs. No-HLI: 2%, p < 0.001) and parenteral nutrition (HLI: 29% vs. No-HLI: 7%, p < 0.001). The ICU-mortality and hospital mortality was 66% (n = 23) and 83% (n = 29) in patients with HLI compared to 17% (n = 170) and 28% (n = 292) in patients without HLI, respectively (both p < 0.001)
Conclusion: HLI is an uncommon but not rare condition in critically ill nonagenarians. Occurrence of HLI is associated with high mortality. Cardiogenic and septic shock were the most common clinical conditions leading to development of HLI

001213 Development of new equations to quantify muscle mass and prognosis in intensive care unit (ICU) patients: an ancillary study of the PHASE ANGLE PROJECT

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Intensive Care Medicine Experimental 2022, **10(2)**:001213

Introduction: Muscle mass evaluation from BIA is an unreliable method to quantify muscle mass in ICU patients because of frequent fluid inflation
Objectives: Taking as Reference the muscle mass measured on third lumbar vertebra (L3)-targeted computed tomography (CT), our aims were to develop a BIA-derived equation to quantify muscle mass in

ICU patients and to assess whether muscle mass is associated with 28-day mortality
Methods: Ancillary study of the PHASE ANGLE PROJECT (1): 10 centres in 9 countries participated in the ulticenter prospective observational study. The inclusion criteria were age > 18 years; expected length of stay > 48 h; absence of pacemaker, heart defibrillator implant, pregnancy and lactation. All patients were performed a BIA as the primary judgment criterion. We selected the patients having performed a CT scan during their ICU stay. Muscle area (cm^2) was measured (threshold range − 29 to + 150 Hounsfield units) on CT scan at the L3 level by one single non-radiologist operator with the ImageJ software. Skeletal muscle index (SMI) cm^2/m^2 was calculated as muscle area/height $(m)^2$. A multivariate linear regression models were performed to set up predictive equations of SMI, vs L3-CT scan as the Reference method, based on clinically relevant covariates or P < 0.20 in the univariate analysis
Results: 209 ICU patients from the 931 included in the PHASE ANGLE PROJECT were included: 61 ± 16 years, men 60%. The decrease in muscle mass (SMI: 40.8 ± 9.5 (dead) vs 47.1 ± 10.5 (alive at day28) cm^2/m^2, P < 0.001) and edemas (65 (48%) vs. 183 (27%), P < 0.001) were associated with higher 28-day mortality. According to the presence or not of edema at admission, we develop two different equations to quantify SMI, derived from raw BIA data (resistance, reactance), height, weight, age and gender. Using the Bland–Altman method, the concordance between the predicted and measured SMIs were good. The correlation coefficients were 0.69 and 0.71 (P < 0.001) for patients with edemas or not, respectively. When applying the new established equations to 775 patients of the PHASE ANGLE PROJECT, the multivariable model including the predicted SMI, gender, age, body mass index, APACHE II, and admission diagnosis allowed a fair prediction of 28-day mortality (area under the curve = 0.76 [95% IC, 0.72–0.80]
Conclusion: We propose two predictive equations to estimate L3-CT-measured SMI based on parameters easy to collect at bedside: BIA-measured reactance and resistance, presence or not of edemas, height, weight, age and gender. Our equations should facilitate the evaluation of muscle mass and patient's prognosis in the ICU daily practice

001238

Evaluation of related-nutrition factors on mortality in patients under enteral nutrition

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Intensive Care Medicine Experimental 2022, **10(2)**:001238

Introduction: The impact on mortality of factors related with nutrition therapy is underrecognized although they strongly influence outcomes
Objectives: To evaluate the impact on mortality of factors directly or indirectly related to nutritional therapy in patients who require enteral nutrition (EN) during their ICU stay
Methods: Multicenter prospective observational study (n = 38) was performed (NCT: 03634943). Adult patients who required EN during the study period were included. Patient characteristics, comorbidities, nutritional status, nutritional therapy, laboratory data, ICU treatment, and complications were recorded in a database. Differences between survivors and non-survivors were analyzed using univariate and multivariate analysis (SPSS 25.0)
Results: 443 patients were included, with a mortality of 25.9% (115). In the subgroup of non-survivors, a higher age was observed (58.33 ± 15.56 *vs* 67.34 ± 12.14; *P < 0.001*), greater comorbidities such as arterial hypertension (36.8% vs 57.39%; *P < 0.001*), chronic obstructive pulmonary disease (15.2% vs 26.9%; *P = 0.007*) and past medical history of neoplasia (12.5% vs 24.3%; *P = 0.004*), as well as a higher nutritional risk (mNUTRIC Score: 3.68 ± 2.19 vs 5.11 ± 1.75; *P < 0.001*)
However, a later EN supply, a lower average caloric-protein intake, or higher rates of complications related to EN (except for a higher incidence of mesenteric ischemia (0.3% vs 5.2%; *P = 0.002*) was seen in non-survivors. Differences were observed in the lipid profile (LDL: Low-Density Lipoprotein) and protein profile (albumin)
The multivariate analysis found that a higher nutritional risk on admission to the ICU (mNUTRIC Score: HR: 1.276; 95% CI: 1.067–1.527; *P = 0.008*) and higher levels of LDL on the seventh day of admission (HR: 0.989; CI 95%: 0.977–0.998; *P = 0.045*) were associated with higher and lower 28-day mortality, respectively
Conclusion: A higher nutritional risk was associated with higher mortality in patients who received EN during their ICU stay in our population. Laboratory parameters, such as the lipid profile, could be associated with mortality in these patients

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001275

Evaluation and Comparison of Nutrition Assessment Tools in Critically-Ill COVID-19 Patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001275

Introduction: Modified Nutrition Risk in the Critically-Ill (mNUTRIC) score, Nutritional Risk Screening 2002 (NRS2002) and Malnutrition Universal Screening Tool (MUST) have been developed to assess nutritional status of outpatients and inpatients (1). There have been no study which evaluates optimum thresholds of these tools and compares their prognostic accuracy in critically-ill COVID-19 patients
Objectives: In this study, we aimed to determine nutritional status of critically-ill COVID-19 patients and to evaluate and compare prognostic accuracy of mNUTRIC score, NRS 2002 and MUST
Methods: We retrospectively analysed the data of laboratory confirmed COVID-19 patients who had been admitted to our medical ICU between 20th March 2020 and 15th June 2021
Results: A total of 397 patients (273 ICU survivors, 124 non-survivors) were analysed. Median age of all patients was 65 (55–76) years. Median BMI of all patients was 26.1 (24.0–29.4) and there was no difference between survivors and non-survivors (26.5 vs 25.7; p = 0.09) while 97 (35.5%) of the survivors and 67 (46.0%) of the non-survivors had a BMI lower than 25 (p = 0.03). Regarding nutrition assessment tools, median mNUTRIC score, NRS2002 and MUST were higher in non-survivors than other patients (5 vs 3, 4 vs 3 and 4 vs 2, respectively; p < 0.01). ICU, 28 days and hospital mortality rates were 31.2%, 24.2% and 33.5%, respectively. Based on Youden index, at a threshold ≥ 4; mNUTRIC score, NRS2002 and MUST had best prognostic accuracy (Table 1). Patients with poor nutritional status had worse outcomes than others (Table 2)
Table 1: Association between ICU mortality and nutritional assessment tools

	Sensitivity	Specificity	AUC	95% CI	p
BMI < 25 kg/m^2 (n = 154, 38.8%)	0.46	0.65	0.55	0.49–0.61	0.10
mNUTRIC score ≥ 4 (n = 166, 41.8%)	0.77	0.74	0.75	0.70–0.81	< 0.01
NRS2002 ≥ 4 (n = 187, 47.1%)	0.63	0.60	0.62	0.56–0.67	< 0.01
MUST ≥ 4 (n = 205, 51.6%)	0.94	0.68	0.82	0.78–0.86	< 0.01

Conclusion: mNUTRIC score, NRS 2002 and MUST had the best prognostic accuracy at a threshold ≥ 4. Among nutrition assessment tools, only mNUTRIC score independently associated with ICU mortality.

Table 2: Characteristics and outcomes of patients according to nutritional risk scores' thresholds (*median, [IQR])

	mNUTRIC < 4 (n = 231)	mNUTRIC ≥ 4 (n = 166)	p	NRS2002 < 4 (n = 210)	NRS2002 ≥ 4 (n = 187)	p	MUST < 4 (n = 192)	MUST ≥ 4 (n = 205)	p
Age*, years	59 [51–67]	75 [66–82]	< 0.0157	[51–63]	77 [71–82]	< 0.0162	[54–73]	68 [56–78]	< 0.01
Male, n(%)	157 (68.0)	97 (58.4)	0.06137	(65.2)	117 (62.6)	0.32127	(66.1)	127 (62.0)	0.22
CFS*	2 [1–4]	6 [4–7]	< 0.012	[1–4]	5 [3–7]	< 0.013	[1–4]	5 [3–7]	< 0.01
APACHE II*	12 [10–14]	20 [17–24]	< 0.0113	[10–16]	17 [14–21]	< 0.0113	[10–16]	17 [13–23]	< 0.01
SOFA score*	3 [2–4]	5 [4–8]	< 0.013	[2–4]	4 [3–6]	< 0.013	[2–4]	5 [4–7]	< 0.01
PaO_2/FiO_2*	164 [120–240]	138 [108–194]	< 0.01	148 [111–225]	154 [118–230]	0.66185	[142–259]	125 [96–178]	< 0.01
BMI*, kg/m2	26.1 [24.2–29.4]	26.0 [23.4–29.4]	0.2126	9 [24.6–29.5]	25.5 [23.1–29.3]	< 0.0127	0 [24.5–29.5]	25.9 [23.4–29.3]	< 0.01
ICU mortality, n (%)	29 (12.6)	95 (57.2)	< 0.0146	(21.9)	78 (41.7)	< 0.017	(3.6)	117 (57.1)	< 0.01
28 days mortality, n (%)	21 (9.1)	75 (45.2)	< 0.0134	(16.2)	62 (33.2)	< 0.017	(3.6)	89 (43.4)	< 0.01
Hospital mortality, n (%)	34 (14.7)	99 (59.6)	< 0.0149	(23.3)	84 (44.9)	< 0.0112	(6.3)	121 (59.0)	< 0.01
ICU LOS*, days	9 [5–15]	14 [7–23]	< 0.0110	[6–18]	12 [6–20]	0.068	[4–12]	14 [8–26]	< 0.01
Hospital LOS*, days	17 [11–29]	23 [15–35]	< 0.0117	[11–29]	22 [13–32]	< 0.0115	[10–25]	24 [15–37]	< 0.01

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001378

Association of nitrogen balance trajectories with clinical outcomes in critical ill COVID-19 patients: a retrospective single center cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:001378

Introduction: The intensity and duration of the catabolic phase in COVID-19 patients might differ between survivors and no survivors.
Objectives: The purpose of the study was to assess the association between NBAL trajectories and outcome in critical ill COVID-19 patients.
Methods: This retrospective study was conducted in intensive care at Clermont Ferrand University Hospital, France. From January 2020 to May 2021. The present study was approved by the Ethics Committee of Clermont Ferrand. Patients over 18 years old with a severe COVID-19 disease were eligible. Patients were excluded if they were referred from another ICU, if their ICU length of stay was < 72 h, and if they were treated by renal replacement therapy during the first seven days after ICU admission.
The primary objective was to compare the profile of NBAL during the first two weeks after ICU admission between the patients with ICU death and the other patients.
All data were prospectively collected and comprised details on ICU admission and during ICU stay. Vital status was collected at day 60. NBAL was estimated as proposed by Dickerson and all (R. Dickerson 2016).
Statistical analysis Comparisons between the evolution of NBAL depending on outcome was achieved using 2 level ANOVA. At day 3, 5 and 7, to represent the relationship between NBAL and protein intake, linear and non nonlinear models were achieved and the protein intakes necessary to reach a zero NBAL were determined. Sub-group analyses were achieved according to BMI, age, gender.
Results: 99 patients were included in the study. Their characteristics are reported in table 1.
On day 3, a negative similar NBAL was observed in survivors and non survivors: − 16.4 g/d [− 26.5; − 3.3] and − 17.3 g/d [− 22.2; − 3.8] (pval = 0.54). Then, the trajectories of NBAL over time differ between survivors and non survivors (pval = 0.01).
In survivors, NBAL increased over time (Patients with a net protein catabolism: 73.9% at day 3 versus 45.5% at day 14) whereas in non survivors, NBAL decreased from day 2 to day 6, and thereafter increased slowly up to day 14 (Patients with a net protein catabolism: 73.3% at day 3 vs 78.9% at day 14).
Administrating higher protein amounts were associated with higher NBALs.

Variables (N (%) or median [IQR])	All N=99	ICU Survivors N=69	Non-ICU survivors N=30	P- Value
Age (years old)	71 [60.6; 76.2]	68.9 [58.7; 75.9]	73.9 [67.6; 78]	0.02
Gender (Male)	64 (64.6)	45 (65.2)	19 (63.3)	0.86
BMI > 30 kg/m²	45 (45.5)	31 (44.9)	14 (46.7)	0.87
Comorbidities				
Cardio-vascular	15 (15.2)	6 (8.7)	9 (30)	<0.01
Respiratory	5 (5.1)	3 (4.3)	2 (6.7)	0.63
Renal	6 (6.1)	2 (2.9)	4 (13.3)	0.05
Immunosuppression	15 (15.2)	10 (14.5)	5 (16.7)	0.78
Diabetes mellitus	15 (15.2)	12 (17.4)	3 (10)	0.35
On admission (Day 1 or Day 2)				
Steroids	86 (86.9)	60 (87)	26 (86.7)	0.97
SAPS II	32 [22; 41]	32 [22; 41]	33.5 [22; 44]	0.55
SOFA score (DM=9)	4 [3; 6]	4 [3; 5]	5 [4; 6]	0.03
PaO2/FiO2	86.9 [68; 138.8]	92.7 [76.3; 140]	86 [61.1; 109.2]	0.24
IMV	7 (7.1)	6 (8.7)	1 (3.3)	0.34
During ICU stay				
IMV	31 (31.3)	11 (15.9)	20 (66.7)	<0.01
RRT	8 (8.1)	2 (2.9)	6 (20)	<0.01
Vasopressors	28 (28.3)	10 (14.5)	18 (60)	<0.01
ICU LOS	8 [5; 14]	7 [5; 10]	15 [7; 24]	<0.01
Hospital LOS	17 [11; 28]	17 [11.5; 29]	15.5 [9; 24]	0.30
ICU Death	30 (30.3)			

Conclusion: We reported a prolonged catabolic state in COVID patients which seemed more pronounced in non survivors than in survivors. Our study underlined the need for monitoring urinary nitrogen excretion to guide protein intakes in COVID-19 patients.

001405

Pilot Study: Evaluation of Bioelectric Impedance analysis in patients with non-invasive ventilation with Acute Respiratory Failure

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Intensive Care Medicine Experimental 2022, **10(2)**:001405

Introduction: The status and function of the respiratory muscles may be important in the occurrence of non-invasive mechanical ventilation (NIV) failure. Bioimpedance analysis (BIA) parameters, which measure body composition (e.g., muscle body composition), have been associated with outcomes in critically ill patients.

Objectives: To evaluate the impact of BIA parameters on NIV failure in patients with hypoxemic acute respiratory failure.
Methods: Observational study. Patients with acute respiratory failure in the intensive care units (ICU) of our hospital were included. We performed BIA during the first 24 h of NIV. Patient characteristics, severity scores, HACOR score, NIV parameters and gas exchange values together with BIA values were included in a database for analysis. We trength the association of BIA values, such as phase angle (PhA), with NIV failure. Univariate and multivariate analysis were performed using SPSS 25.0.
Results: We included 36 patients and mortality was 22.2% (8). Mean age was 59.5 ± 13.2 years, the Body Mass Index was 31.9 ± 8.2 kg·m^{-2} and 83.3% (30) were men. 20 patients (55.5%) required tracheal intubation during NIV support with a mean duration of 4.7 ± 2.9 days from the start of NIV to tracheal intubation.
We found no differences in the univariate analysis between the patients who required intubation and those who did not, except for a trend towards lower PhA in the intubated patients (5.2 ± 1.1 vs 4.41 ± 1.17; P = 0.06). This trend towards a lower incidence of NIV failure with higher PhA was also observed in the multivariate analysis (Hazard Ratio: 0.345; 95% CI: 0.113–1.0.48; P = 0.06).
Conclusion: We found that BIA parameters, such as PhA, related with body composition may be associated with NIV failure. We hypothesized this may be related with baseline metabolic-nutritional status, which may be ultimately reflected by body composition.

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001428

The Role of Vitamin D in Developing the Intensive Care Unit-Aquired Weakness

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Introduction: Critical illness refers to all medical life-threatening condition that should be treated in Intensive care unit (ICU). According to literature, about 50-80% patients treated in ICU because of critical illness develop Intensive care unit—trength weakness, ICUAW. It is defined as diffused, generalised muscle weakness that could only be explained by critical illness [1]. Unsuccessful weaning from ventilator is very often associated with this condition and it causes more complications, more need for reintubation, prolonges hospitalization, there is higher mortal outcome probability. Almost 50% of patients who develop ICUAW, after weaning from ventilator require reintubation and 50% of them die during hospitalization [2]. Considering all of this, ICUAW is very important to diagnose, prevent and treat. There are many established risk factors such as: sepsis, multiorgan failure, the systemic trength response syndrome, immobility, duration of trength and cateholamin support, duration of mechanical ventilation, renal failure and so on. Vitamin D is the most known for its skeletal effects, but 3% of human genom is under vitamin D control, especially cells in neurologic and muscleskeletal system [3]. Recommended vitamin D blood level is more than 75 mmol/L. Ventura J. et al. in their research showed that almost 50% of patient in Department of Neurology, Neuromuscular Ward are vitamin D trength [4]. Meta-analysis of 29 studies established small, but significant muscle strength improvement in patient treated with vitamin D [5]. The association of ICUAW and vitamin D is still not evaluated.
Objectives: Evaluate the importance of vitamin D in developing ICUAW.
Methods: The research was done in COVID ICU Clinic of Anesthesiology, Reanimatology and Intensive care during the February 2022. All trengt that were mechanicaly ventilated more than 48 h, and weaned from ventilator successfuly were included. All patient with trength muscle or neurologic disorder were excluded. The patients were examined after abolition of analgosedation and after weaning from ventilator. The ICUAW diagnosis was made clinically by Medical Research Council test (MRC test). Level of vitamin D was detect at the ICU trength.
Results: During the February 2022 in COVID ICU, 77 patients were treated. In this group 36 patients were successfully weaned from ventilator in a period longer than 24 h and 12 patients developed ICUAW, one patient trengt of impared consciousness was not able to be examined. All patient tested were vitamin D trength. The median value of vitamin D in the group that had sufficient muscle strength was 25,2 (12–54) compared to group that developed ICUAW 17 (7,5–73,3) with statistical significance p = 0,567.
Conclusion: ICUAW is very often complication of patient treated in ICU. Considering the fact that it prolonges mechanical ventilation, hospitalization and increases trength cost it is very important to prevent and treat this condition. Regarding to our research, althought all patients tested were vitamin D trength, there was no statistical significance in the vitamin D blood level of patients who developed ICUAW compared to those with sufficient muscle trength. Further investigation will be needed to define the exact etiopathogenesis in order to prevent ICUAW and treat propertly.

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001358

Are immediate or delayed hypoxic changes on CT head a prognosticator after out-of-hospital cardiac arrest?

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Intensive Care Medicine Experimental 2022, **10(2)**:001358

Introduction: Out-of-hospital cardiac arrest carries with it significant likelihood of death. In England, return of spontaneous circulation (ROSC) is achieved in 25% of cases, and 7–8% of people survive to discharge [1]. CT scan of the head performed after ROSC can detect the cause of cardiac arrest (such as haemorrhage) or sequelae of arrest (such as hypoxic brain injury, HBI). This study aims to quantify the utility of immediate or delayed HBI as a prognosticator in this patient group.

Objectives: To identify the proportion of patients presenting with out-of-hospital cardiac arrest who demonstrate hypoxic changes on CT head after ROSC.
To stratify patients into two groups: immediate hypoxic changes (demonstrated within 24 h) and delayed hypoxic changes (demonstrated after 24 h).
To compare mortality rates between these groups and with the overall patient population.
Methods: An observational retrospective cohort study was designed in a single centre using casenote data covering a five-year period from April 2015 to March 2020. This period was chosen to exclude any changes resulting from the COVID-19 pandemic. A database query was created to identify patients presenting to the emergency department (ED) with cardiac arrest. Successful ROSC was defined as survival to disposition from ED. The hospital Picture Archiving and Communication System (PACS) was searched for record of at least one CT head performed after ROSC. The formal reports were used to identify acute pathology.
Results: 467 patients presented to ED as out-of-hospital cardiac arrest with males outnumbering females 1.6 to 1. Median age was 70 and range was 0–96 years old. 209 patients survived to disposition from ED. 19 patients were subsequently excluded as not 'true' cardiac arrest. 190/448 patients (42%) were therefore confirmed to be true cardiac arrest with successful ROSC. 83 of these (44%) survived to discharge. Overall, 19% of patients presenting with out-of-hospital cardiac arrest survived to discharge.
Of 190 patients, 118 had at least one CT head performed after ROSC. 110 patients were scanned within 24 h of admission.
12 patients demonstrated immediate HBI. 4 of these survived to discharge. All survivors were reported as having 'mild' or 'subtle' signs, compared with 'severe' or 'gross' in the deceased. 1 survivor had a second scan which showed no progression of HBI.
8 patients with a negative initial CT head demonstrated HBI on a second scan performed later. 1 of these survived. Again, the survivor was reported as having 'mild' changes.
An additional 3 patients without early scan demonstrated severe signs of HBI on a delayed scan and did not survive.
Conclusion: Signs of severe HBI carry a dismal prognosis, regardless of whether identified within 24 h or later in admission.
Signs of mild HBI may be reassuring. However, this should be interpreted in the context of many patients with no CT head pathology who did not survive.

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001365

Targeted Temperature Management; efficacy, duration, and the optimal method of implementation on OHCA patients

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Introduction: Out-of-hospital cardiac arrest (OHCA) is associated with a high mortality rate and poor neurological function. Targeted temperature management (TTM) is used with comatose survivors to minimise the secondary brain injury and improve survival rate and neurological function. However, the evidence base behind this intervention is generally weak. Furthermore, the optimal method and interval period with which to implement this intervention has not been well defined.
Objectives: The principal aim is to identify the benefits of implementing TTM on adult OHCA patients in relation to the rate of mortality and neurological outcomes. Additionally, we sought to determine the ideal cooling interval and the optimal method to perform the procedure.
Methods: A systematic search was conducted in the following databases: PubMed, Cochrane Library, and the U.S National Library of Medicine. Only prospective, randomised, and quasi-randomised controlled trials were included.
Results: ***TTM efficacy*** The search yielded 319 citations of which 8 met the inclusion criteria. Two RCTs found superior survival and neurologic outcomes from mild hypothermia compared to normothermia for patients with shockable rhythms. The largest two studies compared TTM with normothermia, however both failed to detect any statistical difference measuring the same outcomes. Notably, they used different targeted temperatures (33° vs 36 °C in the first, 33° vs 37.5 °C with early prevention of fever in the second). For patients with non-shockable rhythms, one study found a significant improvement in neurologic outcome in the TTM arm, albeit with a comparable mortality rate.
TTM interval; Only one study compared cooling for 24 h or 48 h and revealed similar mortality and neurological outcomes.
TTM ideal method; One small RCT compared use of the Arctic Sun device with a standard cooling blanket but identified no difference in either mortality rate or neurological outcome. The paper compared use of an intravascular catheter to external basic methods and reported a similar mortality rate at 90 days, but superior neurologic outcomes in favour of the intravascular catheter.
Conclusion: Despite promise in smaller trials, there is no overall advantage of using TTM on mortality, although TTM could confer an improvement of neurological outcomes in specific subgroups. At this stage, the optimum TTM administration length is unknown, although one study showed no difference between 24–48 h. The intravascular catheter and implementation of surface cooling by the Arctic Sun device appeared to be more efficient compared to conventional techniques. However, only the intravascular catheter showed a high probability of neurological recovery.

Feeding, Rehabilitation, Endocrinology & Metabolism 3

000455 ICU

-acquired hypoglycemia is preceded by a divergence of insulin-requirements and lactate levels depending on the cause

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Introduction: Hypoglycemia in ICU patients can occur as a result of various causes, but two main factors are inadequate glycemic control and liver failure. In our center glucoses are measured in arterial blood gas samples together with lactate. Both glucose and lactate serve as acute fuels in physiology. During insulin-associated hypoglycemia (IAHG) lactate may substitute for glucose. In liver failure, lactates increases because of impaired gluconeogenesis [1]. Thus monitoring of glucose and lactate may help identify discriminate iatrogenic hypoglycemia from impending liver failure.
Objectives: Assess the changes in glucose, lactate and insulin administration rate that precede ICU-acquired hypoglycemia in a large cohort of ICU patients.

Methods: Glycemic control was performed with the glucose regulation for ICU patients (GRIP) computer program, which only prescribes continuous insulin [2]. Adult patients admitted to our ICU between 2008 and 2021 were analyzed for the occurrence of hypoglycemia < 3.5 mmol/L under GRIP-control. Low glucose levels were assessed for potential pre-analytical errors. In case of multiple hypoglycemias the earliest lowest level was taken as Reference. The glucose/lactate ratio (GLR) was calculated to detect impaired gluconeogenesis. Hypoglycemia was classified as insulin-associated when insulin had been administered by GRIP in the 6 h preceding the hypoglycemia (IAHG) or as non-IAHG.
Results: The overall incidence of hypoglycemia was 0.3% on a measurement basis and 5% on a patient basis. After exclusion of 30 presumed preanalytical errrors, 1024 patients had hypoglycemia with a median (IQR) glucose of 2.9 (2.3–3.2) mmol/L, with 68% IAHG with a median

(IQR) insulin dose of 2.6 (1.4–4.1) IU/h over the preceding 6 h. During IAHG, nadir lactate levels were both absolutely and relatively lower than during other phases: 0.9 (0.7–1.3) mmol/L (P < 0.001). In the non-IAHG group, lactate levels were strongly increased during hypoglycemia: 6.1 (1.5–10.5) mmol/L (P < 0.001). Hospital mortality in IAHG and non-IAHG groups was 40% vs 65% respectively (P < 0.001). In non-survivors, survival post-hypoglycemia was 3 (0–11) and 0 (0–1) days respectively (P < 0.001). A GLR of lower than 4.5 in the 24 h to 12 h preceding the actual hypoglycemia, was strongly predictive of liver failure (P < 0.001).
Conclusion: Although hypoglycemia had a low incidence in our population, it was associated with considerable hospital mortality, particularly in patients with non-IAHG. Observing a glucose-lactate ratio < 4.5 in at risk patients could assist in the timely initiation of continous concentrated glucose infusion to avoid frank hypoglycemia.

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Acknowledgements: None.

000588

Association of obesity and mortality in adult patients with acute respiratory distress syndrome secondary to severe COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**:000588

Introduction: Obesity is a global epidemic that predisposes to increased morbidity and mortality. Mexico is among the main countries in the world with the highest incidence of obesity, by 2016 33% of the population was obese. This condition has been associated with the release of proinflammatory factors that predispose to endothelial dysfunction and major cardiovascular events. In the context of acute respiratory distress syndrome (ARDS), obese patients have a higher risk of morbidity due to decreased residual capacity, lower compliance, increased airway resistance, among others; however, it has not been possible to establish whether this condition is associated with higher mortality. Studies have been carried out in patients with severe COVID-19 in obese patients, observing higher mortality compared to non-obese patients.
Objectives: To determine the association of obesity and mortality in adult patients with ARDS secondary to severe COVID-19.
Methods: A retrospective, descriptive, observational cohort study was conducted in patients with ARDS secondary to severe COVID-19 who required invasive mechanical ventilation in an Intensive Care Unit in Mexico, from March to December 2020. A total of 210 patient's records were analyzed, patients with BMI > 30 were classified as obese, regarding sociodemographic characteristics, comorbidities, laboratory, severity scales and ventilation parameters on days 1, 3 and 7, Kolmogorov–Smirnov normality test was applied to each of the variables, those with normal distribution were summarized with mean and standard deviation, those of free distribution in median and interquartile range, qualitative variables were reported in percentages. The comparison of qualitative variables was carried out using chi square test, quantitative variables were analized with Student's T test and for the non-parametric Mann–Whitney U. Binary logistic regression was performed to estimate the odds ratio of independent variables associated with mortality.
Results: The primary outcome was mortality in the ICU, of the 210 patients included in the study, 22.4% (n = 47) died, 71.2% were male, mean age was 60 ± 12.70 (26–89), the most frequent chronic comorbidities were arterial hypertension 51% (n = 107) and diabetes mellitus 26.7% (n = 56). The days of mechanical ventilation had a median of 11 (8–18), median days of ICU stay of 16 (11–24), median days of hospital stay of 21 (16–29). Mortality in patients with obesity (BMI > 30) was 12.32% (n = 9) compared to 27.7% (n = 38) in patients without obesity (BMI < 30), both groups did not present significant differences in the prognostic scales and acute phase reactants at admission: APACHE II of 12 (8–20.5) vs 12 (7.5–18) p = 0.189, SAPS II of 30 (22–48) vs 27 (23–36.5) p = 0.234, SOFA of 6 (3–9) vs 7 (3–9) p = 0.784, C-reactive protein of 13.59 (6.94–24.5) vs 17.72 (8.21–26.80) p = 0.163 and IL-6 of 170 (33.50–335.60) vs 175 (79.30–309) p = 0. 443, in non-obese versus obese patients respectively, during mechanical ventilation lung protection goals were maintained in terms of tidal volume, driving pressure, plateau pressure, with a significant difference in the PaO_2/FiO_2 ratio on day 1 = 137.5 (92.57–216) vs 202 (112.5–269.7) p = 0.006 and on day 7 with 196.5 (142–256.7) vs 231 (173–298) p = 0.005, in obese patients 61.6% (n = 45) required prone position vs 35.7% (n = 49) of non-obese patients with a statistically significant X2 of 12.89, only 24.6% (n = 18) of the obese required prolonged ventilation compared to 37.9% (n = 52) of the non-obese with X2 = 3.79. Obesity was not associated with higher mortality odds ratio (OR) 0.36 (0.16-0.80) after adjustment for age, gender, severity scales, prone position and prolonged ventilation the adjusted odds ratio was OR = 0.56 (0.36-0.84).
Conclusion: In our population, obese patients with ARDS had greater severity however, they did not have higher mortality. There are meta-analyses that have described lower mortality, a phenomenon known as the paradox of the obese, where alterations in innate immunity, greater reserve to cope with catabolic stress, and more aggressive treatment in this population have been proposed as the cause of this protective effect in ARDS. It is important to highlight that the population with BMI less than 30 had a higher prevalence of prolonged ventilation without being able to determine the causes in this study, so prospective studies are required to determine the factors associated with mortality in obese patients.

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000595

Withholding enteral nutrition associated lower hospital mortality in shock patients with candidemia

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Introduction: Lower calorie intake in acute phase of critically ill was recommended by ESPEN guideline. The result of NUTRIREA-2 trial showed early enteral nutrition did not reduce 28 day mortality in critically ill with shock. Updated guidelines also recommend withholding enteral nutrition in patients with uncontrolled shock. Total parenteral nutrition is a well-known risk factor of candidemia. Whether withholding enteral nutrition worsens clinical outcomes or not of shock patients with candidemia is unknown.
Methods: We retrospectively collected patients' data in a tertiary medical center from Jan 2015 to Dec 2019. The study enrolled patients with shock in the first 7 days after ICU admission, candidemia diagnosed during ICU stay and both medical/surgical ICU patients. Patients with ICU stay less than 48 h were excluded.
Results: There were 106 patients enrolled in the study. The hospital mortality rate was 23% (24/106). The average age was 68 ± 15 years old and APACHE II score was 29 ± 7. Male (p = 0.031) and nothing per os prior to candidemi a(p = 0.007) were associated with lower hospital mortality in univariate analysis. In the cox regression model, male (HR: 0.31 95% CI: 0.130–0.723), nothing per os prior to candidemia (HR: 0.16 95% CI: 0.058–0.414) and lower calorie intake (HR: 0.99 95% CI: 0.999–1.000) were associated with lower hospital mortality.
Conclusion: Our present result echoed the enteral feeding might not be an optimal feeding route in critically ill patients with shock. Nothing per os prior to candidemia and lower calorie intake might be associated with lower hospital mortality in candidemic patients with shock. It still needs randomized controlled trial to confirm the finding.

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000715

Evolution of resting energy expenditure in long stay critical ill patients and during their recovery on the ward

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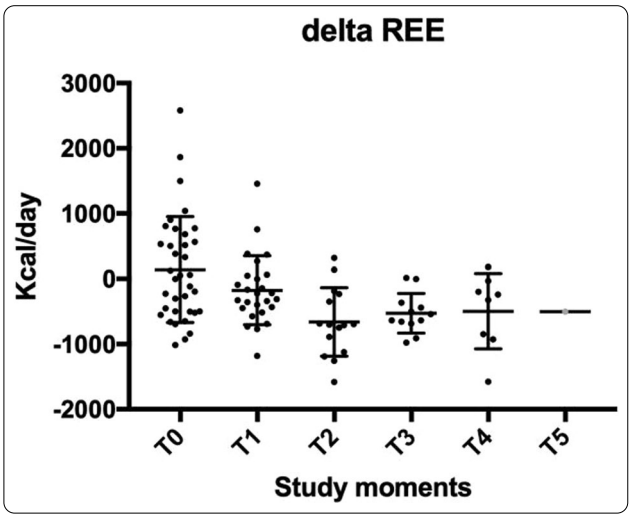
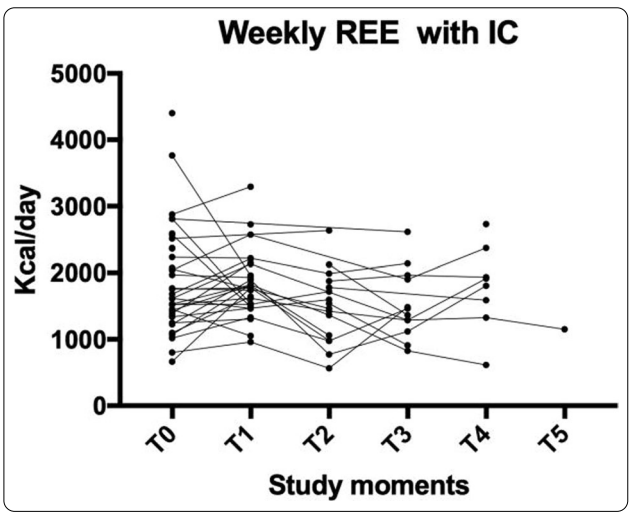
Introduction: Metabolic state changes over time as it is influenced by multiple parameters such as disease state and inflammation. Resting Energy Expenditure (REE) predicted by equations have repeatedly been shown to be highly inaccurate. As nutrition therapy guided by indirect calorimetry (IC) is associated with better survival and lower infections, knowledge of metabolism is of cardinal importance. However, IC is not always present in the intensive care unit (ICU) so measured REE can be used to tailor prescription of artificial nutrition.
Objectives: The aim of this study was to follow REE measured by IC in long stay ICU patients and during their recovery in the ward.
Methods: 50 long stay patients, defined with a minimal length of stay of 7 days were prospectively followed up until hospital discharge or 28 days on the ward. REE was assessed on inclusion (T0) and followed every week defined as T1 until T5. The difference between measured REE with indirect calorimetry and calculated energy expenditure on body weight according to the best-suited ESPEN guideline (ICU, geriatrics, internal medicine) was objectified and expressed as Δ REE. Differences between study moments were explored with one-way Anova.
Results: 3 patient dropped out and were excluded from further analysis. REE could be measured in 103 of 156 study moments (66%). Mean measured REE was on T0 1879 ± 804 kcal/day; T11826 ± 500 kcal/day; T2 1492 ± 539 kcal/day; T3 1530 ± 528 kcal/day; T4 1786 ± 643 kcal/day and on T5 (n = 1) 1151 kcal/day which were not statistically significant different (p = 0,263). However a clinically important intraindividual variability was observed (figure 1). Mean Δ REE, which is plotted in figure 2, was on T0 141 ± 811 kcal/d; T1 − 175 ± 528 kcal/d; T2 − 659 ± 525 kcal/day; T3 − 528 ± 304 kcal/day; T4 − 496 ± 577 kcal/day and on T5 (n = 1) − 501 kcal/day which were statistically significant different (p = 0,001).





Conclusion: Indirect calorimetry is feasible in 66% of cases. Mean REE does not seem to change significantly over time in a general ICU population and on the ward but on an individual base there is a large variability. Individual REE seems to significantly change over time.

Equations seem to be more accurate after 7 days of admission than during the recovery phase where measured REE is lower compared to calculated REE. IC is crucial to correctly objectify REE.

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000752

Chronic non-thyroidal illness is associated with higher mortality in chronic critically ill patients with Covid-19

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Intensive Care Medicine Experimental 2022, **10(2)**:000752

Introduction: Recently the knowledge is growing about the pathophysiology of chronic critical illness. Persistent inflammation, immunosuppression catabolism syndrome, the critical illness endocrinopathy has also been described. The chronic phase of the non-thyroidal illness syndrome is not well described, underdiagnosed, and neglected, while it can be the cornerstone of the metabolic changes in CCI.
Objectives: Our aim was to evaluate the impact of chronic non-thyroidal illness on ICU mortality in CCI patients.
Methods: We collected and retrospectively analysed the medical history and clinical data of our chronic critically ill COVID-19 patients. CCI was defined as at least 11 days of ICU treatment and 7 days of invasive mechanical ventilation. Extensive laboratory test, including thyroid hormones were made on admission, and on days 7th and 14th of ICU care. We used logistic regression analysis to predict ICU mortality. Multivariate models were adjusted to age, sex, and history of hypertension.
Results: We included 89 CCI patients, the median length of ICU stay was 17 days (IQR: 13–24 days). The median age was 62 years (IQR: 54–68), 55 patients died in the ICU (61.8%). 6 patients (6.7%) had history of hypo- and one patient (1.1%) hyperthyroidism, four patients (4.5%) were on chronic thyroid medication on admission. Conventional prognostic markers (age, BMI, APACHE II score) did not differ significantly between survivors and non-survivors.
Lower TSH (OR = 0.58, 95% CI: 0.35–0.99; p = 0.046) and fT3 values (OR = 0.26, 95% CI: 0.07–1.00; p = 0.049) on day 7th showed significant, independent association with ICU death in chronic critically ill patients.
Conclusion: Our results emphasize the importance of chronic critical endocrinopathy in the outcome of ICU patients. Further studies are needed to evaluate the need of substitution in this population.

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000753

Metabolic phenotypes and Vitamin D response in the Critically Ill: a metabolomics subtyping cohort study

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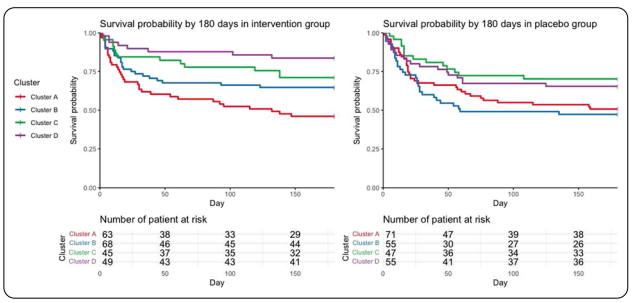
Intensive Care Medicine Experimental 2022, **10(2)**:000753

Introduction: Trials in the critically ill fail to demonstrate benefits of high dose vitamin D3 supplementation in part due to high subject heterogeneity and differential response to intervention. In critically ill subgroups, benefit from high dose vitamin D3 supplementation may exist.
Objectives: We aimed to identify critical illness metabolic phenotypes by applying machine learning clustering methods to the Correction of Vitamin D Deficiency in Critically Ill Patients (VITdAL-ICU) trial metabolomics data. We hypothesized that in a distinct metabolic phenotype, vitamin D3 decreases 180-day mortality.
Methods: The relative abundance of 659 metabolites in 1215 plasma samples from 453 VITdAL-ICU trial subjects were analyzed. We applied an unsupervised consensus clustering method with the partitioning around medoids algorithm to the metabolomics data at randomization. We defined the optimal number of clusters by a combination of the cumulative distribution function, average silhouette scores, a consensus matrix heatmap, and biological plausibility. Cluster-specific associations between vitamin D intervention and 180-day mortality was evaluated by logistic regression analysis with adjustment for age, sex, Simplified Acute Physiology Score (SAPS) II, admission diagnosis, and baseline 25(OH)D value. Further, we performed adjusted mixed effects linear regression to analyze the cluster-specific metabolic response to vitamin D intervention.
Results: The consensus clustering approach identified 4 distinct metabolic phenotypes from 453 samples at randomization: 134 subjects (30%) in cluster A, 123 subjects (27%) in cluster B, 92 subjects (20%) in cluster C and 104 subjects (23%) in cluster D. Clinical characteristics differed between the four clusters. Cluster D subjects had a higher proportion of women, more medical and neurological patients, lower creatinine and procalcitonin as well as a higher increase in 25(OH)D with intervention. In cluster D, vitamin D intervention had a significantly lower risk of 180-day mortality after adjustment (16.3% vs. 34.5%; adjusting odds ratio, 0.28; 95%CI, 0.09–0.89) (Figure 1). Vitamin D intervention was not significantly associated with lower 180-day mortality in the other 3 clusters. Mixed-effects modeling of 1215 total plasma samples from day 0, 3, and 7 showed that 120 metabolites were significantly (adjusted for multiplicity) associated with increased 25(OH)D at day 3 in cluster D, highlighted by increases in long-chain acylcarnitines, sphingomyelins, diacylglycerols, and branched chain amino acids metabolites. This metabolic signature was not observed in the other 3 clusters.



Conclusion: In the VITdAL-ICU trial, clustering analysis of metabolomics data at randomization identified a biological distinct metabolic phenotype that demonstrated a distinct metabolic response and improved 180-day mortality following high dose vitamin D3 intervention. Our findings should encourage further study to validate phenotype-targeted strategies for critical illness.

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Acknowledgements: This work was supported by the National Institutes of Health [R01 GM115774].

000766

Racial Disparities in the Delivery of Enteral Nutrition Delivery in Critically Ill Mechanically Ventilated Patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000766

Introduction: A plethora of data exists regarding rates of malnutrition by race and ethnicity both in the hospital and outpatient settings. Nevertheless, there is minimal to no data on disparities within nutrition delivery, where we have shown that timing has been proven to influence morbidity and mortality in medical and surgical ICU patients. Previous studies evaluating early vs. late (3 days) enteral nutrition (EN) have shown that early enteral nutrition significantly improves outcomes and total hospital costs.
Objectives: This study was designed to evaluate the impact of race and ethnicity on providers' decisions to initiate EN in the intensive care unit (ICU).
Methods: This is a retrospective cohort analysis of patients requiring EN after the initiation of mechanical ventilation (MV) using the eICU Collaborative Research Database (eICU) from 2014–2015. EN episodes were identified by intake/output entries. Patients who had EN on day one of admission or MV less than 4 days were excluded. Race and ethnicity was determined by self-identification in the eICU database; unknown/other race and ethnicity was left as a separate category. For all patients with EN and MV, the timestamp of the first episode of MV was compared to the timestamp for the first episode of EN. Illness severity was measured by the highest SOFA score in the first 24 h after admission. A multivariate linear model to examine the impact of race and ethnicity was developed, controlling for age, gender, and severity of illness in medical and surgical ICU patients. A similar second linear model was regressed, adding a race and ethnicity term, with ANOVA for linear models used to compare the significance. For all analyses, $p < 0.05$ was considered significant.
Results: Of 1704 patients with documented enteral nutrition, 897 patients were identified with enteral nutrition started after MV initiation (Asian = 7, Black = 52, Native American = 26, White = 741, Other = 71) across 14 hospitals. The average time between MV to enteral nutrition was 2.2 ± 2.2 days. When evaluated by race and ethnicity subgroups, White patients were noted to have an earlier time to initiation (2.1 ± 2.0 days) as compared to Black patients (3.2 ± 4.5 days). The multivariate regression of time to enteral nutrition was significant for SOFA score ($p < 0.001$) and was significantly improved by inclusion of race and ethnicity ($p = 0.02$).
Conclusion: Disparities exist with regard to starting EN in the ICU. Black patients have a significantly longer delay between intubation to the start of enteral nutrition when compared to White patients. As the timing of EN has previously been linked to outcomes and hospital costs, future studies understanding the reason behind these disparities in nutrition delivery are warranted.

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Acknowledgements: Paul Wischmeyer and Krista Haines are funded under grants from the NIH, DOD, Baxter, Abbott, and Fresenius Kabi. Paul Wischmeyer is a consultant for Baxter, Abbott, and Fresenius Kabi.

000768

Timing of Acute Initiation of Parenteral Nutrition is Not Altered by Race or Ethnicity in eICU-CRD

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Intensive Care Medicine Experimental 2022, **10(2)**:000768

Introduction: Nutrition delivery and malnutrition directly impact outcomes in critically ill patients. Additionally, the timing of parenteral nutrition (PN) remains controversial. Despite numerous articles on the impact of race and ethnicity on outcomes in critically ill patients, minimal literature exists regarding the initiation of parenteral nutrition delivery in critically ill patients.
Objectives: This analysis was done to determine the impact of race and ethnicity on the timing of parenteral nutrition (PN) initiation in patients in medical and surgical ICUs.
Methods: This is a retrospective cohort analysis of patients who required PN (total parenteral nutrition or parenteral nutrition) using the eICU Collaborative Research Database from 2014–2015. Intake/output entries identified PN episodes. Patients on PN ICU days 1–2 were excluded from this analysis. Race and ethnicity were determined by self-identification in the eICU database; unknown/other race and ethnicity were combined as a separate category. The time of the first episode of PN was compared to admission. The highest SOFA score measured illness severity in the first 24 h after admission. A multivariate linear model was regressed to examine the impact of race and ethnicity was developed, controlling for age, gender, and severity of illness (SOFA) in medical and surgical ICU patients. A second linear model, including a race and ethnicity term, was regressed, and ANOVA for linear models was used to compare the significance of the inclusion. For all analyses, $p < 0.05$ was considered significant.
Results: Of 1544 patients with documented parenteral nutrition status, 1150 had PN started on or after ICU day 2 (Asian = 9, Black = 128, Hispanic = 62, Native American = 4, White = 865, Other/Unknown = 82) across 59 hospitals. The average time to TPN initiation was 4.3 ± 4.0 days. When compared by race and ethnicity subgroups, White patients (4.4 ± 4.2 days) were not significantly different from Black patients (4.4 ± 3.8 days). The multivariate regression of time to parenteral nutrition was significant for SOFA score ($p < 0.001$) but was not significantly improved by the inclusion of race and ethnicity ($p = 0.21$).
Conclusion: Despite the fact that nutrition has been shown to improve outcomes and that race and ethnicity impact outcomes in critically ill patients, this is one of the first studies to evaluate race/ethnicity's impact on the timing of PN initiation in critically ill patients. These data suggest that the timing of PN initiation is not influenced by race and ethnicity in intensive care units and instead depends on patient factors in critically ill mechanically ventilated patients.

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Acknowledgements: Paul Wischmeyer and Krista Haines are funded under grants from the NIH, DOD, Baxter, Abbott, and Fresenius Kabi. Paul Wischmeyer is a consultant for Baxter, Abbott, and Fresenius Kabi.

000777

Initiation of Parenteral Nutrition Delayed for Black Patients vs White Patients in MIMIC-IV

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Intensive Care Medicine Experimental 2022, **10(2)**:000777

Introduction: In critical illness, nutrition delivery and malnutrition are known to portend worse outcomes. Additionally, race and ethnicity overall impact the care and trajectories of critically ill patients. Regardless, despite countless articles on the impact of race and ethnicity on outcomes, minimal literature exists regarding the implementation and timing of nutrition delivery in critically ill patients.
Objectives: This analysis was done to determine the impact of race and ethnicity on the intensivist's decision to initiate parenteral nutrition (PN) in patients in medical and surgical ICUs.
Methods: This is a retrospective cohort analysis of patients who required PN (total parenteral nutrition or parenteral nutrition) using the Medical Information Mart for Intensive Care IV (MIMIC-IV) from 2011–2019. PN episodes were identified by intake/output entries. Patients on PN ICU days 1–2 were excluded from this analysis. Race and ethnicity was determined by self-identification in the MIMIC-IV database; unknown/other race and ethnicity was left as a separate category. The time of the first episode of PN was compared to admission. Mann–Whitney U tests were used for comparison across race and ethnicity subgroups. A multivariate linear regression model to examine the impact of race and ethnicity was developed, controlling for age, sex, and severity of illness (SOFA) in medical and surgical ICU patients. ANOVA for linear models was used to compare the significance of including a race and ethnicity term. $p < 0.05$ was considered significant.
Results: Of 1496 patients with documented parenteral nutrition status, 1275 had PN started on or after ICU day 2 (Asian = 28, Black = 109, Hispanic = 41, Native American = 3, White = 910, Other/Unknown = 127) across 1 hospitals and 7 intensive care units. The average time to TPN initiation was 13.8 ± 15.2 days. When compared by race and ethnicity subgroups, White patients (13.8 ± 16.2 days) were significantly sooner as compared to Black patients (14.6 ± 12.0 days) ($p = 0.02$). The multivariate regression of time to parenteral nutrition across all patients was not significantly improved by including race and ethnicity ($p = 0.63$).
Conclusion: This study is the first of our knowledge to evaluate the impact of race and ethnicity on the provider's decision to initiate PN in critically ill patients. Nutrition improves outcomes, and race and ethnicity have been demonstrated to impact mortality, morbidity, and disposition in critically ill patients. These data suggest that provider decision-making to start PN is potentially influenced by race and ethnicity. Further studies must be conducted to characterize the impact.

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Acknowledgements: Paul Wischmeyer and Krista Haines are funded under grants from the NIH, DOD, Baxter, Abbott, and Fresenius Kabi. Paul Wischmeyer is a consultant for Baxter, Abbott, and Fresenius Kabi.

000871

Low expiratory muscle thickness indicates worst prognostic in the intensive care unit: a prospective observational cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000871

Introduction: During intensive care unit (ICU) stay, muscle wasting is associated with adverse outcome in critically ills (Trethewey et al., 2019). Expiratory muscles are needed in case of high respiratory load, low inspiratory muscle capacity and are involved in coughing, making them key features of ICU management (Shi et al., 2019). It has recently been reported that point of care ultrasound measurement of the expiratory muscle thickness had a good reproducibility and that expiratory muscle were affected by muscle wasting during ICU stay (Shi et al., 2021). Expiratory muscle thickness and function are associated in healthy subjects (Misuri et al., 1997). However, there is no study investigating the prognosis value of expiratory muscle thickness in critically ills. Because in addition to general muscle mass, expiratory muscles are directly related to the respiratory function, we hypothesized that expiratory muscle thickness would have a strong association with outcome in critically ills.
Objectives: To determine whether expiratory muscle thickness was associated with outcome in the ICU.
Methods: Prospective, observational, single-centre study. University-affiliated medico-surgical intensive care unit. Inclusion criteria was age > 18. The exclusion criteria were Amputation, neuromuscular disease, paraplegia, pregnancy, breastfeeding, cardiac failure (LVEF < 50%), advanced chronic obstructive pulmonary disease, body mass index higher than 40. Ultrasound expiratory muscle thickness was performed within the 6 h following ICU admission. The primary endpoint was 28-day mortality.
Results: 310 patients included in the present analysis, 47 (15%) of the patients were dead after 28 days. Median age was 67 [60;77], 65% of patients were men and 59% of the patients were admitted after planned surgery. Twenty-eight-day survival was associated with younger age (66 [58;75 vs 74 [68;80] years, $p < 0.01$) with the type of admission and with lower severity score (SAPS II and SOFA). Higher total expiratory muscle thickness at admission was associated with 28-day survival (16.5 [13.4;20.7] vs 10.8 [10;14.6]). By multivariate analysis, high total expiratory muscle thickness was associated with 28-day survival, independently of the initial severity assessed by the SAPS 2 score (adjusted odd ratio: 0.08 [0.01;0.78]). Total expiratory muscle thickness had an area under the curve to discriminate 28-day mortality of 0.78 [0.71; 0.86]. The optimal cut-off was of 1.15 cm. For this threshold, sensitivity was of 0.60 [0.44;0.73] and specificity was of 0.88 [0.84;0.92].
Conclusion: The ultrasonographic measurement of expiratory muscle thickness was associated with 28-day mortality, independent of the SAPS 2 score. This association could result from the combined evaluation of lean mass and expiratory function.

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Feeding, Rehabilitation, Endocrinology & Metabolism 4

000934

Coverage of nutritional needs in critically ill patients—correlation with the outcome

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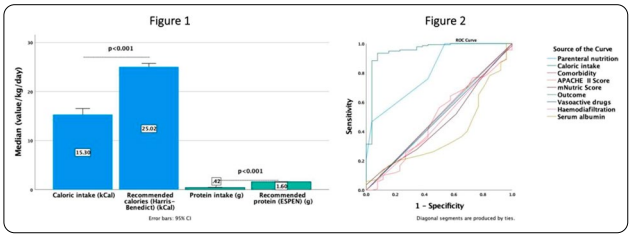
Intensive Care Medicine Experimental 2022, **10(2)**:000934

Introduction: Medical nutrition therapy for intensive care unit (ICU) patients remains a challenge. Current ESPEN guidelines implicate that optimization of protein balance in ICU patients as well as energy balance will improve outcomes. Nonetheless, the determination of the effect of nutrition alone on any possible outcome is complicated by the fact that the severity of illness and the number of comorbidities and complications encountered among adult ICU patients are increasing.
Objectives: The aim of this retrospective study was to assess the nutritional status of adult patients, admitted to the ICU of the University Hospital of Heraklion, Crete between 1/1/2020–31/12/2020, and to assess whether their nutritional needs were met during their hospitalization. Also, to compare their nutritional balance, determined by the difference of provided minus recommended by the ESPEN/ASPEN guidelines energy and protein, with the outcome.
Methods: The data were retrieved from the electronic patient information system. The nutritional coverage (proteins, carbohydrates, and lipids) was recorded, the caloric (Harris-Benedict) and protein (ESPEN recommendations) needs were calculated, and the correlation of these data with the outcome was examined. The balance of calorie and protein intake was also calculated and compared with outcome indices.
Results: The study included 235 patients with a median age of 70 years (IQR 56–78), duration of hospitalization 13 days (8–22), APACHE II 21.6 ± 6.9, mechanical ventilation 80.4%, mNutric Score 3 (2–4), and crude mortality 21.7%. Most patients started enteral feeding on the 3rd–4th day with an average feeding duration of 9 days and a daily feeding interruption duration of 1 h. The daily energy intake, including glucose, protein, carbohydrate, and lipid substrates, showed a significant exponential increase between days 1, 3, and 7 ($p < 0.001$). Compared to the predicted energy expenditure and ESPEN recommended daily protein intake the patient's energy and protein intakes were in a negative balance ($p < 0.001$) (Figure 1). Survivors exhibited a greater negative energy/protein balance compared to non-survivors throughout the study ($p < 0.001$). The use of parenteral alone or in combination with enteral feeding was significantly more common in patients who died compared to those who survived ($p < 0.05$). Only adequate caloric intake (AUROC 0.95 (0.92-1.0), $p < 0.001$) and the type of nutritional support (proportionally increased use of parenteral nutrition (AUROC 0.81 (0.72–)) 0.9), $p < 0.001$), could predict a positive balance energy intake on day 7 (Figure 2).
Conclusion: Although the daily caloric intake, calculated from glucose, protein, carbohydrate, and lipid substrates, showed a significant exponential increase, the energy and protein balance remained negative during the first 7 days of ICU stay. Survivors, who had received less parenteral nutrition, exhibited a greater negative energy/protein balance compared to non-survivors.



000966

The Reference interval for the anion gap, as derived from ICU patients with metabolic acidosis, depends on pH

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Intensive Care Medicine Experimental 2022, **10(2)**:000966

Introduction: Calculation of the anion gap (AG) is important in the differential diagnosis of metabolic acidosis. Sodium and chloride measurements performed in a blood gas analyzer may provide a most accurate basis for determining the anion gap. A frequently used Reference interval (RI) is 12 ± 4 mmol/L, although with modern ion-selective measurements lower Reference intervals are advised, such as 6 ± 3 mmol/L [1,2].
Objectives: Since a RI derived from healthy persons can only be determined at or near and arterial pH of 7.40, we used a large ICU patient-cohort [3] with metabolic acidosis to determine with state-of-the-art measurements the relation between the severity of acidosis, the anion gap and lactate.
Methods: Lithium heparin anticoagulated arterial blood gas samples from patients > 18 years and admitted to our ICU were analyzed. The AG was calculated as AG = [Na]–[Cl]–[bic], and these parameters were measured by the ABL Radiometer 800 Flex or 90 Flex analyzers with ion-selective electrodes at the point of care. No albumin correction was performed. Samples with a base excess < 0 mmol/L were selected to reflect (pure) metabolic acidosis. For each pH decimal we determined the AG and lactate as the median (interquartile range; IQR). Non-arterial blood gasses and extreme values on admission or believed to result from exogenous ions were excluded. The range between P2.5% and P97.5% was considered the RI.
Results: We analyzed 190,000 blood gas analyses from 7300 patients. 1.5% of the blood gas analyses were exluded. At a pH of 7.40 median (IQR) AG was 6 (5–9) and lactate was 1.5 (1.0–2.6) mmol/L. At a pH of 7.0 the AG and lactate had linearly increased to 15 (11–19) and 9.2 (5.7–12.5) mmol/L respectively. At a pH of 6.7 the AG and lactate had further increased to 23 (20–25) and 17.0 (14.6–19.0) mmol/L respectively. The AG was clearly correlated with lactate ($R^2 = 0.29$; $P < 0.001$). Across the pH range the difference between AG and lactate was largely constant with a median (IQR) of 5 (3–7) mmol/L and a 95% patient-based RI of [0–12] mmol/L.
Conclusion: When determined with optimal techniques, the anion gap increases markedly with decreasing pH in ICU patients. When lactate is also taken into consideration, the [AG]-[lactate] difference does not change with decreasing pH, with a RI of 6 ± 6 mmol/L.

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Acknowledgements: None.

001000

Urgent liver transplantation in patients with Acute-on-Chronic Liver Failure

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Intensive Care Medicine Experimental 2022, **10(2)**:001000

Introduction: Acute-on-Chronic Liver Failure (ACLF) is a severe clinical condition corresponding to 5% of hospital admissions for decompensated liver cirrhosis. The mortality rate varies according to the number of organ failure, and is reported to be 22% in ACLF I, 32% in ACLF II and 73% in ACLF III1. Liver transplantation is the only therapeutic approach with significant impact on the survival of these patients2. However, due to the clinical severity, liver transplantation on these patients is associated with worse outcomes, especially in ACLF III, when compared to transplantation of patients with decompensated cirrhosis.
Objectives: Characterization of patients with ACLF undergoing liver transplantation.
Methods: We retrospectively review all patients with ACLF that were admitted to Intensive Care in our Centre in the past 6 years. By using clinical records, we identified patients with ACLF that underwent urgent liver transplantation. Data on demographics, ICU severity scores, confounding and outcome variables were collected and analysed.
Results: A total of 117 patients admitted with ACLF were included. 50% were ACLF III, 31% ACLF II and 19% ACLF I. The mean CLIF-SOFA was 48. Patients were admitted for hepatic encephalopathy (26%), sepsis (15%), haemorrhagic shock (12%), hepatorenal syndrome (12%) and ischemic hepatitis (3%).
24 patients were submitted to liver transplantation, most of them ACLF III (64%) with a mean CLIF-SOFA of 39. All patients underwent immunosuppression with basiliximab, corticosteroids and tacrolimus, and the resulting graft rejection rate was 25%. Among these patients, the hospital mortality rate was 37.5% and the 5-year mortality rate was 50%. The mortality rate of transplanted patients was higher in ACLF III compared with patients with ACLF II and I, corresponding to 50%, 2% and 0%, respectively. In contrast, patients with ACLF who were not submitted to urgent liver transplantation, in-hospital mortality was 69%, and 5-year mortality was 74%.
Conclusion: Liver transplantation has a significant impact on the survival of patients with ACLF, particularly ACLF III.

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001005

Impact of hepatic encephalopathy on the survival of patients with Acute-on-Chronic Liver Failure

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Intensive Care Medicine Experimental 2022, **10(2)**:001005

Introduction: Hepatic encephalopathy (HE) is a clinical entity that reflects the combination of metabolic encephalopathy, cerebral atrophy and cerebral edema. It is a reversible syndrome that occurs in 50% of patients with cirrhosis1,2. The presence of encephalopathy worsens the survival of patients, so liver transplantation should be considered3.
Objectives: To access the prevalence of HE and the association of HE with mortality in patients with acute-on-chronic liver failure (ACLF).
Methods: Retrospective study with a duration of 6 years, including all patients admitted to an intensive care unit of a university hospital. A review of the clinical files was carried out in order to identify which patients with ACLF were admitted for HE. Demographic variables, confounding and outcome variables were collected.
Results: Of these, 117 hospitalized patients with ACLF were included, 30% were admitted for encephalopathy and 53% had grade III/IV of the West-Haven classification. There was no statistically significant association between the West-Haven classification and the ammonia value. There was also no statistically significant association between the ammonia value and hospital mortality. The precipitating factors associated with encephalopathy were digestive bleeding (36%), sepsis (20%), alcoholic hepatitis (15%) and post-Transjugular Intrahepatic Portosystemic Shunt encephalopathy (12%). West-Haven grade III/IV hepatic encephalopathy is associated with a higher mortality when compared to grade I and II of the same classification.
Conclusion: Hepatic encephalopathy is associated with higher mortality in patients with ACLF.

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001010

Prevalence of infection with multidrug-resistant agents in patients with Acute-on-Chronic Liver Failure

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Intensive Care Medicine Experimental 2022, **10(2)**:001010

Introduction: Infection is one of the main reasons for decompensation in a patient with cirrhosis, being the cause of acute-on-chronic liver failure in 27.9% to 32.6% of cases1,2. Infection as a cause of ACLF increases patient mortality3, so antibiotic therapy should be started early. Empirical treatment should take into account the resistance pattern of the most frequent bacteria in these patients. The prevalence of multidrug-resistant bacteria reduces the effectiveness of empirical antibiotic therapy, and it is essential to know the prevalence of multidrug-resistant agents in these patients.
Objectives: To know the prevalence of infection by multidrug-resistant bacteria in patients hospitalized for ACLF grade II/III in an intensive care unit and its effect on patient mortality.
Methods: Retrospective study with a duration of 6 years, including all patients admitted to an intensive care unit of a university hospital. A review of clinical files was carried out in order to identify bacterial agents isolated in patients' biological products. Demographic variables, confounding variables and outcome variables were collected.

Results: A total of 118 patients were included. Although sepsis was responsible for the hospitalization of only 15% of patients, during hospitalization 43% of all patients had sepsis. The most frequent infection was bacteremia associated with intestinal bacterial translocation and pneumonia. The most frequent bacteria were *Enterobacteriaceae* (43%) and gram positive bacteria (21%), with lower expression of *Pseudomonas* bacteria. The prevalence of multidrug-resistant bacteria was 33%, highlighting *Pseudomonas aeruginosa* KPC + (47%) and *Escherichia coli* ESBL + (18%). The presence of sepsis was associated with higher mortality, being 65% in patients with infection *versus* 39% in patients without infection. Infection with multidrug-resistant bacteria significantly increased patient mortality (76% versus 58%).
Conclusion: Sepsis significantly increases the mortality of patients with ACLF. The prevalence of infection with multidrug-resistant bacteria corresponded to one third of infections in patients with ACLF. Infection with these agents was associated with higher patient mortality.
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001088

Early serum ammonia decline was associated with better hospital survival among critically ill cirrhosis patients: a multicenter cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:001088

Introduction: Serum ammonia dynamics is often difficult to interpret in critically ill cirrhosis patients.
Objectives: We assessed the association of serum ammonia decline during the first days of intensive care unit (ICU) stay with survival.
Methods: Observational cohort study including consecutive cirrhosis patients admitted to the ICUs at University of Alberta Hospital (Edmonton, Canada) and Curry Cabral Hospital (Lisbon, Portugal) between 08/2013 and 08/2017. Primary exposure was serum ammonia ratio between ICU days 1 and 2 (D2NH3/D1NH3). Primary endpoint was overall hospital survival.
Results: Among 402 cirrhosis patients included, 265 (65.9%) were men and median (IQR) age was 56 (50–62) years. Median (IQR) SOFA score on ICU day 1 was 13 (10–15). On ICU day 1, median serum ammonia was higher in patients with grade 3–4 hepatic encephalopathy (HE) than those with grade 1–2 HE or no HE (107 vs. 74 mmol/l; $P < 0.001$). Median D2NH3/D1NH3 was lower in patients on renal replacement therapy (RRT) since ICU day 1 than those without RRT (0.61 vs 0.88; $P = 0.09$). Following adjustment for significant confounders (age, HE grade, use of RRT and INR on ICU day 1), higher D2NH3/D1NH3 was independently associated with lower hospital survival (OR (95%CI) = 0.24 (0.07–0.90); $P = 0.033$; model c-statistic (95%CI) 0.82 (0.73–0.90)).
Conclusion: Among critically ill cirrhosis patients, early serum ammonia dynamics may be a therapeutic target with relevant prognostic value.

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001097

Vitamin D deficiency in a Greek ICU: Correlation with albumin and HDL levels and association with patient outcome. A single-center retrospective study

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Intensive Care Medicine Experimental 2022, **10(2)**:001097

Introduction: Vitamin D deficiency (< 20 ng/ml) has been linked with increased risk of sepsis and mortality in critically ill patients. In addition, there is some evidence that albumin and HDL levels are also negatively linked with mortality in patients with sepsis. Thus far, correlation of concurrent vitamin D-, albumin- and lipid-levels with patient outcome has not been studied in Intensive Care Unit (ICU) patients.
Objectives: To identify the prevalence of vitamin D deficiency in our ICU patient population and to investigate whether there is a correlation with laboratory markers such as albumin and lipids and an association with patient outcome.
Methods: We have performed a retrospective study from 10/2018 to 02/2020 including all ICU patients with vitamin D levels measured within 72 h from ICU admission. Patients' demographics, cause of admission, APACHE II and Charlson Comorbidity Index scores, ICU length of stay, complications during ICU stay and mortality along with albumin and HDL levels were recorded for each patient. Two patient groups, i.e., with and without severe vitamin D deficiency, were compared and a correlation analysis was performed in patients dying within 28 days from ICU admission.
Results: Altogether 160 patients were included in our study (67.5% men, 32.5% women) with an overall 28-day ICU mortality being 23.7%. Vitamin D deficiency was evident in 91,25% of our patient population while in 46.5% of the cases vitamin D deficiency was classified as severe (< 10 ng/ml). Patients with severe vitamin D deficiency had a higher risk for developing shock (37% vs 22.6%, $p = 0.019$), acute kidney injury (34.2% vs 20.2%, $p = 0.014$) and coagulopathy (20.5% vs 4.7%, $p = 0.002$), nevertheless, there was no statistically significant difference in hospital mortality (37% severe deficiency vs 25%, $p = 0.186$). Correlation analysis in the subgroup of patients that were not alive by day 28 of ICU admission showed a strong correlation of vitamin D levels with albumin ($r = 0.406$, $p = 0.019$) and HDL ($r = 0.535$, $p = 0.002$) levels.
Conclusion: Vitamin D deficiency in critically ill patients seems to be very common and associated with complications during ICU stay. In our study vitamin D levels show a strong correlation with albumin and HDL levels and 28-day ICU mortality. Whether albumin and HDL levels can assist in stratifying ICU patient risk further remains to be answered in feature trials.

001100

Acute kidney injury in patients with Acute-on-Chronic Liver Failure and its impact on mortality

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Intensive Care Medicine Experimental 2022, **10(2)**:001100

Introduction: Acute-on-chronic liver failure (ACLF) is a syndrome characterized by acute decompensation of chronic liver disease associated with multi-organ dysfunction and high risk of short-term death. The estimated mortality varies from 22 to 73% depending on the number of failing organs (1). Renal dysfunction is common in this entity, and the need for renal replacement therapy is associated with a worse prognosis (2). Renal failure in patients with cirrhosis has a very significant impact on the survival of patients with a one-month mortality rate close to 50% (3) and a 3-month mortality rate greater than 75% (4).
Objectives: To determine the prevalence of acute kidney injury (AKI) in patients with ACLF and its relationship with mortality.
Methods: We performed a retrospective study including all patients with ACLF admitted from 2013 to 2022 in our intensive care unit. Clinical files were reviewed, and patients were characterized according to the presence of AKI, its severity, necessity of renal replacement therapy and survival. Demographic, confounding and outcome variables were collected.
Results: 117 patients with ACLF were included (mean age of 57,3 years). Of these, 49% had AKI on admission and during hospitalization the prevalence increased to 68%. In what severity is due, we found AKIN I in 36%, AKIN II in 36% and AKIN III in 28% of the patients.
Renal replacement therapy was performed in 59% (n = 47) of the AKI population. At the moment of prescription, 46% of the patients were staged as AKIN III; 36% as AKIN II and 18% as AKIN I. The most prescribed modality was continuous renal replacement therapy (47%), followed by conventional hemodialysis (34%) and sustained low-efficiency dialysis (19%).
No relationship was noted between the presence of renal failure and mortality, being even higher in patients who did not have renal failure (59% versus 50%). Nevertheless, mortality was higher in patients with AKIN III when compared to patients with AKIN II and I (69% vs 50% vs 37%, respectively).
Conclusion: In this series of patients, there was no association between acute kidney injury and mortality. A possible explanation could be the low prevalence of severe kidney injury, reflected in the prevalence of 28% of patients with AKIN III.

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001151

Confirmation of nasogastric tube placement in intensive care. The combination of EtCO2 and pH measurement, a new possibility?

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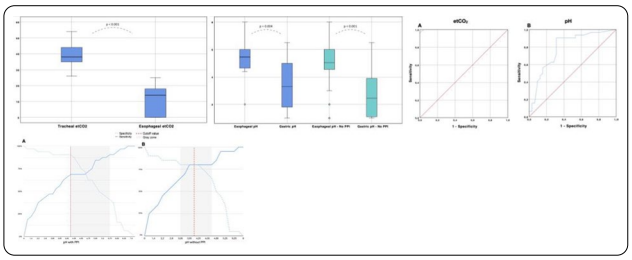
Intensive Care Medicine Experimental 2022, **10(2)**:001151

Introduction: Nasogastric tube (NGT) placement is a commonly performed procedure in the intensive care unit. Chest radiography is the diagnostic gold-standard for confirming correct placement, with the disadvantages of both the need to mobilize patients in the ICU and the inherent risk of actinicity. Other potential methods to confirm NGT placement have shown inferior accuracy to chest radiography; ETCO2 and pH analysis have been studied individually as alternatives to the gold standard.
Objectives: The purpose of this study was to determine thresholds in the combined measurements of ETCO2 and pH values at which correct NGT placement can be confirmed with the highest accuracy.
Methods: This was a prospective, multicenter, observational study; a continuous cohort of eligible patients was assigned to two arms to identify a clear cut-off threshold that could detect correct NGT tip placement with the highest accuracy. Inclusion criteria were patients of both sexes, older than 18 years of age, fasting for at least six hours, undergoing general anesthesia and orotracheal intubation, for whom placement of an NGT was planned according to clinical criteria. Exclusion criteria were patient refusal or inability to give informed consent, pregnancy, known ongoing gastric or esophageal bleeding, coagulation impairment (defined as thrombocytes < 50 G/L, fibrinogen < 1, 0 g/L, INR > 2.5, aPTT > 70 s tested at preoperative evaluation), history of traumatic brain injury or polytrauma, esophago-tracheal fistulas, esophageal varices, ENT malformations and/or tumors, history of radiation therapy for ENT tumors. Patients in whom pH and/or ETCO2 values were not measurable for technical reasons were excluded and considered as dropouts. In the first group, differences between tracheal and esophageal ETCO2 values were assessed. In the second group, differences between esophageal and gastric pH values were determined.
Results: From November 2020 to March 2021, 85 consecutive patients were enrolled: 40 in the ETCO2 group and 45 in the pH group. ROC analysis of ETCO2 to predict NGT trachea misplacement demonstrates an optimal ETCO2 value of 25.5 mmHg, where both sensitivity and specificity reach 1.0 (AUC 1.0, p < 0.001). ROC analysis of pH to predict correct gastric positioning of NGT demonstrated the optimal pH cutoff value at 4.25, with a slight diagnostic accuracy (AUC 0.79, p < 0.001).



Conclusion: In an ICU setting, the use of a device that can combine the presence of a negative marker to rule out NGT misplacement (such as ETCO2) and a positive marker to confirm correct NGT placement (such as a pH assessment) could be accurate enough to improve correct NGT plac ement in unconscious patients. Further studies in this direction are needed to test this hypothesis.

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Neuro-Intensive Care 1

000013

A prospective study of the prevalence of stress cardiomyopathy in the neurocritical patient through myocardial deformation

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Intensive Care Medicine Experimental 2022, **10(2)**: 000013

Introduction: Stress cardiomyopathy (SCM) in a known complication in patients with aneurysmal subarachnoid haemorrhage but rarely described in the rest of neurocritical patients.
Objectives: To compare the prevalence of stress cardiomyopathy in patients diagnosed of subarachnoid haemorrhage (SAH) with respect to other neurocritical patients (non-SAH) through the echocardiographic assessment of myocardial dysfunction.
Methods: Prospective unicentric study on neurocritical patients (SAH vs non-SAH) admitted to an ICU. Sample size is calculated, requiring 45 patients in the SAH group and 45 patients in the non-SAH group to detect a difference equal to or greater than 3 units. We performed an echocardiography at ICU admission. We analysed the left ventricular systolic function through the ejection fraction (LVEF) and the global longitudinal strain (GLS) assessed by speckle tracking, using the normality cut-off points validated in the literature ($\geq$52% for LVEF and $\leq$-18% for GLS1). Demographic data were collected and the severity of neurological damage was stratified according to the Glasgow coma scale (GCS) at admission in mild (13–15), moderate (10–12) and severe (9–3). We carried out a bivariate statistical analysis between both groups using Student's t-test for continuous parametric data and Mann–Whitney U test for non-parametric, and Chi-squared tests for comparison of categorical data. Clinical Research Ethics Committee: CEIC PSMAR 2017/7361/I.
Results: We included a total of 99 patients (45 in the SAH and 54 in the non-SAH group), with a greater percentage of women in the SAH group (64 vs 26%; $p<0.001$), without differences in age (55 ± 11 vs 53 ± 18 years; $p=0.604$), severity scores (APACHE II 13 ± 8 vs 17 ± 9; $p=0.052$, and SOFA 4 ± 3 vs 4 ± 3; $p=0.309$) nor in neurological damage severity (mild 56 vs 39%, moderate 9 vs 22%, and severe 35 vs 39%; $p=0.120$). No differences were observed in LVEF (65 ± 9 vs 64 ± 8%; $p=0.141$) nor GLS (-18.4 ± 4.7 vs -17.3 ± 3.5%; $p=0.263$). The myocardial dysfunction assessed using both techniques tended to be more prevalent with greater neurological severity, although without reaching statistical significance (Table 1). Moreover, GLS presented greater sensitivity to the diagnose of dysfunction in all severity groups. In both groups (SAH vs non-SAH), from the patients with dysfunction diagnosed by GLS a 77% and an 86% respectively presented with a normal LVEF. These results represent interim findings of the on-going study.

Table 1. Echography and severity

	Severity according to GCS			
	mild	moderate	severe	p
GLS > -18%				
SAH, n (%)	5 (26)	2 (50)	6 (60)	0.189
Non SAH, n (%)	7 (44)	5 (56)	9 (64)	0.527
LVEF < 52%				
SAH, n (%)	0 (0)	0 (0)	3 (21)	0.035
Non HSA, n (%)	2 (12)	0 (0)	1 (6)	0.480

p ≤ 0.05 are considered statistically significant

Conclusion: Patients with SAH do not present a greater prevalence of SCM than the rest of neurocritical patients. The prevalence of SCM tends to be greater with more severe neurological damage. In those patients, the use of the LVEF to diagnose SCM leads to an underdiagnosis when compared to GLS. Further analyses are still ongoing to establish the evolution of this cardiac dysfunction throughout the first week of hospitalisation, and its relation to patient's outcome in terms of possible neurological sequelae, cardiac function recovery, and mortality.

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000020

Intrathecal penetration of fosfomycin in patients with ventriculitis—a prospective observational study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000020

Introduction: For treatment of ventriculitis, vancomycin and meropenem are frequently used as empiric treatment but cerebrospinal fluid (CSF) penetration is highly variable and may result in subtherapeutic concentrations. Fosfomycin (FOF) has been suggested for combination antibiotic therapy enhancing gram-positive and gramnegative coverage, but data are sparse, so far. Therefore, we studied CSF penetration of FOF in ventriculitis.
Methods: With ethics approval, patients receiving a continuous infusion of FOF for ventriculitis at a starting dose of 24 g/d were included, and patient data, including serum and CSF concentrations for FOF were prospectively collected twice weekly from CSF drains. Antibiotic CSF penetration ratio was calculated for each patient. The dose was subsequently adapted according to TDM values, targeting CSF concentrations above the antibiotic resistance breakpoint.
Results: Seventeen patients with 43 CSF/serum pairs were included. Infections were caused by coagulase-negative Staphylococci ($n=10$), Enterobacterales ($n=6$), and S. aureus ($n=1$). Mean FOF serum concentration was 257 ± 157 mg/L and the CSF concentration 127 ± 93 mg/L. Considering only the first measurements in each patient before a possible dose adaption, mean serum and CSF concentrations were 268 ± 157 mg/L and 158 ± 120 mg/L. Mean CSF penetration was 50 ± 22% with a coefficient of determination (R^2) of 0.65.

Wefound 98% of CSF levels above the antibiotic resistance breakpoint of 32 mg/L. No adverse toxicity was observed.
Conclusion: Penetration of FOF into the CSF is high, reliably leading to concentrations above the resistance breakpoint. Continuous administration of FOF appears to be a reasonable approach for antibiotic combination therapy in patients suffering from ventriculitis.

000038

Trends in Intensive Care Admissions and Outcomes of Stroke Patients Over 10 Years in Brazil: Impact of the COVID-19 Pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**: 000038

Introduction: The coronavirus 2019 (COVID-19) pandemic affected stroke care worldwide.
Objectives: We aimed to assess the impact of the pandemic in intensive care admissions and outcomes after stroke, in comparison to trends over the last ten years.
Methods: Retrospective cohort study including prospectively collected data from 165 ICUs in a hospital network in Brazil between 2011 and 2020. We analyzed the association between admission in 2020 and hospital outcomes using the following approach: analyses of stroke type (ischemic and hemorrhagic) and trends in mortality over ten years; analysis of variable life-adjusted display of mortality during 2020; a multivariate mixed regression model with admission year as both fixed effect and random slope adjusted for clinical severity.
Results: 17,115 admissions for stroke were analyzed, from which 13,634 were ischemic and 3,481 were hemorrhagic. Overall, in-hospital mortality was lower after ischemic stroke as compared to hemorrhagic (9% vs. 24%, respectively). Changes in VLAD across epidemiological weeks of 2020 showed that the rise in COVID-19 cases was accompanied by an increase in mortality as demonstrated by the decrease in VLAD, mainly in patients with ischemic stroke. In logistic regression mixed models, mortality was higher in 2020 compared to 2019, 2018, and 2017 in patients with ischemic stroke, namely in those without altered mental status. In hemorrhagic stroke, the increased mortality in 2020 was observed only in patients younger than 50 years, as compared to 2019.
Conclusion: We demonstrated worsened hospital outcomes of patients admitted with stroke during the pandemic, interrupting a trend of improvements in mortality rates over 9 years. This effect was more pronounced during the surge of ICU admissions for COVID-19 and affected predominantly patients with ischemic stroke and preserved level of consciousness, and young patients with hemorrhagic stroke.

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Acknowledgements This study was supported by the National Council for Scientific and Technological Development (CNPq), the Coordination for the Improvement of Higher Education Personnel (CAPES)—Finance Code 001, Carlos Chagas Filho Foundation for Research Support of the State of Rio de Janeiro (FAPERJ), the Pontifical Catholic University of Rio de Janeiro, and by departmental funds from the D'Or Institute for Research and Education.

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Clinical characteristics and outcomes of patients with subarachnoid hemorrhage: a prospective multicenter study in a middle-income country

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Intensive Care Medicine Experimental 2022, **10(2)**: 000040

Introduction: Aneurysmal subarachnoid hemorrhage (SAH) is an acute devastating disease associated with high mortality and long-term functional impairment. Data on SAH management and outcomes from developing countries is scarce.

Objectives: We aimed to define patient profiles, clinical practices, and evaluate long-term functional outcomes in patients admitted with SAH in a middle-income Latin American country.
Methods: We prospectively included all consecutive adult patients admitted with aneurysmal SAH to two neurosurgical Reference centers in Brazil from January 2016 to February 2020. Follow up was performed up to September 2020. Clinical and radiological data were collected on admission and during hospital stay. Outcomes were collected on hospital discharge and after 6 months from admission. The main outcome was functional status measured at 6 months using the modified Rankin scale. Multivariable analysis was performed to determine the relationship between premorbid demographic, admission clinical, and radiological variables, as well as complications and surgical treatment implemented, with functional outcome after 6 months.
Results: 666 patients were admitted with SAH in the study period, from which 471 (71%) fulfilled inclusion criteria and were analyzed. The median time from ictus to admission at a study hospital was 4 days (IQR 0–9). The median age was 55 years (IQR 46–62) and 75% were women. 426 (90%) were transferred from nonspecialized hospitals, and 136 (29%) had poor clinical grade (World Federation of Neurological Surgeons 4 or 5). Computed tomography revealed 340 (73%) patients with modified Fisher 3 or 4, and 92% underwent aneurysm occlusion, from which 72% through surgical clipping and 28% endovascular coiling. Only 34 patients (7%) received limitation of life-sustaining therapies, in-hospital mortality was 24% and 40% overall had an unfavorable long-term functional outcome.
Conclusion: Our study demonstrated that despite similar clinical profiles on presentation and admission to high-volume referral centers, management in a middle-income country diverges significantly from published cohorts and current guideline recommendations. Although 60% of patients reached favorable long-term outcomes, earlier aneurysm occlusion and increased use of endovascular therapy could potentially improve mortality and functional impairment in the future.

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Effects of Tranexamic Acid in Patients with Subarachnoid Hemorrhage in Brazil: An Observational Study with Propensity Score Analysis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000041

Introduction: Rebleeding from a ruptured aneurysm increases the risk of unfavorable outcome after subarachnoid hemorrhage (SAH), thus it should be prevented by early aneurysm occlusion. The role of antifibrinolytics before aneurysm obliteration has been studied and remains controversial.
Objectives: We investigated the effects of tranexamic acid on long-term functional outcomes of patients with aneurysmal SAH.
Methods: Single-center prospective observational study conducted in a high-volume tertiary hospital from a middle-income country, from December, 2016 to February, 2020. We included all consecutive patients with aneurysmal SAH that either received or not received TA treatment. Multivariate logistic regression analysis using propensity score-based methods was used to evaluate the association of TA use with long-term functional outcomes, measured by the modified Rankin Scale at 6 months.
Results: 230 aneurysmal SAH cases were analyzed in the study. The median (interquartile range) age was 57 (X–Y) years, 72% were female, 75% good clinical grade (WFNS 1 to 3) and 83% had a Fisher scale of 3 or 4. Around 80% of cases were admitted up to 72 h from ictus. The aneurysm occlusion was surgical in 80% of the cases. For the PSM,128 were selected for the analysis (64 to TA and 64 to non TA group). The long-term rate of unfavorable outcome (mRS 4–6) was the same in the TA and non TA groups (61cases in TA group vs. 33 in non TA group; coefficient 1.39, 95% CI 0.67–2.92; p = 0.377). Our in-hospital mortality was higher in TA group (33% in TA group vs. 10% in non TA group; coefficient 5.64, 95% CI 1.74–23.08; p = p < 0.008), as well as DCI rate (28% in TA group vs. 19% in non TA group; coefficient 4.78, 95% CI 2.03–11.95; p = 0.001). There was no difference between the groups concerning the length of stay in intensive care unit (16 ± 11.22 days in TA group vs. 14 ± 9.24 in non TA group; p = 0.2), neither in hospital (23 ± 13.35 in TA group vs. 22 ± 13.36 in non TA group; p = 0.9). There was no difference in rebleeding (6.2% in TA group vs 7.8% in non TA group; p = 0.305).
Conclusion: Our data reinforce previous data that TA use before aneurysm occlusion do not reduce recurrent bleeding and do not change the long-term funcional outcome of aSAH.

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Procalcitonin (PCT), C-reactive protein (CRP) and relationship in the diagnosis of iVAC in patients with intracerebral haemorrhage; a monocentric pilot study, Hospital Bufalini Cesena

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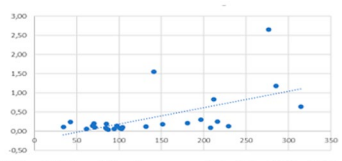
Introduction: Intracerebral hemorrhage (ICH) is a common acute cerebrovascular disease. In patients with ICH, infection-related ventilator-associated complications (iVACs) are due to microinhalation from loss of normal physiological reflexes such as swallowing and coughing, a state of immune paralysis and need of prolonged mechanical ventilation. It occurs in 9–27% of patients intubated for longer than 48 h. iVACS may exacerbate secondary brain injury and it is associated with increases the days of mechanical ventilation, long hospitalization and rising healthcare costs. Procalcitonin (PCT) and C-reactive protein (CRP) are considered a useful biomarkers of infections; especially PCT can be a tool in the guidance of antibiotic stewardship. However, its efficacy remains controversial in ICH patients.
Objectives: The main aim of the study was to investigate the diagnostic role of serum levels of PCT and CRP in ICH patients with iVAC.
Methods: A preliminary retrospective observational study of patients admitted to ICU from January 2020 to January 2021. Patients with ICH diagnosed with iVAC during stay ICU were included. Patients with lower respiratory tract infection already upon admission to the ICU were excluded. During the ICU stay, laboratory tests (blood count, creatinine, urea, PCR) and seriated blood gas analysis were required daily. In the event of suspected iVAC, culture tests, including bronchoalveolar lavage(BAL) or endotracheal aspirates(ETA) and PCT dosage, were performed before administering antimicrobial therapy.
Results: From January 2020 to January 2021 a total of 51 patients meet inclusion criteria (41.17% males and 58.82% females). The average age was 55.9 s.d. ± 12.83. Patients were admitted with a median GCS of 7(IQR 6); 50.98% of patients had cerebral aneurysm and/or vascular malformation, 49% of patients had spontaneous cerebral hemorrhage. We observed clinical worsening with onset of iVAC at 5 days (median value-IQR 2.75) from admission. Considering the median value we divided the patients in two groups: early onset iVAC (39.22%) and late onset iVAC (60.78%). CRP was 123.81 mg/dL (123.81 ± 75.46 mg/dL) and in 92.15% of cases the first PCT value was below the cut off of 0.5 ng/ml (0.23 ± 0.39 ng/mL). We observed poor correlation between PCT and CRP: the Spearman coefficient Rho = 0.249 p 0.121. Only 8% of patients had PCT values > 0.5 ng/ml, in this cohort a progressive downward trend in PCT values was observed following antimicrobial therapy.

Age		55.9 ± 12.83
Gender (women)		58,82%
GCS score at endotracheal intubation		7.43 ±3.43
	median (IQR)	7(6)
Pupillary reactivity bilateral reactivity		80,39%
	midriasis	3.9%
	anisocoria	15,68%
Surgery		66.66%
Endovascular treatment		21.56 %
No treatment		1.76%
Time of tracheotomy		4.98 ±2.33
	median (IQR)	4.5(3)

Baseline characteristics of the study population. Data are given as mean ± standard deviation unless otherwise indicated.



PCT and CRP correlation, Spearman coefficient Rho=0.249 p 0.121

Conclusion: Biomarkers such as PCT and CRP have been proposed for the diagnosis of iVAC, we observed no increase in procalcitonin values in 92.15% of patients with ICH and iVAC. Our data suggest that PCT

values < 0.5 ng /ml does not exclude iVAC and the need to start antibiotic therapy.

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000099

Timing of descompressive cranietomy for acute ischemic stroke

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Introduction: Ischemic stroke is one of the leading causes of death and disability worldwide. Malignant stroke occurs in a subgroup of patients suffering from ischemic cerebral infarction and is characterized by neurological deterioration due to progressive edema, raised intracranial pressure, and cerebral herniation. Decompressive craniectomy (DC) is a surgical technique aiming to open the "closed box" represented by the nonexpandable skull in cases of refractory intracranial hypertension. It is a valuable modality in the armamentarium to treat patients with malignant stroke: the life-saving effect has been proven for both supratentorial and infratentorial DC in virtually all age groups.
Objectives: To study the association between the timing of DC and outcome of patients with malignant middle cerebral artery (MCA) infarct.
Methods: This is a single center, retrospective study that was conducted in patients presenting with middle cerebral artery infarction admitted in Centro Hospitalar Universitário de São João, between January 2019 and December 2020 who underwent decompressive craniectomy due to clinical (according to Glasgow Coma Scale) or structural (neuroimaging) deterioration. Functional outcome was assessed in terms of mortality and modified Rankin Scale (mRS).
Results: A total of 939 patients were admitted with acute ischemic stroke, a decompressive craniectomy performes in 12 patients (1,3%). Eight patients were female and four were male and the mean age was 56,66 years. Out of those 12 patients, 10 (83,3%) had a right middle cerebral artery infarct (RMCAI) and 2 (16,7%) had a left middle cerebral artery infarct (LCAI). The mean initial NIHSS score was 18,25. In 83.3% of the cases, the timing of DC was less than 48 h and the majority of the findings in neuroimaging before DC was midline shit > 5 mm in 66,67%. The mean modified Rankin Scale (mRS) after discharge was 3,0 and no deaths were registered.
Conclusion: We found no diference in outcome when decompressive craniectomy was performed after 48 h in patients with malignant MCA infarct. Contrary to current guidelines and, albeit a limited series, we advocate not to restrict decompressive craniectomy to a period of ≤ 48 h stroke onset.

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000112

Auditing own practice: compliance with local guidelines on use of ICP and Pbt02 monitors in TBI patients admitted to a tertiary centre

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Intensive Care Medicine Experimental 2022, **10(2)**: 000112

Introduction: Severe traumatic brain injury (TBI) remains a high mortality (30–40%) and burden disease. The use of intracranial pressure (ICP) and brain tissue oxygenation (Pbt02) monitors have been used to limit secondary brain injury that will worse outcome or cause death. Local guidelines were developed within our institution targeting patients with moderate to severe traumatic brain injuries for monitoring and management of such patients based on current evidence.
Objectives: Evaluation of local guidelines compliance on the use of ICP and Pbt02 in severe TBI patients admitted to a tertiary trauma centre in London, UK.
Methods: Our local guidelines for management of moderate and severe follow the Brain Trauma Foundation indications for insertion and monitoring of ICP and estate that if an ICP bolt is to be inserted, it should be accompanied by a Pbt02 probe, recognizing the relationship between low Pbt02 and poor outcomes, independently of ICP and CPP. We conducted a retrospective audit of all traumatic brain injury (TBI) patients admitted to intensive care in a tertiary trauma centre in London, UK, from 1st January 2019 to 31st December 2020. Data collected included demographic data (age, sex, ICU length of stay (LOS), ICU and hospital outcome (dead/alive), initial GCS and motor score where possible, insertion of ICP and Pbt02 monitors and reason for them not being inserted.
Results: We identified 203 patients admitted to intensive care in our centre. Of those, n = 40 (19.7%) suffered mild TBI, n = 40 (19.7%) moderate TBI (GCS 9–11) and n = 123 (60.6%) were admitted with severe TBI (GCS ≤ 8). Our focus was on those admitted with moderate and severe TBI.
Demographic data is presented in Table 1.
Table 1 Demographic data of moderate and severe TBI patients

	Severe TBI	Moderate TBI
Sex (n, %)	Male n = 94 (76,4%) Female n = 29 (23.6%)	Male n = 31 (77.5%) Female n = 9 (22.5%)
Age	51	50
Outcome at ICU discharge	Alive 78 (63.4%) Dead 45 (36.6%)	Alive 36 (90%) Dead 4 (10%)
ICU LOS (days)	7	8
Initial GCS	6	10

Patients admitted with moderate TBI that received an ICP monitor were n = 29 (27.5%), whereas a Pbt02 was inserted in only 3 patients (7.5%). Reasons to not insert ICP monitors included catastrophic TBI (N = 7, 17.5%), GCS improved (n = 1, 2.5%) and no clear documented reason was found in 32 patients (80%). When looking at severe TBI patients (n = 123), ICP was inserted in 43 patients (35%), and Pbt02 in 16 patients (13%). Reasons to not insert an ICP bolt nicluded: catastrophic TBI (N = 27, 34.2%), GCS improved (n = 8, 10.1%), no radiological indication (n = 1, 1.3%) and in 43 (54.5%) patients this reason was not documented. With regards the outcome at discharge of the severe

TBI patients, 78 patients (63.4%) left ICU alive and 45 patients (36.6%) died during their stay in ICU.
Conclusion: Only 35% and 13% of patients with severe TBI were monitored following our local guidelines with limited documentation explaining the deviation from the guidelines. Despite, our outcomes are comparable to those previously published. Working in partnership with our neurosurgical colleagues to establish clearer lines of communication has commenced to understand the impact of these practices.

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Acknowledgements No grants received.

000154

Understanding the Relationship Between Arterial Carbon Dioxide and Neurological Injury in Patients Undergoing veno-venous extracorporeal membrane oxygenation. A Prospective Cohort Study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000154

Introduction: Veno-venous extracorporeal membrane oxygenation (VV-ECMO) enables *ex-vivo* gas exchange in a critically ill patient with acute respiratory failure. It enables lung protective ventilation to facilitate recovery from severe disease (1,2). Although VV-ECMO can be life-saving, it has significant complications. Specifically, neurologic injury (e.g., cerebral ischemia or hemorrhage) during VV-ECMO is associated with increased mortality and adverse long-term functional outcomes (3). Studies suggest that among adult patients undergoing VV-ECMO, the incidence of neurological injury ranges from 7 to 40%3. Prospective physiologic studies are needed to further delineate the underlying mechanisms.
Methods: We conducted a prospective cohort study of 59 adult patients undergoing VV-ECMO at Vancouver General Hospital. Timing of arterial blood gas measurements were obtained as per our clinical protocol prior to initiation of VV-ECMO, and at every 2–4 h for first 24 h. Neurological injury was defined as either an acute cerebral hemorrhage or infarct on computerized tomography (CT) head imaging. We visually assessed the relationship by plotting $PaCO_2$ (connected line plot for each patient) over time stratified by injury status. Because of the non-linear relationship between $PaCO_2$ and time, we logarithmically transformed $PaCO_2$ and performed a mixed-methods linear regression between ln ($PaCO_2$) and neurologic injury as a dichotomous variable, with specifying 'patient' as a random-effect (STATA command *xtreg*). We included an interaction variable of time and injury. In order to assess previously published relationships of changes in $PaCO_2$ and injury (4) we also calculated the pre-post percentage (PP%) as the difference between the $PaCO_2$ obtained before and 24 h after initiation of VV-ECMO divided by the pre-VV-ECMO $PaCO_2$. As part of a *post-hoc* sensitivity analysis, we examined various thresholds of max–min percentage (MM%) in $PaCO_2$.
Results: We enrolled 59 patients between April 1st and November 30th, 2021. Patients had a mean age of 50 (SD 12) years in the neurologic injury group and 52 (10) years in the no-injury group. Eleven (19%) of the patients were female and 50 patients (85%) required VV-ECMO for COVID-19. Twelve patients had neurologic injury (9 patients had intracranial hemorrhage and 3 patients had ischemic strokes). Prior to initiation of VV-ECMO, the median $PaCO_2$ was 88 (68–105) mm Hg vs. 67 (IQR 61–80) mm Hg in the injury and no-injury group, respectively. $PaCO_2$ values over first 24 h were analyzed over time in patients with and without neurologic injury. $PaCO_2$ decreased over time in both groups (− 0.18% per 10 min, 95%CI: 0.14 to 0.21%). There was effect measure modification of the $PaCO_2$ over time by neurologic injury (p-interaction < 0.001). Patients with neurologic injury had a steeper reduction in $PaCO_2$ by 0.32% (95%CI: − 0.25 to − 0.39) for each 10 min compared to a reduction of $PaCO_2$ by 0.18% (95%CI: − 0.14 to 0.21) in the no-injury group. Post-hoc analysis of various $PaCO_2$ thresholds were don and a $PaCO_2$ MM% ≥ 50% in first 24 h was associated with an increased odds of neurologic injury (OR 8.8, 95%CI: 2.0 to 37.8).
Conclusion: We characterized the effects of $PaCO_2$ during the first 24 h of VV-ECMO on neurological injury. The decreased of $PaCO_2$ around the time VV-ECMO was steeper in patients with neurologic injury compared to those without. Previous studies had evaluated the effects or $PaCO_2$ using a PP%, however a MM% may be a better predictor of neurological injury (4).

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000171

Continuous infusion of hyperosmolar saline solution (HSS) in patients with brain injury: a systematic review and meta-analysis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000171

Introduction: Brain injury is an important cause of death and disability worldwide. Maintaining normal intracranial pressure (ICP) and preventing secondary brain injury is the central goal of neuro-intensive care management. Continuous infusion of hyperosmolar saline solution (HSS) can be used to optimize hemodynamics, but its use as fluid therapy is not recommended in neuro –intensive care patients.
Objectives: The primary objective was to determine if continuous infusion of HSS enhance outcomes of brain-injured patients. Secondary objective was to assess its tolerance.
Methods: A meta-analysis was performed according to PRISMA (Preferred Reported Items for Systemic Reviews and Meta-Analyses)

guidelines using the MeSH Terms: "HYPERTONIC SOLUTION" and "BRAIN INJURY" from 1990 to 2021. [PROSPERO CRD42021221367]. We included all clinical trials conducted in brain-injured patients hospitalized in ICUs and evaluating continuous infusion of hypertonic saline solutions. The primary outcome was assessed by in hospital mortality. Secondary efficacy outcomes were the rates of intracranial hypertension and neurological recovery assessed by Extended Glasgow outcome scale (GOS-E) or Glasgow Outcome Scale (GOS) as available. Tolerance outcomes were the rate of acute kidney injury (AKI) and severe hypernatremia defined as a natremia > 160 mmol/L. Analyses were performed using fixed-effects models with random-effects models for comparison.
Results: Studies: Our initial search yielded 338 citations. Ninety-one studies were scrutinized, we retained 22 studies on continuous infusion of HSS, and 10 were pooled in the meta-analysis. Studies were published between 1994 and 2021 and 4 (40%) were prospective and randomized. The risk of bias for allocation concealment was deemed high in 6 studies (60%). The risks of incomplete data was low in 9 studies (90%). The overall risk of bias was considered low for 5 studies (50%).
Population: A total of 1883 patients were included in these studies of whom 793 (42.1%) patients were considered as HSS group and 1090 (57.9%) were considered as control group (standard of care). Patients were admitted for a traumatic brain injury for 8 studies (n = 1525, 81%).
Primary outcome: The risk ratio (RR) for death was evaluated at 0.68 (95% confidence interval [CI], 0.54–0.85) in the intervention groups with a fixed effect model, and 0.68 [95%CI 0.54–0.85] with a random effect model. No significant heterogeneity was noted ($I^2 = 0\%$).
Secondary outcome: Episodes of intracranial hypertension was recorded in 137 (37.1%) patients with continuous infusion of HSS versus 200 (47.8%) patients in the control group (RR 0.78 [95%CI 0.48–0.85]). Poor neurological outcome (GOS-E < 6 or GOS $\leq$ 3 at 3 months) was recorded in 204 (58.6%) patients of the HSS group versus 425 (69.9%) patients in the control group (RR 0.7 [95%CI 0.52–0.83]. Regarding tolerance, AKI was recorded in 29 (0.8%) patients in the HSS group, as compared with 38 (0.9%) patients in the control group (RR 0.88 [95%CI 0.52–1.44]. Severe hypernatremia was more frequently reported in the HSS group (n = 74; 15.3%) than in the control group (n = 32; 4%) (RR 4.1 [95%CI 2.8–6.61].
Conclusion: In this meta-analysis continuous infusion of HSS as fluid therapy reduced in-hospital mortality of brain-injured patients hospitalized in ICU. Tolerance was acceptable. Data on long term neurological recovery are still needed before revising guidelines for fluid management in neuro-intensive care.

Neuro-Intensive Care 2

000221

Characterising global resource inequality in management of traumatic brain injury: results from the Global Neurotrauma Outcome Study (GNOS) provider profiling questionnaire

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Intensive Care Medicine Experimental 2022, **10(2)**: 000221

Introduction: Traumatic Brain Injury (TBI) is A Major Cause of Morbidity and Mortality Worldwide.(1, 2) Guideline Implementation is Associated with Improved Outcomes, However Management is Resource Intensive (3) and May Not Always Be Feasible to Implement, Especially in Low Resource Settings (4). Despite This, Little International Data Exists Evaluating Capacity for TBI Management. We Aimed to Characterise International Resource Availability for the Management of TBI and Compare Provisions Across Different Levels of Human Development.
Methods: We Constructed a Questionnaire With 50 Items Assessing Specific Resource Availability at Different Stages of TBI Management: Prehospital, Surgery, Neurocritical Care, and Rehabilitation. This Was Sent To 159 Neurosurgical Units From 57 Countries of Different Levels of Human Development which Participated in the Global Neurotrauma Outcomes Study. Development Was Described Using the Human Development Index (HDI) and Countries Were Stratified as Very High-HDI, High-HDI, Medium-HDI, and Low-HDI. Questionnaire Results Were Analysed Using Descriptive Statistics and Differences Between Development Levels Were Tested Using Appropriate Parametric and Nonparametric Tests. Interrater Reliability Was Assessed by Comparing Answers of Independent Respondents from the Same Institution.
Results: 153 Units (96%) Completed and Returned the Questionnaire and Centres in Very High-HDI, High-HDI, Medium-HDI, and Low-HDI Countries Comprised 51%, 22%, 18% And 9% of Responses Respectively. Most Centres Were Government Funded (85%) and Located in Urban Areas (96%). Median Interrater Reliability Was Found to Be Fair ($\kappa = 0.478$). Resource Availability and Guideline Usage Were Poorest in the Prehospital and Rehabilitation Phases Across All HDI Strata and Best During the Surgical Management Phase. Amongst All Respondents, the Prehospital Phase Was Most Frequently Indicated as the Phase for which Changes Would Most Improve Patient Outcomes. Intensive Care and Prehospital Care Were Chosen Most Amongst Centres of Less Developed Regions While Rehabilitation Was Chosen Most by Very High-HDI Centres. Centres Of Less Developed Regions Had Significantly Fewer Resources at All Phases and Most Notably Lacked Provisions at the Prehospital, Intensive Care and Rehabilitation Phases. No Low-HDI Centre Indicated Regular Access to Basic Monitoring and Treatment During the Prehospital Phase. Low-HDI Centres Were Less Likely Manage Severe TBI Patients in Specialised Intensive Care Units (ICUs). These Centres Had Significantly Limited Access to Basic Management and Investigations Like Intravenous Fluids and Blood Counts in the ICU and Only the Most Developed Centres Had Sufficient Access to Invasive Monitoring. All Centres Other Than the Most Developed Had Extremely Limited Rehabilitation Capacity However This Was Least Indicated by Low-HDI Centres as the Phase for which Changes Would Most Improve Patient Outcomes.
Conclusion: Capacity for TBI Management Varies Between Different Human Development Settings and Populations of Less Developed Regions Greatly Lack Access to Evidence-Based Care. These Findings Highlight the Need for Context Specific Management Guidelines and Help Direct Global Health Efforts Targeting This Disparity.

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Acknowledgements Administrative costs of this study were funded by the National Institute of Health Research (NIHR) Global Health Research Group on Neurotrauma.

000232

Neurologic Pupil Index and Delayed Cerebral Ischemia in Subarachnoid Hemorrhage

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Intensive Care Medicine Experimental 2022, **10(2)**: 000232

Introduction: Delayed cerebral ischemia (DCI) occurs in around 20–30% of aneurysmal subarachnoid hemorrhage (aSAH) patients and

is associated with poor neurological outcome (1). Automated pupillometry is a non invasive easily performed technique that quantifies the quality of pupillary function through a parameter called NPi. The role of NPi in the diagnostic approach and outcome in patients with DCI remains to be elucidated (2,3).

Objectives: The aim of this study was to investigate the association of NPi with the occurrence of DCI in SAH patients, as well as its prognostic value in this setting.

Methods: This is a single center retrospective cohort study of consecutive aSAH admitted to the intensive care unit of at Erasme Hospital, Brussels (Belgium) between January 2018 and December 2020 that had daily NPi recordings (every 8 h)during the first 10 days of admission.A Npi < 3 was defined as pathological. The primary outcome of the study was the number of patients that had NPi < 3 before DCI. Secondary outcomes included the difference in NPi between patients with good and poor grade on admission and the difference in NPi between patients with favorable and unfavorable neurological outcome.

Results: A total of 72 aSAH patients were eligible for the final analysis. Mean age was 53 (± 14) and 63% were female. Twenty-five patients (35%) presented with poor clinical grade on admission (WFNS 4–5) and DCI occurred in 38 (53%) patients. NPi values were similar in patients with DCI and those without DCI.However, patients with DCI (21/38, 55%) had a higher frequency of NPi values < 3 than others (8/34, 24%, p = 0.008. In the multivariable logistic regression, the presence of any NPi < 3 was independently associated with the development of DCI [OR 4.07 (95% CI 1.33–12.40)] when adjusted for Fisher scale on admission [OR 2.09 (95% CI 1.02–4.28)] and poor clinical grade on admission [OR 0.73 (95% CI 0.23–2.36)]. The presence of any NPi < 3 was not independently associated with unfavorable outcome [OR 1.58 (95% CI 0.48–5.23)] when adjusted for DCI [OR 8.93 (95% CI 2.33–34.18)] and poor clinical grade on admission [OR 6.72 (95% CI 1.84–24.54)].

Conclusion: Automated pupilometry is a non-invasive technique that can help in the diagnosis of delayed cerebral ischemia in aSAH patients but its role in predicting outcome remains debatable.

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000273

Brain injury, endothelial injury and inflammatory markers in COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**: 000273

Introduction: Prominent marks of COVID-19 are the inflammatory response and endotheliopathy. However, the effect of COVID-19 on brain injury is also emerging. The relationship of brain injury with the above mechanisms has not been elucidated. On the other hand, erythropoietin (EPO) has been proposed to improve respiration, counterbalance the inflammation caused by the cytokine storm, and exhibit neuroprotective and neuroregenerative actions.

Objectives: We aimed to study brain injury and its probable associations with the inflammatory response in COVID-19.

Methods: The brain injury markers s100b and neuronal specific enolase (NSE), EPO, the interleukins (IL)-6, IL-8, IL-10 and tumour necrosis factor-α (TNF-α), and the established marker of infection, soluble urokinase-type plasminogen activator receptor (suPAR), were measured in the sera of 17 moderate/severe COVID-19 patients, and 53 critically ill, mechanically ventilated COVID-19 patients.

Results: Critically ill COVID-19 patients presented with higher IL-8, TNF-α, s100b, NSE and EPO levels compared to the ward patients. suPAR levels were comparable between the 2 severity groups. suPAR levels strongly correlated with EPO, IL-6, and IL-8 ($0.46 < r < 0.49$, $p < 0.0001$, respectively), and moderately with s100b and IL-10 levels ($0.24 < r < 0.31$, $p < 0.05$) while s100b positively correlated with NSE, IL-8 and TNF-α ($0.27 < r < 0.37$, $p < 0.05$). Interestingly, s100b levels on admission were higher in COVID patients who died compared to survivors (4.25 ng/ml vs. 2.52 ng/ml, p = 0.001). In the generated ROC curves, the prognostic value of s100b was comparable to that of suPAR.

Conclusion: s100b apart from a COVID-19 severity marker, looks like a promising poor outcome biomarker in both critically ill COVID-19 patients and patients hospitalized in the ward.

000286

Risk factors associated with disability and mortality in patients in a neurotraumatic ICU with decompressive craniectomy after discharge. A eight year prospective study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000286

Introduction: Second level therapeutic actions for controlling intracranial hypertension (ICH) proposed by the European Brain Trauma Foundation include barbiturates, moderate hypothermia and decompressive craniectomy (DC), but outcomes are controversial. Our aim was to evaluate the factors associated with disability and mortality after ICU discharge in patients undergoing DC.

Objectives: To assess the factors associated with disability and mortality, after ICU discharge, in DC patients after 8 years.

Methods: Prospective study of patients admitted from January 1, 2013 to December 2020 who required DC. DC was performed due ICH refractory to medical treatment. We analyzed: main admission diagnosis; demographic data; neurological data (clinical examination and Glasgow Coma Score: GCS); hypotension; type of craniectomy and DC complications; Rankin scale, and Glasgow outcome scale (GOS) at 30, 60 days after ICU admission, at ICU discharge and 6 months after ICU discharge; preoperative serum lactate levels; hypo and hyperglycemia; application of mannitol or hypertonic saline solution before and after DC; leukocytes and platelets previous and after DC and other factors related to prognosis. Univariate analysis of disability (Rankin > 3) and mortality in ICU, 60 days after ICU admission and 6 months after ICU discharge were performed. Statistical significance was set at $p \leq 0.05$.

Results: Forty seven DC patients were collected. Demographic data and types of admission are shown in Table 1. Most DC were subarachnoid hemorrhages (SAH) 25 (53.2)). and brain trauma injury (BTI) 16 (34.8)%).The most frequent complications were hydrocephalus 21 (45.6%) and reoperation due to complications 16 (35.6% % of them). Eight patients died at ICU discharge (14,6%), 5 (62,5%) of them were SAH. Five DC patients with BTI died, 2 of them at ICU discharge. Rankin score at ICU discharge was 5 and GOS 3. Rankin score at 6 months after ICU discharge was 5 and GOS was 3. We did not find any significant risk factors associated with disability, six months after ICU discharge. Mortality 6 months after discharge was significantly associated with bilateral pupillary reactivity prior to DC (Table 2).

Table 1. Univariate analysis of DC disability at ICU discharge

	Overall N = 47	Rankin at ICU discharge < 3 N = 9	Rankin at ICU discharge =>3 N = 38	
Age (years)	47 (36 - 56)	42 (39 - 56)	47 (36 - 55)	0.989
Sex female	29 (61.7)	5 (55.6)	24 (63.2)	0.716
APACHE-II	22 (19 - 25.5)	25 (21.5 - 26.5)	22 (18.5 - 24.5)	0.282
GCS at admission	8.5 (5.5 - 13.2)	12 (5 - 13)	8 (6 - 13.5)	0.930
GCS at ICU admission	3 (3 - 7)	3 (3 - 10)	3 (3 - 7)	0.613
ICU-Deaths	8 (17.4)	0	8 (21.1)	0.317
Hospital-Deaths	2 (4.7)	0	2 (5.7)	1
Discharge of the Hospital-Deaths	4 (10.0)	0	4 (12.1)	1
Deaths	14 (29.8)	0	14 (36.8)	0.042
Arterial hypertension	8 (17.0)	3 (33.3)	5 (13.2)	0.167
Dislypemia	8 (17.0)	2 (22.2)	6 (15.8)	0.639
Tumor	3 (6.5)	1 (12.5)	2 (5.3)	0.444
SAH	25 (53.2)	5 (55.6)	20 (52.6)	1
Stroke Malignant middle cerebral artery	11 (23.4)	1 (11.1)	10 (26.3)	0.663
Acute subdural hematoma	15 (32.6)	3 (37.5)	12 (31.6)	1
Obliteration of the cisterns of the base	18 (39.1)	1 (12.5)	17 (44.7)	0.124
Focal contusion with edema and expansivity	18 (39.1)	5 (62.5)	13 (34.2)	0.232
Evacuated injury	9 (19.6)	2 (25.0)	7 (18.4)	0.645
BTI	16 (34.8)	5 (55.6)	11 (29.7)	0.241
Transfusion prior to DC	9 (20.0)	1 (12.5)	8 (21.6)	1
Pre-craniectomy seizures	6 (13.3)	0	6 (16.2)	0.572
Bilateral areactive mydriasis prior to DC	3 (6.7)	0	3 (8.1)	1
Both reactive pupils prior to DC	31 (68.9)	6 (85.7)	25 (65.8)	0.407
One reactive pupil prior to DC	7 (15.9)	0	7 (18.4)	0.568
None-reactive pupils prior to DC	5 (12.8)	1 (14.3)	4 (12.5)	1
Midline shift on CT at admission	5 (0 - 9)	1.5 (0 - 8.5)	5 (0 - 9)	0.557
Number of Platelets prior to DC	224 (183 - 264)	258 (246 - 293)	214 (182 - 256)	0.142

Data are means and medians (IQR) y frequences (%) SAH:subaracnoid hemorrhage;BTI:brain trauma injured; OTI: orotracheal intubation; DC: decompressive craniectomy. T

Table 2. Univariate analysis of DC mortality 6 months after ICU discharge

	Alives N = 33	Deaths N = 14	P-valor
Age (years)	46.6 ± 14.5	48.5 ± 13.0	0.671
Sex male	22 (66.7)	7 (50.0)	0.282
APACHE-II	22 (18 - 25)	22 (20 - 25)	0.475
Arterial hypertension	7 (21.2)	1 (7.1)	0.405
Tumor	2 (6.2)	1 (7.1)	1
SAH	18 (54.5)	7 (50.0)	0.775
Stroke Malignant middle cerebral artery	6 (18.2)	5 (35.7)	0.263
Acute subdural hematoma	11 (34.4)	4 (28.6)	1
Obliteration of the cisterns of the base	12 (37.5)	6 (42.9)	0.732
Focal contusion with edema and expansivity	15 (46.9)	3 (21.4)	0.104
Evacuated injury	6 (18.8)	3 (21.4)	1
BTI	11 (34.4)	5 (35.7)	1
Ninguna pupila reactiva previo CD	3 (9.7)	2 (14.3)	0.639
Transfusion prior to DC	6 (18.8)	3 (23.1)	0.268
Pre-craniectomy seizures	3 (9.4)	3 (23.1)	0.334
Bilateral areactive mydriasis prior to CD	2 (7.1)	1 (9.1)	1
Both reactive pupils prior to DC	25 (80.7)	6 (42.9)	0.017
One reactive pupil prior to DC	3 (10.0)	4 (28.6)	0.184
None-reactive pupils prior to DC	3 (9.7)	2 (14.3)	0.639
ICU-Deaths	-	8 (57.1)	-
Hospital-Deaths	-	2 (14.3)	-
Discharge of the Hospital-Deaths	-	4 (28.6)	-
Midline shift on CT at admission	4 (0 - 8)	7 (1 - 10)	0.218
GCS on admission	8 (5 - 13.5)	9 (6 - 13)	0.928
GCS at ICU admission	3 (3 - 8)	3 (3 - 5)	0.806
Number of Platelets prior to DC	224 (188 - 263)	228 (164 - 280)	0.754

Data are means and medians (IQR) y frequences (%) SAH: subarachnoid hemorrhage;BTI:brain trauma injured; ; DC: decompressive craniectomy.

Conclusion: DC patients showed low ICU mortality (14,6%). DC Patients with BTI had also low rate of mortality of 12,5% at ICU discharge. Rankin and GOS reflected moderate / severe disability of these patients, at ICU and 6 months after ICU discharge. Mortality, 6 months after discharge, was significantly associated with bilateral pupillary reactivity prior to DC.

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Disability associated risk factors in patients with subarachnoid hemorrhage in a neurotraumatic ICU: eight year study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000352

Introduction: Aneurysmal subarachnoid hemorrhage (SAH) is a worldwide health burden with serious outcomes such as permanent disability. It is important to learn the disability risk factors and identify those potentially preventable, to reduce them.
Objectives: To assess disability risk factors in patients admitted with subarachnoid hemorrhage (SAH), admitted in a neurotraumatic ICU.
Methods: Prospectively collected data of patients admitted from October, 2013 to March 2021 to a 10-bed Neurotraumatic ICU. We analyzed: main diagnosis at admission; demographic data, including sex and race; neurological data (clinical examination, pupils reactivity and size, and Glasgow Coma Score (GCS); location and aneurysm size; presence of intracranial hematoma (ICH); presence and volume of intraventricular bleeding; days to develop vasospasm; development of delayed cerebral ischemia (DCI); Fisher scale, modified Fisher scale, Hunt and Hess scale, Word Federation of Neurosurgeons (WFNS) scale; presence of vasospasm in doppler or arteriography; delayed of admission in ICU; treatment of the aneurysm; complications, including infections; Glasgow Outcome Scale (GOS) at ICU discharge and 6 months after ICU discharge and several other risk factors. Disability was defined as GOS ≤ 3. In order to identify those factors that maintain independent association with disability, a multivariate logistic regression analysis were performed. It was considered significant if $p \leq 0.05$.To determine the discriminatory capacity of the Score, an analysis of the receiver operating characteristics (ROC) was performed. The diagnostic capacity of the score was assessed using the area under the ROC curve, which was estimated using a 95% confidence interval. For the chosen cut-off point, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated.
Results: Among 223 SAH admitted patients, 84(37.6%) had GOS ≤ 3. DCI was not significantly different between studied groups (Table 1). Thirty four (15,2%) died at ICU discharge and 16 (7,2%) died in hospital. Decompresive craniectomy was performed in 12 (5.4%) SAH patients, all of them with GOS ≤ 3. The independent risk factors associated with disability were: Apache II at ICU admission per unit OR (95% CI) 1.180 (1.100; 1.265); Hunt and Hess score (HUNTHESS) OR: 1.450 (1.084; 1.939) and mechanical ventilation (MV) (VMgt7D) > 7 days OR: 4.534 (1.937; 10.611) (Table 2).

$$\Pr(GOS \leq 3) = \frac{\exp(-4.489 + 0.165 \times APACHE_{ING} + 1.512 \times VMgt7D + 0.372 \times HUNTHESS)}{1 + \exp(-4.489 + 0.165 \times APACHE_{ING} + 1.512 \times VMgt7D + 0.372 \times HUNTHESS)}$$

From the logistic model the next Score was deduced (Fig. 1):
The area under the curve (AUC) was 0.905 95% IC (0.862;0.948). Cut-off point:0.4172;specificity: 87.6 [80.9; 92.6]; sensitivity 84.5 [75.0; 91.5]; NPV: 90.2 [83.9; 94.7]; PPV: 80.7 [70.9; 88.3] (Fig. 2)

Table 1. Characteristics of the patients: overall and according to the presence or absenc of disability (*GOS* ≤ 3)

		GOS≤ 3		
	Overall N = 223	No N = 139	Yes N = 84	*P*-value
Age (years)	56.1 ± 14.0	53.6 ± 12.8	60.3 ± 15.0	< .001
Sex female	147 (65.9)	92 (66.2)	55 (65.5)	0.914
Apache-II at admission	14.1 ± 7.8	10.3 ± 5.7	20.3 ± 6.6	< .001
Deaths	49 (22.0)	3 (2.2)	46 (54.8)	< .001
ICU-Deaths	34 (15.2)	0	34 (40.5)	< .001
Hospital-Deaths	16 (7.2)	3 (2.2)	13 (15.5)	< .001
MV>7days	73 (32.7)	15 (10.8)	58 (69.0)	< .001
Arterial hypertension	101 (45.3)	54 (38.9)	47 (56.0)	0.013
Number of platelets at ICU admission	20 (9.0)	8 (5.8)	12 (14.3)	0.031
Urgent surgery at ICU admission	31 (13.9)	14 (10.1)	17 (20.2)	0.033
SDD	88 (39.6)	32 (23.2)	56 (66.7)	< .001
Oriented	112 (50.5)	94 (68.1)	18 (21.4)	< .001
Alert	124 (55.6)	98 (70.5)	26 (30.9)	< .001
Confused	36 (16.1)	18 (12.9)	18 (21.4)	0.095
Stuporous	53 (23.8)	17 (12.2)	36 (42.9)	< .001
Bilateral mydriasis	8 (3.6)	1 (0.7)	7 (8.3)	0.005
Anisochoric pupils	26 (11.7)	10 (7.2)	16 (19.1)	0.008
Isochoric pupils	191 (85.7)	128 (92.1)	63 (75.0)	< .001
One reactive pupil	12 (5.4)	5 (3.6)	7 (8.3)	0.139
Both reactive pupil	193 (86.5)	128 (92.1)	65 (77.4)	0.002
None reactive pupil	14 (6.3)	4 (2.9)	10 (11.9)	0.007
Posterior inferior cerebellar artery anurysm	9 (4.0)	3 (2.2)	6 (7.1)	0.084
Aneurysm clipping	42 (18.8)	20 (14.4)	22 (26.2)	0.029
Decompressive craniectomy	12 (5.4)	0	12 (14.3)	< .001
External ventricular device	107 (48.0)	42 (30.2)	65 (77.4)	< .001
Stroke	64 (28.7)	26 (18.7)	38 (45.2)	< .001
Hydrocephalus	90 (40.4)	33 (23.7)	57 (67.9)	< .001
ICH	57 (25.6)	22 (15.8)	35 (41.7)	< .001
Frontal ICH	37 (16.6)	9 (6.5)	28 (33.3)	< .001
Temporal ICH	26 (11.7)	10 (7.2)	16 (19.1)	0.008
Acute Cerebral Ischemia	21 (9.4)	6 (4.3)	15 (17.9)	< .001
Delayed Cerebral Ischemia	52 (23.3)	28 (20.1)	24 (28.6)	0.149
Ventriculitis	20 (9.0)	10 (7.2)	10 (11.9)	0.233
SOFA admission	2 (0 - 6)	1 (0 - 3)	7 (3 - 9)	< .001
Fisher scale	4 (3 - 4)	3 (2 - 4)	4 (4 - 4)	< .001
Fisher modified scale	4 (3 - 4)	3 (2 - 4)	4 (3 - 4)	< .001
Hunt and Hess scale	2 (1 - 4)	1 (1 - 2)	4 (2 - 5)	< .001
WFNS scale	2 (1 - 4)	1 (1 - 2)	4 (2 - 5)	< .001
APACHE- Vasospasm	14 (8 - 18)	12 (7 - 17)	18 (15 - 23)	< .001
SOFA- Vasospasm	3 (1 - 6)	2 (1 - 4)	6 (4 - 9)	< .001
Delayed admission after bleeding	10 (2 - 24)	9 (2 - 24)	12 (4 - 24)	0.287
GCS on site	15 (13 - 15)	15 (14 - 15)	13 (7 - 15)	< .001
GCS in emergency room	14 (9 - 15)	15 (14 - 15)	9 (6 - 14)	< .001
GCS at ICU admission	14 (5 - 15)	15 (12 - 15)	6 (3 - 10)	< .001

Data are means ± DS, medians (RIQ) y frequencies (%). MV: mechanical ventilation; ICH: intracranial heamtoma; SDD: selectiv digestive decontamination.

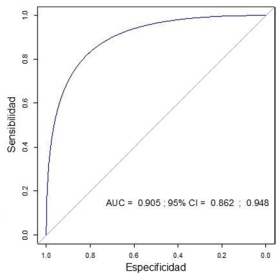
Table 2. Multivariate logistic regression analysis GOS≤ 3 at ICU discharge

	P	BIC	Odd-Ratio (95% IC)
Apache-II at admission (per unit)	< 0.001	206.4	1.180 (1.100 ; 1.265)
Hunt y Hess score	0.012	186.5	1.450 (1.084 ; 1.939)
Mechanical ventilation >7 days	< 0.001	192.4	4.534 (1.937 ; 10.611)

Variables were selected using the best subset regression with the bayesian information criteria (BIC)

(*) Likelihood ratio test

(**) BIC value if the factor is removed from the model (BIC is a measure of lack of fitted). The BIC for the full model is 185.7. Thus, if a factor is removed from the model, the resulting model is worse according to the BIC.



Conclusion: In SAH patients admitted to a neurotraumatic ICU, risk factors that were independently associated with disability were: Apache II at ICU admission per unit, Hunt and Hess score and MV > 7 days. A predictive score was obtained.

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Delayed cerebral ischemia associated risk factors in patients with subarachnoid hemorrhage in a neurotraumatic ICU: a eight-year study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000353

Introduction: Delayed cerebral ischemia (DCI) is a major contributor to the high morbidity and fatality case rates of aneurysmal subarachnoid hemorrhage (SAH). About 30% of the SAH patients present DCI but it is difficult to predict which patients will develop it.

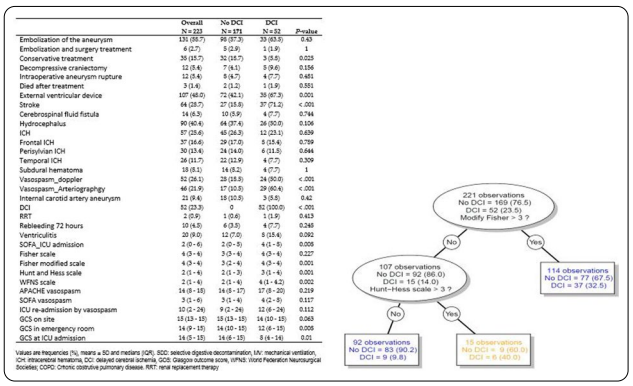
Objectives: To prospectively assess the DCI risk factors in patients with SAH, admitted to a neurotraumatic ICU.

Methods: Prospectively collected data of patients admitted from October, 2013 to March 2021 to a 10-bed Neurotraumatic ICU. We analyzed: main diagnosis at admission; demographic data including sex and race; neurological data (clinical examination, pupils reactivity and size, and Glasgow Coma Score: GCS; localization and aneurysm size; presence of intracranial hematoma (ICH); days to develop vasospasm; development of DCI; Fisher scale, Modified Fisher scale (MFS), Hunt and Hess scale (HHS), Word Federation of Neurosurgeons (WFNS) scale; presence of vasospasm in doppler or arteriography; delayed of admission in ICU; treatment of the aneurysm; complications, including infections; Glasgow Outcome Scale (GOS) at ICU discharge and 6 months after ICU discharge and several other risk factors. A univariate analysis of DCI was performed To obtain a predictive rule for the DCI, a model for the prediction was obtained using the classification and regression trees (CART) procedure [1]. CART classifies data using a sequence of if–then rules. The basis of the decision tree algorithms is the binary recursive partitioning of the data. At each terminal node, the probability of DCI was estimated as the proportion of patients belonging to that node that developed the event. The tree was constructed according to the following algorithm: in the first stage, the tree grows until all cases are correctly classified, and in the second stage, we used the tenfold cross-validation method of successive pruning [1]. Finally, the tree that minimized the error measurement (deviance) was chosen. For this predictor the corresponding ROC curve was obtained and the AUC was estimated by means of a 95% CI.

Results: Two hundred twenty three SAH patients were collected, 52 (23,31%) of them developed DCI. Demographic data and types of admission are shown in Table 1a and 1b. Anterior communicating (Aco) artery aneurysms were the most frequently found and most of them were located in the left side.The most frequent DCI patient complications were stroke 64 (28.7%) and hydrocephalus 90 (40.4%). Thirty-four (15.2%) of the SAH patients died. Eleven (21.1%)of the DCI patients died. There was not statistical significant difference in mortality in DCI vs SAH patients. Classification tree showed: Classification tree showed:MFS < 3 and HHS < 3 have probabilities of 90,2% of no DCI. The AUC was 0.695 (0.621–0.750) and had a high negative predicitive for DCI (0.9 for a cutoff: 0.2) (Fig. 1).

- Table 1 a. Characteristics of the patients: overall and according to DCI

	Overall N = 223	No DCI N = 171	DCI N = 52	*P*-value
Age (years)	56.1 ± 14.0	56.8 ± 14.2	53.8 ± 13.4	0.173
Sex female	147 (65.9)	108 (63.2)	39 (75.0)	0.115
Apache-II at admission	14.1 ± 7.8	13.5 ± 7.9	16.2 ± 7.0	0.025
Death	49 (22.0)	35 (20.5)	14 (26.9)	0.325
Death at ICU discharge	34 (15.2)	23 (13.4)	11 (21.1)	0.176
Hospital death	16 (7.2)	12 (7.0)	4 (7.7)	1
Death	2 (0.9)	2 (1.2)	0	1
MV > 7 days	73 (32.7)	48 (28.1)	25 (48.1)	0.007
Arterial hypertension	101 (45.3)	74 (43.3)	27 (51.9)	0.273
Diabetes	26 (11.7)	20 (11.7)	6 (11.5)	0.975
Dyslipemia	53 (23.8)	41 (24.0)	12 (23.1)	0.894
COPD	5 (2.2)	5 (2.9)	0	0.593
Chronic renal failure	5 (2.2)	4 (2.3)	1 (1.9)	1
Neoplasm	9 (4.0)	9 (5.3)	0	0.121
Malnutrition	3 (1.4)	3 (1.8)	0	1
Smoker	87 (39.0)	64 (37.4)	23 (44.2)	0.378
Caucasian race	212 (95.1)	163 (95.3)	49 (94.2)	0.721
Platelet inhibitors	20 (9.0)	17 (9.9)	3 (5.8)	0.579
Emergency surgery at admission	31 (13.9)	20 (11.7)	11 (21.1)	0.084
Previous surgery	17 (7.6)	15 (8.8)	2 (3.9)	0.372
SDD	88 (39.6)	58 (34.1)	30 (57.7)	0.002
Oriented	112 (50.5)	99 (58.2)	13 (25.0)	< .001
Alert	124 (55.6)	106 (62.0)	18 (34.6)	< .001
Confused	36 (16.1)	26 (15.2)	10 (19.2)	0.49
Stuporous	53 (23.8)	30 (17.5)	23 (44.2)	< .001
Bilateral mydriasis	8 (3.6)	6 (3.5)	2 (3.9)	1
Anisochoric pupils	26 (11.7)	15 (8.8)	11 (21.1)	0.015
Isochoric pupils	191 (85.7)	150 (87.7)	41 (78.8)	0.11
One reactive pupil	12 (5.4)	7 (4.1)	5 (9.6)	0.156
Both reactive pupils	193 (86.5)	151 (88.3)	42 (80.8)	0.163
Bilateral aneurysm	12 (5.4)	9 (5.3)	3 (5.8)	1
Aneurysm in the midline	62 (27.8)	44 (25.7)	18 (34.6)	0.21
Anterior cerebral artery aneurysm	18 (8.1)	13 (7.6)	5 (9.6)	0.576
Anterior communicating artery aneurysm	67 (30.0)	51 (29.8)	16 (30.8)	0.896
Posterior communicating artery aneurysm	31 (13.9)	20 (11.7)	11 (21.1)	0.084
Anterior cerebral artery aneurysm	8 (3.6)	6 (3.5)	2 (3.9)	1
Ophthalmic artery aneurysm	1 (0.5)	0	1 (1.9)	0.233
Anterior cerebral artery aneurysm	30 (13.4)	20 (11.7)	10 (19.2)	0.163
Posterior cerebral artery aneurysm	9 (4.0)	6 (3.5)	3 (5.8)	0.439
Basilar artery aneurysm	15 (6.7)	13 (7.6)	2 (3.9)	0.53
Posterior inferior cerebellar artery aneurysm	9 (4.0)	8 (4.7)	1 (1.9)	0.689
Carotid carotid aneurysm	20 (9.0)	14 (8.2)	6 (11.5)	0.421
Multiple aneurysm	34 (15.2)	22 (12.9)	12 (23.1)	0.073
Aneurysm clipping	42 (18.8)	26 (15.2)	16 (30.8)	0.012
Lumbar drainage	3 (1.4)	2 (1.2)	1 (1.9)	0.551



	Overall N = 223	No DCI N = 171	DCI N = 52	*P*-value
Embolization of the aneurysm	131 (58.7)	96 (57.3)	33 (63.5)	0.43
Embolization and surgery treatment	6 (2.7)	5 (2.9)	1 (1.9)	1
Conservative treatment	35 (15.7)	31 (18.7)	3 (5.8)	0.025
Decompressive craniectomy	12 (5.4)	7 (4.1)	5 (9.6)	0.156
Intraoperative aneurysm rupture	12 (5.4)	8 (4.7)	4 (7.7)	0.481
Died after treatment	3 (1.4)	2 (1.2)	1 (1.9)	0.551
External ventricular device	107 (48.0)	72 (42.1)	35 (67.3)	0.001
Stroke	64 (28.7)	37 (21.6)	37 (71.2)	< .001
Cerebrospinal fluid fistula	14 (6.3)	10 (5.9)	4 (7.7)	0.746
Hydrocephalus	90 (40.4)	64 (37.4)	26 (50.0)	0.106
ICH	57 (25.6)	45 (26.3)	12 (23.1)	0.639
Frontal ICH	37 (16.6)	29 (17.0)	8 (15.4)	0.759
Perisylvian ICH	30 (13.4)	24 (14.0)	6 (11.5)	0.644
Temporal ICH	26 (11.7)	22 (12.9)	4 (7.7)	0.309
Subdural hematoma	18 (8.1)	14 (8.2)	4 (7.7)	1
Vasospasm_doppler	52 (26.1)	28 (18.8)	24 (50.0)	< .001
Vasospasm_Arteriography	46 (21.9)	17 (10.8)	29 (60.4)	< .001
Internal carotid artery aneurysm	21 (9.4)	15 (10.5)	3 (5.8)	0.42
DCI	52 (23.3)	0	52 (100.0)	< .001
RRT	2 (0.9)	1 (0.6)	1 (1.9)	0.413
Rebleeding 72 hours	10 (4.5)	6 (3.5)	4 (7.7)	0.248
Ventriculitis	20 (9.0)	12 (7.0)	8 (15.4)	0.092
SOFA_ICU admission	2 (0 - 6)	2 (0 - 5)	4 (1 - 8)	0.005
Fisher scale	4 (3 - 4)	3 (3 - 4)	4 (3 - 4)	0.227
Fisher modified scale	4 (3 - 4)	3 (2 - 4)	4 (3 - 4)	0.001
Hunt and Hess scale	2 (1 - 4)	2 (1 - 3)	3 (3 - 4)	0.001
WFNS scale	2 (1 - 4)	2 (1 - 4)	4 (1 - 4.2)	0.002
APACHE vasospasm	14 (8 - 18)	14 (8 - 17)	17 (8 - 20)	0.219
SOFA vasospasm	3 (1 - 6)	3 (1 - 4)	4 (2 - 8)	0.117
ICU re-admission by vasospasm	10 (2 - 24)	9 (2 - 24)	12 (6 - 24)	0.112
GCS on site	15 (13 - 15)	15 (13 - 15)	14 (10 - 15)	0.063
GCS in emergency room	14 (9 - 15)	14 (10 - 15)	12 (6 - 15)	0.009
GCS at ICU admission	14 (5 - 15)	14 (6 - 15)	8 (4 - 14)	0.01

Values are frequencies (%), means ± SD and medians (IQR). SDD: selective digestive decontamination, MV: mechanical ventilation, ICH: intracerebral hematoma, DCI: delayed cerebral ischemia, GCS: Glasgow outcome score, WFNS: World Federation Neurosurgical Societies, COPD: Chronic obstructive pulmonary disease, RRT: renal replacement therapy

Conclusion: Our data show 23,31% of our studied patients had DCI. Classification tree showed a high negative predicitive for DCI (0.9 for a cutoff: 0.2).Finally, mortality was not significantly greater in the studied versus total SAH patients.

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1. References and Grant acknowledgments [1] Breiman L, Freidman JH, Olshen RA, Stone CJ (1984) Classification and regression trees. Wadsworth, Belmon

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Effects of positive end-expiratory pressure on intracranial pressure and autoregulation in mechanically ventilated brain injured patients monitored by ICM+

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Intensive Care Medicine Experimental 2022, **10(2)**: 000387

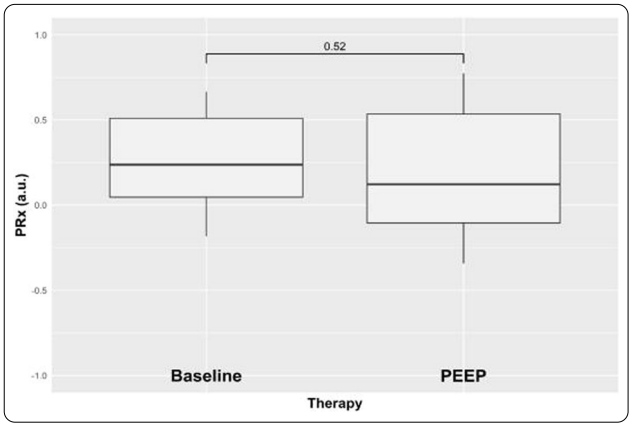
Introduction: Cerebral autoregulation is the mechanism that allows to maintain the stability of cerebral blood flow despite changes in cerebral perfusion pressure. After brain injury, cerebral autoregulation can be impaired, leaving the brain vulnerable to further insults.
Maneuvers which increase intrathoracic pressure such as the application of positive end-expiratory pressure (PEEP) have been always challenged in brain injured patients, for the risk of increased intracranial pressure (ICP) and autoregulation [1].
The primary aim of this study is to assess the effect of PEEP on ICP and cerebral oxygenation and autoregulation. Two different levels of PEEP (5 and 15 cmH20) were evaluated.
Methods: Prospective, observational study including adult mechanically ventilated patients with brain injury requiring invasive ICP. ICM+ (Intensive Care Monitoring) is a clinical research software that offers real time analysis able to obtain an index which expresses cerebral autoregulation (PRx) [2]. This index together with ICP, cerebral oxygenation (rSO2) and arterial blood gas values was analyzed at PEEP 5 and 15 cmH20.

Characteristics of patients	All patients (n=15)
Demographics	
Gender, male [n, (%)]	10 (66,7%)
Age [years], median [IQR]	59 [21-77]
BMI [kg/m^2], median [IQR]	24 [18-27]
PBW [kg], median [IQR]	67 [46-75]
Comorbidities	
Respiratory disease [n, (%)]	0 (0)
Cardiovascular disease [n, (%)	3 (20)
Neurologic disorders [n, (%)]	2 (13.3)
Hypertension [n, (%)]	4 (26.7)
Smoker [n, (%)]	3 (20)
Psychiatric disorders [n, (%)]	3 (20)
Reason for ICU admission, [n, (%)]	
TBI	4 (26.7)
SAH	5 (33.3)
ICH	6 (40)
GCS score at ER admission, median [IQR]	6 [3-14]
Pupils Anisocoria at ER admission, [n, (%)]	4 (26.7)

Table 1. Characteristics of the patients included in the study.
Abbreviations: IQR, Interquartile range; n=number; BMI, body mass index; PBW, predicted body weight; ER, Emergency Room; TBI, traumatic brain injury; SAH, subarachnoid hemorrhage; ICH, intracranial hemorrhage; GCS, Glasgow Coma Scale

	Baseline
ICP	9.0 (5.9-13.1)
CPP	82.3 (70.3-87.8)
ABP	88.7 (80.6-95.9)
PRx	0.24 (0.05-0.51)

Results: Fifteen patients were included in this study. The median age was 59 [Interquartile range IQR = 21–77] and 10 (66.7%) were male. PEEP increase from 5 to 15 cmH20 did not lead to an increase of ICP (from 9 [IQR = 6–13] to 11 [IQR = 9–14], p = 0.053) but increased cerebral oxygenation (from 63 [IQR = 61–67] to 66 [IQR = 63–69], p = 0.031), without affecting cerebral autoregulation (PRx from 0.26 [0.08 to 0.32] to 0.24 [IQR = 0.09–0.29], p = 0.52).



Conclusion: PEEP increase from 5 to 15 cmH_2O can be safe in brain injured patients. Further larger studies are necessary to validate our results.

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Acknowledgements None.

000391

Effects of hyperoxygenation on cerebral autoregulation and cerebral oxygenation in traumatic brain injured patients monitored by ICM+

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Intensive Care Medicine Experimental 2022, **10(2)**: 000391

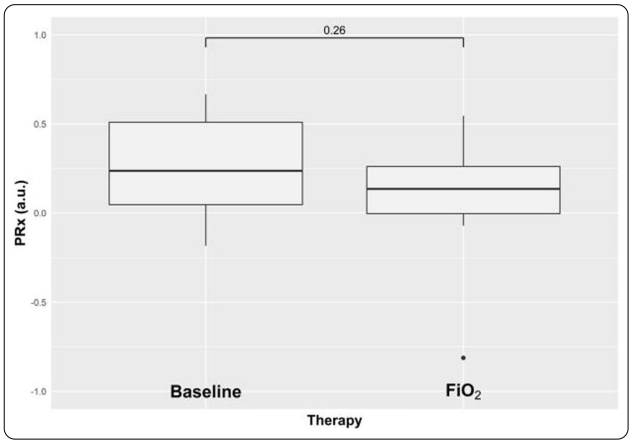
Introduction: According to some authors, hyperoxygenation is considered potentially harmful due to the development of oxidative damage, promoted by the production of radical oxygen species, and arteriolar vasoconstriction secondary to plasma hyperoxia. The aim of this study is to assess the role of hyperoxygenation in brain injured patients and to evaluate possible alterations in intracranial pressure and cerebral autoregulation following induced hyperoxemia.
Methods: Single center, observational prospective study conducted at San Martino Policlinico Hospital, Genoa, Italy. Traumatic brain injured patients with invasive monitoring of intracranial pressure (ICP) were included in the study. We evaluated the effects of hyperoxygenation (inspired fraction of oxygen = FiO_2 100%) on cerebral autoregulation, measured through PRx with ICM+, on cerebral oxygenation, through Near infrared Spectroscopy (NIRS), and on invasive ICP.

Characteristics of patients	All patients (n=15)
Demographics	
Gender, male [n, (%)]	10 (66,7%)
Age [years], median [IQR]	59 [21-77]
BMI [kg/m^2], median [IQR]	24 [18-27]
PBW [kg], median [IQR]	67 [46-75]
Comorbidities	
Respiratory disease [n, (%)]	0 (0)
Cardiovascular disease [n, (%)	3 (20)
Neurologic disorders [n, (%)]	2 (13.3)
Hypertension [n, (%)]	4 (26.7)
Smoker [n, (%)]	3 (20)
Psychiatric disorders [n, (%)]	3 (20)
Reason for ICU admission, [n, (%)]	
TBI	4 (26.7)
SAH	5 (33.3)
ICH	6 (40)
GCS score at ER admission, median [IQR]	6 [3-14]
Pupils Anisocoria at ER admission, [n, (%)]	4 (26.7)

Table 1. Characteristics of the patients included in the study.
Abbreviations: IQR, Interquartile range; n=number; BMI, body mass index; PBW, predicted body weight; ER, Emergency Room; TBI, traumatic brain injury; SAH, subarachnoid hemorrhage; ICH, intracranial hemorrhage; GCS, Glasgow Coma Scale

	Baseline
ICP	9.0 (5.9-13.1)
CPP	82.3 (70.3-87.8)
ABP	88.7 (80.6-95.9)
PRx	0.24 (0.05-0.51)

Results: Fifteen patients with acute brain injury were included in the analysis. Mean age was 59 years [Interquartile Range, IQR = 21–77] (Table 1) and 66.7% were male. The use of hyperoxygenation resulted in increased cerebral oxygenation (from 58% [IQR = 56–65] to 64% [IQR = 62–67], $p < 0.001$) but did not alter intracranial pressure (from 9 [6–13] to 10 [5–16], $p = 0.231$), cerebral autoregulation (from 0.24 [IQR = 0.05–0.51] to 0.22 [IQR = 0.12–0.48], $p = 0.26$) or brain injured patient outcome.



Conclusion: Hyperoxygenation is not harmful, as previously described, and promotes cerebral oxygenation without compromising cerebral autoregulation.

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Acknowledgements None.

000393

Effects of alveolar recruitment maneuvers on intracranial pressure and autoregulation in mechanically ventilated brain injured patients monitored by ICM+

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Intensive Care Medicine Experimental 2022, **10(2)**: 000393

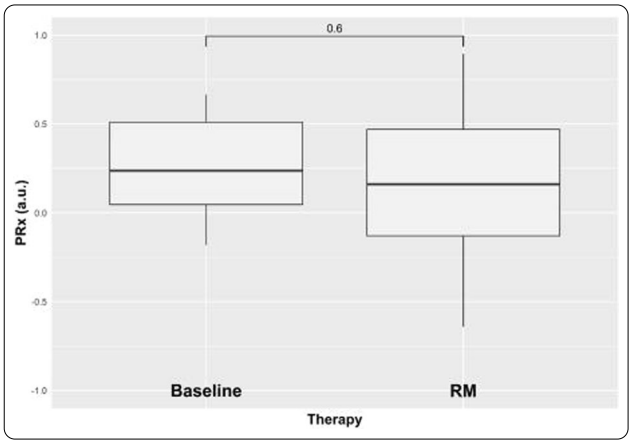
Introduction: Alveolar recruitment maneuvers (RMs) consist of temporary airway pressure increasing during mechanical ventilation in order to open up the collapsed alveoli and raising tidal volume to improve oxygenation. The role of RMs is controversial in brain injured patients: the risks of these maneuvers usually are overdistension and lung damage but more important cerebral hypoperfusion secondary to increased intrathoracic pressures [1]. After brain injury, cerebral autoregulation can be impaired, leaving the brain vulnerable to further insults, especially during RMs. The primary aim of this study is to assess the effect of RMs on ICP, cerebral oxygenation and autoregulation.
Methods: Prospective, observational study including adult mechanically ventilated patients with acute brain injury requiring invasive ICP requiring RMs. All RMs were performed with stepwise increasing levels of PEEP up to 20 cmH20. ICM+(Intensive Care Monitoring) was used to obtain a dynamic index bedside which express cerebral autoregulation (PRx) [2]. PRx, ICP, cerebral oxygenation (rSO_2), arterial blood gas values were analyzed before and after RMs.

Characteristics of patients	All patients (n=15)
Demographics	
Gender, male [n, (%)]	10 (66,7%)
Age [years], median [IQR]	59 [21-77]
BMI [kg/m^2], median [IQR]	24 [18-27]
PBW [kg], median [IQR]	67 [46-75]
Comorbidities	
Respiratory disease [n, (%)]	0 (0)
Cardiovascular disease [n, (%)	3 (20)
Neurologic disorders [n, (%)]	2 (13.3)
Hypertension [n, (%)]	4 (26.7)
Smoker [n, (%)]	3 (20)
Psychiatric disorders [n, (%)]	3 (20)
Reason for ICU admission, [n, (%)]	
TBI	4 (26.7)
SAH	5 (33.3)
ICH	6 (40)
GCS score at ER admission, median [IQR]	6 [3-14]
Pupils Anisocoria at ER admission, [n, (%)]	4 (26.7)

Table 1. Characteristics of the patients included in the study.
Abbreviations: IQR, Interquartile range; n=number; BMI, body mass index; PBW, predicted body weight; ER, Emergency Room; TBI, traumatic brain injury; SAH, subarachnoid hemorrhage; ICH, intracranial hemorrhage; GCS, Glasgow Coma Scale

	Baseline
ICP	9.0 (5.9-13.1)
CPP	82.3 (70.3-87.8)
ABP	88.7 (80.6-95.9)
PRx	0.24 (0.05-0.51)

Results: Fifteen patients were included in this study. The median age was 59 [Interquartile range IQR = 21–77] and 10 (66.7%) were male. RMs did not lead to a change of ICP (from 9 [IQR = 5–13] to 11 mmHg [IQR = 5–17], p = 0.311) cerebral oxygenation (from 59% [IQR = 57–63] to 57% [IQR = 55–61], p = 0.132) and cerebral autoregulation (PRx from 0.21 [IQR = 0.07–0.31] to 0.22 [IQR = 0.1–0.31], p = 0.6).



Conclusion: RMs can be safe in brain injured patients. Additional larger studies are necessary to validate our results.

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Acknowledgements None.

000394

Effects of hyperventilation on cerebral autoregulation and intracranial pressure in brain injured patients monitored by ICM+

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Intensive Care Medicine Experimental 2022, **10(2)**: 000394

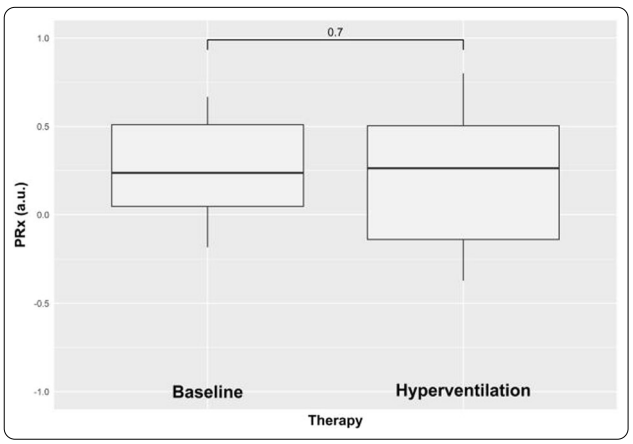
Introduction: Maintenance of cerebral autoregulation and optimal intracranial pressure (ICP) are the main objectives to prevent secondary damage in brain injured patients. The effects of hyperventilation and hypocapnia, currently used in case of refractory intracranial hypertension in these patients are unclear and have been reported by some authors as potentially dangerous as they can alter cerebral oxygenation and dynamics.
Methods: Single center, observational prospective study conducted at San Martino Policlinico Hospital, Genoa, Italy. Brain injured patients with invasive monitoring of ICP were included in the study. We evaluated the effects of mild hyperventilation (target partial pressure of carbon dioxide ($PaCO_2$) = 30–32 mmHg) on cerebral autoregulation, measured through PRx with ICM+, on cerebral oxygenation, through Near infrared Spectroscopy (NIRS), and on invasive ICP.

Characteristics of patients	All patients (n=15)
Demographics	
Gender, male [n, (%)]	10 (66,7%)
Age [years], median [IQR]	59 [21-77]
BMI [kg/m^2], median [IQR]	24 [18-27]
PBW [kg], median [IQR]	67 [46-75]
Comorbidities	
Respiratory disease [n, (%)]	0 (0)
Cardiovascular disease [n, (%)	3 (20)
Neurologic disorders [n, (%)]	2 (13.3)
Hypertension [n, (%)]	4 (26.7)
Smoker [n, (%)]	3 (20)
Psychiatric disorders [n, (%)]	3 (20)
Reason for ICU admission, [n, (%)]	
TBI	4 (26.7)
SAH	5 (33.3)
ICH	6 (40)
GCS score at ER admission, median [IQR]	6 [3-14]
Pupils Anisocoria at ER admission, [n, (%)]	4 (26.7)

Table 1. Characteristics of the patients included in the study.
Abbreviations: IQR, Interquartile range; n=number; BMI, body mass index; PBW, predicted body weight; ER, Emergency Room; TBI, traumatic brain injury; SAH, subarachnoid hemorrhage; ICH, intracranial hemorrhage; GCS, Glasgow Coma Scale

	Baseline
ICP	9.0 (5.9-13.1)
CPP	82.3 (70.3-87.8)
ABP	88.7 (80.6-95.9)
PRx	0.24 (0.05-0.51)

Results: Fifteen patients with acute brain injury were included in the analysis. Mean age was 59 years [Interquartile Range, IQR = 21–77] (Table 1), and 33.3% were female. The use of hyperventilation lead to reduced mean values of ICP (from 29 mmHg [IQR = 24–32] to 21 [IQR = 16–22] $p < 0.001$), but no significant effect was observed on cerebral oxygenation (from 62% [IQR = 59–65] to 61 [60–64], $p = 0.142$) and autoregulation (from 0.24 [IQR = 0.17–0.29] to 0.25 [IQR = 0.16–0.28], $p = 0.7$) (Fig. 1).



Conclusion: Mild, short-term hyperventilation can be safe in traumatic brain injured patients and can reduce ICP without affecting cerebral oxygenation and autoregulation.

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Acknowledgements None.

Neuro-Intensive Care 3

000774

Can we use protective lung ventilation strategies in acute brain injury patients? Preliminary analysis of the BrainVent study

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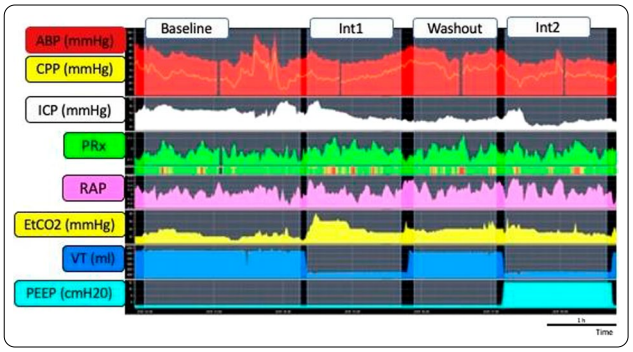
Introduction: It is still unclear whether lung protective ventilation (LPV) can be safely applied to acute brain injury (ABI) patients. Any invasive mechanical ventilation settings in ABI patients should avoid causing increased intracranial pressure (ICP) or deranged cerebral autoregulation (CA). Escalating intrathoracic pressures, changes in arterial oxygenation or carbon dioxide (CO_2) are the main pathophysiological mechanisms involved in the possible impairment of ICP or CA secondary to LPV application in ABI patients.
Objectives: We aimed to investigate the effect of LPV in comparison with conventional ventilator settings on ICP and on CA as measured by the pressure reactivity index PRx, in ABI patients without acute lung injury (ALI). As a secondary objective we aimed to describe the physiological mechanisms implied in those effects.
Methods: BrainVent was a single-centre trial (NCT03278769) running in the ICU at the University Hospital of Northern Norway, Tromsø. Intubated ABI patients without intracranial hypertension or ALI, received two types of ventilatory interventions (cross-over study, Fig. 1): Int1—tidal volume (VT) 6 ml/kg predicted body weight (PBW), PEEP 5 cmH_2O; Int2—VT 6 ml/kg PBW, PEEP 12 cmH_2O. During baseline/washout patients were ventilated with VT 9 ml/Kg and PEEP 5 cmH_2O. CO_2 was kept constant by modulating respiratory rate. Cerebral and respiratory physiological measurements were monitored continuously with ICM + (https://icmplus.neurosurg.cam.ac.uk) and FluxMed software respectively. For each patient, average values of ICP and PRx corresponding to each study period were calculated. Carry-over and period effects were ruled out with linear mixed effect models and baseline comparisons via repeated measurements ANOVA. Values at the intervention were compared with values at the preceding period (baseline/washout). Non inferiority analysis was performed for the ICP investigation. Paired tests were used for PRx analysis. Non parametric tests were used for the secondary objective.
Figure 1 ABP, arterial blood pressure; CPP, cerebral perfusion pressure; ICP, intracranial pressure; PRx, Pressure reactivity index; RAP, compensatory reserve index; $EtCO_2$, end-tidal CO_2; VT, Tidal volume; PEEP, positive end-expiratory pressure.



Results: 27 patients (males 59%) were included in the analysis. Median (IQR) age (years) and BMI were 58 (42.75–65.5) and 26.6 (23.9–28.9) respectively. As compared to baseline/washout, median airway plateau pressure was lower in Int1 (Wilcoxon-test, $p < 0.001$), and mean end-expiratory transpulmonary pressure was higher in Int2 (paired t-test, $p < 0.001$). 8/53 interventions were interrupted for high ICP. Those had lower baseline brain compliance as assessed by the compensatory reserve index RAP (Mann-U, $p = 0.003$). Among the completed interventions, neither average ICP (paired t-test, one tail: $p = 0.987$ for int1; $p = 0.999$ for int2) nor average PRx changed significantly between baseline/washout and intervention (Wilcoxon-test, $p = 0.75$ for int1; paired t-test, $p = 0.56$ for int2).
Conclusion: These pilot results suggest that LPV is feasible in ABI patients, provided continuous neuromonitoring and evaluation of brain compliance is ensured.

000404

The impact of multimodal monitoring and perfusion computed tomography in the diagnosis of delayed cerebral ischemia and prevention of cerebral infarction

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Intensive Care Medicine Experimental 2022, **10(2)**: 000404

Introduction: Delayed cerebral ischemia (DCI) occurs in 20%-30% of patients with aneurysmal subarachnoid hemorrhage (aSAH). The advances in radiologic methods (computed tomography angiography—CTA; perfusion computed tomography—CTP) and in invasive multimodal monitoring (iMMM) could detect reversible DCI and potentially improve outcome of aSAH.
Objectives: To assess whether the use of iMMM and CTA/CTP can reduce the risk of infarction related to DCI.
Methods: This is a retrospective cohort study of patients admitted to the ICU of Erasme Hospital (Brussels, Belgium) with aSAH from 2014–2020. DCI was classified as: clinical definition (Group 1) [1] or based on iMMM and CTP/CTA (Group 2) [2]. The primary outcome was the percentage of patients that developed infarction in the two groups. Secondary outcome was neurological outcome at 3 months (Glasgow outcome scale) and hospital mortality.
Results: Of 230 aSAH patients, 113 (49%) were diagnosed with DCI: 39 (35%) in group 1 and 74 (66%) in group 2. In group 1, 27 (69%) patients developed cerebral infarction, when compared to 41 (55%) patients in group 2 ($p = 0.31$). The use of iMMM/CTA/CTP resulted in an absolute risk reduction of infarction of 14% and a relative risk reduction of infarction of 20%. However, hospital mortality rates (12/39, 31% vs. 27/74, 37%, $p = 0.68$) and the rates of unfavorable outcome in 3 months (26/39, 67% vs. 48/74, 65%, $p = 0.99$) was similar between the two groups.
Conclusion: Modified DCI criteria based on iMMM/CTA/CTP may help to reduce the occurrence of cerebral infarction after aSAH.

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000457

The prognostic role of Neurologic Pupil Index in COVID-19 Patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000457

Introduction: COVID-19 patients are characterized by an excessive inflammatory response, that could affect the autonomic system regulation[1] and, as such, the pupillary activity[2]. Abnormalities of pupillary response, assessed by the Neurologic Pupil Index (NPi) via an automated pupillometer, are associated with neurological deterioration and correlated with poor neurological outcomes[3] in acute brain injury patients. The prognostic role of NPi in COVID-19 patients remains unknown.
Methods: This was a retrospective, observational, monocentric study including COVID-19 patients admitted to the Intensive Care Unit of Erasme Hospital (Bruxelles, Belgium) from June 2020 to March 2022. Only patients with available NPi data were included. NPi was evaluated on admission (lower value of the two eye) and as mean over the ICU stay (mNPi). The primary outcome was the prognostic role of NPi on hospital mortality.
Results: On a total of 356 patients, 218 met the inclusion criteria and were analyzed (median age 61 [50–68] years; 152 patients (70%) were male; 97 patients (44%) died at hospital discharge. The number of NPi measurement over the ICU stay per patient was 18 [6–34]. The median mNPi was similar between non-survivors and survivors (4.6 [4.3–4.7] vs. 4.5 [4.4–4.6]; $p = 0.37$). Also, median values of NPi on admission were similar between groups (4.5 [4.2–4.7] and 4.6 [4.2–4.7]; $p = 0.28$). Also, the proportion of NPi measurements < 3 during the ICU stay were similar between non-survivors and survivors.
Conclusion: In this study, no independent prognostic role of NPi was observed in COVID-19 patients. Further larger prospective studies are needed to better evaluate the role of automated pupillometry in the diagnosis of neurological complications in this setting.

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000466

The effects of $PbtO_2$-guided therapy in traumatic brain injury: a systematic review and meta-analysis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000466

Introduction: Traumatic brain injury (TBI) is a major public health burden, causing death and disability worldwide [1]. Intracranial hypertension [3] and brain hypoxia are the main mechanism of secondary brain injury. As such a management strategies guided by intracranial pressure (ICP) or brain oxygen ($PbtO_2$) monitoring could improve the prognosis of these patients.
Objectives: To summarize the current evidence regarding the impact of $PbtO_2$-guided therapy on the outcome of TBI patients.
Methods: We performed a systematic search of PubMed, SCOPUS and the Cochrane Library databases, following the protocol registered in PROSPERO. Only studies comparing $PbtO_2$/ICP guided-therapy with ICP-guided therapy were selected. Primary outcome was hospital mortality; secondary outcomes included neurological outcome at 3 and/or 6 months, assessed by the Glasgow Outcome Scale.
Results: Out of 6254 retrieved studies, 15 studies (n = 37,245 patients, of which 2184 received $PbtO_2$-guided therapy) were included in the final analysis. When compared to ICP-guided therapy, the use of combined PbO_2/ICP-guided therapy was associated with higher chance of hospital survival [OR 1.15 (95% CI 1.04–1.28)] and favorable neurological outcome at 3 months [OR 2.46 (95% CI 1.64–3.67)] or 6 months [OR 2.03 (95% CI 1.47–2.8]. The heterogeneity (/2) of the studies in each analysis were below 40%. However, the quality of evidence was overall low to very low, using the GRADE tool.
Conclusion: In this meta-analysis, $PbtO_2$-guided and protocolized therapy in the management of severe TBI patients resulted in reduced mortality rates and more favorable short term neurological outcome. These data underline the importance of the ongoing phase-III randomized trials.

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000536

Effect of Dobutamine administration on brain tissue oxygenation in acute brain injury patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000536

Introduction: Brain tissue oxygenation ($PbtO_2$) is an important target in the management of patient suffering from acute brain injury. Fluids and vasopressors can increase $PbtO_2$ in this setting [1–3]. However, the role of inotropic agents has not been entirely evaluated. Moreover, whether the effects on $PbtO_2$ changes are dependent on the effects of inotropic agents on systemic hemodynamic remains unknown.
Objectives: The primary aim of this study was to assess the effects of dobutamine on $PbtO_2$ in a cohort of patient with acute brain injury. Secondary aim was to determine main differences between $PbtO_2$ responders and non-responders to dobutamine.
Methods: We conducted a retrospective monocentric study including all adults patients admitted to the Intensive Care Unit of Erasme Hospital (Bruxelles, Belgium) with acute brain injury requiring $PbtO_2$ monitoring and who were treated with dobutamine from January 2018 to December 2021. $PbtO_2$ values were collected before and then 1 h and 2 h after the initiation of the dobutamine infusion. Responders to dobutamine were identified by a relative increase of $PbtO_2$ values of at least 20% from baseline; a multivariable analysis was performed to assess predictors of $PbtO_2$ response to dobutamine.
Results: A total of 35 patients were included in the study (median age 55 [46–62] years; 18 patients (51%) were male; 31 patients (89%) had subarachnoid haemorrhage, 2 patients (6%) had traumatic brain injury, and 8 patients (23%) had ICH). The median value of $PbtO_2$ at baseline was 20 [14–24] mmHg, which remained unchanged at 1 h and 2 h after dobutamine administrations (at 1 h: 19 [14–25] mmHg; at 2 h: 19 [17–25] mmHg; p = 0.052). We identified 12 (34%) patients as responders; baseline value of $PbtO_2$ was independently associated with response to dobutamine in the multivariate analysis adjusted for cerebral perfusion pressure and intracranial pressure at baseline (OR 0.82 [0.68–0.98] p = 0.03), with best predictive cut-off value of 17 mmHg (AUROC 0.84 [0.70–1.00]).
Conclusion: In this study, dobutamine did not significantly affect brain tissue oxygenation in all patients with an acute brain injury. However, low $PbtO_2$ at baseline independently predict an increase in $PbtO_2$ after dobutamine administration. Further research is needed to better understand the potential role of inotropes in the treatment of brain hypoxia in this setting.

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000543

Chain of choices saves the brain! The role of pre-hospital decision-making in the organisation of patient care in suspected stroke

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Intensive Care Medicine Experimental 2022, **10(2)**: 000543

Introduction: To investigate whether time has an unquestionable role in the disease process of stroke, despite the fact that the connection between time passed and the process of stroke is not linear. In our study, in order to be able to stay within the therapeutic window, we investigated which variables affect the time period of the prehospital treatment.
Methods: For our cross-sectional quantitative study, we gathered data from two ambulance stations in Hungary, comparing the competence of physician (ALS) and non-physician (BLS) units. We processed information from 2021 regarding patients whose initial diagnosis was stroke (N = 220). We investigated whether the unit's decision to treat the patient, was justified or not, moreover we investigated the effect it had upon prehospital times.
Results: We identified that ALS units spend more time with the patient at the incident site than BLS units (p = 0,003). We found that ALS teams treated the patients in 79,17% of all indicated cases, while BLS units treated patients in only 62,50%. However, ALS units treated 42,86% of patients in circumstances for which there was no need of intervention, whilst 82,24% of cases were considered transport priority by the BLS units. In conclusion, the correct choice was made by ALS level units in 59,62%, and by BLS units in 80,36% of cases.
Conclusion: The difference between the shortest and the longest patient transport was 24.28 min. Time was wasted by the ALS team at the site of incidents when there was no need of treatment. This suggests that time could be saved if a BLS unit arrives at the scene. The average prehospital time is lower in cases in which a BLS team is dispatched even if their treatment is not necessary, compared to cases in which an ALS unit is dispatched and does not treat the patient at all.

000648

Understanding the Relationship Between Neurological Biomarkers and Neurological Injury in Patients Undergoing Veno-venous extracorporeal membrane oxygenation. A Prospective Cohort Study

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Introduction: Veno-venous extracorporeal membrane oxygenation (VV-ECMO) enables *ex-vivo* gas exchange in a critically ill patient with acute respiratory failure. It mitigates ventilator-induced lung injury and allows the lungs recover from severe disease (1, 2). Although VV-ECMO can be lifesaving, its use can result in significant complications. Specifically, CNS injury (e.g., intracranial hemorrhage) during VV-ECMO is associated with increased mortality and adverse long-term functional outcomes (3). Neurological injury can be localized to various anatomical structures within the neurovascular unit with the detection of biomarker release (4). Glial fibrillary acidic protein (GFAP) reflects astroglial damage and blood brain barrier permeability and Tau and neurofilament-light (NF-L) reveal axonal damage (5).
Prospective physiologic studies are needed to further delineate the associations with markers of neurologic injury to understand underlying mechanisms.
Methods: We conducted a prospective cohort study of 59 adult patients who received VV-ECMO at the Intensive Care Unit at Vancouver General Hospital Intensive Care Unit (ICU). Bio-specimens for neurological biomarkers were obtained at 4 time points via arterial blood: immediately prior to initiation of VV-ECMO, and a 1-h, 24 h and 7-days following the initiation of VV-ECMO. Brain-specific neurological biomarkers measured were NF-L, GFAP and tau protein using the Quanterix®/Simoa® HD-1 platform. We defined neurological injury as either a new intracranial hemorrhage or infarct on computerized tomography (CT) imaging. We first visually assessed the relationships NF-L, GFAP and tau (connected line plot for each patient over time stratified by injury status. Because of the non-linear relationship between NF-L and GFAP and time, we performed a logarithmic transformation. We did not need to transform tau. We then performed a mixed-methods linear regression of biomarkers over time including injury as a dichotomous variable and specifying "patient" as a random-effect (STATA command xtreg). We also included an interaction term for each biomarker and time.
Results: Patients had a mean age of 50 (SD 12) years in the neurological injury group and 52 (10) years in the no neurological injury group. Twelve patients had neurological injury amongst which 9 patients had intracranial hemorrhage and 3 patients had ischemic strokes. The mean NF-L level over time was higher in the injury group (464 [739] pg/ml) compared to the no-injury group (127 [257] pg/ml) ($p = 0.001$). NF-L levels were higher at each time-point in the injury group and increased over time for both. There was no interaction of time by injury for NF-L. For GFAP, the mean levels over time were higher in the injury group (4278 [11653] pg/ml) compared to the no-injury group (116 [108] pg/ml) ($p < 0.001$). GFAP did not increase over time ($p = 0.06$) and there was no interaction between time and injury. There was no difference in the tau over time in the injury compared to no-injury groups, (2.1 [1.6] vs. 1.5 [1.4] pg/ml, $p = 0.17$), respectively.
Conclusion: In our cohort, patients with neurological injury had elevated NF-L prior to the initiation of VV-ECMO. The mean value of NF-L and GFAP over our four time points was significantly different in patients with neurological injury.

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000725

Functional outcomes over the first year after stroke requiring mechanical ventilation: a prospective multicenter longitudinal cohort study

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Introduction. Importance Outcomes of patients with severe stroke requiring invasive mechanical ventilation remain poorly documented.
Objectives. Objective We aimed to characterize functional outcomes of patients with acute stroke requiring mechanical ventilation.
Methods. Design Prospective multicenter cohort study.
Setting Thirty-three intensive care units (ICU) in Paris area, France (March 7, 2017 to December 26, 2019).
Participants Adult acute stroke patients admitted to the ICU within seven days before or after stroke onset.
Exposure Invasive mechanical ventilation.
Main outcomes and measures The primary endpoint was poor functional outcome at one year, defined by a score of 4 to 6 on the modified Rankin scale, indicating severe disability or death. Multivariable mixed models investigated variables associated with the primary endpoint. Secondary endpoints included quality of life, activity of daily living, and anxiety and depression in survivors.
Results. Among 373 patients prospectively enrolled, 364 (98%) patients (129 ischemic strokes, 128 intracranial hemorrhages, and 107 subarachnoid hemorrhages) were included in the analysis and completed the one-year follow-up. A total of 244 patients (66.5%, 95%CI 61.7–71.3%) had poor functional outcome at one year. Variables

independently associated with poor functional outcome were age 70 years [OR = 2.38 (95%CI 1.26–4.49)], comorbidities [OR = 2.01 (95%CI 1.16–3.49)], a Glasgow coma score < 8 at ICU admission [OR = 3.43 (95%CI 1.98–5.96)], stroke subtype [intracranial hemorrhage: OR = 2.44 (95%CI 1.29–4.63) versus ischemic stroke: OR = 2.06 (95%CI 1.06–4) versus subarachnoid hemorrhage: (Reference)], and a shorter time between stroke diagnosis and initiation of mechanical ventilation [OR = 0.56 (95%CI 0.33–0.94)]. Sensitivity analyses conducted in patients without early decisions of withdrawal of care displayed similar findings. We observed a constellation of persistent physical and psychological problems at 1 year, with more than 50% of survivors reporting problems in at least one dimension of the EQ-5D-3L scale. Those symptoms were significantly worse in ischemic stroke and intracranial hemorrhage patients than in those with subarachnoid hemorrhage.

Conclusion. Conclusions and relevance We observed poor functional one-year outcomes in two-thirds of acute stroke patients requiring mechanical ventilation. Persistent physical and psychological symptoms likely explained the impaired quality of life observed in many survivors.

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1. TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03335995.

Acknowledgements

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2. We thank all the investigators from the 33 centers (SPICE co-investigators)

Funding 1. Agence Régionale de Santé Ile-de-France, Paris, France

000737

Long-term Quality of Life of Pediatric Traumatic Brain Injury Survivors

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Introduction: Traumatic brain injury (TBI) is a leading cause of morbidity and mortality in children and adolescents. Severe injury causes global disease burden to children and has long-term impact on children's daily functioning and health related quality of life (HRQL).
Objectives: The objective of the study was to examine long-term HRQL 11 years after pediatric severe, intensive care requiring TBI.
Methods: This study is a national retrospective, multi-centre observational study. All pediatric patients treated for TBI, and admitted to ICU in four university hospital providing neurointensive care during 2003–2013 were included. Questionnaires regarding HRQL were mailed to survivors including SF-36 and 15D, 16D or 17D HRQL-questionnaires, and questions regarding children´s chronic diagnoses and the need of health care support. The data concerning ICU stay were collected from the Finnish Intensive Care Consortium database. 15D was assessed poor if the total scores were less than − 2SD of Finnish population mean value and SF-36 was poor if scores in general health, physical functioning, physical role functioning or pain were below − 2SD of Finnish population values.
Results: 158 of the 345 (45.5%) surviving patients treated for TBI responded to the questionnaires. The mean follow-up time was 11.3 years. Among the responders 28 (17.7%) got poor 15D, 16D or 17D scores. Patients with low scores were more often female (16, 57.1%, $p = 0.036$). Glascow Coma Scale (GCS) score at admission was 3–8 in 12 cases (44.4 vs 33.3%, $p = 0.48$) with poor 15D scores. Glascow Outcome Scale (GOS) was poor (1–3) in 5 cases (20.0 vs 1.1%, $p < 0.001$) at intensive care admission and in 8 cases (28.6 vs 7.0%, $p = 0.001$) at discharge for those who rated poor 15D scores. There were no statistical difference in age at the time of injury, mechanism of injury, Helsinki CT score, DAI grade, TBI diagnose, number of TBI diagnoses or need of craniectomy between poor or good 15D or SF-36 scores. 121 patients returned SF-36 questionnaire. Seven (5.8%) of them rated poor scores in general health domain, 18 (15.1%) in physical role functioning and 11 (9.2%) in physical functioning. Poor GOS and GCS scores at admission appeared significantly more often in those with poor scores in physical functioning (GOS 50–0% vs 1.1%,$p < 0.001$ and GCS 70.0% vs 33.6%, $p = 0.046$) and physical role function scores (GOS 20.0% vs 2.4%, $p = 0.003$ and GCS 66.7% vs 32.0%, $p = 0.019$). Nearly all patients with poor 15D scores had an increased need for healthcare services; 43% required regular therapy and 60% regular medication. However, only 5.6% of those with normal scores needed therapy and 26% needed medication.
Conclusion: Majority of patients (82.3%) after TBI have normal long-term HRQL after severe TBI as a child according 15D HRQL questionnaire. Poor HRQL is associated with poor GOS scores at intensive care admission.

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Acknowledgements This study was funded in part by Alma and K.A.Snellman Foundation.

000814

Status Epilepticus prognosis and mortality—a single centre retrospective cohort study

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Introduction: Status epilepticus (SE) is a common condition in neurointensive care units (NICU), either as a cause of admission or as complication during NICU stay. SE that progresses despite treatment defines refractory SE (RSE) and super-refractory SE (SRSE), and these are associated with higher morbidity and mortality [1]. Mechanisms for SE progression to RSE and ultimately SRSE and its implications on treatment are purely theoretical [2]. Robust scientific evidence for the treatment of SRSE is lacking.
Objectives: To report the outcomes of a cohort of patients with SE, RSE and SRSE and identify predictors of progression to SRSE and mortality in a single level 3 NICU.
Methods: Retrospective cohort study. Population consisted of all patients admitted to our NICU with a diagnosis of SE, RSE and SRSE from January 2018 to July 2021. Protocoled-based prospective data were retrieved from our electronic data base. Statistical analysis was

performed using binary logistic regression to predict progression to SRSE and 6-month mortality.
Results: A total of 79 patients were included, 15 (19%) fulfilling criteria for RSE, 53 (67,1%) for SRSE and the remainder 11 for SE (13,9%). Median age at admission was 68 (±17), SAPS II 51 (±15) and SOFA 6 (±2.7). Most were non-programmed admissions (96,2%) and about half following a neurosurgery (55,7%). Most patients had an acute symptomatic aetiology for SE (83,5%) and half had non-convulsive SE (51,9%). Only 12 patients (15,2%) had a previous diagnosis of epilepsy. Male gender (72,7%) and programmed admissions (18,2%) were more frequent in SE than RSE or SRSE patients, and SAPS II was higher in RSE. There were no other statistically significant differences between baseline admission characteristics of these three groups. NICU mortality was 40,5%, further 19% patients died in hospital after ICU discharge and another 3.8% after hospital discharge (6-month follow-up), with an overall cumulative mortality of 63,3%. In a multivariate analysis, age (OR 1.1; CI 95% 1–1.1), need for neurosurgery at admission (OR 3.8; CI 95% 1.1–12.8), SRSE (OR 6; CI 95% 1.6–22–4) and shock (OR 9.1; CI 95% 1.5–54.8) were predictors of 6-month mortality. We couldn't find any baseline predictor of progression to SRSE.
Conclusion: Our results highlight the negative impact of progression to SRSE in the prognosis of patients admitted to a NICU. The diagnosis of SRSE, particularly its non-convulsive form, is almost always hampered by the ongoing sedation and lack of clinical clues, therefore delaying treatment. Progression of RSE to SRSE is associated with high mortality, although further prospective studies are needed to address the causes and mechanisms for treatment failure. Developing evidence-based diagnosis and treatment protocols is, therefore, of utmost importance.

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001278

Standardized and Simulation-Based Education of Death by Neurological Criteria

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Introduction: Variation in the determination of death by neurological criteria (DNC), or brain death, is frequent in the United States and has profound medical and ethical implications. [1,2] Optimizing education of DNC is a potential target to improve clinical practice.
Objectives: The purpose of this project was to standardize the education of DNC and provide learners with opportunities for hands-on experience with real-time feedback and evaluation in a controlled environment.
Methods: This was a before/after study to evaluate the effects of an online tool combined with high-fidelity simulation on the education of DNC. Post-graduate year (PGY) II-IV Adult Neurology residents completed the Neurocritical Care Society's Brain Death Determination Course© and then participated in a high-fidelity, mannequin-based simulation scenario where they were expected to identify prerequisite criteria to DNC, perform a clinical examination (including an apnea test), and interpret, document, and disclose results to an embedded participant.[3] Pre- and post-simulation survey data regarding subjective comfort with DNC determinations were collected.
Results: Sixteen participants were enrolled (PGY II = 4, PGY III = 6, PGY IV = 6). Only three (19%) residents reported feeling confident with performing a DNC evaluation prior to this intervention. All participants reported increased confidence with each individual aspect of DNC testing from before to after study completion. The combination of the online course with the simulation activity was subjectively more effective than either tool individually. Prior to this activity, the aspect of DNC which most residents were uncomfortable with was the apnea test (63%), which improved to 80% afterwards. After completing the study, residents remained most uncomfortable with conveying results (63%).
Conclusion: Combining an online course with high-fidelity simulation is feasible and effective in improving resident confidence in performing DNC determinations. Communicating results of DNC evaluations remains an area for improvement. Large-scale studies investigating the effects of standardized teaching and high-fidelity simulation on education and clinical performance of DNC are warranted.

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Acknowledgements Funding awarded by the Southwestern Academy of Teachers (SWAT).

001284

The association between serum amyloid A and phenotypes of acute brain injury in a neurocritical care unit

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Introduction: Serum amyloid A (SAA) is a known acute-phase response protein. Elevated SAA concentration were reported in the mouse model of traumatic brain injury and human basal ganglia hemorrhage. We aimed to analyze the association between SAA and types and severities of acute brain injuries.Serum amyloid A (SAA) is a known acute-phase response protein. Elevated SAA concentration were reported in the mouse model of traumatic brain injury and human basal ganglia hemorrhage. We aimed to analyze the association between SAA and types and severities of acute brain injuries.
Methods: We retrospectively reviewed the patients admitted to our neurocritical care unit with an acute brain injury including ischemic stroke (IS), subarachnoid hemorrhage (SAH), traumatic brain injury (TBI) and intracerebral hemorrhage (ICH). Serum SAA was measured at arrival to emergency department. The association between the concentration of serum SAA and characteristics of brain injuries were analyzed.
Results: We analyzed 26 patients (mean age, 61.3 ± 17.6; female, 53.8% [n = 14]). Average SAA level was 47.5 ± 86.4 mg/L and 42.3% (n = 11) was abnormal (> 10 mg/L). Mean SAA was 47.5 ± 93.7 mg/L in the mild (Glasgow Coma Scale [GCS] 13–15, n = 10), 38.8 ± 69.3 mg/L in the moderate (GCS 9–12, n = 4) and 53.8 ± 91.4 mg/L in the severe (GCS 3–8, n = 10) group. There was no significant difference among those groups (p-value = 0.96). Mean SAA were 13.5 ± 20.4 mg/L in IS (n = 10), 53.3 ± 109.0 in SAH (n = 7), 161.0 ± 149.5 mg/L in TBI (n = 3) and 45.2 ± 57.6 mg/L in ICH (n = 6). No significant difference was observed between those groups (p-value = 0.069). However, compared between intracranial hemorrhage (SAH, ICH and TBI; mean SAA 70.5 ± 104.0 mg/L) and IS, the difference was statistically significant (p-value = 0.049).

Conclusion: In this study, the difference among was not statistically different among each brain injuries, possibly due to the limited number of samples. Although there is no SAA level difference by GCS at arrival, there was a signal that SAA was higher in hemorrhagic brain injury than ischemic brain injury, which suggest the nature of brain injury is more important to elevation of SAA level.

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Acknowledgements This research was supported by the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT (Grant No. NRF-2020M3E5D9079768).

001329

Anaesthesia and surgery in the steep Trendelenburg position and its impact on cerebral perfusion

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Introduction: Surgery in the steep Trendelenburg position carries potential risks such as pulmonary dysfunction (1–2). It may also cause impaired venous return from the head, resulting in cerebral oedema, increased intracranial pressure, and reduced cerebral blood flow (3–5). Several studies demonstrate that cerebral oxygenation measured with Near Infra-Red Spectroscopy (NIRS) during steep Trendelenburg position is adequate (6). However, NIRS can only measure the oxygenation of the brain tissue close to the sensors (7). Several studies indicate that brain injury biomarkers such as Glial Fibrillary acidic protein (GFAP) and S100B can be detected in the bloodstream during cerebral hypoperfusion (8–9). There are no studies to our knowledge of brain injury biomarkers in blood during and after anaesthesia and surgery in the steep Trendelenburg position.
Objectives: This prospective observational study aims to answer if anaesthesia and surgery in the steep Trendelenburg position affect cerebral perfusion by correlation of mean arterial pressure and cerebral oxygenation and levels of brain injury biomarkers in blood.
Methods: This prospective observational study occurred at Sahlgrenska University Hospital, Gothenburg, Sweden, between September and November 2021. The study was approved by the Swedish Ethical Review Authority (Dnr 2020–00,169). All patients received oral and written information before consenting to participate in the study. The patients were identified from the operating schedule. Inclusion criteria were adult patients $\geq$ 18 years of age, planned for elective lower abdominal surgery in the Trendelenburg position. Exclusion criteria were previous ischemic stroke, previous traumatic brain injury and pre-existing neurological disease. Before anaesthesia induction, standard monitoring equipment was applied, including an arterial line in the radial artery for continuous arterial blood pressure. Furthermore, the patients were equipped with bilateral NIRS (INVOS 5100C cerebral oximeter, Medtronic, Minneapolis) adhesive pads on the forehead. The Moberg CNS monitor (Moberg ICU Solutions Micromed group) collected and stored all data. Data collection started before anaesthesia induction and continued until two h postoperatively. Blood samples before induction, 2 h after induction and 24 h after induction were drawn from the arterial line. Blood samples were analyzed with a previously described in house ELISA technique and the single-molecule array technique.
Results: This is still an ongoing study but our premilnary results indicate that prolonged steep Trendelenburg position during anaesthesia and surgery does not affect cerebral perfusion to any significant degree and that cerebral autoregulation seems to remain intact even during lengthy procedures. However, brain injury biomarkers Glial Fibrillary Acidic Protein and S100B may be affected, mainly due to venous stasis.
Conclusion: In the steep Trendelenburg position, cerebral perfusion may be affected by anaesthesia and surgery.

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Acknowledgements The authors wish to express their gratitude to Wilhem and Martina Lundgren foundations for granting this study.

001437

Correlation between heart rate variability and cerebral autoregulation in septic patients

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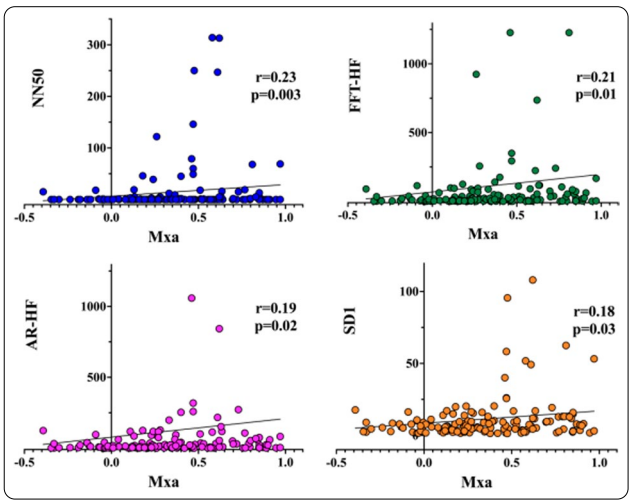
Intensive Care Medicine Experimental 2022, **10(2)**: 001437

Introduction: Heart rate variability (HRV) may provide an estimation of the autonomous nervous system (ANS) integrity in critically ill patients. Disturbances of cerebral autoregulation (CAR) may share common pathways of ANS dysfunction.
Objectives: To explore whether changes in HRV and CAR index correlate in critically ill septic patients.
Methods: Prospectively collected data on septic adult (> 18 years) patients admitted into a mixed Intensive Care between February 2016 and August 2019 with a recorded transcranial doppler CAR assessment. CAR was assessed calculating the Pearson's correlation coefficient (i.e. mean flow index, Mxa) between the left middle cerebral artery flow velocity (FV), insonated with a 2-MHz probe, and invasive blood pressure (BP) signal, both recorded simultaneously through

a Doppler Box (DWL, Germany). MATLAB software was used for CAR assessment using a validated script; a Mxa > 0.3 was considered as impaired CAR. HRV was assessed during the same time period using a specific software (Kubios HRV 3.2.0) and analyzed in both time-domain and frequency domain methods. Correlation between HRV-derived variables and Mxa were assessed using the Spearman's coefficient.

Results: A total of 141 septic patients was studied; median Mxa was 0.35 [0.13–0.6], with 77 (54.6%) patients having an impaired cerebral autoregulation. Mxa had a significant although weak correlation with HRV time domain (SDNN, r = 0.17, p = 0.04; RMSSD, r = 0.18, p = 0.03; NN50, r = 0.23, p = 0.006; pNN50, r = 0.23, p = 0.007), frequency domain (FFT-HF, r = 0.21; p = 0.01; AR-HF, r = 0.19; p = 0.02), and non-linear domain (SD1, r = 0.18, p = 0.03) parameters. Impaired CAR patients had also all of these HRV-derived parameters higher than those with intact CAR.



Conclusion: These findings suggested a potential role for ANS failure in the occurrence of CAR disturbances during sepsis.

001442

Practice of Therapies Intensity Levels in Acute Brain Injury. Insights from the SYNAPSE-ICU study

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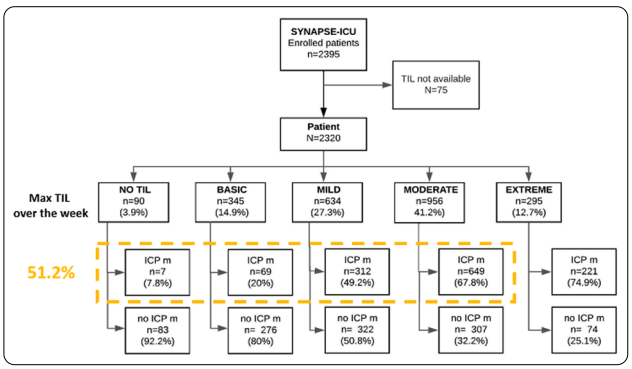
Introduction: Therapies intensity levels (TIL) score is a scale to assess the intensity of ICP (intracranial pressure) lowering management based on 5 levels (no therapy, basic, mild, moderate, extreme). Extreme TIL (eTIL), defined as the most extreme therapies to control ICP, include extreme hypothermia (T < 35°), metabolic suppression, profound hypocapnia ($PaCO_2$ < 4.0 kPa; < 30 mmHg) and secondary decompressive craniectomy. The indications for the use of eTIL are mostly based on traumatic brain injury (TBI), whereas uncertainties remain in the use of eTIL in non TBI (subarachnoid haemorrhage (SAH) and intracerebral haemorrhage (ICH)). Given this uncertainty, we performed an analysis aimed to investigate the current practice of TIL after ABI (acute-brain-injury) analysing the SYNAPSE-ICU-study cohort focusing on the prevalence in the use of the extreme TIL and their variability.

Methods: The SYNAPSE-ICU is an international, prospective, observational, cohort study (NCT03257904) including patients in coma after acute traumatic and non-traumatic brain damage admitted to > 200 Intensive Care Units. Demographic information, clinical condition, treatments and TIL during the first week in ICU were collected. Characteristics between eTIL and no-eTIL were compared by Mann–Whitney U test for continuous data and χ^2 test for categorical data.

Results: At day 1, of 2320 ABI patients, 102 (4.4%) not received specific ICP directed therapy, 364 (15.7%) received basic, 860 (37.1%) mild, 847 (36.5%), moderate TIL and 147 (6.3%) received eTIL. 94 of 147 of subjects with extreme therapies had TBI as primary diagnosis and 53 (36.1%) no-TBI (26 were ICH and 27 SAH). The most frequent extreme therapies were metabolic suppression (48.3%), profound hypocapnia (41.5%) and then hypothermia < 35 °C (10.2%).The median age of the extreme therapies group (eTIL) was lower 50 (I-III quartile, Q1–Q3 = 32.50, 63.50) than no-eTIL groups (median, Q1–Q3 = 55 (40, 69), p = 0.005). At hospital admission, no differences were found in GCS (Glasgow Coma Scale), pupil reactivity, arterial hypertension, and all types of abuse. Neuroworsening was more frequent in eTIL group (82, 57.7% eTIL-group vs 731, 34.7% no-eTIL group, p < 0.001). Overall, 295 (12.7%) patients received at least one of the eTIL during the week. 93 (31.5%), 84 (28.4%) and 50 (16.9%) patients received a TTT at day 1, day 3 or day 7; 68 (23%) patients received more than one eTIL over the week. During the week, the ICP monitoring was insert in 1258 (54.2%). The frequency of ICPm was higher in eTIL groups than no-eTIL one (74.9% vs 51.2%). The ICP monitor patients received more frequently extreme TIL than no-ICP monitored ones (221 (17.6%) and 74 (7.0%), p < 0.001). The median of the ICP maximum value was higher in eTIL group than the no-eTIL group (28, Q1-Q3 = 18, 44.2 and 21, Q1–Q3 = 14, 38, p < 0.001).

Conclusion: The frequency of eTIL over the week was 12.7% and the most frequent treatments were extreme suppression and extreme hypocapnia. eTIL-group was younger and more often experienced neuroworsening than the no eTIL group. The ICP-monitor is more used in eTIL group, in which higher values of ICP were observed.

Figure 1 Diagram of enrolled patients; Abbreviations: TIL = therapy intensity Levels; ICU = Intensive Care Unit; ICPm = ICP monitored patients



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001446

Stroke in a Neurocritical Care Unit

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Introduction: Stroke was known as the XXI century epidemic. Despite reductions in mortality and disability-adjusted life years over the last decade, acute ischaemic stroke (AIS) remains one of the leading causes of death and a major cause of permanent disability worldwide. To highlight this fact, in Portugal stroke is the number one cause of death, and the most important cause of morbidity, with enormous social and economic consequences. Nevertheless, only a minority of cases require admission to an intensive care unit (ICU), as they need care and interventions that cannot be provided on a stroke unit. However there is a lack of information about the characteristics and outcomes of patients admitted in the ICU with stroke.
Objectives: To analyse the characteristics and outcome of patients admitted with acute ischaemic stroke in a Neurocritical Care Unit.
Methods: This is a single center, retrospective study that was conducted in patients admitted in the Neurocritical Care Unit (NCCU) of the Centro Hospitalar e Universitário de São João, between 1st January 2019 and 31st December 2020, presenting with middle cerebral artery infarction.
Results: A total of 939 patients were admitted in Centro Hospitalar e Universitário de São João, a tertiary hospital, with acute ischemic stroke, 9,80% of those patients (n 92) required admission in the NCCU. The main reasons for admission were decreased conscious level, need for respiratory support and haemodynamic management. The mean age was 66,61 years (SD ± 13,97), the ratio of males and females was pretty balanced (male 52,75%), the mean Acute Physiology And Chronic Health Evaluation II (APACHE II) score was 13,98 (SD ± 7,86), and the median length of stay in the NCCU was 5 days (IQR 2–11). The mean admission NIHSS score was 18,08 and the mean Glasgow Coma Scale score was 11,03. Notably the proportion of patients receiving thrombolytic therapy (23,91%) or mechanical thrombectomy (15,22%) was not very high, and 13,04% had craniotomy. About 29,35% of the patients needed mechanical ventilation. About 61,59% were classified as having a poor outcome, defined as a modified Rankin Scale (mRS) score 4–6. The NCCU mortality was 19,57% and the hospital mortality was 26,09%.
Conclusion: Severe stroke patients are frequently admitted in an intensive care unit setting, however mortality rates and other outcome variables reported in the literature vary widely. In this population the mortality rate was not high, which may be explained by the existence of a dedicated neurocritical care team or by more strict admission criteria. However, despite early aggressive treatment some patiens do not have a satisfactory recovery, as such, it is extremely important to discuss the prognosis and functional outcome with relatives.

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Acknowledgements The authors thank the Neurocritical Care Unit for the time and expertise provided.

001309

Antibiotic sequence and bacterial clearance in a Steptococcus pneumoniae rat model of septic shock

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Introduction: Higher microbial load and antibiotic delay are associated with increased morbidity and mortality in septic shock. Antibiotic combination is the basis of empiric treatment for sepsis and septic shock, current recommendations suggest the use of a combination of antibiotics to broaden the initial spectrum of coverage to treat some multi-resistant bacteria. Antibiotic combination therapy leads to more rapid pathogen clearance, which may translate into improved patient outcomes.
While antimicrobial synergy has been established for betalactam combinations with aminoglycosides or fluoroquinolones, antimicrobial sequence has been studied mostly in vitro. Herein we sought to confirm this in our Streptococcus pneumoniae peritonitis rat model of septic shock.
Methods: Our peritonitis rat model of septic shock consists on a peritoneal infection caused by implanting a gelatin capsule with a known Streptococcus pneumoniae inoculum, where the capsule dissolves with time and the inoculum will grow generating a severe infection. After letting the infection evolve to septic shock, we resuscitate the rat and provide supportive care (mechanical ventilation, vasopressors, fluids and temperature control). Then we experiment with the order of antimicrobials (cefotaxime and levofloxacin), and compare bacterial counts in treated animals with different combination therapy strategies to monotherapy and untreated controls, for a total of 6 treatment arms and 6 rats per arm. At several time points we measure blood bacterial load, cytokine profile and lactate, and the organ bacterial load after euthanizing the animal. In this nonsurvival experiment, we follow the ethics guidelines for animal experimentation and have the approval of animal ethics at University of Manitoba.
Results: Rats treated with cefotaxime or levofloxacin monotherapy had slow but steady bacterial clearance in the blood (see Fig. 1). Staggered dosing regimens showed a synergistic effect, with faster initial blood bacterial clearance that maintained over time after 1.5 h. These trajectory differences showed to be statistically significant when compared to simultaneous administration of antibiotics or either of the monotherapy strategies ($p < 0.001$ in all three comparisons). Interestingly, simultaneous administration of both antibiotics behaved similarly as either of the monotherapy cohorts ($p > 0.025$). At experiment end levofloxacin monotherapy had the lowest bacterial clearance, showing significant differences with either of the staggered combination strategies ($p = 0.012$ C->L vs. L and $p = 0.001$ L->C vs. L).

Peritoneal and organ bacterial clearance didn't differ between treated strategies ($p > 0.025$), see Fig. 2.
Conclusion: Antibiotic sequence showed significant synergistic effects in initial bacterial clearance when we compared staggered administration of antibiotics and simultaneous administration. Altering the antimicrobial sequence had no significant impact in peritoneal or organ bacterial counts in our Streptococcus pneumonia septic shock model.

001334

Effects of angiotensin-II administration on vascular properties and association with inflammatory response in a polymicrobial septic shock experiment

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Introduction: Sepsis is known to severely impair vascular function (1), leading to altered pulse wave transmission (2). The different hemodynamic response to sepsis therapy may depend on the complex interaction between triggered inflammatory processes and pharmacological actions. Recently, angiotensin-II (ATII) has been proven to be effective in catecholamine-resistant vasodilatory shock (3). However, pro-inflammatory and pro-oxidative effects secondary to excessive ATII activity may question its potential benefits (4).
Objectives: The objective of this study is to evaluate the vascular response to ATII administration in comparison to noradrenaline (NA) in a swine model of polymicrobial septic shock. Moreover, the relationship between vascular indices and inflammatory markers was assessed to investigate possible different interactions between inflammatory and therapy response.
Methods: 16 pigs underwent a protocol of polymicrobial sepsis followed by standard resuscitation to reach blood pressure (BP) target: 8 animals were treated with fluids and NA, 8 with ATII. The latter pigs were further subdivided according to the total ATII dosage administered: Low-ATII group (5 pigs, dose $< < 10 \times 104$ ng/Kg) and High-ATII group (3 pigs, dose $> 10 \times 104$ ng/Kg). Continuous cardiac output (CO), BP in central aorta and in femoral artery were recorded. We estimated the arterial compliance (AC) and the total peripheral resistance (TPR) according to the 2-element Windkessel model(5); the pulse pressure (PP) amplification as the ratio between aortic and femoral PP, representing the peripheral vascular decoupling (6). Plasma inflammatory markers include IL6 and lactate. Finally, correlation analyses were performed between vascular indices and inflammatory markers.
Results: At the end of the experiment, Low-ATII pigs showed better vascular conditions with higher values of AC, TPR, and lower values of PP amplification (Table 1), despite all the animals achieved the recommended targets, such as mean BP > 65 mmHg, and showed a similar overall cardiovascular condition (Table 2).
Table 1 Values of vascular indices at the end of the experiment

	AC [mL/mmHg]	TPR [dyne*s*cm-5]	PP amplification
NA	0.84 (0.76, 0.93)	710.1 (667.8, 745.2)	1.3 (1.2, 1.7)
High-ATII	1 (0.9, 1.1)	592.2 (506.2, 650.2)	1.8 (1.6, 2.1)
Low-ATII	1.1 (1.1, 1.3)	789.1 (708.1, 937.1)	1.1 (1, 1.2)*

*Mann–Whitney *U*-test p-value < 0.05 Low- vs High-ATII (Kruskal Wallis p-value < 0.05).
Table 2 Values of hemodynamic variables at the end of the experiment

	MAP [mmHg]	CO [L/min]	SV [mL]
NA	66.3 (63.7, 71.5)	8.5 (7.5, 9.5)	55.9 (53, 61.4)
High-ATII	63.7 (62.4, 63.9)	9.5 (8.3, 11.6)	62.2 (52.1, 75)
Low-ATII	72.1 (63.2, 75.6)	7.4 (6.9, 8.4)	55.2 (52.8, 62.4)

IL6 and lactate concentration were lower in Low-ATII pigs compared to the other groups at the end of experiment (IL6 [pg/mL] NA: 749.7 (386.5,1254); High-ATII: 1177.5 (724,1271.1); Low-ATII: 320.3 (179.8,478.6). Lactate [mmol/L] NA: 1.5 (1,2.8); High-ATII: 1.4 (1.4,1.9); Low-ATII: 0.9 (0.9,1.6)). A negative correlation was found between IL6 and AC and TPR ($r = -0.6$ and $r = -0.3$, respectively), and a positive correlation characterizes the relationship between IL6 and PP amplification ($r = 0.6$).
Conclusion: A persistent alteration of the arterial system properties has been observed in all animals even after successful resuscitation. Elevated IL6 concentration is related to a worse prognosis in septic patients (7) and serum IL6 is known to be correlated with endothelial dysfunction (8). Our results suggest that too elevated dosage of ATII in non-responsive subjects may have a deleterious effect on vascular function, despite the achievement of the recommended hemodynamic therapy targets. The role of inflammation on the alteration of arterial characteristics during sepsis resuscitation needs further investigations to shed light on possible associations which may help to identify new therapy targets for a more personalized therapy.

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001415

Sympathoexcitation induced by microglial activation in the brain plays an important role in sepsis in rats with chronic kidney disease

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Intensive Care Medicine Experimental 2022, **10(2)**: 001415

Introduction: Sympathoexcitation plays an important role in the pathogenesis of various diseases such as sepsis and chronic kidney disease (CKD). Inflammation in the brain induced by microglial activation is involved in sympathoexcitation. The prognosis of sepsis accompanied with CKD is poor; however, the precise mechanism is not fully elucidated.
Objectives: We aimed to clarify the association between end organ damage and sympathoexcitation induced by microglial activation in sepsis in rats accompanied with CKD.
Methods: Protocol 1) Male Sprague–Dawley (SD) rats were implanted telemetry system to monitor the electrocardiogram at 10-week-old, and performed 5/6-nephrectomy (Nx) or sham-operation. 4 weeks

after the Nx, we performed cecal ligation and puncture (CLP) or sham, and divided into 4 groups (sham-sham: n = 4, sham-CLP: n = 8, Nx-sham: n = 5, Nx-CLP: n = 9). The end organ damage was evaluated by the serum creatinine (cre) and total bilirubin (bil) levels. Using telemetry throughout the experiment course, we analyzed the power spectrum of heart rate variability and assessed a ratio of low and high frequency (LF/HF) as an indicator of sympathetic nerve activity (SNA). Protocol 2) In Nx-CLP group, we implanted osmotic minipump before CLP for intracerebroventricular administration of minocycline, which is commonly used to inhibit microglial activation, or artificial cerebrospinal fluid (CSF) and divided into 2 groups (Nx-CLP-Mino: n = 5, Nx-CLP-CSF: n = 4) and examined the above parameters. Statistical analyses were performed using unpaired t-test and two-way ANOVA.
Results: In Nx-rats at 4-weeks after nephrectomy, the cre (0.57 ± 0.04 vs. 0.35 ± 0.03 mg/dL, $p < 0.01$, n = 5 for each) level was significantly increased compared with control. In Nx-CLP at 2-days after CLP, the cre (0.93 ± 0.07 vs. 0.57 ± 0.04 mg/dL, $p < 0.01$, n = 5 for each) and total bil (0.19 ± 0.02 vs. 0.08 ± 0.01 mg/dL, $p < 0.01$, n = 5 for each) levels were significantly increased compared with those in Nx-sham. In Nx-CLP at 0, 1, 2-days after CLP, LF/HF ratio were significantly higher compared with those in Nx-sham (Two-way ANOVA, $p < 0.001$). In Nx-CLP at 2-days after CLP, the cre level (0.93 ± 0.07 vs. 0.64 ± 0.06 mg/dL, $p < 0.05$, n = 5 for each) was significantly increased compared with those in sham-CLP. In Nx-CLP at 0, 1, 2-days after CLP, LF/HF ratio were significantly higher compared with those in sham-CLP (Two-way ANOVA, $p < 0.01$). In Nx-CLP-Mino compared with Nx-CLP-CSF, both the cre (0.72 ± 0.08 vs. 0.95 ± 0.17 mg/dL, n = 4–5, $p < 0.05$) and bil (0.13 ± 0.03 vs. 0.20 ± 0.04 mg/dL, n = 4–5, $p < 0.05$) levels were significantly lower at 2-days after CLP, and the LF/HF ratio were significantly suppressed at 0, 1, 2-days after CLP (Two-way ANOVA, $p < 0.01$).
Conclusion: These data indicate that the end organ damage was exacerbated in association with activated SNA, through augmentation of microglial activation in the brain, in the early phase of infection in rats with sepsis accompanied with CKD.

001443
Pulmonary co-infections and superinfections in COVID-19 critically ill patients. An observational study from Morocco

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Intensive Care Medicine Experimental 2022, **10(2)**: 001443

Introduction: There is a growing literature showing that COVID-19 critically ill patients have an increased risk of pulmonary co-infection and superinfection. However, studies in developing countries, especially African countries, are lacking. In Morocco, there have been more than one million confirmed cases of COVID-19, with more than 15,000 deaths.
Objectives: The objective of this study was to determine the prevalence of co-infection and superinfection with severe COVID-19 pneumonia in a Moroccan ICU, the micro-organisms involved, and the outcome of patients.
Methods: This retrospective observational study was performed between April 2020 and April 2021 in the intensive care unit (ICU) of Avicenna Military Hospital. We included adult patients consecutively admitted for COVID-19 pneumonia with acute respiratory distress. The diagnosis of pulmonary co-infections and superinfections was based on the isolation of pathogens from blood or lower respiratory tract samples culture: sputum or mini-broncho-alveolar lavage (mini-BAL) for patients under mechanical ventilation. Co-infection was defined as the identification of a respiratory pathogen, diagnosed concurrently with SARS-Cov2 pneumonia. Superinfection includes hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) as defined according to current guidelines.
Results: During the study period, 155 patients were analyzed, 87% were males, with a median age of 68 years [IQR, 62–72]. Nearly half of the patients received antibiotics before ICU admission, with third generation cephalosporin (3GC) being the most prescribed antibiotic. A large proportion also received azithromycin and hydroxychloroquin as antivirals. Regarding ventilatory management, the majority of patients (88%) underwent non-invasive ventilation (NIV). Sixty-five patients (42%) were placed under invasive mechanical ventilation, mostly after failure of NIV. Ninety-two blood cultures, 82 sputum cultures, and 88 mini-BALs were achieved. Among the mini-BAL samples, 37 were also examined by multiplex PCR. The prevalence of co-infections was 4.5%. The micro-organisms isolated were staphylococcus aureus, hemophilus influenza, proteus sp, and Klebsiella pneumoniae. Forty-five patients developed pulmonary superinfections (prevalence = 29%) of which 19 were HAP and 26 were VAP. The prevalence of VAPs was 64 VAP episode / 1000 ventilation days. Multi-drug resistant (MDR) gram negative bacilli (GNB) were the predominantly isolated pathogens in superinfections (86%), in particular Klebsiella pneumoniae for HAP and Acinetobacter Baumanii for VAP. Overall mortality was 64.5%. Patients with pulmonary superinfections had a worse outcome. We observed a high frequency of superinfections among COVID-19 critically ill patients, with MDR-GNB being the most identified microorganism. Mortality was significantly impacted by the development of superinfections.
Conclusion: We observed a high frequency of superinfections among COVID-19 critically ill patients, with MDR-GNB being the most identified microorganism. Mortality was significantly impacted by the development of superinfections.

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000878 C-Reactive Protein-to-Serum Lactate Ratio to predict mortality in Status Epilepticus—single centre proof-of-concept study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000878

Introduction: Status epilepticus (SE) is a life-threatening emergency responsible for high disability and mortality burden1. The mortality prediction in this population is challenging and led to the development of prognostic scores, such as the STESS2 and the EMSE3. Unfortunately, the utility of these scores is limited when seizure history at SE onset is uncertain or electroencephalography is not readily available. Ideally, a prognostication tool should rely upon simple and readily accessible information. Some previous evidence suggests that systemic inflammation, as reflected by C-reactive protein (CRP) level, might affect the prognosis of SE4–6; on the other hand, serum lactate may be useful to differentiate type of seizures (generalized-convulsive vs. non-convulsive seizures) at SE onset with prognostic impact 7,8. In line with this evidence, we hypothesized that CRP-to-serum lactate ratio (CLR) could be useful as a mortality predictor in SE.
Objectives: To evaluate the predictive value of CLR for hospital mortality at SE onset.
Methods: We designed an observational cohort study, using our SE database from a tertiary neurocritical intensive care unit (NICU). From 2018 to 2021, all adult patients (≥ 18-year-old) with a diagnosis of SE (according to the International League Against Epilepsy definition9), established at NICU admission or during NICU stay, were included. CLR ratio was calculated using the first simultaneous values of both variables (in mg/dL) obtained within 24-h of SE onset. Logistic regression was used to evaluate the association of CLR with hospital mortality, both with crude and adjusted analysis for age, sex, presence of infection, STESS, SOFA and SAPS-II scores. CLR area under the receiver operating characteristic curve (AUROC) was calculated.

Results: Ninety-five patients with SE were included. Median age was 66 years (interquartile range [IQR]: 47–76) and 56% were females. Mean SAPS-II score was 49 ± 17, mean SOFA score was 6 ± 3 and median STESS was 4 (IQR: 3–5). Hospital mortality rate was 60% in this cohort. At SE onset, the median CLR was 0.43 (IQR: 0.07–1.41). Increments in CLR were associated with higher hospital mortality, both in the crude (odds ratio [OR] 1.82; 95% confidence interval [95% CI]: 1.12–2.98; $p = 0.016$) and adjusted analysis (OR 1.79; 95% CI: 1.07–2.97; $p = 0.025$). The precision of CLR alone to predict hospital mortality was 0.67, as calculated by AUROC, and 0.77 when included in the adjusted model.
Conclusion: Our findings suggest that CLR has prognostic value as a mortality predictor at SE onset. It may be useful not only as a simpler stand-alone predictor but also as an add-on to the current prediction scores. Its validation in other SE cohorts' merits further research.

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Acknowledgements None.

000881

Serial neuroinflammatory markers and cognition in hospitalized COVID-19 patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000881

Introduction: Cognitive complaints occur in a high percentage of patients suffering from long-COVID and can have lasting negative impact on rehabilitation, daily functioning and quality of life. COVID-19-induced neuroinflammation may account for this: innate immune cells of the brain become activated, due to systemic inflammation and a compromised blood–brain barrier, causing a neuroinflammatory state of the brain resulting in neuronal damage. Neurological damage markers are often measured once at admission, but not serially and their trajectory is unknown.
Methods: This prospective single centre study serially assessed brain damage related biomarkers in plasma during hospital admission in COVID-19 patients (ICU patients and ward patients) between March and May 2020. We measured plasma neurofilament light-chain (NfL), Ubiquitin carboxy-terminal hydrolase L1 (UCHL-1), glial fibrillary acidic protein (GFAP) and tau protein at admission and every other 7 days, until discharge. We also assessed the following cytokines during the same sampling points: IL-6, IL-8, IL-10, TNF-a. Additionally, we assessed the cognitive outcomes in survivors at 6 months post-hospital discharge using a full neuropsychological examination.
Results: 73 ICU patients and 51 ward patients were included. Median age was 62 [58–70] and 67% was male. We have recently finished the analysis of the biomarkers and collection of the long-term cognitive data. First, we will report the trajectories of brain specific proteins and their relation to systemic inflammation and ICU related outcomes. Second, we will analyze whether systemic inflammation or brain specific protein levels predicted cognitive outcomes at 6 months follow-up.
Conclusion: While previous studies assessed brain specific proteins at one sampling point in patients with COVID-19, within this unique longitudinal setup we will be able to generate new insights into brain damage in COVID and outcomes based on a) the trajectories of biomarkers related to brain damage, b) relation between systemic inflammation and brain markers, and c) the relation between brain specific biomarkers and long-term cognitive outcomes.
Acknowledgements ZonMw Clinical Fellowship grant 90715610.

000913

Outcomes of adult patients with meningoencephalitis requiring intensive care: the international prospective multicenter EURECA study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000913

Introduction: Importance Outcomes of adult patients with severe central nervous system infections remain poorly documented.
Objectives: Objective We aimed to characterize functional outcomes of adult patients with suspected meningoencephalitis requiring intensive care.
Methods: Design ESICM-endorsed, prospective multicenter international cohort study (2018–2019).
Setting Sixty-eight intensive care units (ICU) in 7 countries.
Participants Eligible patients were adults admitted to the ICU with symptoms suggestive of encephalitis, defined by an acute onset of encephalopathy (score on the Glasgow coma scale (GCS) ≤ 13), a cerebrospinal fluid (CSF) pleocytosis ≥ 5 cells/mm^3, and at least two criteria among the following: fever, seizures, focal neurological deficit, parenchymal abnormalities on neuroimaging, and EEG alterations compatible with encephalitis.
Main outcomes and measures The primary endpoint was poor functional outcome at 3 months, defined by a score of 3–6 on the modified Rankin scale (moderate-to-severe disability or death). Multivariable analyses investigated variables associated with the primary endpoint. Sensitivity analyses were performed to investigate two a priori-defined subgroups, namely patients with bacterial meningitis, and patients

with primary encephalitis, after adjustment for main etiologies (e.g., viral, immune-mediated, and unknown origin).

Results. Results Among 599 patients enrolled, 589 (98.3%) completed the 3-month follow-up and were included. Among them, 247 (41.9%) had bacterial meningitis and 140 (23.6%) had an encephalitis of infectious origin (viral causes, n = 101; other bacterial causes, n = 25; fungal/parasitic causes, n = 14). Other causes were immune-mediated encephalitis (n = 38, 6.5%), neoplastic/toxic encephalitis (n = 11, 1.9%), and encephalitis of unknown origin (n = 155, 26.3%). At admission, 137 (23%) patients were immunocompromised, and the median SAPS2 and GCS scores were 42 (interquartile range, 30–57) and 9 (interquartile range, 6–11), respectively. Main reasons for ICU admission were altered mental status (n = 431, 73.2%) and seizures/status epilepticus (n = 88, 14.9%), and 426 (72.3%) received invasive mechanical ventilation. A total of 298 patients (50.5%, 95%CI 46.6%-54.6%) had poor functional outcome, including 150 deaths (25.5%). Variables independently associated with the primary endpoint were age > 60 years [OR = 1.69 (95%CI 1.19–2.40)], immunocompromised status [OR = 2.02 (95%CI 1.31–3.12)], time between hospital and ICU admission > 1 day [OR = 1.99 (95%CI 1.36–2.91)], and the following ICU admission variables: a motor component on the GCS ≤ 3 [OR = 2.29 (95%CI 1.49–3.50)], the presence of hemiparesis/hemiplegia [OR = 2.19 (95%CI 1.32–3.64)], respiratory failure [OR = 1.82 (95%CI 1.10–3)], and cardiovascular failure [OR = 1.69 (95%CI 1.10–3)]. Among patients with bacterial meningitis, only a motor response on the GCS ≤ 3 and hemiparesis/hemiplegia remained independently associated with the primary endpoint. Among patients with primary encephalitis, those with immune-mediated causes had the worst outcomes.

Conclusion. Conclusions and relevance We observed a poor prognosis in half of the patients with meningoencephalitis requiring intensive care. Main outcome indicators were immunocompromised status, the severity of neurological presentation, and associated respiratory or cardiovascular failures. Among patients with primary encephalitis, those with immune-mediated causes had the worst outcomes.

Reference

1. TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03144570

Acknowledgements The EURECA study was funded by the European Society of Intensive Care Medicine (ESICM): Romain Sonneville, Established investigator award 2017.

000930

Ventilation settings in early brain-injured patients: preliminary data of VENTIBRAIN STUDY

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Intensive Care Medicine Experimental 2022, **10(2)**: 000930

Introduction: Mechanical ventilation is often used in brain-injured ill patients. Although it is necessary to optimize oxygen delivery to the brain, mechanical ventilation may itself cause pulmonary and cerebral damage, leading to an increase in morbidity and mortality. 'Protective lung ventilation', which includes the use of low tidal volumes and plateau pressure (Pplat), application of Positive end-expiratory pressure (PEEP), and recruitment maneuvers (RM), has shown to reduce morbidity and mortality in intensive care unit (ICU) patients with acute respiratory distress syndrome (ARDS); additionally, it seems to have a beneficial effect on ICU patients with healthy lungs. These recommendations often come into conflict with the management of patients with acute brain injury, in which permissive hypercapnia and increased intrathoracic pressure, as a consequence of protective ventilation strategies, can be dangerous. However, it remains poorly described how current protective lung ventilation recommendations are applied in this setting.

Objectives: The primary objective of this multi-center prospective study is to describe the ventilatory settings and targets used in the brain injured patients during their ICU stay.

Methods: This is an ongoing international, multicenter, prospective, observational study on practice of ventilation in brain injured patients (VENTIBRAIN study). Inclusion criteria are brain injured patients ≥ 18 years old, with a diagnosis of Traumatic Brain Injury (TBI), Subarachnoid Haemorrhage (SAH), Intracranial Haemorrhage (ICH) or acute ischemic stroke (AIS) undergoing invasive mechanical ventilation and admitted to the ICU. Clinical characteristics at the baseline and ventilation settings in the first 24 h of ICU stay were recorded.

Results: This preliminary analysis included 419 patients from 18 countries enrolled from October 2021 to March 2022. The median age was 58 (IQR, 44–70) years and 264 (63%) were males. One hundred fifty-one (36%) were admitted with a diagnosis of TBI, 87 (20.7%) of SAH, 130 (31%) of ICH, and 51 (12.2%) of AIS. Two hundred ninety-five (70.4%) patients had a history of hypertension and 15 (1.96%) suffered from chronic obstructive pulmonary disease. At the first neurological evaluation, the patients had a median motor Glasgow Coma Scale score of 4 (2–5). Median tidal volume was 480 (440–530) mL, median tidal volume per ideal body weight was 7.15 (6.37–8.22) mL/Kg, respiratory rate 16 (14–18) breaths/min, positive end-expiratory pressure 6 (5–8) cmH20 and inspiratory plateau pressure 15 (13–18) cmH_2O. Median compliance of the respiratory system was 47.6 (38–61.1) mL/cmH_2O and driving pressure 10 (8–12) cmH_2O. The median arterial partial pressure of oxygen/ fraction of inspired oxygen ratio was 275 mmHg (IQR 184.2–483.2).

Table 2. Ventilatory settings and pulmonary mechanics at ICU admission

	Overall (n=419)
Ventilatory setting and pulmonary mechanics at ICU admission	
Respiratory rate, breaths/min, median (IQR)	16.0 (14.0; 20.0)
Positive end-expiratory pressure, cmH_2O, median (IQR)	6.00 (5.00; 8.00)
Plateau pressure, cmH_2O, median (IQR)	15.0(13.0; 18.0)
Tidal volume, mL, median (IQR)	480 (440; 550)
Tidal volume, mL/kg PBW, median (IQR)	7.15 (6.37; 8.22)
Driving pressure, cmH_2O, median (IQR)	10.0 (8.00; 12.0)
Compliance of the respiratory system, mL/cmH_2O, median (IQR)	47.6 (38.0; 61.1)
Gas exchange	
Fraction of inspired oxygen (FiO_2), %, median (IQR)	40.0 (30.0; 50.0)
PaO_2, mmHg, median (IQR)	110 (92.1; 145.0)
PaO_2/ FiO_2 ratio, mmHg, median (IQR)	275 (184.2; 483.3)
$PaCO_2$, mmHg, median (IQR)	37.8 (34.0; 42.0)
pHa, median (IQR)	7.41 (7.35; 7.46)

Table 1. Baseline characteristics of patients at ICU admission

	Overall (n=419)
Baseline patient characteristics	
Age, years, median (IQR)	58 (44; 7)
Gender, male, n (%)	264(63)
Height, cm, median (IQR)	170 (165; 180)
Weight, kg, median (IQR)	76 (65; 85)
BMI, kg/m^2, median (IQR)	26.3 (24.1; 29.7)
Chronic comorbidities	
Hypertension, yes, n (%)	87(29.5)
Diabetes mellitus, yes, n (%)	82 (19.4)
Cardiological history, yes, n (%)	42(10.1)
Smoke, yes, n (%)	67(16)
COPD, yes, n (%)	9(1.9)
Cancer, yes, n (%)	36(9.5)
Type of brain injury	
TBI n (%)	151(36)
SAH n (%)	87 (20.7)
ICH n (%)	130 (31)
Stroke n(%)	51(12.2)
GCS motor ,median (IQR)	4 (2-5)

Conclusion: The findings of this preliminary analysis show that acute brain-injured patients during the first 24 h after the admission in ICU

are usually ventilated with a lung protective approach using low tidal volumes, low to moderate level of positive end-expiratory pressure and low inspiratory plateau pressure.

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001109

Standard versus individual positive end-expiratory pressure (PEEP) by electrical impedance tomography in neurocritical care: a pilot prospective study

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Intensive Care Medicine Experimental 2022, **10(2)**: 001109

Introduction: Introduction: Optimization of mechanical ventilation with Positive End-Expiratory Pressure (PEEP)in neurocritical care patients is an important aspect on which we have to put a proper attention due to a secondary brain damage and possible intracranial hypertension which could be worsened with excessively high PEEP.
Objectives: Objectives: We tried to determine whether a mechanical ventilation with individualized PEEP obtained from PEEP titration procedure guided by Electrical Impedance Tomography (EIT) results in a better distribution of lung ventilation, compared to the ventilation with standardised PEEP of 5 cm H_2O (standard recommended PEPP for neurointensive patients with an acute brain diseases without intracranial hypertension [1]).
Methods: Methods: 55 acute adult neurocritical care patients started the mechanical ventilation with standardised PEEP of 5 cm H_2O with their lungs monitored by EIT over three days in average. Within one day EIT PEEP-titration was performed and optimal PEEP was identified (PEEP when lung overdistensions and collapses are minimal). Then, optimal PEEP was set and homogeneity of lung ventilation using global inhomogeneity index (GII) [2], as well as SpO_2 and $EtCO_2$ were evaluated before and after this change of PEEP.
Results: Results: Optimum PEEP based on EIT-PEEP titration procedure ranged from 2 to 8 cm of H_2O. However, this did not cause improved ventilation homogeneity or changes in SpO_2 or $EtCO_2$ compared to standardised PEEP of 5 cm of H_2O. Besides analysing the effect of PEEP on the GII, we also evaluated the effect of patient positioning on the GII value, and found statistically significant changes in GII with patient body position (lateral tilt by approx. 10°, every 2 h, R, L, H).

GII region; change of PEEP after EIT PEEP titration	P value Before vs. after setting EIT-titrated PEEP		
	GII	SpO_2	$EtCO_2$
Whole lungs GII; PEEP increase or decrease	0.945	0.44	0.61
Right lung GII; PEEP increase or decrease	0.347		
Left lung GII; PEEP increase or decrease	0.931		
Whole lung GII; PEEP increased > 2 cmH_2O	0.754	0.74	0.44
Whole lung GII; PEEP decreased > 2 cmH_2O	0.419	0.53	0.25
Whole lung GII; PEEP increase	0.945	0.54	0.87
Whole lung GII; PEEP decrease	0.327	0.55	0.67

Conclusion: In neurocritical care patients, the EIT-titrated PEEP could be 2 cm H2O and still not changing the GII, SpO_2 and $EtCO_2$ compared to standard PEEP of 5 cmH_2O.

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Acknowledgements TAČR FW01010679.

001208

A Single center, Prospective, Observational study to determine the effect of Fibrinogen levels in Thrombolysis of Stroke Patients (Before, after 06 h and 24 h of Thrombolysis) on various outcome indicators

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Intensive Care Medicine Experimental 2022, **10(2)**: 001208

Introduction: Cerebrovascular Accident (CVA), commonly called as Stroke is a debilitating disease. Cerebral angiography conducted soon after the onset of stroke demonstrates arterial occlusions in 80 percent of acute infarctions. [1,2]. Thrombolytic canalization of occluded arteries may reduce the degree of injury to the brain if it is done before the process of infarction has been completed. Since intracerebral haemorrhage was a frequent major complication reported in early trials of thrombolytic therapy [3,4] the use of recombinant human tissue plasminogen activator (t-PA) for cerebral arterial thrombolysis requires a careful evaluation of both the risks and the potential benefits. In our study we tried to find the benefits (Improvement in NIHSS) and risks (Intracranial Bleed)in relation to Fibrinogen levels at 0 (Before Thrombolysis), 6 h after and 24 h after thrombolysis.
Objectives: To determine the effect of Fibrinogen levels in Thrombolysis of Stroke Patients (Before, after 06 h and 24 h of Thrombolysis) on various outcome indicators.
Methods: The study population consists of Patients with Non Hemorrhagic CVA presenting within window period of 0–4.5 Hour. We collected the following data for each patient: Demographics, history of hypertension, time from symptom onset (of stroke) to alteplase infusion, National Institutes of Health Stroke Scale (NIHSS) scores before alteplase infusion and 6 and 24 h after alteplase infusion, Blood pressure 1 hrly during and 24 h, level of fibrinogen before, after 06 h and 24 h of Thrombolysis, Incidence of intracranial (IC) bleeding and its potential association with fall in fibrinogen level. All Statistical Analysis done using licensed statistics/ data analysis software SPPS IBM Corp Released 2017 for data analysis.

Results:
We studied 40 Patients.

Mean age 67.95.
Male (N) 25.
Female (N) 15.
As per our data analysis fibrinogen levels and NIHSS improvement at 0–6 h, 0–24 h and 6–24 h was statistically significant. 3 patients out of 40 had IC bleed but they did not have significantly higher fall in fibrinogen levels as compared to patients who didnt have IC bleed. Statistical tables and images could not be shared due to limitation of space. However we are ready to share additional data if asked for.
Conclusion: To summarise it appears that fibrinogen level reduction after thrombolysis has a good correlation with NIHSS improvement. The risk of bleeding doesnt increase with lower initial fibribinogen level, hence it should not stop us from giving thrombolysis which reduces morbidity and mortality. The study has a limitation of small sample size. However to the best of our knowledge it is largest study where fibrinogen levels and its correlation with NIHSS imrovement and IC bleed is studied In Indian population when patients reached hospital within window period and were thrombolysed. Stroke awareness is lacking in India and very few patients reach hospital within 4.5 h of onset of stroke. This has been the biggest challange in getting more number of patients. Still this study might give an insight for the importance of fibrinogen levels in these patients and may be a stimulation to start a multicenter study in India for more powered studies.

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001221

Preoperative serum alkaline phosphatase and neurological outcome of cerebrovascular surgery: A retrospective study

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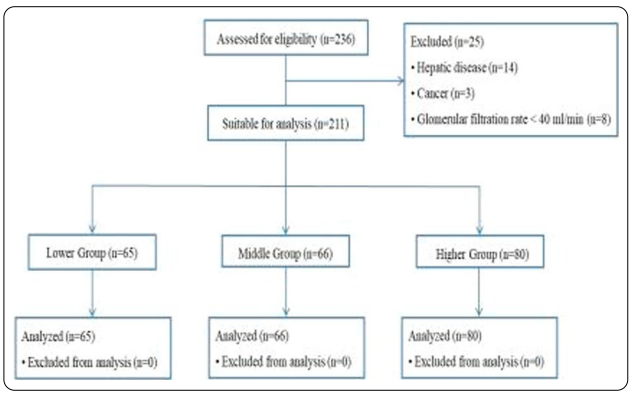
Intensive Care Medicine Experimental 2022, **10(2)**: 001221

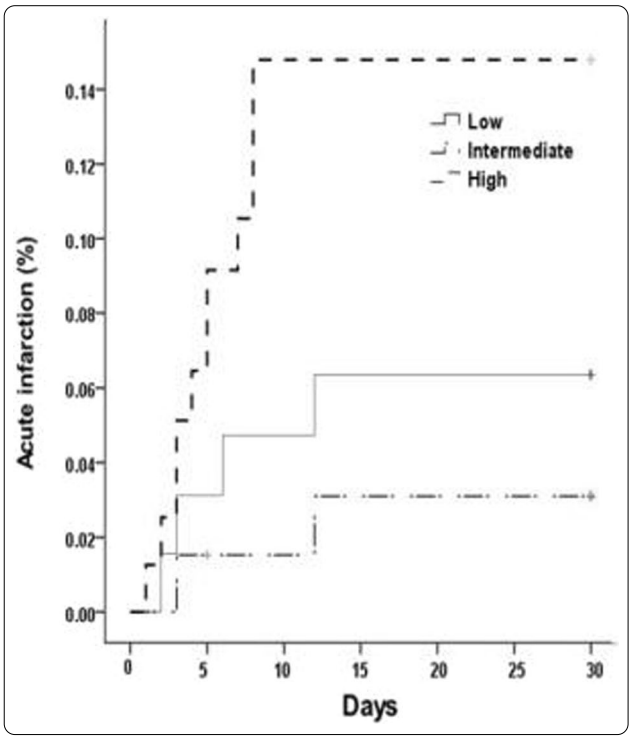
Introduction: The purpose of cerebral bypass is to improve blood flow in the ischemic brain area and to repair a blocked or damaged artery. However, postoperative complications such as subsequent stroke or hemorrhage can occur. Alkaline phosphatase (ALP) is a phosphatase that releases inorganic phosphoric acid from organophosphorus esters. In terms of cerebrovascular disease, ALP is a reliable predictor of the recurrence of cerebrovascular disease and mortality after stroke. Therefore, this study retrospectively evaluated the relationship between preoperative ALP levels and major neurological complications in patients who underwent cerebral bypass surgery after a diagnosis of cerebrovascular stenosis or occlusion.
Methods: Data were collected from electronic medical records dating from May 2003 to August 2017.). The inclusion criteria were a patient with American Society of Anesthesiologists physical status classes I–Ш, over 18 years old with diagnosed cerebral stenosis or cerebral artery occlusion, who underwent cerebral bypass surgery under general anesthesia at single tertiary hospital. The patients were classified into 3 groups by tertiles based on preoperative serum ALP levels.: low (ALP < 63 IU/mL), intermediate (ALP 63–79 IU/mL), and high (ALP > 79 IU/mL) ALP groups. An adverse neurological event was postoperative acute infarction, defined as a new cerebral infarction or an increase in the size of a previous lesion that occurred within 1 month postoperatively and was confirmed by magnetic resonance imaging. The incidence of neurological events according to the ALP level were analyzed.
Results: This study enrolled and analyzed 211 patients (Fig. 1).



Except for ALP and phosphorus levels, the demographic data, medial history, and laboratory data did not differ significantly among the three groups. The incidence of acute infarction in each group differed significantly among the three groups (P = 0.007). In the logistic regression analysis, only serum ALP tertile was related to the incidence of acute infarction. (OR 3.356, 95% CI 1.026–10.974, P = 0.045).

	Lower group (n = 70)	Middle group (n = 70)	Higher group (n = 71)	P value
Acute infarction	4 (5.7%)	2 (2.9%)	12 (16.9%)	0.007

	OR (95% CI)	P-value
ALP third tertile	3.356 (1.026–10.974)	0.045
Cholesterol	0.995 (0.983–1.006)	0.372
AST/ALT ratio	0.995 (0.983–1.006)	0.971
AST/ALT ratio	3.356 (1.026–10.974)	0.045



On Kaplan–Meier time-to-event curves, the incidence of acute infarction increased significantly with the ALP (log rank = 0.048). As the ALP increased, the incidence of acute infarction increased significantly. According to the Cox proportional hazards regression analysis, the hazard ratio of acute infarction was 1.013 (95% CI 1.004–1.022, P = 0.007).

Conclusion: In conclusion, the preoperative serum ALP level was an independent predictor of acute infarction in patients undergoing cerebral bypass surgery. Patients with a high serum ALP may require more careful patient management to prevent postoperative complications.

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Acknowledgements

Conflicts of Interest:

1. None.
2. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

001255

Clinical effects of cerebral near-infrared spectroscopy monitoring (NIRS) and guide intervention versus standard usual care in Comatose patients

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Introduction: Comatose patients with cerebral deoxygenation is associated with various adverse systemic outcomes and increase disability and mortality. We hypothesized, by using the brain as an index organ, with interventions to improve cerebral oxygenation would have systemic benefits in intensive care unit.

Methods: This study is an interventional study. Data from all 60 patients were randomized to either intra and post-operative cerebral regional oxygen saturation (rSO_2) monitoring with active display and treatment intervention protocol to keep $rSO_2 \geq 55\%$ by induced increasing cardiac output, mean arterial pressure, adjust ventilator to hypoventilation (keep $PaCO_2$ 40–45 mmHg) (avoid in patients with significant or radiographic brain herniation) and increase FiO_2 (intervention, n = 30), or underwent blinded rSO_2 monitoring (control, n = 30). Predefined clinical outcomes were assessed by a blinded observer. Both group were retrieved during June 1st, 2018 to January 31st, 2022 comparing NIRS group with standard usual care. Data collection comprised of patients' demographic data, treatment process and outcomes of treatment assess by modify Rankin scale (mRS) at 1 year follow up.

Results: There were no difference in baseline characteristics and no difference in overall incidence of adverse complications between 2 groups. Compared to standard usual care, NIRS group had significantly more good clinical outcome at 1 year follow up (33.3% vs 6.7%, p = 0.01) and no difference in ICU length of stay, ventilator and vasopressor free day. There was a significant (r = 0.459, p < 0.001) positive correlation between rSO_2 and ICU length of stay in patients requiring > 3 days with NIRS guide-intervention. CO ≤ 2 L/min and mean arterial pressure ≤ 65 mmHg were significantly associated with in hospital mortality (Hazard ratio 87.45,8.43, p = 0.024, 0.001 respectively). Outcomes of treatment; mortality rate (mRS = 6), NIRS group was significantly lower than usual care (60% vs 63.3%, p = 0.048).

Conclusion: Monitoring cerebral rSO_2 in comatose patients avoids profound cerebral desaturation and is associated with significantly more incidences of good clinical outcome at 1 year follow up and decrease mortality. CO ≤ 2 L/min and mean arterial pressure ≤ 65 mmHg were factors associated with hospital mortality.

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Acknowledgements My grateful thanks to Mrs Dollapas Panpanich for her helpful doing the data analysis, and extend to the staff of the surgical and medical intensive care unit of Phramongkutklao hospital for their help in offering me the resources in running the study.

001272

Risk of Epilepsy in Elderly Stroke Patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 001272

Introduction: The incidence of epilepsy in elderly stroke patients has been significant attention because planning future needs for health services and improved primary and secondary prevention of stroke are

important. We evaluated the relationship between stroke and the subsequent development of epilepsy within 10 years follow-up.
Methods: This retrospective, nationwide, longitudinal study used National Health Insurance Service-Senior cohort (NHIS-Senior) comprising 550,000 random subjects who were selected from over than 60 years old. This study included a cohort of 42,925 patients who were first diagnoses as stroke between 2009 and 2011. To match each stroke patient, 218,478 control subjects were selected from the data-base.
Results: In this cohort, the prevalence of stroke was higher in female(62%) than in male(38%). A higher prevalence of stoke was observed in the 60–70 years age and more than 80 years age group in urban area. The incidence of stroke was increased from 2002 to 2009, but decreased from 2010 to 2013. The diagnosis of epilepsy was done at averagely 20 months after the diagnosis of stroke. Cox regression analysis showed that the HR of epilepsy was 7.658 times greater for patients with stroke (95% CI: 7.402–7.923) than for control group after adjusting for other risk factors. The HR of epilepsy was 1.08 (95% CI: 1.045–1.116) in female patients, 1.66(95% CI: 1.607–1.715) in diabetic patients, 1.679(95% CI: 1.625–1.734) in hypertensive patients, 1.831(95% CI: 1.626–2.062) in chronic kidney disease and 1.647(95% CI: 1.593–1.703) in hypercholesterol patients.
Conclusion: Our findings suggest that stoke may be independent risk factor for epilepsy in elderly patients(HR 7.658, 95% CI: 7.402–7.923). So we need to control and pay attention to epilepsy in elderly stroke patients.

Systemic Inflammation & Sepsis 1

000009

Timing to use norepinephrine with vasopressin for septic patients: A post-hoc analysis of a multicenter prospective study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000009

Introduction: Clinical practice guidelines for management of sepsis have been published. Although vasopressin (VP) is considered as a second-line vasopressor for sepsis, the optimal timing remains unclear.
Objectives: To clarify how to initiate VP after norepinephrine (NE) administration for septic patients in the real worlds.
Methods: This study was a post-hoc analysis of a multicenter prospective study, which was conducted in 23 intensive care units (ICU) in Japan [1]. We included 67 septic patients who were administered VP and NE. We calculated the following values to estimate how to initiate VP: Time of NE administration until the start of VP administration, NE dosage at the start of VP administration, NE exposure until the start of VP administration, and mean time-weighted dose of NE until the start of VP administration. We compared ICU survivors with non-survivors and created a Cox regression model to assess 30-days mortality according to NE exposure before VP administration.
Results: Twenty of 67 septic patients (29.9%) patients were initiated on NE and VP at the same time and other patients were initiated VP after NE administration. Before VP was initiated, NE was administered for median 1.4 interquartile range [0.0, 6.1] h, and NE dosage was 0.31 [0.20, 0.42] mcg/kg/min. NE was exposed to 16.0 [0.0, 71.3] mcg/kg until the initiation of VP administration, and the mean time-weighted dose of NE was 60.0 [0.00, 100.00] mcg/mL. ICU survivors had lower NE exposure than non-survivors (ICU non-survivors; 33.6 [0.87, 107.3] mcg/kg, ICU survivors; 7.7 [0.0, 34.1] mcg/kg, $p = 0.06$). Using the Cox regression model, exposure of NE $\geq$ 75 mcg/kg until VP administration was associated with increase of 30-days mortality (adjusted hazard ratio, 4.15; 95% confidence interval, 1.75–9.82, $P < 0.01$).
Conclusion: The association between mortality and VP usage was investigated using real-world data. Increased cumulative doses of NE before VP administration might be risk for mortality in septic shock patients.

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000016

Effect of age on abdominal sepsis features and innate immune cell function

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Intensive Care Medicine Experimental 2022, **10(2)**: 000016

Introduction: Sepsis is a life-threatening dysregulated host response to infection that compromises organ health, and abdominal sepsis is a commonly presenting critical illness in intensive care units (ICU). As a greater number of people age into elderly status, it is important to characterize the effect of age on intra-abdominal sepsis outcomes.
Objectives: In this study, we investigate the effect of age on clinical sepsis characteristics and innate immune cell (neutrophil and monocyte) functionality in abdominal sepsis patients.
Methods: We recruited 32 patients with abdominal sepsis from the Beijing Ditan Hospital's ICU from December 2020 to September 2021, and selected 18 healthy volunteers that were age- and sex-matched as controls for a prospective cohort study.
Results: Elderly abdominal sepsis patients had the following altered characteristics compared to controls: lower mean arterial pressure, monocytes percentage, and red blood cell volume distribution width ($p < 0.05$); higher neutrophils percentage and neutrophils-to-lymphocytes ratio ($p < 0.05$); significantly increased monocyte-produced reactive oxygen ($p < 0.05$); increases neutrophilic secretion of TNF-α, as well as lower monocytic secretion of TNF-α ($p < 0.05$); higher neutrophil percentage (which was significantly higher in peripheral blood than monocyte percentage).Elderly patients also had significantly increased phagocytic activity in their neutrophils and monocytes ($p < 0.05$), significantly reduced neutrophils-produced reactive oxygen ($p < 0.001$), and significantly increased TNF-α secretion by monocytes and neutrophils ($p < 0.05$).
Conclusion: This paper focuses on the effect of aging on the clinical sepsis characteristics and immune function. We found that elderly patients have decreased immune cell function and increased release of cytokines compared to younger patients, suggesting individualized treatment plans targeting the elderly septic microenvironment could help prevent organ failure in elderly septic patients and improves patient survival.This paper focuses on the effect of aging on the clinical sepsis characteristics and immune function. We found that elderly patients have decreased immune cell function and increased release of cytokines compared to younger patients, suggesting individualized treatment plans targeting the elderly septic microenvironment could help prevent organ failure in elderly septic patients and improves patient survival.

000017

Identification of immune-related genes in sepsis patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000017

Introduction: Sepsis is defined as a life-threatening organ dysfunction that is caused by a dysregulated host response to infection. The systemic immune response plays a crucial role in the pathogenesis of severe sepsis. Currently, growing evidence suggests that novel immunological biomarkers can be used as potential predictors of the outcome of sepsis.
Objectives: Therefore, the exploration of immune-related diagnostic markers is an important focus of studies on sepsis.V

Methods: Gene expression data of whole blood of sepsis patients and controls were downloaded from GEO database. Firstly, we analyzed and identified the differentially expressed genes (DEGs) between sepsis and control. Meanwhile, the ssGSEA was used to analyze the infiltraion of 28 immune cells in sepsis samples. WGCNA analysis was used to search for co-expressed gene modules associated with immune cells. Then, key networks and hub genes were found in the PPI network. ROC curve was used to evaluate the ability of the hub genes to differentiate sepsis from controls, and miRNA and transcription factor regulatory network analysis were performed for hub genes.
Results: In total, 184 DEGs were identified, including 89 upregulated and 95 downregulated genes in sepsis patients compared with controls. SsGSEA analysis showed that the abundance of CD56 bright natural killer cell, gamma delta T cell, macrophage and natural killer T cell were different between sepsis and controls. WGCNA further identified 20 modules involved in the immune infiltration of sepsis. 1059 genes were extracted from the 7 most relevant important modules. We obtained 27 immune-related DEGs by overlapping 1059 module genes and DEGs. We used 27 immune-related genes to construct a PPI network, and 10 genes with the highest degree were selected as hub genes. ROC curve showed that the AUC values of 6 hub genes were greater than 0.7 in both training set and the validation set, indicating that they were potential biomarkers of sepsis.In total, 184 DEGs were identified, including 89 upregulated and 95 downregulated genes in sepsis patients compared with controls. SsGSEA analysis showed that the abundance of CD56 bright natural killer cell, gamma delta T cell, macrophage and natural killer T cell were different between sepsis and controls. WGCNA further identified 20 modules involved in the immune infiltration of sepsis. 1059 genes were extracted from the 7 most relevant important modules. We obtained 27 immune-related DEGs by overlapping 1059 module genes and DEGs. We used 27 immune-related genes to construct a PPI network, and 10 genes with the highest degree were selected as hub genes. ROC curve showed that the AUC values of 6 hub genes were greater than 0.7 in both training set and the validation set, indicating that they were potential biomarkers of sepsis.
Conclusion: Immune-related hub genes, including ADAR, AP3B1, CNBP, PCBP1, PRDX3 and USP14 may play key roles in the development of sepsis. These results provide novel markers or targets for the diagnosis and treatment of sepsisImmune-related hub genes, including ADAR, AP3B1, CNBP, PCBP1, PRDX3 and USP14 may play key roles in the development of sepsis. These results provide novel markers or targets for the diagnosis and treatment of sepsisImmune-related hub genes, including ADAR, AP3B1, CNBP, PCBP1, PRDX3 and USP14 may play key roles in the development of sepsis. These results provide novel markers or targets for the diagnosis and treatment of sepsisV.

000023

Favorable oxygen target ranges change over time in patients with septic shock—a retrospective cohort study

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Introduction: Adequate oxygenation in patients with septic shock is imperative and hyperoxia has been suggested to improve neutrophil activity [1]. However, hyperoxia increases formation of reactive oxygen species, leads to vasoconstriction, and may thus induce oxygen toxicity. We postulated changing optimum target ranges for oxygen partial pressures (PaO_2) over the course of sepsis and sought to study the association with mortality in the intensive care unit (ICU).
Methods: In this exploratory retrospective single-center cohort study patients admitted to twelve ICUs (140 beds) of the University Medical Center Hamburg-Eppendorf with septic shock and mechanical ventilation > 48 h were included. Data were obtained from electronic records. We calculated time-weighted mean PaO_2 from admission to end of day 1 (d1), day 3 (d3), day 7 (d7), and day 14 (d14). Time weighted mean PaO_2 was categorized in deciles. Finally, we conducted multivariable logistic regression analyses adjusted for age, sex, and length of stay (LOS) in ICU.
Results: From 01/2016 until 12/2021, 2587 patient records were retrieved. Mean age was 63 ± 15 years (males: 66%), the Simplified Acute Physiology Score (SAPS) II was 49 ± 14, and 1687 patients died in ICU (65%). The lowest mortality was associated with a time-weighted PaO_2 between 96 and 103 mmHg on d1 ($p = 0.002$), 82 and 85 mmHg on d3 ($p = 0.023$), 83 and 86 mmHg on d7 ($p = 0.118$), and 83 and 86 mmHg on d14 ($p = 0.001$). Age and LOS were independent predictors of mortality at all timepoints. Favorable PaO_2 ranges on d1 were significantly higher than on d3, d7, and d14 (all $p < 0.001$).
Conclusion: PaO_2 ranges associated with the lowest mortality in patients with septic shock differed over time with higher values being favorable on d1. These results suggest that future studies should consider different oxygen targets over the time course of treatment.

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000072

Impact of Polymyxin B Hemoperfusion Therapy on High Endotoxin Activity Level Patients after Successful Infection Source Control: A Prospective Cohort Study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000072

Introduction: We sought to evaluate the clinical implication of endotoxin levels in gram-negative bacilli (GNB)-induced abdominal septic shock patients with polymyxin B-hemoperfusion (PMX-HP) treatment.
Methods: A prospective cohort of 60 patients who received surgical infectious source control for abdominal sepsis from January 2019 to December 2020 was included in the study. Endotoxin activity (EA) levels and Sequential Organ Failure Assessment (SOFA) scores were assessed immediately after surgery (baseline), 24, and 48 h post baseline. With receiver operating characteristic curves, the patients were stratified into two groups by the EA cut-off value (high-risk group vs low-risk group) and the clinical outcomes were compared. Logistic regression was performed to identify the clinical impact of PMX-HP on in-hospital death.
Results: Among the 31 high-risk patients (EA level ≥ 0.54), 16 patients (51.6%) received PMX-HP treatment and showed significant decreases in EA levels compared to patients who underwent conventional treatment only ($-$ 0.34 vs $-$ 0.12, $p = 0.01$). SOFA scores also showed significant improvement with PMX-HP treatment (12.8 to 8.9, $p = 0.007$). Fourteen in-hospital deaths occurred (45.2%), and PMX-HP treatment had a protective effect on in-hospital death (odds ratio (OR) 0.04, $p = 0.03$). In 29 low-risk patients (EA level < 0.54), seven patients (24.1%) received PMX-HP treatment and showed significant decreases in EA levels (0.46 to 0.16, $p = 0.018$). However, SOFA scores and in-hospital deaths were not improved by PMX-HP treatment.
Conclusion: PMX-HP treatment accelerated endotoxin removal and might be a useful option to improve organ impairment and in-hospital deaths in abdominal septic shock patients with EA levels of ≥ 0.54.

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Acknowledgements Te authors would like to thank all the participants for their valuable contribution to this study and the staf for their friendly cooperation. Te equipment for measuring endotoxin activity assay in this trial was supported by KOLON Pharma.

000073

Prediction of postoperative sepsis using change of presepsin level in surgical intensive care unit patients with acute kidney injury after abdominal surgery

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Intensive Care Medicine Experimental 2022, **10(2)**: 000073

Introduction: Presepsin (PSP) is a viable biomarker for detection of bacterial infection, but lacks accuracy when acute kidney injury (AKI) develops. In this study, we determined the diagnostic power and the cut-off value of PSP in predicting postoperative sepsis respective to the degree of AKI after abdominal surgery.
Methods: 311 patients who underwent abdominal surgery and admitted to surgical intensive care unit were enrolled. Patients were classified into non-AKI, mild-AKI (Risk, Injury, Failure) and severe-AKI (Loss, ESKD) group according to RIFLE criteria. In each group, PSP and other biomarkers were statistically analyzed between non-sepsis and postoperative sepsis at the admission (T0), 24 h (T1), 48 h (T2) and 72 h (T3) after surgery.
Results: Comparison of PSP level between postoperative sepsis and non-sepsis, PSP levesl were significantly higher in postoperatve sepsis in non-AKI and mild-AKI group, whereas no difference was observed in severe-AKI group. Cutoff values of PSP in mild-AKI group for prediction of postoperative sepsis were 544 pg/ml (AUC:0.757, $p < 0.001$) at T0 and 458.5 pg/ml (AUC:0.743, $p < 0.001$) at T1, prominently higher than those of non-AKI group. In multivariate analysis, predictors of postoperative sepsis in mild-AKI group were PSP at T2 [Odds ratio (OR):1.002, $p = 0.044$] and PSP at T3 (OR:1.001, $p = 0.049$).
Conclusion: Not only for patients without AKI, PSP can be clinically applicable to predict postoperative sepsis with modified cutoff values for patients with transient AKI after abdominal surgery.

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Acknowledgements No additional investigators participated in this research project.

000126

Prospective Analysis Of Patients Followed Up İn The İntensive Care Unit With The Diagnosis Of Sepsis By Phenotypically Classifying Them According To Their Temperature Trajectories

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Intensive Care Medicine Experimental 2022, **10(2)**: 000126

Introduction: Sepsis is a heterogeneous syndrome with a high mortality rate, which has a different clinical course depending on the patient and the location of the infection. Identifying the subphenotypes of this heterogeneous syndrome is essential in therapeutic management.
Methods: 150 patients over the age of 18 who were followed up in the intensive care unit with the diagnosis of sepsis were included in the study. All temperature measurements were recorded for 72 h after admission to the intensive care unit. Temperature measurements were made with an infrared device via axillary, oral, tympanic and temporal routes. At the end of the study, the patients were divided in to 4 groups according to their body temperature: hypothermic (α), normothermic (β), hyperthermic fast resolvers (γ) and hyperthermic slow resolvers (δ).
Results: 150 sepsis patients were included in the study. The median age of all patients was 65 years and 49% were female. Patients; 36 (24%) were hypothermic, 49 (33%) were normothermic, 34 (23%) were hyperthermic fast soluble and 31 (21%) were hyperthermic slow soluble. The median of the patients included in the study; 96 (64%) of the patients died. The ages of the hypothermic and normothermic patient groups were significantly higher than the other two groups (α: 70, β: 70, γ: 64, δ: 57; p = 0.026). Charlson comorbidity index was significantly higher in the hypothermia group (α: 8 ± 3, β: 7 ± 3, γ: 5 ± 3, δ: 5 ± 3; p: 0.006). The number of days of stay in the ICU (α: 10, β: 7, γ: 5, δ: 9) was significantly lower in the hyperthermic rapidly dissolving group (α: 10, β: 7, γ: 5, δ: 9; p = 0.002). Mortality was significantly lower in the hyperthermic rapidly dissolving group (α:26, β:28, γ: 13, δ:29; p < 0.005).

Demographic and Clinical Characteristics Table

	All patients n:150	Hypothermic (α) n:36	Normothermic (β) n:49	Hyperthermic, fast resolvers (γ) n:34	Hyperthermic, slow resolvers (δ) n:31	P
Age, yr, median (IQR)	65 (50–74)	70 (59–76)	70 (54–77)	64 (41–73)	57 (48–66)	**0.026**
Female sex, n (%)	73(49)	16 (44)	26 (53)	18 (53)	13 (42)	0.695
Procalcitonin, ng/mL, median (IQR)	3.7 (1.2-18.57)	2.66 (1.06–15.27)	3.67 (1.26–17.10)	4.18 (1.45–46.10)	7.72 (1.13–24.30)	0.832
CCI, ± SD	6 ± 3	8 ± 3	7 ± 3	5 ± 3	5 ± 3	**0.006**
SOFA (IQR), median (IQR)	11 (7–14)	12 (9–15)	11 (5–15)	8 (3–13)	12 (8–14)	0.065
APACHE-II, median (IQR)	24 (20–29)	28 (22–32)	23 (18–29)	23 (17–29)	25 (21–29)	0.090

Demographic and Clinical Characteristics Table

	All patients n:150	Hypo-thermic (α) n:36	Normo-thermic (β) n:49	Hyper-thermic, fast resolvers (γ) n:34	Hyper-thermic, slow resolvers (δ) n:31	P
LOS in ICU, d, median (IQR)	7 (4–13)	10 (5–16)	7 (4–10)	5 (4–8)	9 (4–21)	**0.002**
LOS in hospital, d, median (IQR)	14 (8–26)	14 (8–21)	11 (8–23)	14 (7–25)	22 (9–37)	0.150
Mortality, n (%)	96 (64)	26 (72)	28 (57)	13 (38)	29 (94)	< 0.005

Conclusion: In this prospective study, 4 clinical phenotypes were identified according to temperature associated with clinical outcomes. The results led to the idea that these phenotypes could be helpful in understanding the heterogeneity of treatment effects. More research is needed to determine the clinical utility of these phenotypes and to determine their effects on patient outcomes.

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000145

Variation of beta-lactam antibiotic concentrations in critically ill patients after adjustments according to clinical characteristics

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Introduction: Antibiotic concentration target attainment is known to be poor in critical ill patients. Dose adjustment is recommended in patients with altered clearance, volume of distribution and according to bacterial susceptibility. The effect of beta-lactam antibiotics depends on the concentration above the minimal inhibitory concentration (MIC). A concentration above the MIC during the whole dosing interval (100%ft > MIC) is a suggested minimum requirement and four times the MIC gives the maximal bactericidal effect (100%ft > 4MIC). The aim of this study was to investigate the variation of antibiotic concentration in critically ill patients with standard and adjusted dose according to patient characteristics and microbiology findings.
Methods: This prospective pilot study included and measured concentration of the three most common beta-lactam antibiotics prescribed in the ICU, cefotaxime, piperacillin/tazobactam and meropenem. All patients had confirmed or suspected infection and had received at least four doses of the beta-lactam antibiotic to reach steady state. Mid-dose and trough values were collected during a single dosing interval. The primary pharmacokinetic/pharmacodynamic targets were one- and four times free antibiotic concentrations above the minimum inhibitory concentration (MIC) during the whole dosing interval (100% ft > MIC) and (100% ft > 4MIC). MIC breakpoints for cefotaxime were 1 mg/L, piperacillin/tazobactam 8 mg/L and meropenem 2 mg/L.
Results: We included 102 patients (38 cefotaxime, 30 piperacillin/tazobactam, 34 meropenem) at the intensive care unit at Skane University Hospital, Malmö during 2020 and 2021. The median age was 65.5 ([IQR], 57–73) years and 27% were females. Target attainment for 100%ft > MIC was 74% for Cefotaxime, 67% for Piperacillin/tazobactam and 88% for Meropenem. Target attainment for 100%ft > 4MIC was 34% for cefotaxime, 30% for piperacillin/tazobactam and 53% for meropenem. In patients with standard dose 71% attained 100%ft > MIC and 37% for 100%ft > 4MIC. All patients with reduced dose attained 100%ft > MIC and 27% attained 100%ft > 4MIC. In patients with increased dose 79% attained 100%ft > MIC and 48% 100%ft > 4MIC respectively.
Conclusion: Beta-lactam antibiotics concentration vary widely in critically ill patients. The dosage regime currently employed are not sufficient to reach even the lowest target concentration in approximately a quarter of the patients. In patients whom dose adjustment was performed, the group with reduced dose had higher target attainment compared to the group with increased dosing suggesting the need for even higher dose increase in this group. Alternatively, therapeutic drug monitoring can be applied to further increase target attainment.

Systemic Inflammation & Sepsis 2

000162

Mitochondrial and immunosuppressive effects of norepinephrine in a septic monocyte model: physiological or supra-physiological?

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Intensive Care Medicine Experimental 2022, **10(2)**: 000162

Introduction: The use of norepinephrine may further aggravate the dysregulated immune response seen in sepsis [1]. Increasing ß-adrenergic (β-AR) anti-inflammatory affinity of norepinephrine occurs at higher concentrations. Thus, neither the dose–effect relationship nor the mechanisms contributing to adverse immunological effects of norepinephrine are well understood [2]. As optimal immune cell effector functions use energy, we tested the hypothesis that altered mitochondrial bioenergetics in sepsis, alongside mitochondrial reactive oxygen species (mROS) may adversely impact immune cell function [3,4].
Objectives: To study the effects of physiological and supraphysiological concentrations of norepinephrine, as found in septic patients, on monocyte mitochondrial and effector function in an *ex-vivo* model of infection.
Methods: Fresh peripheral blood mononuclear cells (PBMCs) were isolated from healthy volunteers ($n = 6$) and incubated for 6 h with *S. Aureus* (SA) (10^8/mL) and three different concentrations of norepinephrine representing levels found in sepsis (1 ng/mL), septic shock (10 ng/mL) and a supraphysiological dose (100 ng/mL) [5]. PBMCs were stained for flow cytometry with pan-leukocyte anti-CD45, anti-CD14 and anti-CD16 to identify monocyte subpopulations, anti-HLA-DR for HLA-DR receptor expression as a surrogate for effector function, TMRM and MitoSox™ as measures of mitochondrial membrane potential (MMP) and mROS production, and Live/Dead™ as a marker of viability. Appropriate positive-, negative-, and fluorescence minus one (FMO) controls were used. Samples were measured using a BD LSR Fortessa flow cytometer and analysed using FlowJo. Prism was used for statistical analysis comparing unstimulated with SA-treated cells by Wilcoxon matched-pairs signed rank test, and the effects of norepinephrine on SA-treated cells by Friedman test with subsequent uncorrected Dunn's test.

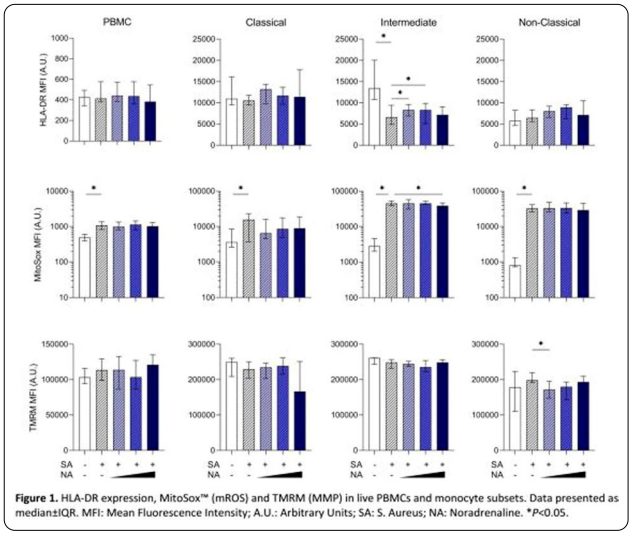

Figure 1. HLA-DR expression, MitoSox™ (mROS) and TMRM (MMP) in live PBMCs and monocyte subsets. Data presented as median±IQR. MFI: Mean Fluorescence Intensity; A.U.: Arbitrary Units; SA: S. Aureus; NA: Noradrenaline. *P<0.05.

Results: Incubation of cells with SA resulted in decreased HLA-DR expression on intermediate monocytes, and increased MitoSox™ in all cell types ($P=0.03$ for all) (Fig. 1). In intermediate monocytes, norepinephrine at low and medium concentration resulted in partial recovery of HLA-DR ($P=0.04$ for both), but this effect disappeared with high dose. High dose did however decrease mROS ($P=0.04$). Low dose decreased MMP in non-classical monocytes ($P=0.04$).

Conclusion: Lower physiological levels of norepinephrine induce an immunostimulatory effect by restoring HLA-DR expression which is lost at high dose. Supraphysiological levels also decreased mROS production in intermediate monocytes. Altered MMP could not explain these effects in the current model. This study highlights the importance of using physiologically relevant doses in *ex-vivo* models to improve translation to the clinic. Future experiments should include more measures of immune function and different exposure times to determine beneficial or detrimental effects in individual patients.

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Acknowledgements MJM is supported by the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 676129.

000176

Interpretable real-time prediction of sepsis mortality using machine-learning algorithms

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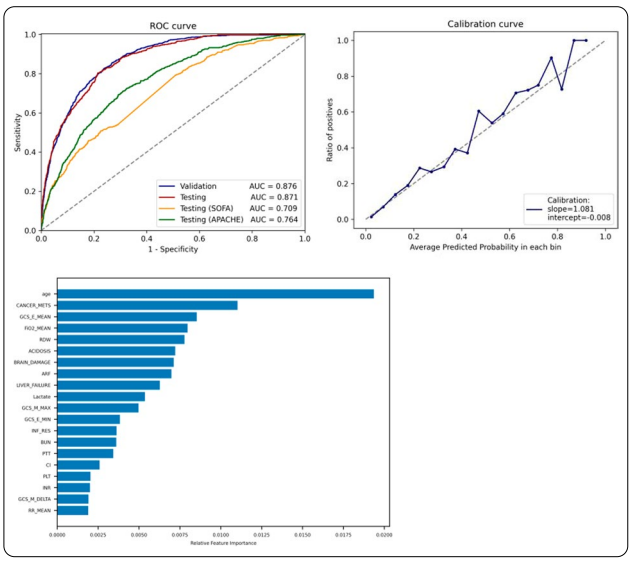
Introduction: Prognosis prediction for sepsis patients has always been a challenging task. While there are several scores being applied in clinical practice, these scores require a relatively long period of data follow-up, and large-scale evaluation is still not available.

Objectives: Using state-of-the-art machine-learning algorithms on the MIMIC-IV dataset, this study aims to develop a real-time risk stratification tool for mortality prediction at sepsis onset. With emphasis on interpretability, we also paid special attention to the calibration properties, in addition to the traditional discrimination metrics such as AUROC.

Methods: From the MIMIC-IV dataset, we extracted the vital signs and lab data on an hourly basis, in addition to the infection focus and past history information. SOFA scores and modified 6-h APACHE II scores were assessed, and sepsis patients were labeled following the SEPSIS-3 criteria. In-hospital mortality outcomes were then specified depending on the pre-defined (30-day) window of prediction. A variety of machine learning models were applied for prediction of mortality at the time point of sepsis onset. Both discrimination and calibration metrics were considered for evaluation of model performance.

Results: Using the record most recent to sepsis onset as well as the 6-h difference in value, the ensembled model of XgBoost and SVM yielded the best performance for 30-day mortality prediction, giving the AUROC of 0.876 (95% CI 0.864–0.888), sensitivity of 0.825 (95% CI 0.799–0.851), and specificity of 0.763 (95% CI 0.751–0.776) on the validation dataset, while producing the AUROC of 0.871 (95% CI 0.857–0.885), sensitivity of 0.859 (95% CI 0.831–0.887), and specificity of 0.710 (95% CI 0.693–0.727) on the testing dataset. For calibration property analysis, the reliability diagram gave the regression slope of 1.081 (95% CI 1.008–1.151) and intercept of -0.008 (95% CI − 0.035–0.02); Spiegelhalter's z test and Hosmer–Lemeshow goodness of fit test yielded insignificant p values (0.426 and 0.092 respectively), indicating reliability in risk estimation in addition to binary classification. Feature importance analysis revealed patient age, comorbidities such as metastatic cancer, the Glasgow coma scale, and FiO_2, being determinative factors on sepsis mortality prediction.



Conclusion: With fair performance on real-time prediction of long-term sepsis mortality, our model revealed a valuable approach for early alarming as well as risk stratification, with emphasis on calibration properties in terms of interpretability. For potential incorporation and identification of alarming patterns in serial features, a deep-learning approach would be explored in the near future.

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000189

Candidemia in non neutropenic COVID 19 patients during the ICU stay: Incidence, patients characteristics and mortality

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Introduction: A higher incidence of candidemia has been reported in COVID-19 critical care patients compared to other ICU patients. We aimed to describe clinical characteristics and outcome in candidemia cases.
Methods: We retrospectively analyzed all COVID 19 patients (diagnosis with polymerase chain reaction) admitted to our ICU from September 2021 to January 2022. We identified a total of 10 patients with candidemia. Candidemia defined as a detection of one or more Candida species in at least one blood culture in patients with clinical signs of infection. Data regarding candidemia episode were analyzed.
Results: Characteristics of patients with Candidemia (n = 10) are shown in Table 1. All of them were unvaccinated. Compared with the rest of the cohort (n = 77), mean age of candidemia patients was 64,6 ± 8,2 vs 62,4 ± 11, females 40% vs 45%. A total of 5 non-albicans species of *Candida(NAC) were* isolated (*Parapsilosis* 3,*Glabrata* 1, *Lusitaniae* 1). Fluconazole resistance was found in 1/5 Albicans and in 2/5 NAC species. Mean ICU days before Candida isolation was 14.8 ± 8.2 Mean Hospital days before ICU was 7.1 ± 5.2. In 7/10 cases *Candida* spp. were also isolated from *sites other* than blood. Only 1/10 patients was diabetic while none of them received parenteral nutrition.
Mortality of candidemia patients was 60%
Table 1 Characteristics of Candidemia Covid 19 ICU pts

Gender/ age	Candida species	Fluconazole Susceptibility MIC	Comorbidities	Other sites of candida	ICU pre-candida days	Hospital pre ICU days	Death
M,51	Glabrata	R (echinocandin S)	0	0	16	6	0
M,57	Albican	S (1)	0	CL	15	7	0
M,68	Lusitaniae	R (Voriconazole S)	Carotid dis HPT	0	16	2	0
F,65	Parapsilosis	S (< 0.5)	0	Urine	17	16	1
F,75	Albican	S (1)	HPT, Parkinson	Bronchial secretions	6	5	1
M73	Albicans	S (< 0.5)	Thrombophilia Coronary dis	Urine	2	16	1
F 69	Parapsilosis	S (2)	HPT	Clurine	15	1	1
F 52	Parapsilosis	S (< 0.5)	HPT	Urine	7	7	0
M 73	Albicans	R(16)	HPT, DM	Urine	29	8	1
M 63	Albicans	S (< 0.5)	0	0	25	3	1

(CL = central line, DM = diabetes mellitus, HPT = Hypertension.

Conclusion: Risk of candidemia in COVID-19 patients admitted to ICUs is high. Corticosteroid administration and prolonged ICU stay with broad spectrum antibiotic therapy are predisposing factors. In our Covid ICU the incidence of Candidemia was 11.5%. Half of the cases were non-albicans species of *Candida*. Candidemia develop within 2 weeks from ICU admission.Mortality rate was high (60%).

000211

Initiation timing of Hydrocortisone in Adults with Septic Shock: A Machine Learning-Based Approach to Estimate Time-Varying Treatment Effects

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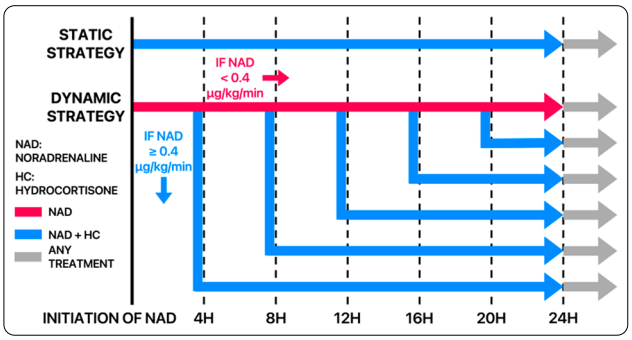
Introduction: Critical illness-related corticosteroid insufficiency (CIRCI) is known to be associated with hemodynamic instability and poor response to vasopressors in patients with septic shock [1–3]. A meta-analysis indicated that hydrocortisone as a treatment of CIRCI achieved septic shock reversal and might reduce 28-day and in-hospital mortality among patients with sepsis [4]. Some guidelines have recommended hydrocortisone use for patients with septic shock [3, 5], and early initiation of hydrocortisone was found to be associated with improved survival among patients with septic shock requiring a high dose of noradrenaline [6]. However, the optimal timing of hydrocortisone initiation remains unclear: should hydrocortisone be initiated together with noradrenaline, or should it be reserved to patients requiring high-dose noradrenaline?
Methods: This was a retrospective cohort study using the MIMIC-IV (Medical Information Mart for Intensive Care IV) dataset [7]. We identified adults with septic shock based on the Sepsis-3 criteria. We considered the administration of hydrocortisone as a time-varying treatment [8] and compared the treatment effects of the following two treatment strategies (Figure): (1) hydrocortisone is started immediately (within 4 h) after noradrenaline initiation (static treatment strategy) and (2) hydrocortisone is not started until the dose of noradrenaline exceeded 0.4 mcg/kg/min (dynamic treatment strategy). An extended framework [9] based on g-estimation and double machine learning was applied to estimate the debiased treatment effects of two hydrocortisone administration strategies on in-hospital mortality adjusted for potential confounders (e.g., patient demographics, vital signs, laboratory tests, concomitant treatments).



Results: Among 8,684 patients with septic shock based on the Sepsis-3 criteria, the median age was 68 years (IQR: 57–69 years), 5,015 (58%) were male, and 287 (3.3%) patients were started on hydrocortisone within 24 h of noradrenaline initiation (i.e., a diagnosis of septic shock). Of all patients with septic shock, we identified 74 patients treated with the static strategy and 6540 treated with the dynamic strategy. In-hospital mortality among patients categorized in either the static or dynamic treatment strategy was 24.7%. Based on our

machine learning-based approach for estimating time-varying treatment effects of hydrocortisone, the dynamic treatment strategy was significantly associated with lower in-hospital mortality compared to the static treatment strategy (adjusted risk difference − 20.9%; 95%CI − 35.7 to − 4.4%).
Conclusion: In patients with septic shock, hydrocortisone initiation upon requirement of high-dose noradrenaline was associated with lower in-hospital mortality compared with hydrocortisone initiation immediately after the diagnosis of septic shock. Our findings could facilitate future interventional trials to optimize the timing of hydrocortisone initiation in septic shock.

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Acknowledgements The authors have no conflicts of interest to declare.

000222

Longstanding splanchnic hemodynamic dysfunction in sepsis survivors may be related to high morbidity. Experimental study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000222

Introduction: The mortality rate of sepsis survivors is high, and the mechanisms that lead to accelerated death have not yet been elucidated [1,2]. The hemodynamic and cellular changes in sepsis result from the effects of pro-inflammatory mediators involved in the host's response to infection, leading to organ dysfunction. Gut immunity has been related to systemic inflammatory exacerbation in critical illnesses [3].
Objectives: This study evaluated the kinetics of blood flow distribution to splanchnic territory in the acute phase of sepsis and after sepsis recovery periods in rats.
Methods: Following the induction of a DL50 sepsis model (2 mL *E.coli* 108 CFU/ mL, iv) in adult Wistar female rats, the animals were monitored for macro (MAP, and abdominal aorta blood flow by Transonic, TS420 transit-time flowmeter), regional (mesenteric artery and vein, celiac trunk artery and portal vein flow by Transonic, TS420 transit-time flowmeter), and micro hemodynamics (liver and ileum). Animals were monitored before sepsis (T-0) and for 6 h, 30, 90, and 180 days (T-6 h, T30, T90, and T180) post-sepsis periods (n = 5/period). Naïve animals (N) were used as a control. (n = 5). All rats were euthanized at the end of the experiments.
Results: The MAP did not vary throughout the periods. (110 + 4 Naive, 102 + 8 T-6 h, and 106 + 9 mmHg in T-30, 60, and 90 days). However, a rapid and significant decrease in the aorta's blood flow was observed up to 6 h after sepsis, with partial recovery at 30 and 60 days (Fig. 1). The blood flow recovery, similar to T-0 values, was only achieved after 180 days. The celiac trunk did not show significant changes over time. The mesenteric artery and vein, as well as the portal blood flow, showed a significant decrease at 6 h and remained low until 90 days after sepsis. In 180 days, all flow returned to the basal level (Fig. 1). Tissue perfusion showed different behavior between organs (Fig. 2). The liver showed significantly lower values in 30 days after sepsis when compared to the controls, while in the ileum a significant drop occurred at 90 days. The results showed that despite the hypoflow seen in post sepsis groups, no changes in MAP were observed. Overall, a significantly prolonged hypoxia effect persisted in the liver and small intestine for 3 months. Besides, images of SDF-videomicroscopy showed persistent microvessel and tissue alterations comprised of venular congestion and tissue edema in splanchnic organs (Fig. 3.).
Conclusion: In rats sepsis survivors, the splanchnic organs undergo prolonged hypoxia, and their recovery period appears to be around 6 months. The splanchnic organs' hemodynamic dysfunction may be a contributing factor implicated in post-sepsis high morbidity. Ongoing studies are evaluating other organs' hemodynamics to better address this issue.

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Acknowledgements Grant 2017/21052-0, São Paulo Research Foundation (FAPESP).

000224

Prognostic utility of early determination of troponin I associated to death in patients with sepsis at intensive care unit "Dr Mario Shapiro" ABC Medical Center

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Intensive Care Medicine Experimental 2022, **10(2)**: 000224

Introduction: Sepsis is one of the most frequent causes of admission to intensive care. Mortality ranges is 10–15%. Cardiovascular abnormalities are frequent in sepsis related to myocardial injury. Cardiac-specific troponins I and T are found only in the heart, when there is damage to heart muscle cells, cardiac-specific troponins I and T are released into circulation. Cardiac troponin elevation among patients with sepsis is common, but its role in risk stratification of patients with sepsis is still debated. The pathophysiology of troponin elevation in sepsis is thought to be due to myocardial dysfunction. Proposed mechanisms for myocardial dysfunction in sepsis includes demand ischemia, direct cardiac myotoxic effects of endotoxins, cytokines or reactive oxygen radicals, and alterations in regional coronary blood flow. Troponin I is a marker of myocardial damage associated with worse prognosis and death.

Objectives: To determine the prognostic utility of early determination of troponin I to predict death in patients with sepsis.
Methods: A simple cohort study was carried out with 65 patients admitted to the Intensive Care Unit of the ABC Medical Center with sepsis criteria according to the 3rd definition and 18 years or older were included. Patients were excluded from the study if they had history of myocardial infarction, angina pectoris, coronary angioplasty, pulmonary embolism, or chronic renal failure. Demographic and clinical variables were determined in all cases. Troponin I was determined in the first 24 h after admission. The outcome variable was death.
Results: Sixty-five patients with sepsis were enrolled in the study. Thirty (46%) patients had elevated serum Troponin I. Mortality 33% vs 26% compared to normal troponin I patients. A ROC curve was performed to find a cut-off point with troponin values of 50 ng/dl with a sensitivity of 73% to predict death. ORs were determined for troponin outcomes with an OR of 6.6 for death with 95% CI (1.24–34.9).
Conclusion: The determination in the first 24 h of troponin I values greater than 50 ng/dl was shown to be a predictor of death in patients with sepsis with 73% of sensitivity. Serum troponin measurement can be done to detect myocardial injury in patients with sepsis. Therefore, an elevated troponin value during the first days of admission may be a reliable test to identify septic patients who are at high-risk for mortality and select them for more aggressive management.

000234

Use of non-invasive measurement of indocyanine green plasma disappearance rate in patients with septic shock

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Intensive Care Medicine Experimental 2022, **10(2)**: 000234

Introduction: Indocyanine green plasma disappearance rate (ICG-PDR) is a dynamic test of liver function and flow with predictive value of mortality in hepatectomised patients and in several groups of critically ill patients.
Objectives: Our aim was to analyse the correlation of serial values of the ICG-PDR with hospital mortality in the first 48 h of ICU admission in patients with septic shock (SS).
Methods: Prospective analytical observational study carried out over 12 months of patients admitted to the ICU with SS. Each patient underwent non-invasive determination of ICG-PDR at 24 and 48 h with the LiMON® module. Follow-up was performed until hospital discharge or exitus. For each clinical variable recorded, the values corresponding to the time of diagnosis of SS and the values obtained at 24 and 48 h were analysed. For the descriptive analysis, absolute frequency (N), relative frequency (%), mean values, median, standard deviation (SD), and 25th, 50th and 75th percentiles were calculated. T-tests: Chi-square, independent samples t-test, Mann–Whitney U-test for independent samples and Wilcoxon signed-rank test. A two-stage clustering was performed for the classification of the hospital mortality variable with different prognostic variables (ICG-PDR, SOFA, APACHE II).
Results: Results: 63 patients. Age 61.1 ± 12.3 years. 60.3% men. SOFA on admission 8.7 ± 3.3 and APACHE II 27.9 ± 10.7 points. 44.4% of patients died. These patients maintained low ICG-PDR values: 10.5 (5.7–13.0) and 10.5 (3.9–13.6) %/min at 24 and 48 h respectively. In survivors: 15.9 (11.4–28.0) and 20.8 (18.0–27.0) %/min at 24 and 48 h. There are differences in ICG-PDR measurements between survivors and deceased ($p < 0.001$). The silhouette measure of ICG-PDR cohesion and separation for the clusters analysed (deceased and survivors) was satisfactory (0.6). ICG-PDR < 11.7%/min was related to in-hospital mortality, ICG-PDR > 18%/min to survival and the interval between 11.7% and 18%/min covered a range of uncertainty. In the two-stage cluster, ICG-PDR, SOFA and APACHE II are good and similar predictors of mortality in SS patients.
Conclusion: ICG-PDR in our setting is a useful clinical prognostic tool and can optimise the decision tree in patients with SS.

000236

Prognostic utility of the non-invasive measurement of the indocyanine green plasma disappearance rate in patients with septic shock who develop acute liver dysfunction

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Introduction: Our aim was to analyse the correlation of serial values of the indocyanine green plasma disappearance rate (ICG-PDR) and hospital mortality in the first 48 h of ICU admission in patients with septic shock (SS) who develop acute liver dysfunction (ALD) during admission.
Methods: Prospective analytical observational study carried out over 12 months of patients admitted to the ICU with SS. Each patient underwent non-invasive determination of ICG-PDR at 24 and 48 h with the LiMON® module. Incidence of ALD during admission was studied. Follow-up was performed until hospital discharge or exitus. For each clinical variable of liver function recorded, the values corresponding to the time of diagnosis of SS and the values obtained at 24 and 48 h were analysed. For the descriptive analysis, absolute frequency (N), relative frequency (%), mean values, median, standard deviation (SD), and 25th, 50th and 75th percentiles were calculated. T-tests: Chi-square, independent samples t-test, Mann–Whitney U-test for independent samples and Wilcoxon signed-rank test. Two-stage clustering was performed for the classification of the hospital mortality variable with ICG-PDR.
Results: 63 patients. Age 61.1 years ± 12.3 years. 60.3% men. SOFA at admission 8.7 ± 3.3 and APACHE II 27.9 ± 10.7 points. 44.4% of patients developed ALD associated with SS. Of this group, 57.1% died. These patients had ICG-PDR values of 9.2 (4.2–12.9) and 7.1 (0.6–11.0) %/min at 24 and 48 h. In survivors: 14.7 (11.6–29.6) and 21.5 (17.3–27.6) %/min at 24 and 48 h. There were differences in ICG-PDR measurements between survivors and deceased ($p < 0.001$). Serum INR and lactate showed similar time course to ICG-PDR in deceased and survivors ($p < 0.05$). Bilirubin, AST, ALT, GGT, FA and LDH showed no statistically significant differences between survivors and deceased. The silhouette measure of ICG-PDR cohesion and separation for the clusters analysed (deceased and survivors) was satisfactory (0.7). ICG-PDR < 10.6%/min was related to in-hospital mortality, ICG-PDR > 17.8%/min to survival and the interval between 10.6 and 17.8%/min spanned a range of uncertainty.
Conclusion: ICG-PDR is a dynamic liver function test with prognostic utility in SS patients who develop ALD, superior to static tests such as bilirubin and transaminases and similar to INR and lactate.

000268

Serial change of endotoxin tolerance in a polymicrobial sepsis model

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Intensive Care Medicine Experimental 2022, **10(2)**: 000268

Introduction: Immune suppression is known to occur during sepsis. Endotoxin tolerance is considered a mechanism of immune suppression in sepsis. However, the timing and serial changes in endotoxin tolerance have not been fully investigated.
Objectives: To investigate serial changes in endotoxin tolerance in a polymicrobial sepsis model.
Methods: We used a rat model of fecal slurry polymicrobial sepsis. After induction of sepsis, endotoxin tolerance of peripheral blood mononuclear cells (PBMCs) and splenocytes was measured at various time points (6 h, 12 h, 24 h, 48 h, 72 h, 5 days, and 7 days) by measuring TNF-α production after stimulation with lipopolysaccharide (LPS) in an ex vivo model. At each time point, we checked for plasma tumor necrosis factor (TNF)-α, interleukin (IL)-6, and IL-10 levels. We also

analyzed reactive oxygen species (ROS) as measured by 2′,7′-dichlorodihydrofluorescein, plasma lactate, serum alanine aminotransferase (ALT), and creatinine levels. Nuclear factor (NF)-κB, IL-1 receptor-associated kinase (IRAK)-M, and cleaved caspase 3 levels were measured in the spleen.
Results: Endotoxin tolerance, measured by TNF-α production stimulated by LPS in PBMCs and splenocytes, was induced early in the sepsis model, starting from 6 h after sepsis. It reached a nadir at 24 to 48 h after sepsis, and then started to recover. Endotoxin tolerance was more prominent in the severe sepsis model. Plasma cytokines peaked at time points ranging from 6 to 12 h after sepsis. ROS levels peaked at 12 h and then decreased. Lactate, ALT, and serum creatinine levels increased up to 24 to 48 h, and then decreased. Phosphorylated p65 and IRAK-M levels of spleen increased up to 12 to 24 h and then decreased. Apoptosis was prominent 48 h after sepsis, and then recovered.
Conclusion: In the rat model of polymicrobial sepsis, endotoxin tolerance occurred earlier and started to recover from 24 to 48 h after sepsis.

000283

Pattern of inflammatory immune responses in patients with septic shock receiving vitamin C, hydrocortisone, and thiamine: unbiased clustering analysis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000283

Introduction: Sepsis is characterized by the initial overwhelming systemic inflammation which is rapidly counterbalanced by an anti-inflammatory response [1]. Despite its heterogeneity, most sepsis studies have failed to select patients based on their immune status and focused on a one-size-fits-all treatment approach [2]. Thus, it may be useful to identify biomarkers to monitor the immune status of sepsis patients and identify those who could benefit from immunomodulatory therapies.
Objectives: To identify distinct patterns of inflammatory immune responses in patients with septic shock receiving vitamin C, hydrocortisone, and thiamine.
Methods: A single center, prospective observational study of 95 adult septic shock patients who were treated using a vitamin C protocol (intravenous vitamin C 1.5 g every 6 h for 4 days, hydrocortisone 50 mg every 6 h for 7 days, and thiamine 200 mg every 12 h for 4 days) in the medical intensive care unit (ICU) between September 2019 and July 2021. Blood samples were collected at days 1–2, 3–4, and 6–8 after shock onset and evaluated for lymphocyte count, C-reactive protein (CRP), interleukin (IL)-6, tumor necrosis factor (TNF)-α, and IL-10. The group-based multi-trajectory modeling [3] was performed to define the trajectories of serial biomarker patterns regardless of clinical information. Then, associations between the resulting patterns and clinical outcomes were assessed.
Results: Twenty-six patients (27%) died in the ICU. Biomarker levels on days 1–2 were not significantly different between survivors and non-survivors. However, CRP, IL-6, and IL-10 levels were significantly higher in non-survivors compared to survivors on days 3–4 and 6–8. Lymphocyte counts on days 3–4 and 6–8 were also lower in non-survivors. Unbiased clustering analysis classified the study patients into two distinct groups. Group 1 ($n = 41$) was characterized by lower IL-6, TNF-α, and IL-10 levels, which remained low or increased over time. Conversely, group 2 ($n = 54$) presented with higher IL-6, TNF-α, and IL-10 levels, but decreased over time. Both groups had high CRP levels and low lymphocyte counts on days 1–2, although the improvements over time were greater for group 2. The baseline characteristics were generally similar between the groups. However, the changes in vasopressor dose and Sequential Organ Failure Assessment score from days 1–2 to days 6–8 were significantly higher in group 2 ($p < 0.001$ and $p = 0.001$, respectively). The ICU mortality rates were 39% for group 1 and 19% for group 2 ($p = 0.03$).
Conclusion: Our data support the prognostic utility of longitudinal changes in inflammatory biomarkers over using a single measurement. Vitamin C protocol may be more effective in patients with higher proinflammatory and anti-inflammatory immune responses.

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Acknowledgements This research was supported by the National Research Foundation of Korea grant funded by the Korea government (Ministry of Science, ICT & Future Planning) (2019R1G1A1099373).

Systemic Inflammation & Sepsis 3

000284

Mortality risk factors in patients with nosocomial infection, in an ICU after ten years application of Selective Digestive Decontamination

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Intensive Care Medicine Experimental 2022, **10(2)**: 000284

Introduction: Recognition of mortality risk factors and early intervention with appropriate broad-spectrum antimicrobial administration in patients with nosocomial infection (NI) may significantly improve outcomes. Selective Digestive Decontamination (SDD) has been associated with reduced ICU mortality and acquired infection rates.
Objectives: To analyze mortality risk factors in patients with NI in an ICU after 10 years of SDD.
Methods: Patients with NI were prospectively included from October 1, 2010 to September 30, 2021 in a polyvalent ICU of 30 beds. SDD was applied for 10 years, from October 1, 2011 to September 30, 2021. Patients requiring mechanical ventilation for more than 48 h, an enteral solution and a paste with colistin, tobramycin and nystatin every 8 h until discharge were applied. Also intravenous cefotaxime were administered during the first 4 days. Rectal and pharyngeal exudates were collected on admission and weekly. We used ENVIN NI criteria.The categorical variables were summarized in frequencies and percentages and the numerical variables as means and standard deviations or in medians and interquartile ranges. The percentages were compared with the X2 test or the Fisher exact test, the means with the t-test and the medians with the Wilcoxon test for independent data. A multidimensional logistic analysis was carried out. It was considered significant if $p \leq 0.05$.
Results: Of 9715 patients admitted, 275 (35,38%) out of 802 patients with NIs died. In an univariate analysis we did no find statistically significant difference in ICU stay. Multiresistant (MR) *Pseudomonas* and MR Gram negative bacteria (GNB) were significantly higher in patients who died (Table 1). Independent mortality risk factors were: renal replacement therapy OR: 4.694 (3.315; 6.646); neoplasm OR 3.008 (1.702; 5.316); septic shock OR: 2.215 (1.559; 3.147); parenteral nutrition OR 2.054 (1.382; 3.052); ventilator associated pneumonia (VAP):OR: 1.965 (1.363; 2.832) and APACHE II Odds Ratio (OR)1.057 (1.033; 1.082) (Table 2).

Table 1. Characteristics of the patients according to survival

	Alives N = 527	Deaths N = 275	p-value
Age, years	59.8 ± 15.1	63.9 ± 13.3	< .001
APACHE II	19.6 ± 7.4	23.8 ± 7.6	< .001
SDD	453 (86.0)	239 (86.9)	0.71
Sex male	345 (67.8)	180 (67.2)	0.862
Trauma patients	76 (14.4)	12 (4.4)	< .001
Coronary artery disease patient	106 (20.1)	60 (21.9)	0.555
Emergency surgery	129 (24.5)	65 (23.8)	0.834
Immunosuppression	41 (7.8)	51 (18.6)	< .001
Neutropenia	11 (2.1)	19 (6.9)	< .001
Parenteral nutrition	85 (16.1)	94 (34.3)	< .001
Ventricular device	63 (11.9)	8 (2.9)	< .001
RRT	119 (22.6)	176 (64.0)	< .001
Malnutrition	34 (6.5)	40 (14.6)	< .001
Diabetes mellitus	137 (26.0)	114 (41.5)	< .001
COPD	68 (12.9)	59 (21.4)	0.002
Renal failure	77 (14.6)	86 (31.3)	< .001
Cirrhosis	19 (3.6)	21 (7.6)	0.013
Neoplasm	29 (5.5)	43 (15.6)	< .001
VAP	167 (31.7)	129 (46.9)	< .001
CRB	208 (39.6)	83 (30.2)	0.008
Secondary bacteremia	125 (23.9)	78 (28.4)	0.164
Urinary infection	143 (27.1)	68 (24.8)	0.48
ATB 48 hours before admission	119 (23.3)	96 (36.4)	< .001
Acinetobacter baumannii	13 (2.5)	7 (2.5)	0.946
MRSA	11 (2.1)	5 (1.8)	0.796
ESBL	118 (22.4)	72 (26.2)	0.231
MR Pseudomonas	30 (5.7)	34 (12.4)	< .001
MR GNB	18 (3.4)	21 (7.6)	0.009
Admission:			< .001
Medical	358 (68.0)	225 (82.1)	
Scheduled surgery	85 (16.1)	16 (5.8)	
Emergency surgery	84 (15.9)	33 (12.0)	
Inflammatory response:			< .001
Non sepsis	19 (3.6)	8 (2.9)	
Sepsis	137 (26.0)	37 (13.5)	
Septic Shock	371 (73,4)	230 (83.7)	
ICU days	32 (19 ; 50)	35 (20 ; 57)	0.231

Values are means ± SD and frequencies (%) .SDD: Selective digestive decontamination;RRT: Renal replacement therapy; VAP: ventilator associated pneumonia;CRB: Catheter related bacteremia; COPD: chronic obstructive pulmonary disease; MRSA: methicillin resistant Staphylococcus aureus; ESBL: extended spectrum betalactamase; MR: multiresistant; GNB: gram negative bacteria

Table 2. Multivariate logistic regression for *Death*

	p-value	Odd-Ratio (95% CI)
APACHE II	< .001	1.057 (1.033 ; 1.082)
Septic shock	< .001	2.215 (1.559 ; 3.147)
Parenteral nutrition	< .001	2.054 (1.382 ; 3.052)
RRT	< .001	4.694 (3.315 ; 6.646)
Neoplasm	< .001	3.008 (1.702 ; 5.316)
VAP	< .001	1.965 (1.363 ; 2.832)

RRT: Renal replacement therapy;VAP: ventilator associated pneumonia;

Conclusion: In an ICU with SDD, factors that were independently associated with mortality were: renal replacement therapy, neoplasm, septic shock, parenteral nutrition, VAP and APACHE II. MR *Pseudomonas* and MR GNB also had significantly higher mortality.

000288

Ex vivo and in vitro leukocyte responses do not reflect in vivo immune responses and tolerance

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Intensive Care Medicine Experimental 2022, **10(2)**: 000288

Introduction: Sepsis is a highly heterogeneous inflammatory syndrome, and can lead both to hyperinflammation as well as a profoundly immunotolerant state known as sepsis-induced immunoparalysis. A common method to gauge immune function in critically ill patients is to determine ex vivo (EV) cytokine production by leukocytes that are stimulated with bacterial lipopolysaccharide (LPS) or other inflammatory stimuli, but whether this accurately reflects the in vivo (IV) immune response is largely unknown. The repeated experimental human endotoxemia model is a highly standardized IV model of systemic inflammation, which captures aspects of both hyperinflammatory and immunoparalytic phenotypes of sepsis.
Objectives: To determine whether EV leukocyte stimulation assays accurately reflect IV responses and tolerance.
Methods: 110 healthy volunteers were intravenously challenged with 1 ng/kg lipopolysaccharide (LPS) twice: on day 0 to determine the extent of the (hyper)inflammatory response and on day 7 to determine the degree of IV endotoxin tolerance as a model for immunoparalysis. Plasma cytokines were serially measured and area under the time-concentration curves (AUCs) were calculated for both LPS challenges, reflecting integral measures of IV cytokine responses over time. Monocytes were isolated and stimulated one hour before the first LPS challenge (T = − 1) on day 0 (to determine baseline cytokine production capacity) four hours after the LPS challenge (T = 4) on day 0 (to determine short-term EV tolerance), and on T = − 1 before the second LPS challenge on day 7 (to determine long-term EV tolerance). The TLR ligands LPS, β-glucan, R848, Pam3Cys, poly I:C and CpG motifs as well as heat killed pathogens *E. coli, P. aeruginosa, S. aureus* and *C. albicans* were used as EV stimuli. Relationships between IV and EV responses and tolerance where analyzed using Pearson's correlation.
Results: EV cytokine responses of monocytes isolated at baseline did not robustly correlate with IV cytokine responses to LPS administration, except for the EV responses to *S. aureus*, for which weak but significant inverse correlations between IV tumor necrosis factor plasma levels and EV production of TNF (r = − 0.30; p = 0.004), interleukin (IL)-6 (r = − 0.23; p = 0.03), IL-8 (r = − 0.25; p = 0.02) and interferon gamma-induced protein (IP)-10 (r = − 0.26; p = 0.01) were observed (Fig. 1). However, robust and widespread inverse correlations were found between EV responses of monocytes isolated 4 h after IV LPS administration and IV cytokine responses (Fig. 1), suggesting that high IV responses drive more extensive development of EV tolerance. Although IV LPS administration resulted in profound IV tolerance (median reduction in cytokine responses upon the second LPS challenge compared with the first ranging from 18–86%), as well as short- and long-term EV tolerance, no correlations between IV and EV tolerance were observed (data not shown).

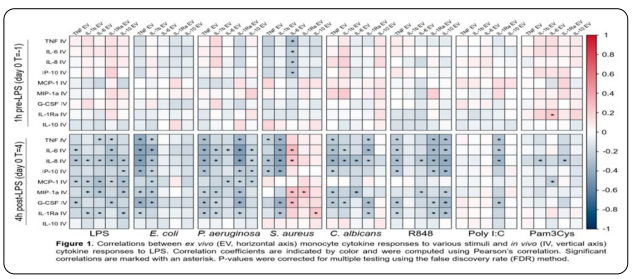

Figure 1. Correlations between *ex vivo* (EV, horizontal axis) monocyte cytokine responses to various stimuli and *in vivo* (IV, vertical axis) cytokine responses to LPS. Correlation coefficients are indicated by color and were computed using Pearson's correlation. Significant correlations are marked with an asterisk. P-values were corrected for multiple testing using the false discovery rate (FDR) method.

Conclusion: EV leukocyte stimulation assays poorly reflect IV cytokine responses and tolerance. Low EV cytokine responses probably reflect ongoing IV hyperinflammation rather than immune suppression, and clinicians and researchers should interpret results of such assays cautiously.

000297

Effect of discontinuation of immunosuppression therapy on mortality in kidney transplant patients with sepsis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000297

Introduction: Kidney transplantation (KT) is the most common solid organ transplant performed worldwide. New advances in transplant immunosuppressants have expanded donor pools for kidney transplantation, and nowadays, many kidney transplant recipients (KTR) possibly have more comorbidities. Up to 6% of KTRs experience a life-threatening complication requiring intensive care unit (ICU) admission, and one of the most common medical complications requiring ICU admission is infection. Up to date, there has been no guidelines about maintaining immunosuppression therapy (IST) in KTRs with sepsis.
Methods: We conducted multicenter retrospective study in four university-affiliated hospital to effect of adjusting IST in KTRs with sepsis, since January 2010 to December 2020. "Any reduction" was defined as dosage reduction or discontinuation of at least one immunosuppressant except calcineurin inhibitors was carried out during ICU stay and "complete withdrawal of IST" was defined as all of immunosuppressants were concomitantly discontinued.
Results: During study period, 1,552 patients received KT and 112 episodes of sepsis or septic shock were identified: 72 (64.3%) male, median age 61.0 (IQR 55.5–67.5) years. "Any reduction" was made in 94 (83.9%) cases and "complete withdrawal of IST" was made in 61 (54.5%) cases. In-hospital mortality rate was 35.7%, varying from 47.5% to 11.8% ($P = 0.008$) in case with and without "complete withdrawal of IST". Simple logistic regression showed higher SAPS3 score (OR 1.01, $P < 0.001$), septic shock (OR 4.50, $P < 0.001$), complete withdrawal of IST (OR 3.30, $P = 0.005$) as independent risk factor for in-hospital mortality. After adjusting potential confounding factors, complete withdrawal of IST remained significantly associated with in-hospital mortality.
Conclusion: Complete withdrawal of IST was common and was associated with worse outcome in critically ill KTRs with sepsis.

000298

Outcomes of Hemoperfusion for Critical COVID-19 Infection in a Cardiovascular Specialty Hospital in the Philippines: A Single Center Experience

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Intensive Care Medicine Experimental 2022, **10(2)**: 000298

Introduction: Cytokine storm is the most feared complication of COVID-19 and immunomodulatory therapies have become the cornerstone in its management. Hemoperfusion for cytokine removal has gained wide acceptance, although with limited evidence on patient outcomes.
Objectives: This study aims to review critical COVID-19 patients with and without hemoperfusion and its effects on their outcomes.
Methods: This is a retrospective cohort study. Patients aged $\geq$ 19 years old with critical COVID-19, confirmed with RT-PCR testing, who were admitted between March 2020 to May 2021 in the medical ICU in a cardiovascular specialty hospital in the Philippines were randomized and 93 patients were included in this study. Charts and electronic records were reviewed. Outcomes evaluated include in-hospital mortality, ICU and hospital length of stay, duration of non-invasive and invasive mechanical ventilation.
Results: Thirty-two patients (34%) underwent hemoperfusion and 61 patients (66%) were treated without hemoperfusion. Mean age was 64.19 (SD $\pm$ 14.91) years old. Majority were males (72.04%), hypertensive (83.87%), diabetic (59.14%), current smoker (54.84%) and admitted due to a cardiac problem (54.84%) with the most common cardiac diagnosis being coronary artery disease. Median admission SOFA score was 4 with an interquartile range of 3 to 6. Steroid treatment was given in 91.4% and tocilizumab was given in 24.73%. There was heterogeneity in characteristics in terms of presence of diabetes, history of stroke, treatment with steroids and tocilizumab, neutrophil count, NT-proBNP and D-dimer levels. There were significantly more diabetics in the hemoperfusion group (p-value 0.028) and more stroke patients in the group without hemoperfusion (p-value 0.048). There were significantly more patients in the hemoperfusion group who received tocilizumab (p-value 0.001) and steroid treatment (p-value 0.047). NT-proBNP was significantly higher in the group without hemoperfusion (p-value 0.019). Mortality rate was 65.59% and there was no significant difference in mortality (p-value 0.819) between both groups. Patients with hemoperfusion had a slightly higher mortality but did not achieve statistical significance. Days on non-invasive ventilation, invasive ventilation, ICU and hospital length of stay were not significantly different between both groups.
Conclusion: Although there was some heterogeneity in the study population, our data suggest hemoperfusion has no effect on outcomes in terms of mortality, duration of high-flow nasal cannula, non-invasive mechanical ventilation, intubation, ICU length of stay and hospital length of stay. Our study showed a slightly higher mortality rate, although not statistically significant, in the hemoperfusion group despite having a higher proportion of patients receiving tocilizumab and steroids. From these findings, the need for further studies is emphasized before routinely recommending hemoperfusion for critical COVID-19.

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000322

Incidence of candidaemia in critically ill COVID-19 patients during the first year of pandemic in a University Hospital

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Introduction: In the months after the start of the COVID-19 pandemic in 2020, there were few publications describing a possible association between SARS-CoV-2 infection and invasive fungal infections. Koehler et al. published a retrospective review of five patients, without known immunosuppression, with COVID-19 and ARDS, finding an association with invasive pulmonary aspergillosis. *Aspergillus fumigatus* was isolated in the different culture media, in addition to the positivity of specific biomarkers and compatible chest CT images. Three patients died. The authors suggested a possible increased risk of developing coinfection with *Aspergillus sp.* in critical COVID-19 patients in addition to an increase in mortality. Prattes et al. and Blaize et al. described in two separate cases the association between Coronavirus SARS-CoV-2 disease and invasive pulmonary aspergillosis. Both patients died.
Objectives: The aim of this study was to evaluate the incidence and mortality of invasive fungal infection in critically ill COVID-19 patients admitted in ICU during the first year of world pandemic in a Spanish University Hospital.
Methods: This is a retrospective study of patients admitted to Intensive Care Unit because of COVID-19 pneumonia and ARDS at La Paz University Hospital in Madrid, from February 28th 2020 to March 3rd 2021. All demographic variables, invasive fungal infection risk factors, incidence and mortality rates were registered.
Results: During the study period, 189 critically ill COVID-19 patients were admitted. *Aspergillus fumigatus complex* was isolated from cultures of respiratory samples obtained by bronchoalveolar lavage in 3 patients. In addition, *Candida sp.* was isolated in urine cultures from 8 patients. 19 candidaemias were diagnosed (*C. albicans*: 11; *C. parapsilosis*: 5; *C. glabrata*: 3). The mean age of the patients with candidaemia was 58.7 ± 17.5 years; 60% men and 40% women. All patients were on mechanical ventilation, with vasoactive support with norepinephrine, and had a central venous catheter. In addition, they had received parenteral nutrition, broad-spectrum antibiotic therapy, and corticosteroid treatment for ARDS. Mortality in the subgroup of patients with candidaemia was 40%.
Conclusion: The high rate of candidaemia (10%) in this 12 months duration study contrasts strikingly with previous published data of candidaemia from our Critical Care Unit in a 7 years observation period (Agrifoglio et al.) Usually and in relation to our local epidemiology, the annual incidence rate is 1.07–2.19 candidaemia for every 1000 patients admitted to ICU. *C. albicans* is the most commonly isolated species (50%) in blood cultures followed by *C. parapsilosis* (20%), *C. glabrata* (13%), *C. tropicalis* (10%) and *C. krusei* (7%). These results should be confirmed in further studies to determine the potential role of invasive candidiasis in patients patients with COVID-19. In any case, according to the data we already have and to our series of critical patients we find necessary to stablish recommendations such as epidemiological vigilance, consisting on perform periodically screening for *Candida sp* colonization, take risk factors into account and re-evaluate them, optimize early diagnosis and introduce treatment protocols in ICU, which leads to consider to start empirical antifungal treatment in case of worsening septic patient, depending on each local epidemiology, at least until microbiology results.

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Acknowledgements To all our COVID-19 patients, their gratifying families and all the health team that has fought day by day against the pandemic.

000325

Early administration of intravenous immunoglobulins improve outcome of septic shock. A retrospective observational study

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Introduction: The use of intravenous immunoglobulins (IVIG) as supportive therapy in sepsis or septic shock is controversial. So we hypothesized that the administration of IVIG combined with antibiotics could improve outcome of patients with septic shock [2,3].
Objectives: To evaluate the effectiveness of IVIG combined with antibiotics for the treatment and improvement of the prognosis of septic shock.
Methods: In this retrospective observational study, we collected and analyzed between 2019 and 2021, the data of 2 groups of 20 patients in septic shock according to definition of Sepsis 3 criteria,admitted in ICU university hospital. The patients were 65 + -10 years old and mechanically ventilated,with the same baseline characteristics and severity scores on admission. The first group received IVIG and empirical antibiotics (IVIG group). The second group received placebo and antibiotics (control group). On the first hour of admission in ICU, IVIG preceded by administration of antibiotics were infused continuously at a a dose of 0.5 g/kg with a flow of 3 ml/kg/h during 3 days. We recorded in the 2 groups: SOFA score day 1 and Day 4, C-reactive protein (CRP) mean arterial pressure (MAP), P/F ratio day 1 and day 3,ICU stay, hospital length of stay (LOS), time on vasopressors, duration of mechanical ventilation (MV), dosage of immunoglobulins and 28 day mortality.

Results:
Table 1 Variables in relation with outcome in control and IVIG group

	Group 1 Control Group		Group 2 IVIG Group		
	MEAN	STD	MEAN	STD	P
SOFA score Day 4	7.55	1.15	4.4	0.68	P < 0.0001
Lactate Day2 mmol/l	4.45	0.76	3.04	0.43	P < 0.0001
CRP Day 3	70.15	14.67	26.90	4.22	P < 0.0001
P/F ratio Day 3	203.7	37.70	307.35	26.68	P < 0.0001
Time on MV(days)	10.55	2.42	6.45	0.89	P < 0.0001

	Group 1 Control Group		Group 2 IVIG Group		
	MEAN	STD	MEAN	STD	P
Time on vasopressors(days)	6.1	1.62	4.17	0.95	P < 0.0001
ICU Stay (days)	16.05	2.95	10.95	1.15	P < 0.0001

Statistical analysis used Student's t- test and Results expressed as Mean ± Standard deviation

Conclusion: Our study showed that the use of IVIG in patients with septic shok may have a rationale and seems to be associated with a reduced morbidity [1,4] and with a tendency to a decrease in mortality(7patients died in the control group and 4 patients died in the IVIG group p < 0.3) A large Randomized controlled trial, well designed is needed to confirm this results in terms of morbidity and mortality.

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Acknowledgements Thanks to my colleagues of Algiers University for their contribution.

000331

Evaluation of the Efficacy of Tocilizumab in Patients Developing Cytokine Release Syndrome Due to COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**: 000331

Introduction: Cytokine Release Syndrome is one of the important causes of mortality due to COVID-19. Although more than one agent is used to treat cytokine release syndrome and its related complications, studies are still ongoing. We aimed to investigate the effectiveness of tocilizumab, its effect on mortality and complications that may occur due to tocilizumab in cytokine release syndrome developed in patients followed in the intensive care unit due to COVID-19.
Methods: Following the ethics committee approval, patients who developed cytokine release syndrome, who were being followed up in the intensive care unit due to COVID-19 between October 2020 and August 2021, were included. The patients were grouped as those who received tocilizumab and those who did not receive tocilizumab. In the study, which was planned as a case–control study, SOFA and GCS scores, P/F values, intensive care treatments, laboratory parameters (on the day of receiving the treatment, 3rd, 5th, 7th days), morbidity and survival of the patients in both groups were compared. P < 0.05 was accepted as statistical significance.
Results: During the date of the study, a total of 1509 COVID-19 patients were followed, and there were 312 patients diagnosed with cytokine release syndrome. Fifty patients who received tocilizumab treatment were included study group, and 50 patients who did not receive tocilizumab were included in the control group. Patients in both groups were similar in terms of demographic characteristics and comorbidity. The two groups in the study were comparable in terms of secondary infection, mechanical ventilation, time to weaning and survival. Ferritin levels in the tocilizumab group were significantly higher on the day of diagnosis, on the 3rd day and on the 5th day compared to the control group (p:0.019). On the 5th day of treatment, SOFA score, AST and ALT values were higher in the tocilizumab group compared to the control group (p:0.02,p:0.07,p:0.016) CRP value and fibrinogen were lower in the tocilizumab group (p < 0.001).
Conclusion: We concluded that tocilizumab was not superior to standard care in terms of mechanical ventilation, weaning time, length of hospital stay and survival in cytokine release syndrome caused by COVID-19. However, we found that tocilizumab treatment did not increase the risk of secondary infection but caused hypofibrinogenemia.

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000396

PSP kinetics in the prediction of VAP diagnosis

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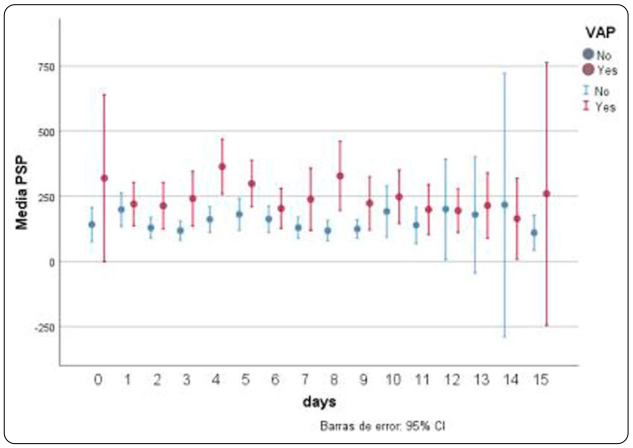
Introduction: Ventilator-associated pneumonia (VAP) is the most frequent nosocomial infection in the ICU. Early, adequate antibiotic treatment reduces complications and associated mortality. Pancreatic stone protein (PSP) may start to increase above the normal level range before the development of clinical signs and symptoms of sepsis.
Objectives: We aimed to evaluate the predictive performance of kinetic of PSP to VAP development in all non-infected patients during the first days of mechanical ventilation.
Methods: This was a post hoc study of the observational, multicenter, prospective BioVAP study. Patients were included when they were on mechanical ventilation for > 72 h, and no infections were suspected. PSP was measured in frozen samples taken on consecutive days during mechanical ventilation duration. The kinetics of each variable, from day 1 to day 6 of mechanical ventilation, was assessed with individual PSP slopes (rate of biomarker change per day), and the highest level. Pneumonia was diagnosed by clinical radiographic criteria and microbiological criteria.
Results: Thirty-five patients out of 138 developed VAP. During the first 6 days, PSP was higher on days 3, 4, and 5 in patients who developed VAP (p < 0.05). Median (1st–3rd qt) values of PSP at the day of VAP diagnosis were 144 ng/ml (79–440 ng/ml). The slope of PSP and the highest PSP concentration were not significantly associated with VAP (aOR 1.01, CI97,5% [0.98, 1.03]), (aOR 1, CI97,5% [0.99, 1] respectively).



Conclusion: Conclusion: In this cohort of patients, the kinetics of PSP did not show predictive value for VAP diagnosis. More studies evaluating PSP as a VAP predictor are warranted.

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000399

Impact of the COVID-19 pandemic on management and outcomes in patients with septic shock in the emergency department

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Introduction: This study aimed to determine the impact of modifications in emergency department (ED) practices caused by the coronavirus disease 2019 (COVID-19) pandemic on the clinical outcomes and management of patients with septic shock.
Methods: We conducted a retrospective study utilizing prospectively collected multicenter data from the Korean Shock Society. Patients with septic shock who presented to the ED between January 1, 2018, and January 19, 2020 were allocated to the pre-COVID-19 group, whereas those who presented between January 20, 2020, and December 31, 2020 were assigned to the post-COVID-19 group. We used propensity score matching to compare the septic shock-related interventions and clinical outcomes. The primary outcome measure was in-hospital mortality.
Results: Of the 3697 patients included, 2254 were classified as pre-COVID-19 and 1143 as post-COVID-19. A total of 1140 [A1] propensity score-matched pairings were created from these patients. In a matched cohort, the post-COVID-19 group had delayed lactate measurement (27.0 min *vs.* 37.0 min), blood culture test (82.0 min *vs.* 117.0 min), and infection source control (12.9 h *vs.* 16.1 h) (all $p < 0.05$). There was no significant difference in time to IV antibiotics (140.5 min *vs.* 138.0 min, $p = 0.19$) or vasopressors (133.0 min *vs.* 143.5 min, $p = 0.09$) between the groups. Overall, the in-hospital mortality rate was 25.5% (n = 582), with no statistically significant difference between the pre-and post-COVID-19 groups (25.4%, n = 290 *vs.* 25.6%, n = 292, respectively; $p = 0.92$).
Conclusion: While delaying septic shock-related interventions during the COVID-19 pandemic, there was no significant difference in the in-hospital mortality between the pre-and post-COVID-19 groups.

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000406

Mortality from Sepsis in Cancer Patients: A Review and Meta-Analysis

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Introduction: The number of cancer patients being admitted to intensive care unit (ICU) with sepsis and septic shock has increased in recent years (1,2). Despite this, there is a limited amount of research on critically ill cancer patients with sepsis. Consequently, the risk of mortality from sepsis and septic shock in this cohort is unclear.
Objectives: To perform a literature review and meta-analysis to establish the mortality from sepsis and septic shock in patients with cancer admitted to ICU, and to assess for any trends in mortality over time.
Methods: A systematic literature search using Medline/Embase of adult patients was conducted. The medical subject headings (MeSH) terms "sepsis", "septic shock" and "neoplasm" (including synonyms) were combined. To estimate a pooled mortality of sepsis and septic shock from these studies, we performed a random effects meta-analysis of 28–30-day, ICU, and hospital mortality. To assess the relationship between mortality and time, we performed a multivariable meta-regression for ICU and hospital mortality over time, adjusting for age and proportion of haematological cancer patients.
Results: 416 articles were identified, and, after exclusions, 26 articles were included to review. The average 28-30-day, ICU, and hospital mortality for sepsis was 44.8 (95% CI 38.2 to 51.7), 47.0% (95% CI 44.0 to 48.2) and 57.6 (95% CI 49.1 to 65.7) respectively. The average 28–30-day, ICU, hospital mortality for septic shock was 51.8 (95% CI 45.7 to 57.7), 53.6 (95% CI 48.8 to 58.3) and 64.2 (95% CI 54.7 to 72.7) respectively. Meta-regression identified a decreasing trend in ICU mortality from sepsis (coefficient (B) = − 0.019, p = 0.031), hospital mortality from sepsis (B = − 0.017, p = 0.033) and ICU mortality from septic shock over time (B = − 0.010, p = 0.005). An inverse relationship between age and hospital mortality from sepsis was present after accounting for year (B = − 0.014, p = 0.044). This association was no longer significant after adjusting for the proportion of haematological cancer patients within each study, and so it is likely that variation in casemix may account for this finding (after adjustment, B for age = − 0.020, p = 0.067).
Conclusion: There is a significant risk of mortality in cancer patients admitted to ICU with both sepsis and septic shock, which appears to be greater than the general population, with a recent study estimating hospital mortality from sepsis in general patients admitted to ICU at 35.3% (3). Mortality appears to be improving over time; however, sepsis remains a significant burden in this population, and further research is required to inform management and improve outcomes in cancer patients with sepsis.

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000426

Early versus delayed vasopressor administration in patients with septic shock

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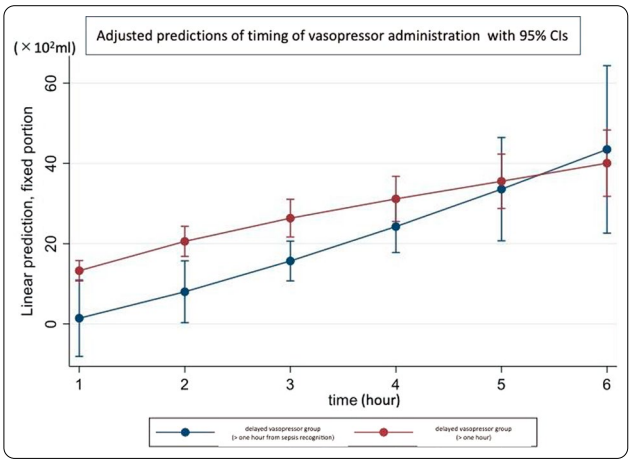
Intensive Care Medicine Experimental 2022, **10(2)**: 000426

Introduction: The timing of vasopressor initiation for patients with sepsis and fluid-resistant hypotension has ambiguous guidelines, although earlier initiation of key therapies, including appropriate antibiotics and fluid resuscitation, can definitely reduce mortality risk.
Objectives: This study aimed to investigate the association of early vasopressor initiation with improved fluid-resistant septic shock outcomes.
Methods: This multicenter observational study was conducted in 17 intensive care units (ICUs) at tertiary hospitals in Japan and included all adult patients diagnosed with sepsis by sepsis-3 and admitted to the ICU from July 2019 to August 2020. Patients were divided into the early vasopressor group ($\leq$1 h from sepsis recognition) and the delayed vasopressor group (>1 h). The primary outcome includes in-hospital mortality, whereas the secondary outcome includes fluid volume within 6 h of sepsis recognition. The impact of early vasopressor administration on risk-adjusted in-hospital mortality was estimated using logistic regression analyses that were adjusted using an inverse probability of treatment weighting (IPTW) analysis with propensity scoring. Patient age, sex, admission source (emergency department, ward, or ICU), Charlson comorbidity index, mechanical ventilation use, Sequential Organ Failure Assessment (SOFA) score in each organ, 1-h bundle adherence except vasopressors administration, and the amount of fluid by 6 h after sepsis were adjusted. The relationship between the fluid volume within 6 h and the timing of vasopressor administration, as well as the primary analysis, were examined.
Results: Among the 97 patients with fluid-resistant hypotension, 67 (69.1%) received vasopressor within 1 h from sepsis recognition and 30 (30.9%) received vasopressor after 1 h. The median SOFA score was 10 (Q1–Q3: 8–12) in the early vasopressor and 9 (Q1–Q3: 6–10) in the delayed vasopressor group ($p<0.01$). The median fluid volume from sepsis recognition to 6 h was 3,000 (Q1–Q3: 2200–4250) ml in the early vasopressor and 2,645 (Q1–Q3 1740–3900) ml in the delayed vasopressor group ($p=0.120$). The 28 day mortality was 25.4% (17/67) in the early vasopressor and 23.3% (7/30) in the delayed vasopressor ($p=0.830$). The in-hospital mortality was 32.8% (22/67) in the early vasopressor and 26.7% (8/30) in the delayed vasopressor group ($p=0.543$). The adjusted odds ratio for in-hospital mortality in the early vasopressor and delayed vasopressor group was 0.76 (95% confidence interval: 0.17–3.29). The fit curve from the mixed-effects model, which was adjusted with IPTW, showed a relatively lower trend toward an infusion volume in the early vasopressor group than in the delayed vasopressor group over time.



Conclusion: The study findings did not support the benefit of early vasopressor administration with fluid therapy for septic shock recognition. However, early vasopressor administration may help avoid volume overload in the long course of sepsis care.

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Acknowledgements This work was supported by JSPS KAKENHI Grant Number JP19K19376.

000431

Prognostic Value of Near-infrared Spectroscopy in Mortality and Organ Dysfunction in Patients Recovery from Septic Shock

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Introduction: Sepsis or septic shock results in the alteration of blood flow at the microcirculatory level, which is associated with death. Near-infrared spectroscopy (NIRS) with vascular occlusion test (VOT) is used to assess microcirculatory function in early septic shock, but this option is still a gap of knowledge in the recovery phase.
Objectives: To study the association between microcirculatory dysfunction in subjects recovering from septic shock and in-hospital mortality.
Methods: We conducted a prospective observational study of patients who recovered from septic shock. We performed NIRS with VOT within 24 h of hospitalization in ICU (T0), then at the time of

recovery from septic shock (D0), on day 3 (D3), day 5 (D5), and day 7 (D7) after recovery from septic shock. We recorded a de-oxygenation (DeO_2) slope, the re-oxygenation (ReO_2) slope, and the area under the hyperemic response curve. The outcomes of interest were the association between microcirculation dysfunction, in-hospital mortality, and in-hospital complications.
Results: A total of 97 patients were included for analysis. The in-hospital mortality was 29%. Regarding recovery from septic shock, the survivors had higher de-oxygenation slope (0.1 (0.07, 1.51) vs. 0.08 (0.06, 0.1); p = 0.02) and reperfusion area (701.6 (405.5, 1096.4) vs. 411 (186, 606) p = 0.02) at the day of recovery than non-survivors. De-oxygenation slope and reperfusion area provided area under the ROC curve for mortality of 0.69 and 0.66 respectively. For hospitalcomplications, de-oxygenation slope < 0.1014 was associated with new onset of acute kidneyinjury (16.7% vs. 83.3% RR 6.33 p = 0.04), nosocomial infection (28.1% vs. 71.9% RR 3.74 p = 0.01) and new sepsis/ septic shock (31.5% vs. 68.5% RR 5.98 p = 0.002).
Conclusion: The remaining microcirculatory alteration in patients recovering from septic shock is associated with in-hospital mortality and in-hospital complications.

000491

A candidate gene study to identify associations between steroid pathways and sepsis outcomes

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Introduction: The mortality benefit of corticosteroids in sepsis remains uncertain. Steroids are consistently associated with reduction in the duration of shock, but there is conflicting evidence about their effect on survival. Differences in response to these drugs may be explained by genetic variability amongst patients. Understanding this relationship could allow us to stratify those patients with sepsis who may gain maximal benefit from corticosteroids.
Objectives: The aim of this candidate gene study was to explore the association between genetic variants in corticosteroid pathways and outcomes of sepsis.
Methods: The study population included 1709 patients from the GenOSept (Genetics of Sepsis and Septic Shock in Europe) and GAiNS (Genomic Advances in Sepsis) studies who had undergone genotyping. SNPs identified from the literature associated with corticosteroid responsiveness in a range of diseases were used as candidate SNPs. A pairwise tagging approach was used with a linkage disequilibrium threshold (r2 0.8) to minimise collinearity amongst candidate SNPs. The primary endpoints of the study were ICU and 6-month mortality and development of shock. The combination of SNPs predictive of each outcome was extracted using a machine learning L1 regularised (LASSO) variable selection model. The association between every individual SNP and outcome was explored using multiple adjusted generalised linear models (GLMs), with Bonferroni correction for multiple comparisons. For the SNPs selected as predictive of ICU and 6-month mortality, survival analyses were performed for individual SNPs and groups defined by genotype combinations across SNPs.
Results: The individual SNP-by-SNP analysis did not identify any single SNP that was predictive study outcome alone. The LASSO model selected two SNPs associated with both ICU and 6-month mortality (rs56149945 and rs10482704 both from the NR3C1 gene which encodes the glucocorticoid receptor). Time to event analyses demonstrated a reduction in mortality with one copy of the minor allele of rs10482704 (AC) at 6-months versus homozygosity for the major allele (CC) (hazard ratio: 0.45, 95% CI: 0.25–0.83, p = 0.008). Increased mortality was seen with one copy of the minor allele of rs56149945 (CT) at 14-days versus homozygosity for the major allele (TT) (hazard ratio: 1.80, 95% CI: 1.12–2.89, p = 0.01). Considering the combination of these two SNPs showed that individuals who lacked the protective allele of rs10482704 (CC) whilst harbouring the risk allele of rs56149945 (CT) showed increased mortality at both 14-days and 6-months (p = 0.02 and p = 0.02 respectively). The SNP rs56149945 was also selected by the LASSO model as predictive of shock with an association with an increased risk of developing shock (odds ratio: 1.63, 95% CI: 1.00–2.64).
Conclusion: This study identified SNPs associated with mortality and development of shock from sepsis. These findings need to be validated in external data sets but highlight that genetic variation in corticosteroid pathways could explain differences in outcomes from sepsis and may lead to novel ways to identify those patients most likely to benefit from supplementary corticosteroids as adjunctive treatment for septic shock.

000532

Association between level of low high-density lipoproteins and poor long-term outcome in sepsis patients

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Introduction: Cholesterol plays an important role in multiple biological functions, including maintenance of cellular membrane processes, immunity, signaling, and pathway regulation, and it also acts as a precursor for the synthesis of steroid hormones, vitamin D, bile acids, and oxysterols1). Previous studies showed that serum cholesterol levels are decreased in sepsis patients2), 3). Another study showed an association between regulation of cholesterol metabolism and control of tissue inflammation and revealed a mechanism underlying T cell immunoregulatory functions4). However, the clinical significance of low cholesterol levels has been largely unrecognized.
Objectives: The aim of this study was to determine the clinical usefulness of serum cholesterol levels in sepsis patients for predicting prognosis.
Methods: We carried out a retrospective observational study. The study subjects were sepsis patients who were admitted to the ICU during the period from January 2010 to December 2020 and whose serum cholesterol levels were determined on ICU admission. The definition of sepsis was according to Sepsis-35). We obtained information on the characteristics of patients including age and sex, SOFA score, APACHE II score, focus of infection, length of ICU stay, shock, renal replacement therapy (RRT), number of ventilation days, total cholesterol, high-density lipoproteins (HDL), low-density lipoproteins (LDL), 28-day mortality and 90-day mortality. The primary endpoint was 90-day mortality. We performed multivariate logistic regression analyses to clarify the predictive factors for long-term outcomes.
Results: A total of 293 patients were included in this study. The 28-day mortality rate was 24.7%. As for the long-term outcome, the 90-day mortality rate was 38.9%. The serum total cholesterol and HDL levels were significantly lower in the non-survivors than in the survivors (p = 0.020 and p = 0.015, respectively). The levels of LDL were not significantly different in non-survivors and survivors (p = 0.968). The level of HDL was found to be an effective predictive factor for 90-day mortality (odds ratio = 0.98, p = 0.034) by multivariate logistic regression analysis.
Conclusion: Serum total cholesterol and HDL levels might be prognostic markers in sepsis patients at ICU admission. A low level of HDL has the potential to predict 90-day prognosis. On the other hand, this study did not show that those markers are superior to other severity scores. Further study is needed to extend our study on important interactions and roles of HDL in sepsis.

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000544

Risk stratification of the potentially septic patient in the emergency department

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Introduction: Sepsis is a medical emergency requiring immediate attention. Each hour that treatment is delayed increases mortality rates by 5–10%, early diagnosis and monitoring of treatment effectiveness are the keys to saving patients' lives. Early detection remains a challenge, despite the fact that a number of scoring systems have been created in recent years.
Objectives: Our aim was to examine the effectiveness of score systems in patients with suspected sepsis in the emergency care.
Methods: This study included 631 consecutive patients $\geq$ 18 years of age who presented to 3 emergency department in Hungary during 2013–2018. Clinical, laboratory, and follow-up data were acquired independently from documentation by ED physicians. The study team independently rated quality of sepsis classification (Society of Critical Care Medicine definitions), diagnostic workup, and guideline-adherent therapy in the ED. Retrospective score calculations were performed. Application and time of administration of antibiotics, use of biomarkers, i.e. lactate, and procalcitonin, disposition of patients were assessed.
Results: The diagnosis was 45,3% before the intensive care. The most sensitive score was PRESEP 79%. (SIRS:72%, BOMBARD:70,1%, qSOFA 48,1). In terms of specificity indicators, qSOFA performed the highest value: 98,15% (SIRS 92%, BOMBARD: 90,1%). The negative predictive values of the risk-scores: PRESEP: 80%, SIRS 77%, BOMBARD 75,1.
Conclusion: Currently, we still lack an ideal biomarker and risk-assessment to aid in the diagnosis of sepsis. In the future, biomarkers with better diagnostic value as well as a combined diagnosis using multiple biomarkers and scores are expected to solve the challenge of the diagnosis of sepsis. Early diagnosis of sepsis is critical for successful treatment.

000552

Phosphodiesterase 3 inhibitors do not influence lactate dynamics and clinical outcomes in patients with septic shock; a multicentre cohort study

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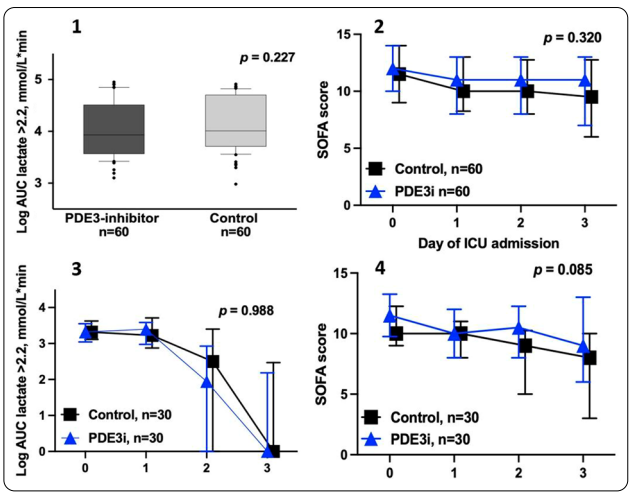
Introduction: In patients with septic shock and persistently elevated lactate levels, inodilatory phosphodiesterase 3 inhibitors (PDE3i) are sometimes used to treat hypoperfusion. However, their effect on lactate dynamics and clinical outcomes is not established.
Objectives: To investigate the association between the administration of PDE3i and lactate dynamics, resolution of organ failure, ICU length of stay (LOS) and hospital mortality in a retrospective cohort of patients with septic shock and persistently elevated lactate.
Methods: Patients admitted to Dutch ICUs, with septic shock and two arterial lactate concentrations $\geq$ 4 mmol/L with at least 4 h between measurements were eligible. Clinical data of the first four days of admission were collected in an online database. For each patient, the area between the lactate curve and 2.2 mmol/l (AUClact) was calculated per day. The results were analysed in three steps: First, a multivariate model was developed to determine covariates for the AUClact. Next, using these covariates, patients receiving PDE3i were propensity matched with control patients to compare AUClact, SOFA scores, ICU-LOS and mortality. Finally, as a sensitivity analysis, patients who continually received PDE3i from day 0 to 3 of ICU admission were selected, and matched with controls surviving to day 3 or longer to compare changes in AUClact and SOFA scores.
Results: Data on 229 eligible patients from ten hospitals were collected. Of these, 123 (54%) received PDE3i. A linear multivariate model, including APACHE IV score, highest lactate, highest leucocyte count, highest noradrenalin infusion rate, and total urinary output in the first 24 h of admission predicted AUClact with an R^2 of 0.57. Adding the use of PDE3i as a cofactor did not affect R^2. Propensity score matching using these five covariates plus a history of heart failure resulted in a cohort of 60 patients receiving PDE3i and 60 matched controls. Patients treated with PDE3i did not differ from controls in AUClact (Fig. 1), change in SOFA scores (Fig. 2), ICU LOS and hospital mortality (6 days [IQR 3–15] vs. 6 days [IQR 3–11], $p = 0.748$, and 56.7% vs. 53.3%, $p = 0.714$, respectively). Propensity score matching of 30 patients receiving PDE3i from day 0 to 3, with 30 control patients alive on day 3, resulted in similar changes in AUClact (Fig. 3) and SOFA scores (Fig. 4) on days 1–3.



Conclusion: In this multicentre, retrospective cohort of patients with septic shock and persistently elevated lactate levels, no association was found between the administration of PDE3i and improvement of lactate dynamics, resolution of organ failure, ICU-LOS, or hospital mortality compared to a matched control group.

000568

Intracellular expression of apoptotic and antiapoptotic molecules in sepsis

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Introduction: The predominance of sepsis leads to the activation of apoptotic and antiapoptotic pathways. Apoptosis is controlled by initiator caspases-8/-9 and executioner caspases-3/-7 (1). Pyroptosis, another form of programmed cell death, is highly associated with sepsis and is mainly driven by caspase -1 (2). On the contrary, certain apoptotic cascades are inhibited by antiapoptotic molecules, such as survivin protein. Both apoptotic and antiapoptotic mediators seem to be upregulated during sepsis and their fragile balance defines the viability of the cell (3).
Objectives: The purpose of the study is to investigate whether the expression of apoptotic or antiapoptotic proteins in peripheral blood cells (PBMCs) characterizes sepsis in adult and pediatric ICU patients.
Methods: The study sample of this prospective single-center study consists of adult and pediatric ICU patients with sepsis (S), compared to non-infectious inflammation (I) and healthy controls (H). Consecutive whole blood samples were collected on the 1st, 3rd, and 7th days of admission. The expression of the study's apoptotic and antiapoptotic molecules in PBMCs was determined by flow cytometry, through the use of specific fluorescent-labeled inhibitors of caspases (FLICA), which bind to activated caspases, or through cell staining with specific conjugated monoclonal antibodies with affinity for survivin protein.
Results: Out of 45 patients enrolled in the study, 29 were adults (12 S, 7 I and 10 H), and 20 patients were children (6 S, 6 I and 4 H). The results of the study showed an increased expression of survivin in lymphocytes (S = 0,65% (0,17–2,05), I = 0,4% (0,25–1,05), H = 0,2% (0,1–0,95), p = 0,370), monocytes (S = 3,05% (1,42–7,3), I = 1,1% (0,9–6), H = 3% (1,12–6,6), p = 0,567), and neutrophils (S = 8,2% (1,02–17,5), I = 5,8%(2,1–26,9), H = 3,4% (1,5–6,3), p = 0,672) in septic adult patients (Fig. 1), as well as a consecutive increase in its expression during sepsis in both adult and pediatric patients. Among non-survivors, necrosis of apoptotic lymphocytes that express caspase-1 (1,9% (1,75–5,8) vs 0,9% (0,62–1,22), p = 0,003), caspases-3/-7 (2% (1,35–4,75) vs 1,25% (0,9–1,5), p = 0,011) and caspase-8 (1,9% (1,15–9,6) vs 0,65% (0,52–1,07), p = 0,006) is particularly increased.

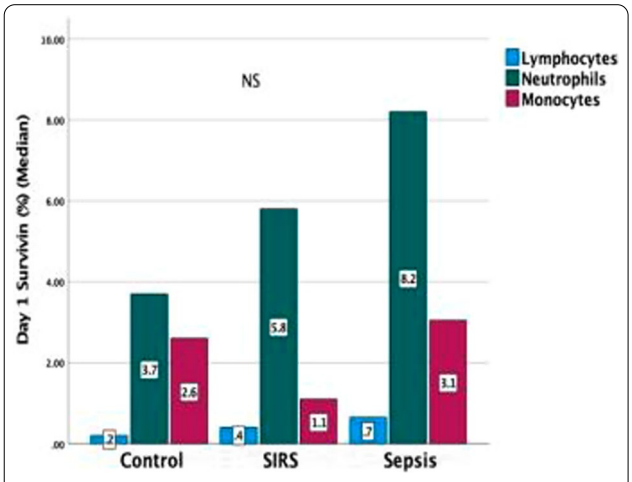

Fig. 1 Upregulated survivin expression in lymphocytes (p = 0,370), neutrophils (p = 0,672) and monocytes (p = 0,567) in septic adult patients compared to non-infectious critically-ill patients and to healthy controls

Conclusion: Increased expression of the antiapoptotic survivin protein in parallel with central apoptotic caspases activation during the septic cascades indicates a competitive apoptotic/ antiapoptotic procedure, while the augmented necrosis of apoptotic lymphocytes seems to have a prognostic value for non-survivors.

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000575

Comparison of molecular endotypes and clinical subphenotypes in sepsis patients admitted to the Intensive Care

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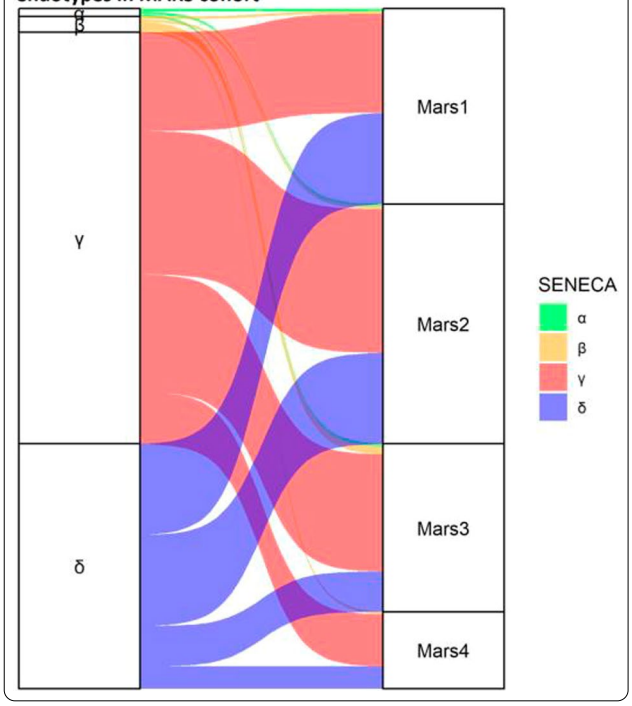
Introduction: The heterogeneity in sepsis may be responsible for the lack of specific sepsis treatments. A shift towards precision medicine has been suggested. Unsupervised learning to identify differential subgroups has been put into practice. Recent work identified 4 sepsis subphenotypes based on clinical parameters and 4 sepsis endotypes based on whole-blood leukocyte transcriptomic data (1,2). However, it is unknown how the different phenotypes represent different biological entities, comparing host-response signatures.
Objectives: To provide insight into how previously identified endotypes relate to currently known subphenotypes in patients admitted to the ICU with sepsis.
Methods: Using the Molecular Diagnosis and Risk Stratification of Sepsis (MARS) prospective observational cohort, molecular classification of 522 sepsis patients as four endotypes was performed using whole blood leukocyte transcriptomic features collected in the first 24 h after ICU admission. Clinical subphenotypes were also applied using membership probabilities from clinical characteristics of α, β, γ and δ cluster members from the Sepsis Endotyping in Emergency Care (SENECA) derivation cohort. Differences between endotype and subphenotype adjudication in clinical parameters, biomarkers and transcriptomics for all subtypes were compared using appropriate statistical testing.
Results: The γ and δ subphenotype were more abundant in the MARS endotype cohort compared to the original SENECA cohort (61% in MARS versus 27% in SENECA for γ and 36% versus 13% for δ), whereas only few patients were classified as α and β (1% versus 33% and 2% versus 27%). There was no clear association between the distribution of clinical subphenotypes compared to endotypes (Fig. 1). Moreover, the subphenotype membership probability was not correlated to endotype (p = 0.36 for γ, p = 0.66 for δ). Patients in the δ subphenotype and Mars2 endotype both had enhanced systemic inflammation, coagulation activation and more disturbed endothelial barrier function compared to other groups. Gene expression data of the four subphenotypes showed alterations relative to healthy controls. However, only few gene expression signatures were specific to each subphenotype. Pathway analysis revealed downregulated pathways involved in the immune system in δ, compared to the other clinical subphenotypes.
Conclusion: In this study, critically ill patients with sepsis classified as subphenotypes, based on clinical parameters, or endotypes, based on transcriptomic data, did not share common ground. Since they do not share common ground, combining multiple data types could yield better results for prediction of treatment in future observations.

Fig 1. Alluvial plot showing distribution of subphenotypes across endotypes in MARS cohort



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Acknowledgements

1. Dr. Seymour is supported in part by grants from the NIH (R21GM144851, R35GM11951).
2. Lonneke A van Vught was supported by the Netherlands Organisation for Health Research and Development ZonMW (Nederlandse Organisatie voor Wetenschappelijk Onderzoek NWO) VENI grant 09150161910033 and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Research Grant.
3. Supported by the Center for Translational Molecular Medicine (http://www.ctmm.nl), project MARS (grant 04I-201).

Systemic Inflammation & Sepsis 5

000637

Factors associated with mortality in critical obstetric patients with SARSCoV2 infection

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Introduction: During the beginning of the SARS-Cov2 pandemic, the principal cause of death in Mexico for pregnant and puerperal patients is respiratory failure. The factors associated with mortality are unknown. The evaluation of the clinical characteristics and the association with mortality in the intensive care unit is relevant. The objective was to determine the factors associated with mortality in obstetric patients with SARSCoV2 infection.
Objectives: The objective was to determine the factors associated with mortality in obstetric patients with SARSCoV2 infection.
Methods: Retrospective and descriptive study, women over 18 years, pregnant and/or postpartum with mechanical ventilation and positive test PCR for SARSCoV2 admitted to the Intensive Care Unit in a tertiary care hospital.
Results: Results were obtained from 20 obstetric patients; 3 (15%) died and 17 (85%) survived. The mean stay in the ICU of the patients who died was 35 days, with a (95% CI 32.5–59), p = 0.02, and the culture of bronchial secretion was reported positive for Acinetobacter Baumanii, however, it did not present significance statistics when associating it with mortality plus ICU days, Log Rank 0.782 p = 0.377.
Conclusion: The risk factor for mortality in these patients is nosocomial infections and staying more than 35 days in the ICU. The limitation was a small sample because it was an obstetric population. With the results obtained, it is proposed to prevent prolonged days of stay and better control of nosocomial infections.

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000645

Excessive long-term mortality after critical community-acquired sepsis—a nationwide case–control study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000645

Introduction: The World Health Organisation has recognised sepsis as a global priority and states that the true burden of sepsis remains unknown(1). The literature suggests a complex interaction between severe illness, intensive care treatment, co-morbidity and socioeconomic factors that affect the patient's vulnerability over time (2).
Objectives: The aim was to investigate the long-term mortality after critical community-acquired sepsis on a national level in Sweden and classify causes of late death compared with a matched control population.
Methods: Patients with sepsis admitted directly from an emergency department to an intensive care unit (ICU) were identified in the Swedish Intensive Care Registry from January 2008 to December 2017. Controls were matched at the time of ICU admission on age, sex, and region in a ratio of 1:5. By linkages to national registries, co-morbidity status classified by Charlson´s Co-morbidity Index (CCI), data on socioeconomy, long-term mortality and causes of death were identified. Causes of death were categorized according to ICD-10 diagnoses. Excess mortality was analysed by calculating the all-cause mortality compared to controls. Survival curves were estimated using a standard Kaplan–Meier estimator and compared by log-rank test. Cox proportional hazard regression models were used to adjust the comparison

of 30, 90, 365 days and 3 years mortality of sepsis patients and controls for potential confounders.
Results: In total, 10 072 sepsis patients and 50 322 controls were included. The majority was male, mean age 67 years. More than half of the sepsis patients presented with a CCI of ≥ 2 compared to 18% of the controls. Sepsis patients had sustained excessive mortality during the entire follow-up period. At 30-days the mortality was 27% vs. 0%, 90-days 32% vs. 1%, 1-year 41% vs. 3% and 3-year 60% vs. 12% among sepsis patients vs. controls. A similar pattern was seen also for patients without a history of co-morbidity on ICU admission. In the adjusted analyses there was an increase in all-cause mortality for up to 3 years with an adjusted hazard ratio of 5.4 (95% CI 5.2–5.6). When splitting into different time intervals, an adjusted hazard ratio of 96.4 (95% CI 80.3–115.6) was seen for days 0–30, 11.1 (95% CI 9.5–13.0) for days 31–90, 4.0 (95% CI 3.6–4.4) for days 91–365 and 3.0 (95% CI 2.8–3.2) for 1–3 years. Again, similar findings were noted for patients without co-morbidity. The causes of death differed between sepsis patients and controls. In early deaths the majority were infectious causes and later more cancer and circulatory related deaths.
Conclusion: The overall mortality was significantly increased during the entire follow-up time for sepsis patients compared to controls. This finding was also seen for sepsis patients with no previous co-morbidity. Causes of death for sepsis patients change over time.

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Acknowledgements Financial support provided through the regional agreement on medical and clinical research (ALF) between Stockholm County Council and Karolinska Institute.

000686

The association between time from emergency department visit to ICU admission and mortality among patients with sepsis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000686

Introduction: The Surviving Sepsis Campaign Guidelines 2021 recommends that adult patients with sepsis requiring intensive care should be admitted to the ICU within 6 h of their emergency department (ED) visits [1]. However, there is limited evidence on whether 6 h is the best target time [2–5]. Furthermore, there are conflicting findings as to whether ICU admissions within 6 h of ED visits are associated with better prognostic outcomes among patients with sepsis [6–7]. We aimed to identify the optimal time from ED visits to ICU admission.
Methods: This is a retrospective cohort study on patients from the Medical Information Mart for Intensive Care IV (MIMIC-IV) [8] and MIMIC-IV-ED databases [9]. We identified adult patients (aged ≥ 18 years) without trauma who were transferred from the ED to ICU and subsequently diagnosed with sepsis based on the Sepsis-3 criteria within 24 h of ICU admission. Patients determined to be non-urgent at triage and those who took more than 9 h from ED visit to ICU admission were excluded from our analysis. Using patient characteristics (e.g., demographics, vital signs at the initial triage, and laboratory results) as covariates, we conducted a multivariable logistic regression analysis to evaluate the association between time from ED visit to ICU admission and 28-day mortality. In addition, we categorized the time from ED visit to ICU admission into quantiles and repeated the analysis using the time quantiles as categorical variables.
Results: We identified 2,188 eligible patients with sepsis. In the multivariable analysis, time from ED visit to ICU admission was not significantly associated with 28-day mortality (adjusted odds ratio [aOR] per hour increase, 1.03; 95% CI 0.96–1.11; p = 0.4). However, when we categorized all patients into time quantiles (time from ED visit to ICU admission: < 3.3 h, 3.3–4.6 h, 4.6–6 h, and > 6 h), patients in the higher time quantiles (e.g., 3.3–4.6 h) had higher 28-day mortality compared with those in the lowest time quantile (< 3.3 h) (e.g., aOR for patients in the second time quantile (3.3–4.6 h), 1.54; 95% CI 1.03–2.30; p = 0.03), as shown in Fig. 1.

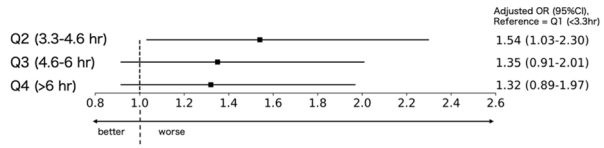

Figure 1

Conclusion: Earlier admission to the ICU (e.g., within 3.3 h of ED visits) was associated with lower 28-day mortality in patients with sepsis. Our findings suggest that adult patients with sepsis who require intensive care should be admitted to the ICU within 3 h.

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000710

Extracorporeal hemoperfusion with Efferon LPS for rapid reconstitution of vital parameters and decreasing proinflammatory biomarkers in patients with intra-abdominal sepsis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000710

Introduction: Post-surgery infections in ICU cause intra-abdominal sepsis (IAS) including septic shock associated with increased mortality. Rapid abrogation of endotoxin and\or excess of cytokines using extracorporeal hemoperfusion (EH) therapies may improve treatment outcomes in patients with septic shock [1–5].
Objectives: to evaluate the efficacy of the Efferon LPS device in extracorporeal therapy in patients with IAS complicated by septic shock.
Methods: Thirty-three post-surgery patients admitted to the same ICU (20 men and 13 women, average body mass 88 kg, median age 67 years, range 39–89 years, with IAS, complicated by septic shock as revealed by SEPSIS-3(2016) criteria) were subdivided in two groups. One group received conventional treatment for septic shock (control, n = 13), another one additionally underwent EH (n = 20). EH was carried out by Efferon LPS adsorber containing cytoking-adsorbing mesoporous hypercross-linked polystyrene beads with surface-immobilized LPS-selective ligand [6–8]. During three days, patients were receiving 1–2 EH procedures, a day apart, 4–6 h each, using MultiFiltrate blood perfusion machine (Fresenius) at a rate of 100–150 ml/min, followed by continuous veno-venous hemodiafiltration. Groups did not differ significantly in age and sex, and in any of the parameters studied except PCT (Table, day 0). Statistical analysis was performed using Microsoft Excel with Real-Statistics add-in and XLStat (USA). Significance of intergroup differences was determined by Student's t test, Wilcoxon test, or Mann–Whitney test, whatever appropriate, and significance of differences was considered at $p < 0.05$.
Results: Mortality during septic shock tended to decrease in EH patients vs.control group at a marginal significance ($P = 0.065$). There was a trend in increased survival in 3, 7, and 14 days post-EH vs. control. EH resulted in a significant fourfold decrease in septic shock duration in survived EH patients: 46(34–74) hours vs. 168 (71–272) hours (HE vs. control patients, respectively, $cP = 0.0025$), accompanied by decreasing endotoxin and IL-6 levels, SOFA score, leukocyte, CRP, lactate and creatinine levels, whereas PfO_2/FiO_2 oxygenation index and MAP values were increasing. The most significant effects were revealed in patients < 80 years old. EH led to rapid decreasing the multiple organ failure in patients exhibiting both lower (< 8) and higher (> 8) SOFA scores values. In contrast to a control group, on day 3 post-EH patients did not require norepinephrine support any more.
Conclusion: EH with Efferon LPS adsorber resulted in rapid improval of vital indices (SOFA, MAP, oxygenation index) and proinlammatory biomarkers (IL-6, PCT, CRP) in IAS patients associated with a rapid shock abrogation and a trend to decreasing mortality in an ICU setting.

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000716

Refractory Septic Shock: A Retrospective Review of Circulatory Support in a Tertiary Intensive Care Unit

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Introduction: Septic shock is the most severe subset of sepsis in which underlying circulatory, cellular and metabolic abnormalities are profound enough to cause a mortality of around 40% [1]. Refractory septic shock has no consensus definition; the presence of hypotension, with end-organ dysfunction requiring a threshold of 0.5mcg/Kg/min of noradrenaline is often used in clinical trials[2–4]. The Surviving Sepsis Campaign (SSC) Guidelines provide a structured approach to managing those with septic shock [4]. Despite advances in treatment, in 6–7% of patients there is a treatment failure and they develop refractory shock[6,7]. The mortality rises to 60% in this group [8–10], however, the literature is often poorly described. Conclusive evidence is required to guide management, and improve patient outcomes, often with the utilisation of pharmacological and mechanical support.
Objectives: This retrospective review aims to describe patients with refractory septic shock admitted to a regional tertiary intensive care unit (ICU), in order to advance understanding of the efficacy of pharmacological and mechanical support used. The primary outcomes were to investigate the incidence of refractory septic shock, factors associated with ICU mortality and the use of cardiac monitoring. This will allow development of a guideline or'bundle' to potentially improve outcomes.
Methods: Patients with septic shock who were admitted to the Royal Infirmary of Edinburgh ICU between January 2018 to November 2021 on noradrenaline (NA) ≥ 0.5mcg/Kg/min within first 24 h of ICU admission were included. The Mann Whitney U test for continuous data and Chi Squared for categorical data were used. Univariate analysis was performed to identify factors independently associated refractory septic shock ICU mortality.
Results: 248 patients were screened, with 26.6% in refractory septic shock. Median age 61 years (IQR 46–70), 37.9% male. Overall mortality was 47.0%. Highest NA dose in the first 24 h was median of 0.79 mcg/Kg/min (IQR 0.61–1.26). 54.5% were on one vasoactive agent, 36.4% on two and 9.1% on three vasoactive agents. 81.8% were initiated on corticosteroids at median NA dose 0.59mcg/Kg/min (IQR 0.47–0.83). 56.1% had an echocardiogram. One patient had invasive cardiac output monitoring. Mechanical circulatory support was utilised in 2 patients (3.0%). Lactate clearance at 36 and 48 h was independently associated with ICU mortality.
Conclusion: A significant mortality still exists in this cohort. High compliance with SSC guidelines was shown. Our unit bundle will address increasing echocardiogram use and cardiac output monitoring. Further prospective data is required to establish factors associated with mortality outcomes to guide a more tailored approach to circulatory support.

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000750

Epigenetic endotypes derived from genome-wide histone modification patterns predict the risk for secondary infections and mortality in patients with sepsis

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Introduction: The dysregulated and harmful host response to infection is a hallmark of sepsis. As the main driver, the immune system exerts a dynamic and complex activation state, which is shaped by the patients' characteristics and the causative pathogen. While specific components of the immune system—such as neutrophils—demonstrate a highly activated state, many patients during and after sepsis encounter recurrent secondary infections, often caused by opportunistic pathogens (1). This phenomenon indicates a functional breakdown of relevant parts of the immune system, which is not apparent using routine lab parameters. Epigenetic modifications—e.g., histones—have emerged as a potential source of diagnostic information, and monocytes from patients with sepsis possess distinct alterations of histone modification associated with promotors of immune-related genes (2).
Objectives: Our study aims to identify potential epigenetic endotypes among patients with sepsis, based on the genome-wide and promotor-associated distribution of histone modifications.
Methods: Patients with sepsis according to Sepsis-3 criteria (n = 50) were enrolled in this single-center observational study (German Clinical Trial Register ID DRKS00018867). Blood was sampled within 24 h after sepsis diagnosis. The genome-wide distribution of distinct histone modifications (trimethylation of lysine 4 (H3K4me3) and acetylation of lysine 9 (H3K9ac) of histone 3) was analyzed using ChIP-mentation assay followed by *Next Generation Sequencing* on an Illumina NextSeqTM 550 platform. The resulting high-throughput data was analyzed bioinformatically and histone distribution within promotor regions (± 2,000 base pairs around transcriptional start) served as input data for unsupervised cluster analysis. The identified subgroups were compared for their demographic, immunological, and clinical characteristics.
Results: The study cohort shows in-hospital mortality of 24% (n = 12), with 32% of patients (= 16) developing secondary infections beyond 48 h after admission. We identified three distinct subgroups for both H3K4me3 and H3K9ac datasets. While the subgroups contained only partly overlapping patients between the modifications, no systematic demographic and immunologic differences became evident for subgroups of a modification. Relevant differences exist for the clinical endpoints "secondary infection" and "hospital mortality", predominantly between subgroups of H3K4me3. High-risk "cluster 1" implicates a risk for secondary infections of 40% in combination with a mortality of 33%. In comparison, "cluster 2" patients exhibit a comparable secondary infection incidence of 42%, but without an associated mortality risk (11%), and "cluster 3" patients show high mortality (31%) with low secondary infections (13%).
Conclusion: We here provide the proof of principle that genome-wide histone modifications are able to identify epigenetic endotypes with non-redundant information. Associated risk profiles for secondary infection and mortality warrant further evaluation, of how this source of biological information can be made available as a tool for clinical risk assessment.

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Acknowledgements The SEPSDIA project (Reference number 11501) has been conducted within the framework of the European funding program "Eurostars". The German consortium partner has received financial support from the German Federal Ministry of Education and Research (BMBF), Berlin.

000785

Early cytokine adsorption in septic shock reduces volume responsiveness-guided fluid requirement after initial hemodynamic stabilization in sheep

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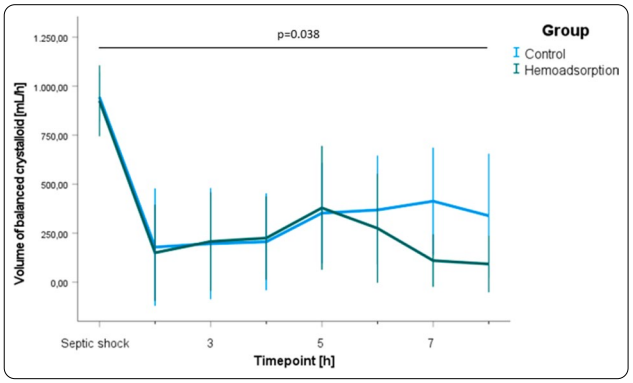
Intensive Care Medicine Experimental 2022, **10(2)**: 000785

Introduction: Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection [1]. One of the key mechanisms of the development from a local infection to a systemic disease is the excessive release of pro- and anti-inflammatory cytokines. The clearance of those cytokines might attenuate the course of sepsis [2]. It is hypothesized that early cytokine adsorption in septic shock is beneficial before profound damage to capillaries and organs occurs [3].
Objectives: The objective of this study was to investigate the effect of early use of hemadsorption on fluid requirements, fluid balance, vasopressor requirements and microcirculation in an ovine model of septic shock.
Methods: After approval by the animal welfare committee, septic shock was induced in 20 sheep by inoculation of feces in the peritoneal cavity. A causal sepsis therapy was performed with intravenous antibiotics. As supportive therapy, norepinephrine (NE) was titrated to maintain mean arterial pressure (MAP) between 65–70 mmHg. Initial fluid resuscitation was performed with 20 mL/kg balanced crystalloids over 60 min. Afterwards, sheep were randomized into two groups. The therapy group underwent hemoadsorption (CytoSorb®, CytoSorbents Europe GmbH, Germany) with a blood flow of 150 mL/min for 6 h (N = 9). The control group underwent a sham procedure (N = 10). Fluid therapy was continued with bolus infusions (4 mL/kg) of balanced crystalloids guided by response to fluid challenges. After the end of hemoadsorption, therapy was continued for one hour. Groups were compared using independent samples t-test and generalized estimating equations.
Results: All sheep developed septic shock with decreases in MAP (baseline [BL] 75 ± 9 vs. shock 45 ± 9 mmHg, $p < 0.001$) and increased lactate concentration (BL 0.9 ± 0.3 vs. shock 2.0 ± 0.2 mmol/L, $p < 0.001$). Conjunctival microcirculation showed serious disturbance with almost halved proportion of perfused vessels (PPV, BL 95.3 ± 5.3 vs. shock 50.2 ± 18.2%, $p < 0.001$). Shock therapy with fluid and NE restored macro- and microcirculation. After 8 h of shock therapy, fluid balance (therapy 5.5 ± 1.9 vs. control 5.1 ± 1.7 L, $p = 0.629$) and cumulative dose of NE (therapy 0.65 ± 0.23 vs. control 0.65 ± 0.20 mg/kg, $p = 0.974$) did not differ between groups. In addition, MAP ($p = 0.669$), lactate concentration ($p = 0.769$) and PPV ($p = 0.955$) did not differ between groups during the experimental therapy. However, animals of the hemoadsorption group received significantly fewer intravenous fluid as guided by fluid challenges ($p = 0.038$, Fig. 1), especially in the last hours of sepsis therapy.
Fig. 1 Amount of fluid administered for hemodynamic stabilization during the experiment



Conclusion: In a clinically relevant model of septic shock, hemoadsorption with CytoSorb® reduced the need for intravenous fluid administration without increased vasopressor requirements, but did not impact on fluid cumulation or vasopressor load. Future studies on early hemadsorption are needed to analyze the reasons for reduced fluid requirements.

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Acknowledgements This work was supported, in part, by CytoSorbents Europe GmbH, Berlin, Germany as an Investigator Initiated Trial.

000818

Persistent inflammation and chronic critical illness in patients with Covid-19

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Intensive Care Medicine Experimental 2022, **10(2)**: 000818

Introduction: The definition of chronic critical illness (CCI), or persistent critical illness is not yet well clarified1. The mortality of the CCI is higher than the acute disease, and due to the prolong ICU treatment and the typical complications represents a big medical challenge and financial burden2. Widely accepted the theory of persistent inflammation, immunosuppression catabolism syndrome3,4 in critically ill patient which with high probability play role of the development of CCI. Some promising makers have been found supporting the PICS hypothesis 5, like CRP clustering 1, carbamide/creatinine ratio6, and haematologic alteration7.
Objectives: Our goal was to find predictive markers of CCI outcome in severe Covid-19 patients in a tertiary intensive care unit in a university centre. The definition of the CCI was more than 7 days invasive mechanical ventilation and more than 11 days ICU treatment.
Methods: During our retrospective study medical data was collected from adult patient admitted in the ICU between 1 November 2020 and 31 October 2021. We include patients who fits into the CCI definition, and exclude who admitted from another ICU, or ECMO centre.
Medical history and clinical parameters were collected on the day of admission, and on the day of 7th, and 14th days of treatment. We compared survivors and non-survivors with Mann–Whitney U-test and performed uni- and multivariate logistic regression models to predict ICU mortality. The latter were adjusted to age, gender, and hypertension.
Results: We included 89 participants, 55 of them died in the ICU (61.8%). The median age was 60.5 (IQR: 44.5–64) years in the survivor, and 63 (IQR: 57–72) years in the non-survivor group. There was no significant difference between survivors and non-survivors in conventional prognostic markers (age, BMI, APACHE II score). History of hypertension (67.3% vs. 44.1%, respectively; $p = 0.033$) were more frequent among deceased patients. With multivariate logistic regression serum albumin levels (OR: 0.72, 95%CI: 0.585–0.887, $p = 0.02$), and CRP (OR: 1,012, 95%CI: 1.005–1.018, $p < 0.001$) on day 7 were independently associated with ICU mortality. Nonetheless, ascending CRP levels from day 0 to 14 (OR: 1.007; 95% CI: 1.003–1.012; $p = 0.001$) and elevation in carbamide levels from day 7 to 14 showed also higher risk for ICU death (OR: 1.144, 95%CI: 1.046–1.251, $p = 0.03$).
Conclusion: CCI cause high mortality and huge medical challenge in the ICU. According to our results, persistently elevated CRP, high carbamide and low albumin levels in the chronic phase showed correlation with ICU mortality.

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000821

Blood Transcriptomic Endotypes and the Response to Treatment Modalities in Sepsis: A Prospective Cohort Study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000821

Introduction: Sepsis is a life-threatening syndrome, caused by a dysregulated host response to an infection. Current treatment guidelines reflect an insufficient appreciation of the heterogeneity in sepsis. Stratifying patients into more homogeneous groups having common biological or clinical features may increase the likelihood of beneficial

treatment effects. We hypothesized that sepsis transcriptomic endotypes respond differently to specific treatment strategies in the intensive care unit (ICU).
Objectives: To test the association between sepsis transcriptomic endotypes, glucose control, fluid balance, corticosteroid treatment and outcome in the ICU.
Methods: Patients were included in a prospective observational cohort study in the ICUs of two tertiary teaching hospitals in the Netherlands. Sepsis transcriptomic endotypes (Mars1–4) were defined based on a previously derived leukocyte gene expression classifier. A glucose measurement was considered in protocol range between 5.0–8.0 mmol/L. Glucose variability was expressed as the daily coefficient of variation (CV) of all measurements. We used the first record (typically day 1) of fluid balance in mL divided by the weight of the patient in kg (mL/kg/day). We defined a high (or low) first fluid balance for each endotype as having a first fluid balance above (or below) the median within the endotype. The cumulative intravenous dose of hydrocortisone administered throughout a patient's ICU stay was used as a measure of corticosteroid treatment (mg/kg/days). Non-parametric Kruskal tests were followed by Dunn's post-hoc tests. Linear or logistic regression models were fit where applicable. Multivariate models included demographics, comorbidities and indices of clinical severity as covariates where applicable. Significance was demarcated by $p < 0.05$.
Results: A total of 522 patients were included in the study, of whom 150, 184, 129 and 59 were classified as Mars1, Mars2, Mars3 and Mars4 transcriptomic endotypes, respectively. Mars1 patients were at highest risk of mortality relative to other endotypes. Mars1 patients were more often out of glucose protocol range in the first 7 days. A multivariate logistic regression model showed that for patients classified as Mars1 a higher glucose CV on days 1, 4 and 7 was associated with 28-day mortality (Fig. 1).

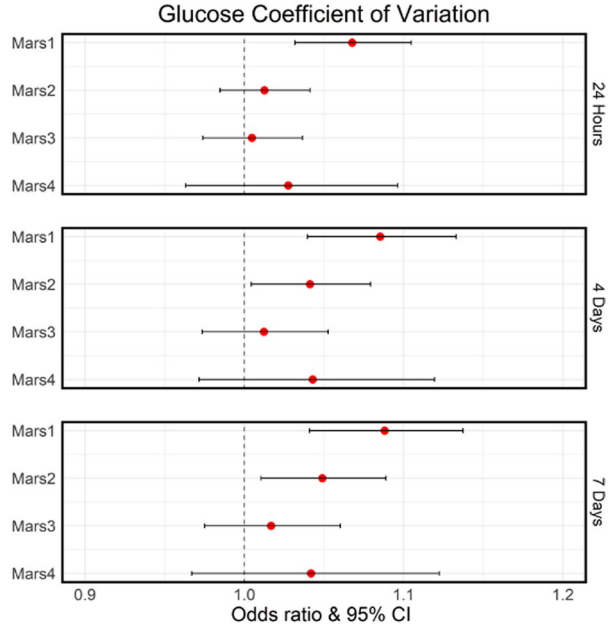

Figure 1 - Forest plot of the association between glucose coefficient of variation and 28-day mortality at 24 hours, 4 days and 7 days after ICU admission.

For Mars2, increased glucose CV calculated on days 4 and 7 was associated with 28-day mortality. No discernible effect of glucose variation was observed for the other endotypes.

Patients classified as Mars3 had a significantly lower first fluid balance when compared to Mars1 or Mars2 patients. Multivariate linear regression showed that this difference in first fluid balance in Mars3 relative to Mars2 patients was independent of clinical severity. Logistic regression showed that a high first fluid balance was associated with increased 28-day mortality for Mars3 patients, while this was not observed in the other endotypes. Overall, 300 patients received intravenous corticosteroids: 96 (64%) were classified as Mars1; 112 (61%) as Mars2; 55 (42.6%) as Mars3 and 37 (62.7%) as Mars4. Corticosteroid treatment was significantly less prevalent in Mars3 compared to the other endotypes. Multivariate logistic regression uncovered no association between the dose of hydrocortisone administered and 28-day mortality.
Conclusion: Sepsis transcriptomic endotypes show differences in blood glucose levels and fluid balance, which were associated with adverse outcome. Patients classified as Mars1 and 2 may benefit from strict glycemic control strategies, while Mars3 patients may benefit from restrictive fluid therapy. Our findings lend weight to the clinical applicability of transcriptomic endotypes in critical care, which need to be confirmed in prospective interventional studies.
Acknowledgements The authors acknowledge the support of the European Union through the MSCA-ESA-ITN project (676129), European Sepsis Academy. In addition, the research leading to the results herein reported was conducted as part of the MARS consortium that received support from the Center for Translational Molecular Medicine (http://www.ctmm.nl; grant 04I-201). Lonneke A. van Vught was supported by the Netherlands Organisation for Health Research and Development ZonMW (Nederlandse Organisatie voor Wetenschappelijk Onderzoek NWO) VENI grant 09150161910033 and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Research Grant.

000835

Identification of the causative microorganism in septic or septic shock patients admitted to the Intensive Care Unit: Does it make a difference?

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Intensive Care Medicine Experimental 2022, **10(2)**: 000835

Introduction: Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection [1]. However, approximately 40–60% of septic patients will not have a causative microorganism identified by culture [2,3].
Objectives: We aim to compare the clinical characteristics and outcomes of septic or septic shock patients with a culture-identified causative microorganism (MO) to those without it.
Methods: We conducted a retrospective, observational, single-centre study in the Intensive Care Unit (ICU) of a University Hospital in Spain, over 2 years (2018–2019). All the patients who were admitted to the ICU with sepsis or septic shock, as defined by Singer M et al. [1], were included. Clinical characteristics, results of microbiological tests and outcomes were retrieved from the electronic medical record. A waiver for informed consent was granted due to the retrospective nature of the study. Data are expressed as median (interquartile range) or frequency (%). χ^2 or Mann–Whitney U tests were applied as appropriate.
Results: We analyzed 191 patients. A causative microorganism was recognized in 145 (76%) (Table 1). Multi-drug resistance was identified in 18% of the patients with a recognized microorganism (17% in community-acquired sepsis *vs* 19% in hospital-acquired sepsis, $p = 0.80$). Empiric antimicrobial therapy (EAT) was adequate in 87% of the patients. Mortality was 13% with adequate EAT *vs* 32% with inadequate EAT, OR 0.32, 95%CI 0.11–0.92, $p = 0.03$.
Table 1 Characteristics of the patients based on MO identification

	Causative MO not identified (n = 46)	Causative MO identified (n = 145)	p-value
Age, years	67 (55–75)	68 (60–77)	0.28
Female, %	44	48	0.57
APACHE-II	18 (14–24)	21 (16–25)	0.03
ICU Mortality, %	9	15	0.26
In-hospital mortality, %	17	19	0.85
Community-acquired sepsis mortality, %	0	12	0.07
Hospital-acquired sepsis mortality, %	18	20	0.86
Respiratory source sepsis mortality, %	25	22	0.85
Non-respiratory source sepsis mortality, %	5	14	0.15
ICU LOS, days	2 (1–4)	4 (2–9)	< 0.01
In-hospital LOS, days	14 (6–20)	15 (9–31)	0.12
Days of antibiotic treatment	4 (3–10)	6 (4–15)	< 0.01
Need for vasopressor support, %	63	81	0.01
Need for mechanical ventilation, %	20	33	0.08
Need for renal replacement therapy, %	2	16	0.01

Conclusion: Septic or septic shock patients without a recognized causative microorganism scored lower in severity scales, required less vasopressors and renal replacement therapy, and had shorter ICU stays. Overall in-hospital mortality was similar regardless of microbiological identification. We observed a downtrend in mortality in community-acquired sepsis and non-respiratory sepsis when a causative microorganism was not identified.

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000840

Sepsis mimics among culture negative sepsis patients in the intensive care unit

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Introduction: To diagnose sepsis remains a challenge because of the lack of gold standard diagnostics. The 2016 sepsis-3 criteria suggest that a Sequential Organ Failure Assessment (SOFA) score of 2 or more should be used as cutoff for sepsis in a patient who is suspected of having an infection (1). Organ failure is present in a majority of Intensive Care Unit (ICU) patients and since there are no simple, broadly accepted criteria for infection, the risk of false positive sepsis patients (sepsis mimics) is high. This issue has been explored in previous studies using the sepsis-2 criteria (2, 3). To our knowledge, no study has investigated the proportion of sepsis mimics when the sepsis-3-criteria are used.
Objectives: To investigate the proportion of non-infected patients (= sepsis mimics) among ICU patients classified as having sepsis at ICU admission.
Methods: We have previously screened 7727 ICU admissions retrospectively (3.5 years, 4 ICUs) for fulfilment of the sepsis-3 criteria (4). Proxy criteria for suspected infection were obtained blood culture(s) and concomitant antibiotic administration, as suggested by the sepsis-3 taskforce(1). A post-hoc analysis of culture negative patients within this sepsis cohort is ongoing, with classification of infection according to an infection tool (5). Culture negativity was defined as no clinically relevant positive culture results 48 h before/after ICU admission.
Results: The ICU sepsis cohort (2527 ICU admission) was culture negative in 42% of cases (n = 1061). We have so far screened 50% of these for infection and an interim analysis reveals that 54% of culture negative sepsis patients do not fulfil criteria for probable infection, thus yielding a total of 23% sepsis mimics within the sepsis cohort. The most common reasons for ICU admission among sepsis mimics were respiratory failure of multifactorial or unknown cause, massive hemorrage or cardiac arrest/cardiogenic shock. A comparison between the mimics and the infected among the culture negative patients showed no difference in admission SOFA score (median 7), sex or age, but a higher hospital mortality among the infected than among mimics (30% vs 22%, p = 0.06) and that the infected were slightly more severely ill according to SAPS-3-score (67 vs. 64 points, p = 0.07). The level of C-reactive protein was higher among the infected (102 vs 60 mg/L, p < 0.001) but leukocyte count was the same (14 × 10^9/L).
Conclusion: Almost one fourth of an ICU sepsis population, identified according to recommended criteria, are sepsis mimics. This sheds light on the low specificity of sepsis criteria, as a consequence of higher sensitivity. The high proportion of sepsis mimics has a potential dilutional effect on the true sepsis population, which threatens the validity of results from sepsis studies using recommended criteria.

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Acknowledgements The study was partly funded by research grant from Region Skåne regional grant support.

000866

Resistant and Refractory Septic Shock: A Retrospective Analysis of the Clinical Features and the Pattern of Use of Norepinephrine and Adjuvant Therapies

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Introduction: Vasopressor-resistant or refractory shock (VRRS) is variably defined as the presence of hypotension, with end-organ dysfunction, requiring high-dose norepinephrine (NE). Regardless of the definition, there is an associated mortality of up to 60%, so early identification of patients evolving to this state is paramount.
Objectives: To describe the clinical characteristics and outcomes of septic patients who develop VRRS, defined as NE $\geq$ 0.3 mcg/kg/min. To assess whether the pattern of use of NE or adjuvant therapies are related to the outcome.
Methods: We retrospectively analyzed a cohort of septic patients in the Intensive Care Unit (ICU) of a University Hospital in Spain, over 2 years (2018–2019). All the patients who were admitted to the ICU with sepsis were included. Clinical features, vasopressor use and outcomes were retrieved from the electronic health record. Informed consent for data collection was waived due to the observational nature of the study. Results are described as median (P25–P75) or frequency (%). Chi^2, Mann–Whitney U and Wilcoxon test for paired data were used as appropriate.
Results: From the 191 patients who were admitted with sepsis during the study period, 146 (76%) received NE and 37 (19%) met VRRS criteria (Table 1). The use of NE differed in non VRRS *vs* VRRS patients in terms of maximum dose used in the first 24 h (0.11 [0.08–0.15] *vs* 0.51 [0.39–1], p < 0.01), hours to achieve the maximum dose (4 [1–12] *vs* 11 [3–20], p = 0.01), days of therapy (2 [2–4] *vs* 5 [2–8], p < 0.01), and mean dose per hour of treatment (0.09 [0.05–0.12] *vs* 0.30 [0.19–0.44], p < 0.01). Compared to patients who did not develop VRRS, patients with VRRS received more adjuvant therapies, including corticosteroids (3 *vs* 49%, p < 0.01), calcium (34 *vs* 60%, p < 0.01), bicarbonate (22 *vs* 65%, p < 0.01) and albumin (8 *vs* 57%, p < 0.01). Mortality in patients with VRRS who were treated corticosteroids was higher than in those who were not (72 *vs* 32%, p < 0.01), but these patients tended to be more severely ill, with an APACHE-II 33 (27–37) *vs* 24 (20–32), p = 0.08. Yet, NE dose was reduced from 0.4 (0.3–0.62) to 0.22 (0.14–0.47) in the next 24 h after administration of corticosteroids, p = 0.03.
Table 1 Features of the septic patients who received NE

	Non VRRS	VRRS	p
	(N = 109)	(N = 37)	
Age, years	72 (62–77)	67 (60–76)	0.28
Male sex, %	55	51	0.70
APACHE-II	20 (16–23)	28 (22–36)	< 0.01
SOFA score, day 1	7 (5–9)	10 (9–11)	< 0.01
Comorbidity-Polypharmacy Score	9 (5–13)	12 (9–15)	0.06
Isolation of MDR microorganism, %	15	11	0.55
Adequate empiric antimicrobial treatment, %	91	78	0.04
Arrhythmia while on vasopressors, %	22	54	< 0.01
Ischemic events while on vasopressors, %	1	22	< 0.01
Need for renal replacement therapy, %	6	51	< 0.01
Withdrawal of life support, %	14	46	< 0.01
ICU stay, days	3 (2–6)	7 (3–13)	< 0.01
Hospital stay, days	15 (8–24)	18 (9–43)	0.29
ICU mortality, %	6	51	< 0.01
Hospital mortality, %	9	62	< 0.01

Conclusion: Patients developing VRRS scored higher in severity scales and tended to be younger, with more comorbidities and less adequate empiric antimicrobial treatment. Complications and mortality were more frequent in these patients. Failure to reestablish arterial pressure within the first hours of ICU admission may help identify and timely treat patients at risk of VRRS.

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000870

Novel Biomarkers in Patients with Septic Shock

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Introduction: Novel biomarkers are gaining increased interest as diagnostic and prognostic tools in septic cardiomyopathy. Growth differentiating factor 15 (GDF15), neuregulin 1 (NRG1) and calprotectin are potential mediators that might be associated with clinical outcomes such as myocardial injury and mortality. Also, in vivo and in vitro studies show that these molecules might be promising targets for sepsis treatment [1–3].
Objectives: This study investigates the dynamic levels of plasma GDF15, NRG1 and calprotectin in patients with septic shock for seven days, or until discharge from the Intensive Care Unit (ICU). The association between biomarker levels and acute myocardial injury (AMi), defined as at least one high-sensitivity troponin T (hsTnT) value of $\geq$ 14 ng/L and an acute change of $\geq$ 20%, was studied. We also evaluated the association between biomarkers and echocardiographically defined left ventricular (LV) systolic dysfunction, vasopressor/inotropic treatment, ICU and 30-day mortality.
Methods: This observational, prospective study is part of the multicenter Sepsis in the Intensive Care Unit-2 study (NCT04695119) and included 61 patients of $\geq$ 18 years, admitted to the ICU at Linköping University Hospital, Sweden, between September 2018 and November 2021. The biomarkers were measured using enzyme-linked immunosorbent assays. Friedman's test was used to study the temporal development of biomarkers. Linear and logistic regression analyses were performed to study the relationship between biomarkers and secondary outcomes.

Results: Out of 61 patients, 48 had a valid set of echocardiography and biomarker variables. 85% suffered from AMi and 60% had LV systolic dysfunction. ICU mortality was 11%. Mortality within the first 30 days after ICU admission was 13%. Of all biomarkers, only GDF15 showed significant temporal changes with peak values on day one of ICU admission. When comparing patients with and without AMi, no statistically significant changes were found in peak, admission or maximum delta biomarker levels, but the median GDF15 values for the first days were higher among patients with AMi. ICU mortality, 30-day mortality, left ventricular dysfunction and number of days with vasopressors or inotropes were increased among patients with higher GDF15 levels, however predominantly not reaching statistical significance. Similarly, calprotectin levels were higher among those with left ventricular dysfunction, but with statistical significance only on day one of ICU admission.
Conclusion: In this preliminary study, novel biomarker levels seem to be associated with left ventricular dysfunction and poor clinical outcomes, although predominantly not reaching statistical significance. This is likely due to a small sample size but supports the conduct of a larger study to explore the value of novel biomarkers for outcomes in septic cardiomyopathy.

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Acknowledgements Funded by Linköping University-Region Östergötland ALF grants (935252).

000895

Penetration of linezolid into the pleural cavity in critically ill patients with proven or suspected gram-positive bacterial infections

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Intensive Care Medicine Experimental 2022, **10(2)**: 000895

Introduction: Linezolid (LZD) penetration into the pleural cavity (PC) have not been yet well evaluated. In this regard, only an animal study performed in rabbit empyemic fluid, and a single case clinical report recently suggested that LZD penetrates the PC (1,2). Human studies on this topic would be very important to improve treatments in this population.
Objectives: To evaluate the penetration of LZD into the PC of a critically ill patient cohort with proven or suspected gram-positive bacterial infections.
Methods: Unicentric, prospective and observational pharmacokinetic (PK) study including critically ill patients with pleural drainage and proven or suspected gram-positive bacterial infections treated with intermittent intravenous LZD 600 mg twice daily. LZD levels were measured at steady state at two timepoints (pre-dose and at the end of the 1 h infusion) in both plasma (Cminss and Cmaxss respectively) and pleural fluid (PF) (PF0h and PF1h respectively) by a validated high-performance liquid chromatography method. Demographics, comorbidities, clinical and analytical data, illness severity and LZD data were also collected. PF type were classified according to the Light's criteria. Continuous variables are presented as medians (interquartile range [IQR]) and qualitative variables as number of patients (%). Spearman coefficient was used to correlate plasma and PF data.
Results: Fourteen patients were finally included in the study, 64% female with 62 (16) years, APACHEII 15 (7) and BMI 27 (5) kg/m2. Five patients (36%) had renal failure at inclusion and only one of them was under renal therapy replacement. Most PF were classified as exudate (43%), followed by empyema (36%) and transudate (21%). LZD penetration into the PC was 2.2 (3.6) at pre-dose time and 0.4 (0.3) at the end of 1 h infusion. Pre-dose PF levels below the usual MIC in our center (2 mg/L) was showed in 39% of patients. Individual Pk data in plasma and PF are shown in image 1 (*CVVHDF). LZD plasma and PF concentrations had a high correlation at pre-dose time (Rho 0.8; $p \leq 0.001$).

Patient	PF[1]	Gender Age (years)	BMI[1] (kg/m²)	Serum creatinine (µmol/L)	eGFR[2] (CKD-EPI) (ml/min)	APACHE II score	RAPID score	LZD dose (mg/kg/day)	Plasma Cminss (mcg/mL)	PF0h (mcg/mL)	PF0h/ Plasma Cminss ratio	Plasma Cmaxss (mcg/mL)	PF1h (mcg/mL)	PF1h/plasma Cmaxss ratio
1	transudate	Male 62	26	2.28	31	20	3	16.0	28.3	31.6	1.1	38.1	45.2	1.2
2	transudate	Male 61	32.5	0.52	127	22	4	13.3	0.2	1.3	6.5	7.8	3.8	0.5
3	transudate	Female 55	27.6	0.39	133	10	1	16.0	1.1	0.6	0.5	7.3	3.5	0.5
4	exudate	Female 62	35.2	0.38	116	17	3	12.6	1.1	0.9	0.8	13.8	7.1	0.5
5	exudate	Female 67	23.4	0.32	105	19	3	28.1	1.9	8.9	4.7	23.6	9.5	0.4
6	exudate	Male 48	29.3	0.59	161	14	2	12.6	<0.5	<0.5		7.2	<0.5	
7	exudate	Male 27	24.1	1.91	58*	14	1	15.4	0.9	2.9	3.2	8.8	3.6	0.4
8	exudate	Female 51	24.2	0.97	61	14	2	17.1	0.4	2.6	6.5	6.4	4.1	0.6
9	exudate	Male 74	26.8	1.33	39	16	6	16.4	2.9	6.2	2.1	16.2	4.8	0.3
10	exudate empyema	Male 60	21.5	0.32	229	23	3	18.5	0.6	4.2	7.0	17	4.2	0.3
11	exudate empyema	Male 67		0.53	118	16	3	17.9	1.3	1.7	1.3	11.4	1.8	0.2
12	exudate empyema	Female 84	27.9	0.66	44	12	4	17.9	6.1	13.6	2.2	20	13	0.7
13	exudate empyema	Male 44	29.8	0.74	147	11	2	10.9	0.2	0.9	4.3	2.9	0.7	0.2
14	exudate empyema	Male 75	22.5	1.96	31	20	5	18.5	12.8	10.8	0.8			

Conclusion: There is a high interindividual variability in the penetration of LZD into the PC, probably related to the large differences observed in the plasma exposure. Pre-dose plasma concentrations of LZD could be used to predict PF concentrations. The findings suggest that therapeutic drug monitoring of linezolid might be helpful for adequate dosing of linezolid in critically ill patients with pleural infection (PI). At pre-dose time, LZD concentrations in PF were higher than those in plasma. However, in more than 30% of patients PF levels were below a MIC of 2 mg/L, what suggests the need to assess the possible benefits of administering higher LZD doses or extended/continuous infusion regimen in critically ill patients with PI.

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000925

Evaluation of cardiovascular performance and tissue perfusion during a vasopressor test in patients with septic shock

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Intensive Care Medicine Experimental 2022, **10(2)**: 000925

Introduction: Among resuscitative interventions in patients with septic shock, current guidelines recommend to increase mean arterial pressure (MAP) to 80–85 mmHg in previously hypertensive patients (a vasopressor test), when tissue hypoperfusion did not recover after initial resuscitation with fluids and MAP reached 65 mmHg with vasopressors, preferably with norepinephrine. Nevertheless, the impact of

increasing norepinephrine dose or adding a second vasopressor such as vasopressin could lead to stroke volume (SV) deterioration due to an increased afterload, thus leading to further impairment on tissue perfusion.

Objectives: To study the impact of a vasopressor test in the cardiovascular performance and tissue perfusion in mechanically ventilated, fluid unresponsive previously hypertensive patients with septic shock, by means of incremental titration of norepinephrine alone or norepinephrine plus vasopressin.

Methods: We evaluated previously hypertensive patients with septic shock on mechanical ventilation after initial fluid resuscitation and norepinephrine administration. MAP was increased from 65 to 85 mmHg in patients with persistent hypoperfusion despite attaining a fluid unresponsiveness status and a MAP of 65 mmHg. A comprehensive echocardiographic assessment was performed at baseline and after 1 h of reaching the new MAP target (85 mmHg). Mean systemic filling pressure (Pmsf) was calculated using the Parking method. Left end-systolic elastance (Ees) was calculated by Chen's method. Contractility and afterload variables were assessed. Peripheral perfusion was evaluated by capillary refill time (CRT), perfusion index and lactate. Statistical analysis was performed with Wilcoxon signed-rank test, a p-value < 0.05 was considered as significant.

Results: Nineteen mechanically ventilated patients with septic shock (47% female, age 72 ± 9 yrs, APACHE II 21 ± 6, SOFA at admission 10 ± 3) were included in this preliminary report.

Table 1	Baseline	Vasopressor test
Macro-hemodynamics		
SAP (mmHg)	101 [96-114]	136 [128-152]*
MAP (mmHg)	67 [64-69]	85[84-88]*
DAP (mmHg)	47 [46-53]	58 [54-65]*
NE (mcg/kg/min)	0.17 [0.10-0.35]	0.24 [0.12-0.43]*
HR (beats/min)	90 [77-105]	93 [82-101]
PPV (%)	5 [4-6]	3 [3-5]*
CVP (mmHg)	9 [7-12]	9 [6-12]
Pmsf (mmHg)	17.5 [15.20-19.5]	18.8 [16.1-20.8]
Pvr (mmHg)	7.8 [6.30-8.9]	9.1 [7.6-10.4.]*
Stroke volume (ml)	63 [50-79]	71 [53-82]*
CO ($L \cdot min^{-1}$)	5.5 [4.8-6.6]	5.7[4.8-7.1]
RVR ($mmHg \cdot min \cdot ml^{-1}$)	1.49 [1.26-1.62]	1.55 [1.36 -1.83]*
SVR ($mmHg \cdot min \cdot ml^{-1}$)	824 [723-926]	1005 [845-1323]*
Aortic elastance	1.5 [1.2-1.8]	1.8 [1.6-2.3]*
LV End-systolic-elastance	2.4 [1.4- 3.1]	2.6 [2.2-3.7] *
Ventriculoarterial coupling	0.64 [0.47-1.23]	0.67 [0.49-1.13]
Tissue perfusion		
Capillary refill time (sec)	3 [2-5]	3 [2-5]
Perfusion index	1.3 [0.5-1,9]	1.0 [0.7-2.2]
Lactate (mmol/L)	2.6 [1.8-4.8]	2.4 [1.7-4.7]
Left ventricular function		
LV EF (%)	66 [60-69]	68 [56-75]
TDI S' wave	13.1 [7.3-16.0]	16.2 [10.7-18.4]*
IVA (cm/sec^2)	392 [231-583]	469 [280-566]
MPI	0.58 [0.46-0.94]	0.55 [0.42-0.72]*

Data are shown as median [IQR 25,75]. Legend: SAP, systolic arterial pressure; MAP, mean arterial pressure; DAP, diastolic arterial pressure; NE, Norepinephrine; HR, heart rate; PPV, pulse pressure variation; CVP, central venous pressure; Pmsf, mean systemic filling pressure; Pvr, driving pressure for venous return; CO, cardiac output; RVR, resistance to venous return; SVR, systemic vascular resistance; LV, left ventricular; EF, ejection fraction; TDI, tissue Doppler imaging; IVA, isovolumetric acceleration; MPI, myocardial performance index. * equal to p<0.05.

In 13/19 (68%) patients norepinephrine was the only vasopressor used. In the remaining 6 (32%) vasopressin was added to norepinephrine as indicated. Main cardiovascular performance parameters are showed in Table 1. SV increased > 10% in 11 patients (58%), remained unchanged in 7 (37%) and decreased > 10% in one patient (5%) after reaching a MAP of 85 mmHg. The rise of SV was associated with an increase in Pmsf and venous return pressure, and was accompanied by a direct increase in left ventricular contractility besides a significant increasing in aortic elastance. In addition, ventriculo-arterial coupling was not deteriorated by the increase in afterload due to concomitant enhancement in Ees. Tissue perfusion improved in 8 (42%) patients, did not change in 7 (37%) and deteriorated in 4 (20%) patients.

Conclusion: In previously hypertensive, mechanically ventilated patients with septic shock, exhibiting persistent hypoperfusion despite reaching a fluid unresponsiveness status and a MAP of 65 mmHg, increasing MAP from 65 to 85 mmHg induced a significant increase in SV in the majority of the cases, despite of a significant increase in afterload. Tissue perfusion parameters did not deteriorate. However, CRT or lactate improved after a vasopressor test in 42% of patients.

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Acknowledgements FONDECYT Iniciación 11201220.

000948

Identification of clinical phenotypes in sepsis patients admitted to the Intensive Care

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Intensive Care Medicine Experimental 2022, **10(2)**: 000948

Introduction: The heterogeneity in sepsis impedes the development and use of specific treatments. Stratification of sepsis patients into more homogenous subgroups using unbiased clustering techniques on clinical and host response data may allow prediction of outcome (prognostic enrichment) and likelihood of beneficial treatment effects (predictive enrichment).

Objectives: To identify and characterize subgroups of patients admitted to the Intensive Care Unit (ICU) fulfilling the sepsis-3 criteria, and determine their outcomes.

Methods: This study was done as part of the Molecular Diagnosis and Risk Stratification of Sepsis (MARS) prospective observational cohort [1], in which 2498 patients fulfilled the sepsis-3 criteria upon ICU admission. Clinical variables, biomarker and transcriptomic data were collected in the first 24 h of admission. Cluster analysis to determine phenotypes was performed on 28 clinical variables, using Monte Carlo Reference-based k-means consensus clustering. Missing values were imputed. Data were normalized as appropriate. Sensitivity analysis was performed using hierarchical clustering. Host response biomarkers reflecting systemic inflammation, coagulation activation and endothelial cell function providing insight into pathophysiological mechanisms implicated in the pathogenesis of sepsis were assessed for each phenotype. Transcriptomic analysis was conducted using the limma method and Reactome database. The identified phenotypes were validated in two different ICU sepsis cohorts; (1) the Medical Information Mart for Intensive Care (MIMIC)-IV [2] and (2) the Dutch National Intensive Care Evaluation (NICE) registry.

Results: Cluster analysis revealed an optimum of 3 different phenotypes. Phenotype 1 was the least common (15%) and included patients with the lowest bicarbonate and highest lactate levels. Phenotype 2 (41%) comprised patients with the highest white blood cell count and platelet count, whereas phenotype 3 (43%) included patients with highest age and most impaired kidney function (Fig. 1). The phenotypes had a prognostic value for in-hospital mortality (Fig. 2). Sensitivity analysis using a different cluster technique also revealed 3 phenotypes with similar characteristics and distribution. Furthermore, validation of the phenotypes in different cohorts yielded similar results (Table 1).

Patients with phenotype 3 displayed the highest levels of inflammatory (e.g. IL-6, TNF-α), coagulation (e.g. D-dimer, PAI-1) and endothelial markers (e.g. ANG1/ANG2) compared to the other phenotypes. Transcriptomic analysis revealed downregulation of adaptive and innate immune genes in phenotype 3 compared to the other phenotypes.

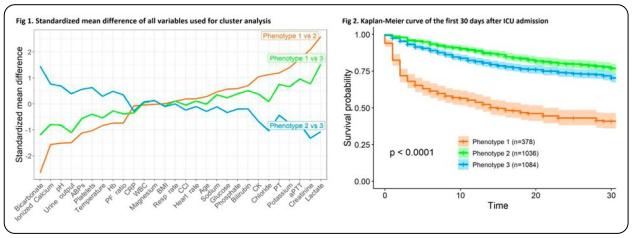

Table 1. Frequencies of phenotypes across different cohorts

	Phenotype 1	Phenotype 2	Phenotype 3
MARS	15%	41%	43%
MIMIC-IV	12%	41%	47%
NICE	12%	42%	46%

Conclusion: In this study, three novel sepsis phenotypes with potential prognostic value were identified using cluster analysis on clinical variables. Furthermore, these clusters were robust to different clustering techniques and across different cohorts.

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1. Lonneke A van Vught was supported by the Netherlands Organisation for Health Research and Development ZonMW (Nederlandse Organisatie voor Wetenschappelijk Onderzoek NWO) VENI grant 09150161910033 and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Research Grant.
2. Supported by the Center for Translational Molecular Medicine (http://www.ctmm.nl), project MARS (grant 04I-201).

000961

Effect of high dose intravenous ascorbic acid on the microcirculation during sepsis and septic shock

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Introduction: Previously published studies indicate that supplemental vitamin C attenuates systemic inflammation, vascular injury and improves microcirculation in septic animals.
Objectives: Our randomized, double-blind placebo-controlled trial aimed to investigate whether a high dose of intravenous ascorbic acid might improve microcirculatory parameters in septic patients.
Methods: Twenty-three adult septic patients were enrolled in the study within 24 h following admission to the intensive care unit. They were all resuscitated according to international sepsis management guidelines. Participants were randomly assigned to a placebo or vitamin C group in a 1:1 ratio. 50 mg/kg of ascorbic either placebo was administered intravenously every 6 h for 96 h. Direct in vivo observation of the sublingual microcirculation was performed with a Cytocam IDF imaging device before the first infusion, 30 min after it and also after 6, 12, 24, 48, 72, 96 h. Microcirculatory flow (microvascular flow index (MFI), proportion of perfused vessels (PPV)) and density (perfused vessel density (PVD) and total vessel density (TVD)) parameters were assessed using validated AVA v.3 software. Vessels were separated into large (mostly venules) and small (primarily capillaries) using a diameter cut-off value of 20 µm.
Results: There were no significant differences among baseline characteristics between the groups initially. No differences in microcirculation flow and density parameters were found between the groups at the beginning. PPV after 6 h from the beginning of the trial was significantly higher in patients receiving ascorbic acid—89.68 (82.52 – 93.29)%, compared to placebo 79.86 (73.53 – 86.40)%, p = 0.041. No significant differences in microcirculatory parameters between the groups were found during subsequent measurements.
Conclusion: High-dose parenteral ascorbic acid may increase the proportion of perfused small vessels in the early period of sepsis and septic shock.

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000965

Feasibility study of longitudinal bioelectrical impedance analysis to evaluate body water status during fluid resuscitation in a swine sepsis model

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Intensive Care Medicine Experimental 2022, **10(2)**: 000965

Introduction: Fluid resuscitation is crucial in the initial management of sepsis, yet little is known about the serial change and ultimate distribution of fluids administered into the body. In a previous clinical study, the increasing trend of extracellular water to total body water ratio (ECW/TBW) among non-survivors of sepsis during initial fluid resuscitation was identified.
Objectives: To identify the feasibility of longitudinal bioelectrical impedance analysis during the progression of sepsis and fluid treatment, a preclinical study using the porcine sepsis model was conducted.
Methods: Total 12 pigs were utilized for the study. Bipolar electrodes of bioelectrical impedance analysis (InBody M20, InBody) were attached to left extremities. To induce sepsis, the diluent of extended-spectrum beta-lactamase (ESBL)-producing Escherichia coli (*E. coli*, 5.0 * 10^9 CFU) in 1000 mL of normal saline was intravenously injected. The pigs were monitored up to either 12 h after bacterial infusion or until death. Maximal support including fluid and vasopressor was provided to maintain mean arterial pressure over 65 mmHg. Longitudinal measurement of bioelectrical impedance was performed every 10 min. Impedance at zero frequency (R0; reflects extracellular water content), impedance at infinite frequency (Rinf; reflects total body water content), and phase angle was derived and Ri, which reflect intracellular water, was calculated. The fluid input and urine output were measured by 30-min intervals and the difference was calculated as fluid balance.

Results: Among 12 subjects, 7 pigs (58.3%) expired before the end of monitoring period and the median survival time was 9.5 h. After induction of sepsis and treatment with fluid resuscitation, the trend of R0 which is inversely proportional to extracellular water decreased and Ri which is inversely proportional to intracellular water increased. Phase angle constantly decreased throughout the monitoring period and all non-survivors in the study expired at the period when the phase angle decreased by more than 10%. Compared to survivors, the ECW/TBW ratio during study period tended to increase in non-survivors (2-way RM AVOVA, group * time interaction, $p < 0.001$).
Conclusion: In a porcine sepsis model, continuous measurement of bioelectrical impedance was feasible and it may reflect the change of body water profile during the initial fluid resuscitation. Further studies should be prompted to investigate the usefulness of continuous monitoring of bod water profile in sepsis.

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000971

Mast cells activation is a key event in sepsis progression

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Introduction: The striking fact that survival rates markedly decrease with progression of sepsis to septic shock highlights the need for strategies specifically aimed to prevent the development of shock. However, targetable mechanisms that drive underlying derangements remain unknown. Septic shock is a complex vascular syndrome characterized by vasomotor disturbances, endothelial leakage, and abnormal microvascular blood flow. Because mast cells (MCs) can rapidly release potent vasoactive mediators from preformed stores, we hypothesized that they may play a critical role in disease progression to septic shock.
Methods: Animal and human studies were performed following institutional approval. Septic shock in mice was induced by iv. injection of 4 × 10E8 E. coli into C57BL/6J or MC–deficient KitW-sh mice. Shock was quantified by monitoring core temperature or invasive blood pressure. Vascular permeability was quantified by measuring tissue extravasation of Evans blue after iv injection. Microvascular perfusion parameters for vascular density, small vessel diameter and tissue oxygen saturation were obtained using photoacoustic tomography. Mast cell inhibition was achieved after intraperitoneal injection of Ketotifen 25 mg/KG 2 h before experiment. Human and murine plasma samples were analysed by ELISA.
Results: In mice, MC activation was specifically associated with a septic shock model (4 × 10E8 E. coli), but not with bacteremia without shock (1 × 10E8 E.coli). Consequently, we defined the impact of MCs in the high-dose sepsis model. Mast cell deficiency prevented both drop in core temperature (A) and in blood pressure after injection of bacteria and ensured prolonged survival in a model where WT animals succumbed to shock within 12 h. In addition, MC deficiency significantly reduced vascular leakage (B) and protected microvascular perfusion in the skin as evidenced by maintained small vessel density (C), lack of vasoconstriction of small arterioles, and largely unchanged levels of microvascular oxygen saturation. These results were reproduced when mice were pretreated with the MC inhibitor Ketotifen. Supporting the human relevance of our findings, we found significant MC activation together with corresponding changes of markers of endothelial activation (Angiopoietin 1/2) in the plasma of patients with septic shock vs. those with sepsis without shock and non-infectious emergency room patients (n = 13/group).

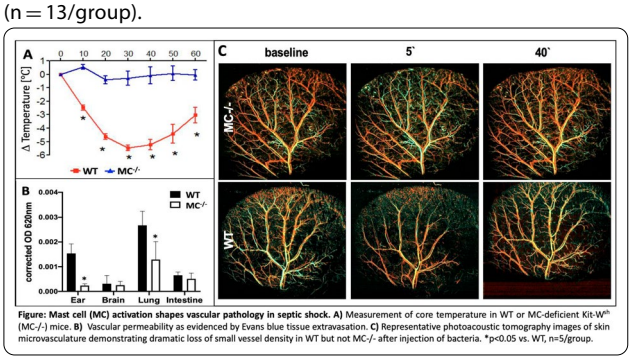

Figure: Mast cell (MC) activation shapes vascular pathology in septic shock. A) Measurement of core temperature in WT or MC-deficient Kit-W^{sh} (MC-/-) mice. **B)** Vascular permeability as evidenced by Evans blue tissue extravasation. **C)** Representative photoacoustic tomography images of skin microvasculature demonstrating dramatic loss of small vessel density in WT but not MC-/- after injection of bacteria. *p<0.05 vs. WT, n=5/group.

Conclusion: Our data identifies, for the first time, the critical role of MCs in the progression of sepsis towards septic shock and closely delineates how MCs shape the key vascular anomalies of septic shock: hypotension, vascular leakage, and microvascular perfusion abnormalities. As a consequence, prevention of wide-spread MC activation in advanced sepsis may serve as a specific therapeutic approach to prevent shock and associated tissue damage.
Acknowledgements Work was supported by the National Institute of Health grants 1R21NS117973-01 and 1R01GM144606-01 (to JK).

000978

Stroke Volume Change May Predict Renal Replacement Therapy

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Introduction: Cardiac function is known to be negatively impacted by sepsis. Monitoring Cardiac Output (CO) and Stroke volume (SV) trends over the course of treatment may provide insight into cardiac function and may be used to predict patient outcome. In the FRESH study1, we have previously shown that patients who improve CO and SV exhibit improved outcome such as decreased mortality and decreased need for ventilation. The goal of this study was to explore the relationship between the change in stroke volume and renal function in critically ill patients.
Objectives: The Starling Registry study is an observational registry study evaluating trends in CO and SV over time as related to patient outcome (NCT04648293). Patients that exhibited an overall improvement in SV (first SV measurement compared to last SV measurement) were compared to those who did not exhibit improvement.
Methods: The Starling Registry study is an observational registry study evaluating trends in CO and SV over time as related to patient outcome (NCT04648293). Patients that exhibited an overall improvement in SV (first SV measurement compared to last SV measurement) were compared to those who did not exhibit improvement.
Results: 85 critical care patients received hemodynamic monitoring during their ICU stay at one hospital. 42% were female, and the average age was 65 years. 76% of the patients had sepsis, and 20% of patients were positive for COVID. The average time between first and last SV measurement of approximately 25 h. 55% of patients improved SV between first and last measurement, and 45% of did not improve. Notably, patients who exhibited an overall improvement in SV exhibited a decrease in the need for RRT (8.5%) compared to those who did not improve (21.1%, $p = 0.09$).
Conclusion: We have previously shown that patients who show an improvement in SV in response to the resuscitation exhibited improved outcome. In this study, we were able to confirm this trend in a separate patient population. Trending cardiac output over a 1–3 day

monitoring period revealed additional usefulness in predicting patients with improved outcome. These results highlight the importance of trending hemodynamics in therapy.

Reference

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Acknowledgements The Starling Registry study is supported by Baxter Healthcare.

Systemic Inflammation & Sepsis 8

000980

Recovery from Acute Immune Failure in Septic Shock by Immune Cell Extracorporeal Therapy—ReActIF-ICE: Study update from the randomized controlled clinical trial

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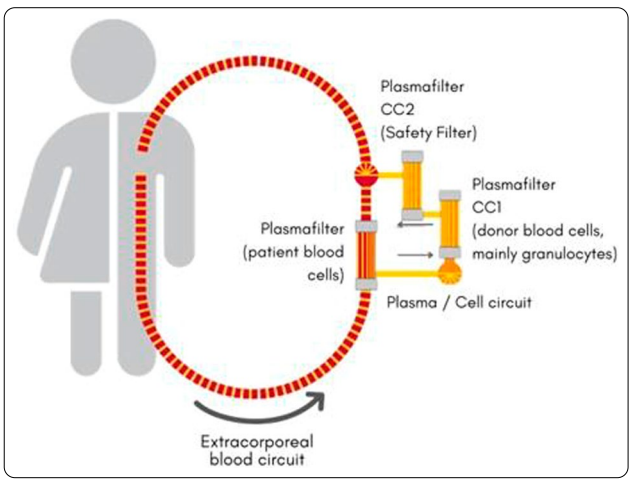
Introduction: Immune cell dysfunction is a crucial part in sepsis and in particular in septic shock. Granulocyte concentrate (GC) transfusions, as the only available immune cell concentrates, potentially induce tissue damage via local effects of neutrophils. Therefore, using donor immune cells purely extracorporeally is an attractive option. Clinical trials with standard GC in an extracorporeal plasma treatment achieved beneficial effects in 20 patients. In this clinical trial, purified GC with longer storability will be investigated in a simplified extracorporeal plasma treatment in 120 patients.



Objectives: Primary Objective.
The primary objective of this clinical trial is to investigate the safety and tolerability of the therapy.
Secondary Objective. The secondary objective is to identify any clinical benefit of the granulocyte concentrate when used in an extracorporeal immune cell treatment in a septic shock population. Furthermore, immunological parameters will be evaluated regarding the immune dysfunction of the patients after septic shock and the influence of the therapy on these parameters.
Methods: We describe a prospective, phase II, multicenter, randomized controlled parallel-group clinical trial in patients with refractory septic shock. Subjects suffering from septic shock according to Sepsis-3-Definition who additionally require norepinephrine at a dose of $\geq$ 0.2 mcg/kg/min (and/or vasopressin at any dose) for a minimum of 6 h (within the last 48 h) are randomized to receive either standard of care therapy or extracorporeal immune cell therapy on top of standard of care, in a 1:1 ratio. A total of 120 evaluable patients will be enrolled at 4 sites within Germany. Primary endpoint is safety and tolerability consisting of new onset of serious adverse events. A key secondary endpoint is showing recovery from immune dysfunction after extracorporeal immune cell treatment.
Results: This study has been submitted to independent ethics committees and responsible agencies in Q4/2021 and is expected to start in June/2022. First results of the ongoing study will be presented. Results of previous clinical trials are expected to be confirmed, in which extracorporeal treatments were well tolerated, norepinephrine doses were significantly reduced, and C-reactive protein, procalcitonin, and human leukocyte antigen DR (HLA-DR) also showed significant improvement.
Conclusion: The extracorporeal immune cell plasma perfusion therapy may on one hand provide immune support and may avoid unwanted local side effects on the other hand. Recovery from immune dysfunction is a prerequisite for avoiding secondary infections and ultimately also for recovery from sepsis.

000983

Mild induced hypothermia and coagulation and platelet function in patients with septic shock: Secondary outcome of a randomized trial

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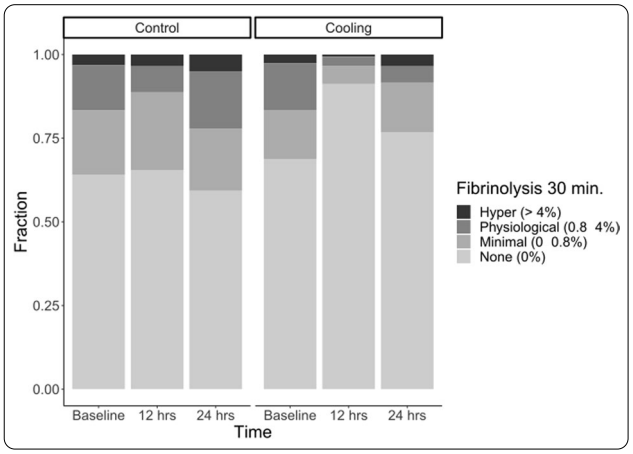
Intensive Care Medicine Experimental 2022, **10(2)**: 000983

Introduction: Septic shock is the most severe manifestation of infection, and it is characterized by hypotension, hypoperfusion, and organ dysfunction. Coagulation abnormalities and microthrombi contribute to septic shock, but the impact of body temperature regulation on coagulation in patients with sepsis is unknown.
Objectives: We tested the hypothesis that mild induced hypothermia reduces coagulation and platelet aggregation in patients with septic shock.
Methods: Secondary analysis of randomised controlled trial. Adult patients with septic shock who required mechanical ventilation from eight intensive care units in Denmark were randomly assigned to mild induced hypothermia for 24 h or routine thermal management. Viscoelastography and platelet aggregation were assessed at trial inclusion, after 12 h of thermal management, and 24 h after inclusion.
Results: A total of 326 patients were randomized to mild induced hypothermia (n = 163) or routine thermal management (n = 163). Mild induced hypothermia slightly prolonged APTT and thrombus initiation time (R time 8.0 min (IQR 6.6–11.1) vs 7.2 min (IQR 5.8–9.2); p = 0.004) and marginally inhibited thrombus propagation (angle 68 degrees (IQR 59–73) vs. 71 degrees (IQR 63–75); p = 0.014). The effect was also present after 24 h. Clot strength remained unaffected (MA 71 mm (IQR 66–76) with mild induced hypothermia vs 72 mm (65–77) with routine thermal management, p = 0.9). The proportion of patients with hyperfibrinolysis was not affected (0.7% vs. 3.3%; P = 0.19.). 0.7%) assigned to mild induced hypothermia and just 5 (3.3%, p = 0.19) to routine thermal management. We conducted an exploratory analysis of the proportion of patients with any fibrinolysis after 30 min of thromboelastographic analysis. This proportion was substantially lower after 12 h of mild induced hypothermia

compared to routine thermal management (8.8% vs. 32.7%, p < 0.001), an effect that was also found after 24 h (22.9% vs. 40.4%, P = 0.002), Fig. 1.



Conclusion: In patients with septic shock, mild induced hypothermia slightly impaired clot initiation but did not change clot strength or hyperfibrinolysis. Platelet aggregation was slightly impaired. In summary, mild induced hypothermia does not have a clinically important effect on coagulation.

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1. The Research Foundation for the Capital Region of Denmark (A6052)
2. Danish National Research Foundation [grant number DNRF126]
3. Lundbeckfonden (application no. R54-A5342)
4. Trygfonden (App. No. 7-10-1301)

000993

Effects of nonselective hemadsorption method (Cytosorb) in porcine model of progressive peritoneal sepsis—experimental study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000993

Introduction: Recently, the therapeutic approach using the extracorporeal high-capacity hemadsorption (HCHA) attracted much attention in critical care setting. Despite the lack of convincing pre-clinical evidence of benefit and potential harms, this method currently penetrates into clinical practice as adjunctive therapy of sepsis.
Objectives: To evaluate effects of nonselective hemadsorption technique (Cytosorb) in a well-established and clinically relevant porcine model of progressive peritonitis-induced sepsis.
Methods: 25 anesthetized, mechanically ventilated and instrumented pigs were randomly assigned into four groups: 1) sepsis group with standard supportive care (SEPSIS, n = 5), 2) sepsis group with concomitant HCHA and norepinephrine initiation in the moment of shock development (EARLY, n = 7), 3) sepsis group with HCHA initiation with reaching the norepinephrine dose equivalent of 0,3 μg/kg/min (LATE, n = 8), and sham operated group with HCHA (SHAM, n = 5). In all septic groups, the peritonitis was induced by intraperitoneal administration of autologous feces (2 g/kg). Before the sepsis induction, and after 6,12,18,24 and 30 h we measured systemic and microvascular (sublingual mucosal) hemodynamics, oxygen (DO_2/VO_2) kinetics, organ function (SOFA score), energy metabolism (lactate kinetics, acid base balance), systemic inflammation (cytokines) and nitrosative/oxidative stress (isoprostanes). Besides, these parameters were assessed also before the initiation of HCHA and in 6 h period until the end of experiment (irreversible organ failure resulting in death or 12 h run of HCHA).
Results: Peritoneal sepsis was associated with typical hemodynamic pattern of hyperkinetic septic shock, progressive organ dysfunction (kidney injury, pulmonary function, vasoplegia) and increasing modified SOFA score. The HCHA use did neither attenuate sepsis-induced hemodynamic alteration nor reduce the norepinephrine dose. We did not observe any measurable effect on the individual organ function (SOFA score) and on the energy metabolism (lactate and oxygen kinetics). In HCHA treated animals, the body temperature ceased to further rise and serum albumin level decreased during the procedure. In SHAM animals, the initiation of HCHA was associated with the development of vasopressor-requiring hypotension and increased SOFA score. Further analyses of sublingual microcirculation, cytokine levels, inflammation markers and nitrosative/oxidative stress are ongoing.
Conclusion: To the best of our knowledge, this experimental study is the first report to evaluate effects of Cytosorb in large animal (porcine) model of septic shock. In this study, both early and late Cytosorb treatment failed to demonstrate the evidence for beneficial effects in clinically relevant outcome measures and even suggested possible harm in healthy controls. Thus, the adoption of this technique for clinical use warrants further rigorous scientific evaluation.
Acknowledgements This project was supported by the Charles University Research Fund (project no.Q39), and project no. CZ.02.1.01/0.0/0.0/16_019/0000787 "Fighting Infectious Diseases" awarded by the MEYS CR, financed from EFRR.

001009

Exploring the relationship between capillary refill time, skin blood flow and microcirculatory reactivity during early resuscitation of patients with septic shock

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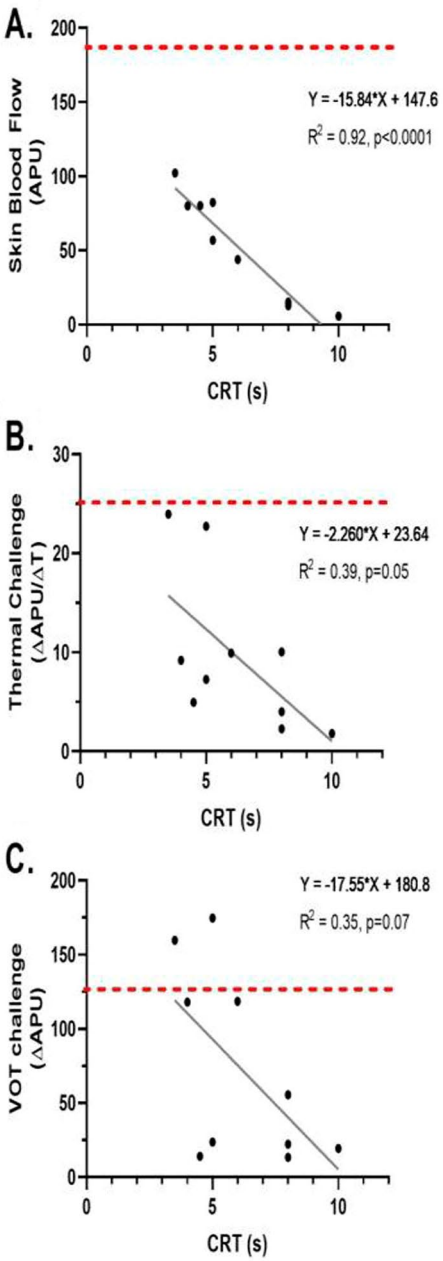
Intensive Care Medicine Experimental 2022, **10(2)**: 001009

Introduction: Multiple epidemiological and physiological studies and a large RCT have shown that an abnormal (> 3 s) capillary refill time (CRT) is associated with generalized tissue hypoperfusion and worse clinical outcomes in patients with septic shock. However, there are still doubts if CRT really reflects the skin blood flow or if a relationship exists between CRT and microvascular reactivity.
Objectives: To assess if an abnormal CRT is associated with impaired skin blood flow (SBF) and microvascular reactivity measurements in early septic shock patients.
Methods: Consecutive patients with septic shock, resuscitated with a common algorithm, were subjected to multimodal perfusion and hemodynamic monitoring protocol for 24 h. Three timepoints (0, 1, and 24 h) were registered. Multimodal assessment included: hemodynamic variables, cardiac output, capillary refill time, arterial lactate, temperature, vasoactive and fluid administration. Skin blood flow was measured in the index finger by the laser doppler technique (PeriFlux System 5000; Perimed, Jarfalla, Sweden). We performed a baseline SBF measurement (APU: arbitrary perfusion unit) and two microvascular reactivity tests: one with thermal challenge at 44 °C (Delta APU/maximum finger temperature – baseline temperature) and other with a vascular occlusion test (VOT challenge: APU max—baseline). 10 healthy volunteers were also analyzed to obtain Reference values. Data is presented as median [interquartile range], and Mann–Whitney and linear regressions were used when appropriate. A p-value < 0.1 was considered as significant.

Fig 1. Correlation between abnormal capillary refill time, skin blood flow and microvascular reactivity



Intermittent red lines represent median values from healthy volunteers

Results: 10 septic shock patients were included in the study. 50% were female, median age was 73[68–77] years, and 100% were connected to mechanical ventilation. Median APACHE II score was 16 [14–22] and median baseline SOFA 11 [9–12]. Baseline CRT was 3.3 [2.6–5] seconds and lactate was 3.5 [2.6–4.7] mmol/L. Median norepinephrine dose was 0.21 [0.14–0.3] mcg/kg/min, and vasopressin was used as a second vasoactive drug in 50% of the cohort. Of 30 measurements available, 10 presented abnormal CRT values. In pooled data analysis, abnormal CRT presented a significantly lower APU when compared to normal CRT (44 [13.3–80.3] vs 193.2 [99.4–285], p = 0.0001). When analyzing the subgroup of abnormal CRT measurements, CRT strongly correlated with SBF (R2 0.92, p < 0.0001) (Fig. 1, panel A). An abnormal CRT also correlated with microvascular reactivity with both techniques tested (Fig. 1, panel B and C).

Conclusion: An abnormal CRT is strongly associated with an impaired objective measurement of SBF and microvascular reactivity.

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Acknowledgements

1. FONDECYT Regular Grant 1200246, ANID
2 . Concurso Becario Residente DIDEMUC No. 201015009, PUC

001026

Reproducibility of sepsis clinical phenotypes among critically ill patients in 3 observational cohorts

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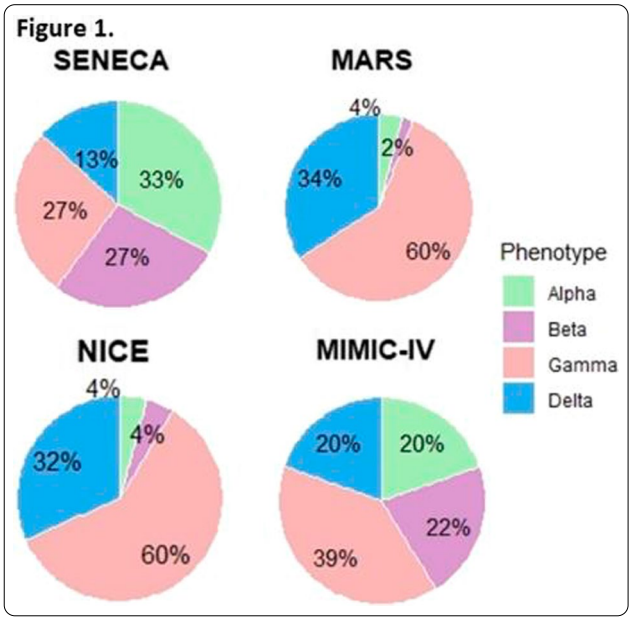
Intensive Care Medicine Experimental 2022, **10(2)**: 001026

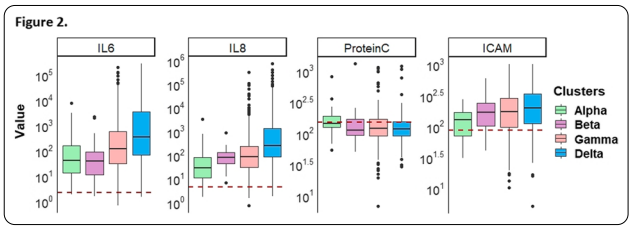
Introduction: The heterogeneity in sepsis may be responsible for the lack of sepsis treatments. Recent work indicated that patients in the emergency department (ED) with sepsis can classified into four groups (named α, β, γ and δ) based on machine learning of clinical data in the electronic health record (1). It is less understood if these clinical sepsis phenotypes are reproducible outside the ED in a population admitted to the Intensive care unit (ICU).

Objectives: To determine phenotypic clinical characteristics, outcomes and host response aberrations of clinical sepsis phenotypes in multiple large observational ICU cohorts.

Methods: Sepsis clinical phenotypes were identified in three observation ICU cohorts: (I) The Molecular diAgnosis and Risk stratification of Sepsis (MARS) including patients fulfilling the Sepsis-3 criteria upon ICU admission (N = 2499), (II) the Dutch National Intensive Care Evaluation registry (NICE) (N = 44,584) and (III) MIMIC-IV (2); the Medical Information Mart for Intensive Care including (N = 18,661). All clinical variables were mapped to algorithms for phenotype derivation from the Sepsis Endotyping in Emergency Care (SENECA) study. Missing values were imputed using Multiple Imputation by Chained equations. In each dataset the clinical phenotypes were found using the Euclidean distance from each patient to the centroid of each of the four phenotypes. Clinical characteristics, outcome and host response biomarkers reflecting systemic inflammation, coagulation activation, and endothelial cell function were analyzed to understand pathophysiological mechanisms implicated in each phenotype.



Results: The frequency distribution of the clinical phenotypes in MARS was different from SENECA with 4% for α in MARS vs 33% in SENECA, 2% for β in MARS vs 27%, 60% for γ in MARS vs 27% and 34% for δ in MARS vs 13% (Fig. 1). However, clinical characteristics of each group in MARS were comparable to the SENECA study. Biomarkers on ICU admission from MARS showed increased inflammation in γ and δ, more abnormal coagulation and endothelial cell activation in γ and δ (Fig. 2). As in SENECA, patients in δ showed highest mortality rates (41% versus 23% in α, 26% in β and 19% in γ, $p < 0.001$). In the NICE cohort, the distribution of the clinical phenotypes was comparable to MARS with 4% for α, 4% for β, 60% for γ and 32% for δ. In MIMIC-IV cohort, the distribution of the clinical phenotypes was more comparable to SENECA with 20% for α, 22% for β, 39% for γ and 20% for δ.



Conclusion: Clinical sepsis phenotypes are reproducible in the intensive care unit, yet the frequency distribution varied widely between US and European cohorts. The clinical characteristics, outcomes, and host response biomarkers were comparable to patterns in the SENECA study.

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Acknowledgements

1. Lonneke A van Vught was supported by the Netherlands Organisation for Health Research and Development ZonMW (Nederlandse Organisatie voor Wetenschappelijk Onderzoek NWO) VENI grant 09150161910033 and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Research Grant.
2. Supported by the Center for Translational Molecular Medicine (http://www.ctmm.nl), project MARS (grant 04I-201).

001044

Metabolic measurements using indirect calorimetry: predictors in survival of the patients with septic shock?—A machine learning perspective

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Intensive Care Medicine Experimental 2022, **10(2)**: 001044

Introduction: Sepsis and septic shock still remain a major worldwide health threat. Despite the current tendency to focus on long term mortality in septic shock, short-term mortality may be a more appropriate outcome, since early management is decisive in septic shock.
Objectives: Based on metabolic measurements provided by indirect calorimetry, we aimed to develop an artificial intelligence algorithm that can predict 28- day survival in septic shock.
Methods: In this prospective observational study, we have continuously performed metabolic measurements through indirect calorimetry during the early phase of septic shock in 20 patients admitted to our ICU. In the first five days of evolution we have measured the resting energy expenditure (MREE1->5) and the volume of oxygen consumption (VO_2), quantified muscle waste through ultrasound measurements of the cvadriceps (D1->5). Demographic and clinical data collected included age, gender, body mass index, estimation of energy requirements (ESPEN guidelines), arterial lactate, procalcitonine, APACHE II score and SOFA score calculated based on data available on the day of ICU admission. Survival at 28 days was assessed.
Results: The collected data were processed using a machine learning algorithm. Using the principal component analysis (PCA), two major components (eigenvectors with highest variance) which influence short term-mortality, were identified: PC1 = 50,24% and PC2 = 15.54%. The eigenvalues related to the eigenvectors graphical represented were 7.633 for PC1 and 2.641 for PC2. The two major components were constructed from data with different loadings, as it follows: PC1: MREE3 (loading = − 0.953), MREE4 (loading = − 0.944), MREE5(loading = − 0.924), MREE2(loading = − 0.880), cvadriceps D1(loading = − 0.824), VO_2 (loading = − 0.740); PC2: age (loading = − 0.659), APACHE(loading = − 0.454) and SOFA (loading = − 0.445). The decision tree approach identified that VO2 and REE measured during the first day in ICU after admission, may predict prognosis in patients with septic shock. ROC curve analysis identified that the following cut off-values: $VO_2 < 252$ mL/min and a measured REE in the first day > 1828 kcal were associated with 100 percent mortality at 28 days, (AUC = 1, $p < 0.001$).
Conclusion: This algorithm identified with 100 percent accuracy survival at 28 days in patients with septic shock using metabolic measurements through indirect calorimetry. Further validation studies are necessary to confirm the universality of our method in the septic shock population.

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Acknowledgements This research received no external funding. The authors declare no conflict of interest.

001052

Association between the site of infection and surgical ICU mortality in patients with sepsis and septic shock- five years retrospective review from a tertiary care hospital of a low-middle-income country

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Introduction: Sepsis is a medical emergency and remains one of the major causes of morbidity and mortality. In the resource-depleted parts of the world, the mortality rates of up to 80% has been reported. Lower middle-income countries (LMIC) face particular health care issues. In 2012–2013, a two-year retrospective observational study was conducted in our hospital which showed a high incidence of sepsis (43.23%) with a mortality rate of 51.1% in surgical ICU. The literature suggests that the anatomic source of infection may influence the progression and clinical outcome of septic shock. Abe T et al. found the highest mortality in the patients with CNS infections i-e 47% whereas, other studies suggested disseminated (84%) and abdominal infection (39–77%) as a major cause of mortality.
Objectives: To find the association between the site of infection and surgical ICU mortality in patients with sepsis/septic shock.
Methods: Duration of Study January 2016- December 2020.
Design Retrospective observational study.
Sample Size: All admitted patients due to sepsis / septic shock will be included during the study mentioned period.

Inclusion criteria
- Age > 18 years.
- Admission due to sepsis/ septic shock.

Exclusion criteria
- In-complete Record.
- DNR on ICU admission.
- Death/ Discharge from ICU within 24 h.

The medical record numbers of all patients fulfilling the inclusion criteria were obtained from the hospital database and then file records will be retrieved and reviewed. Data was collected on a specially designed form for the study. Patient demographic variables including age, BMI, gender, history of addiction, and comorbid conditions will be collected. In addition, infection-related data including the site of infection and the causative organism was identified on admission and during ICU stay. Data on Sepsis-related outcomes, including mechanical ventilation, renal replacement therapy, acute respiratory distress syndrome, vasopressor/ inotropic support, and length of ICU stay were collected.
Results: A record of 246 patients was reviewed. Among which 79 patients were excluded due to missing data, unavailability of records, or mortality due to noninfectious causes. Regarding mode of admission, the emergency department accounted for 70% (117 patients) of admissions followed by ward (30%). A majority (64%) of the patients were admitted under general surgery, followed by neurosurgery and vascular. Complicated Abdominal infection was identified as the most common source of sepsis and in the abdominal culture, E. Coli was most frequent. The most common multi-drug resistant organism identified was MDR- Acinetobacter. The abdominal infection was also associated with a higher APACHE score, more requirement for vasopressor, renal replacement therapy, mechanical ventilation days, and longer ICU stay.
Conclusion: In our population mortality due to septic shock was identified mostly in patients with abdominal infection. One reason can be the inability to effectively control the source. We conclude these patients have more hemodynamic variability requiring more vasopressor and organ support.

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001057

Albumin leakage during early sepsis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000013

Introduction: Sepsis is a global health problem with substantial suffering. Early recognition and initiation of treatment is critical. A cornerstone in the treatment of sepsis is fluid resuscitation, although the evidence behind this treatment is not complete. Hypoalbuminemia has been linked to higher mortality, but the mechanisms behind this are still unknown. The loss of albumin is at least partly due to leakage of albumin from the circulation to the interstitium but the etiology and the relation to outcome are not well known.
Objectives: To estimate the leakage of albumin from the circulation into the interstitium during early sepsis and relate this to clinical outcome.
Methods: This was a retrospective, observational analyses of a study including patients with suspected sepsis arriving to the emergency room (ER) at Karolinska University Hospital Huddinge in 2017 and 2018 (n = 590). All patients with at least two albumin measurements were included for this analysis. Data from medical records were retrieved for a 7-day period after presentation at the ER. Albumin leakage was estimated as Cumulative Albumin Shift (CAS) which in short is the mass balance of albumin calculated from the proportional changes in albumin and hemoglobin concentrations over time and adjusting for all albumin infusions, albumin losses in drains and bleeding ect [1]. CAS then represents the sum effect of leakage from the circulation, assumed to the interstitium, and lymphatic return. Patients were dichotomized based on a deterioration (bad outcome) or an improvement (good outcome) after arriving to the ER. Deterioration was defined as patients transferred to the high dependency unit (HDU) or intensive care unit (ICU) or death within 28 days. The groups were compared using t-test or Mann–Whitney U-test depending on the normality of the data. Data is represented as mean ± SD or median and interquartile ranges.
Results: 256 patients with a good outcome and 162 with a bad outcome were included in this analysis. Plasma albumin levels were low in relation to Reference values in both groups but significantly lower in the group with bad outcome vs the group with good outcome (27.3 ± 6.5 g/L vs 29.8 ± 5.6 g/L, P < 0.0001). CAS after approximately 2 days was 0.1 g (− 5.3 to 8.5) in the good outcome group vs 2.5 g (− 4.6 to 10.6) in the bad outcome group (P = 0.253). After approximately 5 days CAS was 1.4 g (− 6.2 to 8.3) in the good outcome group vs 4.1 g (− 5.7 to 14.9) in the bad outcome group (P = 0.02).
Conclusion: Patients with suspected sepsis that arrive to the emergency room have low albumin levels and a statistically significant leakage of albumin from the circulation. On a group level, there is a small albumin leakage in sepsis but with a large heterogeneity between individual patients. Initially there is no difference in the amount of

albumin leakage between the patients that recover and the ones that deteriorate (transfer to HDU, ICU or death within 28 days), but later on the patient that deteriorate have a significantly higher albumin leakage.

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001080

Cardiovascular response to dobutamine and norepinephrine after infusion of cholesterol formulations in septic rats

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Intensive Care Medicine Experimental 2022, **10(2)**: 001080

Introduction: Cardiomyopathy, loss of vascular tone and hyporesponsivity to catecholamines are hallmarks of sepsis. Hypocholesterolaemia is another feature of sepsis with magnitude related to the severity and worse outcomes. We previously found in our septic rat model that hypocholesterolaemia is accompanied by reduced cholesterol levels in the cardiomyocyte cell membrane (unpublished data). Here we present an analysis of cardiovascular responses to dobutamine and norepinephrine in septic rats after cholesterol infusion.
Objectives: To assess the haemodynamic response to catecholamines in septic rats after cholesterol treatment.
Methods: Awake, instrumented male Wistar rats (300 ± 50 g) received an i.p. injection of faecal slurry. i.v. fluid resuscitation commenced after two hours. Control animals were treated identically, except they did not receive slurry. Six hours after sepsis induction, baseline haemodynamic measures were performed (invasive BP, echocardiography). Septic animals were randomly stratified into placebo or cholesterol-treated groups (6–10 per group). The cholesterol-treated animals received a 15-h i.v. Infusion of either cholesterol-loaded liposomes or bovine HDL-cholesterol. At 21 h, under isoflurane anaesthesia, the response to catecholamines was tested by consecutively administering 10-min infusions of dobutamine (10 mcg/kg/min) and norepinephrine (0.5 mcg/kg/min for 10 min) with a 30-min washout period in between. Repeated measures ANOVA was performed with post-hoc Tukey's test corrected for multiple comparisons.
Results: Baseline mean BP in septic controls at 21 h' post-sepsis induction was significantly lower ($p < 0.05$) compared to both sham rats and septic animals treated with either cholesterol preparation (Table 1). With dobutamine, no effect was seen in stroke volume in septic controls, whereas cholesterol-treated animals showed significant increases ($p < 0.05$).
Table 1 Response to Dobutamine

	Sham		Sepsis		Sepsis + HDL-C		Sepsis + Liposome-C	
	Pre-Dob	Dob	Pre-Dob	Dob	Pre-Dob	Dob	Pre-Dob	Dob
SV (ml)	0.41 (0.05)	0.5 (0.04)	0.42 (0.08)	0.44 (0.09)	0.36 (0.03)	0.48 (0.05) †	0.39 (0.07)	0.46 (0.08)
HR (bpm)	442 (58)	505 (38)	470 (29) **	521 (27)	488 (30) **	516 (20)	487 (18) **	529 (18)
CO (ml/min)	183 (41)	247 (36) ††	200 (46)	226 (50)	178 (25)	248 (32)	201 (49)	253 (46)
Mean BP (mmHg)	107 (15)	110 (10)	90 (11) *	84 (9)	107 (7)	94 (8)	105 (11)	97 (13)

Norepinephrine treatment significantly increased BP in sham rats but had no pressor effect in septic groups.
Table 2 Response to Norepinephrine

	Sham		Sepsis		Sepsis + HDL-C		Sepsis + Liposome-C	
	Pre-Nor	Nor	Pre-Nor	Nor	Pre-Nor	Nor	Pre-Nor	Nor
SV (ml)	0.43 (0.09)	0.47 (0.07)	0.44 (0.11)	0.46 (0.12)	0.46 (0.06)	0.5 (0.08)	0.45 (0.12)	0.5 (0.12)
HR (beat/min)	447 (51)	476 (32)	485 (26)	505 (14)	471 (25)	481 (34)	486 (11)	503 (12)
CO (ml/min)	190 (41)	220 (41)	212 (60)	231 (61)	219 (35)	240 (48)	212 (52)	250 (62)
MBP (mmHg)	108 (13)	127 (8) ††	86 (9) **	96 (9)	101 (11)	106	96 (5)	95 (7)

Conclusion: A 15-h cholesterol infusion to septic rats augmented both blood pressure and the inotropic effect of dobutamine over untreated septic animals, but no difference was seen in noradrenaline vasopressor responsiveness. The usefulness of cholesterol to treat sepsis needs to be investigated in further preclinical and clinical studies.
Acknowledgements This work was supported by an ESICM Senior Investigator Award.

001099

Rapid Multiplex PCR for the guidance of probabilistic antimicrobial therapy in critically ill patients with hospital-acquired pneumonia: a multicenter, before-after study

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Intensive Care Medicine Experimental 2022, **10(2)**: 001099

Introduction: Hospital-acquired pneumonia (HAP) is the major cause of nosocomial infection and antibiotic consumption in intensive care units (ICU) [Vincent 2009, Hessels 2020]. The incidence of resistant germs is increasing, significantly impacting morbi-mortality [EU-VAP 2013, Bassetti 2017]. Bacterial identification and determination of antimicrobial susceptibility last for up to 72 to 96 h. It is thus necessary to initiate optimal probabilistic antimicrobial therapy to reduce the risk of failure and limit unnecessary broad-spectrum therapy. In a previous study evaluating a Rapid Multiplex PCR diagnosis that enables pathogen identification within 4 h [Crémet 2020, Guillotin 2020] we have validated the accuracy of this rapid test in comparison with standard cultures. Thus, we hypothesized that rapid pathogen identification to guide antimicrobial therapy could decrease morbidity and mortality associated with HAP.
Objectives: We aimed to evaluate the efficacy of Rapid Multiplex PCR identification for probabilistic antimicrobial therapy guidance for the treatment of HAP in ventilated critically ill patients.
Methods: We conducted a two-centers, before-after study between August 2018 and November 2021. This study was approved by an ethic committee (CERAR IRB 00010254-2021-106). Patients and next-of-kin were informed of the data collection and could express their opposition to the data collection. Adult critically ill patients requiring invasive mechanical ventilation were included if they had HAP. Non-inclusion criteria were immunosuppression, no bacteriological sampling, and civil guardianship. In the "baseline" period (2018–2020), treatment followed 2017 European guidelines for the treatment of HAP. In the «

intervention» phase (2020–2021), empiric antimicrobial therapy was chosen according to identification by rapid Multiplex PCR (BioFireFilmArray Pneumonia plus Panel (bioMérieux)) in case of risk factors of resistance and or acute respiratory distress syndrome, or on European guidelines in patients with no risk factors. After bacterial identificationby standard culture, retrocession to the narrowest spectrum therapy for seven days was recommendedin the two periods. The primary endpoint was a composite endpoint made of clinical cure between days 7 and 10, invasive mechanical ventilation free days at day 28, and death at day 28. The primary outcome was compared between the two periods with a DOOR/RADAR strategy, according to the COMBACT-NET Consortium[Timsit, 2017].

Results: We included 220 patients in the intervention phase and 223 in the baseline phase. Rapid Multiplex PCR was performed in 85 (38.6%) patients in the intervention period. Patient outcomes are shown in Table 1 (preliminary data analysis). RADAR/DOOR analysis is in progress at the time of abstract submission. The number of broad-spectrum antibiotics free-days on day 28 was 21 (8–16) with the intervention vs. 22 (12–28) during the baseline (p = 0.03).

Table 1 Patient's primary outcome on day 28 of the diagnosis of pneumonia

	Intervention	Baseline	p-value
No. of patients (n =)	220	223	
Clinical cure* between D7-D10, *yes, N (%)*	136 (61.8%)	148 (66.7%)	0.35
Death at D28, *N (%)*	43 (19.6%)	38 (17.0%)	0.45
Invasive mechanical ventilation free days at D28, median [IQR]	9.0 [0.0;20.0]	10.0 [0.0;19.0]	0.94

*Clinical cure is defined as the regression of the symptoms leading to the diagnosis and the resolution or lack of progression of radiological signs.

Conclusion: Guidance of probabilistic antimicrobial therapy for HAP with Rapid Multiplex PCR was not associated with enhanced outcomes in critically ill patients at risk of resistant pathogens.

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Systemic Inflammation & Sepsis 9

001117

Difference in immune response to ex vivo Gram positive and negative stimulation of peripheral blood mononuclear cells in healthy volunteers

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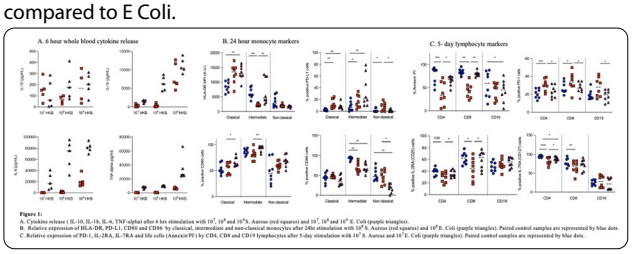
Intensive Care Medicine Experimental 2022, **10(2)**: 001117

Introduction: The dysregulated host response to infection occurring in sepsis is associated with short and long-term mortality [1]. Multiple factors influence this response, including host immunity, treatment and pathogen related factors. Clinical studies have highlighted important differences in the immune responses of patients with Gram positive (G +) and Gram negative (G −) sepsis [2]. Differences in immune responses to Gram positive and negative organisms may highlight specific patient cohorts most likely to benefit from immunotherapy in sepsis [3].

Objectives: Our objective was to evaluate differences in immunological responses to Gram + (*S. Aureus*) and Gram – (*E. coli*) heat killed bacteria (HKB) using healthy volunteer cells ex vivo.

Methods: Peripheral blood mononuclear cell (PBMC) samples of 8 volunteers were stimulated with heat-killed *S. Aureus* or *E. Coli* at a concentration of 10^8 and 10^7 per ml respectively for 24 h (monocytes) or 5 days (lymphocytes). Monocyte function was assessed using flow cytometry panels including antigen presentation and cell signalling (HLA-DR, CD80, CD86, PD-L1), cell death (annexin and live-dead stain, PD-1), and intracellular cytokines (IL-1b, IL-6, IL-10, IFN-y and TNF-a). Lymphocyte function was evaluated using flow cytometry panels including intracellular cytokines (IL-2, IL-6, IL-10, IFN-y and TNF-a), cell death (annexin and live-dead stain) and proliferation markers (IL-2RA, IL-7RA).

Results: Cytokine release (IL-1b, TNF-a, and IL-6) were higher with 10^7 *E. Coli* compared to 10^8 *S. Aureus* (Fig. 1). In contrast, *S. Aureus* was associated with lower intermediate monocyte HLA-DR, and lower co-stimulatory CD-80 in all monocyte subsets. *S. Aureus* bacteria was also associated with increased PD-1 (CD4 and CD8), lower cell viability (CD4 and CD8), lower IL-2RA (CD4 and CD8), and lower IL-7RA (CD4) compared to E Coli.



Conclusion: We found that E. Coli stimulation resulted in greater early cytokine release (at 6 h), and although S Aureuswas associated with lower levelsmore features consistent with late-onset (5 days) sepsis-induced immune suppression of immune suppression. (monocyte HLA-DR and lymphocyte PD-1, IL-2RA, and IL7RA).

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Acknowledgements ESICM Next Start Up (2018).

001123

Downregulation of CD59 complement regulatory protein expression in critically ill COVID-19 patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 001123

Introduction: Complement activation has been verified in COVID-19 and is considered to contribute to disease progression and possibly critical disease (1). Complement regulatory proteins (CRPs) decay accelerating factor (DAF, CD55), membrane cofactor protein (MCP CD46) and CD59 act in order to prevent complement activation and MAC formation (2). CRP defective expression might sustain complement hyperactivation leading to increased MAC formation and promotion of coagulation and thrombosis. The role of CRPs has not been investigated before in COVID-19 patients.
Objectives: To determine CRPs expression profiles in COVID-19 patients.
Methods: 52 patients were recruited; 31 with severe and 21 with critical disease. Healthy volunteers were included as healthy controls (n = 10). Whole blood samples were obtained on admission and stored at – 80 °C for RNA extraction or analysed directly for protein expression. Serum samples were isolated on admission. RNA extractions were performed from whole blood samples followed by reverse transcription and Real-time PCR amplification for CD55, CD46 and CD59 expression levels.
Results: Mean age was 60 years and 66 years for severely and critically ill COVID-19 patients. A significant increase in C3a and C5b-9 was observed in critically ill patients compared to patients with severe disease ($p < 0.001$ and $p < 0.0001$ respectively) and healthy controls ($p < 0.05$ and $p < 0.0001$ respectively). CD55 mRNA levels were significantly increased in patients with critical COVID-19 compared to patients with severe COVID-19 ($p < 0.01$) and healthy controls ($p < 0.001$). This was coupled by an increase in CD46 mRNA levels in both severely and critically ill COVID-19 patients, albeit non-significant. A reduction in CD59 mRNA levels was observed in critically ill COVID-19 ($p < 0.0001$) patients following an initial increase in patients with severe ($p < 0.001$) disease. Receiver operating characteristic curves for prediction of intensive care need, revealed an AUC of 0.753 (95% 0.617 -0.888, $p = 0.002$), 0.828 (95% 0.7152 to 0.9407, $p < 0.0001$) for CD55 and CD59 respectively while analysis was non-significant for CD46 mRNA levels.
Conclusion: The drop in CD59 expression levels in critically ill patients indicates a dysregulated expression pattern of CRPs in critically ill COVID-19 patients possibly affecting the immune response and contributing to a pro-coagulant and pro-thombotic profile in these patients.

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001183

Right ventricular systolic dysfunction is common and associated with myocardial injury in patients with septic shock in the ICU: an observational cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**: 001183

Introduction: The incidence of sepsis is increasing and has an in-hospital mortality of approximately 10%, for patients with septic shock > 40% (1, 2). Septic cardiomyopathy (SCM), including right ventricular systolic dysfunction (RVSD), may be present in 20–83% of septic patients (3). Echocardiography is frequently used in hemodynamically unstable patients to evaluate cardiac function. However, the optimal parameter to measure RVSD is not well established. In addition to the traditionally used indices of RV systolic function, the relatively new variable right ventricular free wall longitudinal strain has been proposed as a sensitive marker for myocardial dysfunction (4, 5).
Objectives: To investigate the frequency of RVSD, assessed by echocardiography, in a Swedish septic shock population in the ICU. A secondary aim is to assess echocardiographic parameters of RV systolic function and their association with myocardial injury (defined as hsTnT ≥ 45 ng/L), organ failure and 30-day mortality.
Methods: Three data repositories with 133 prospectively included patients admitted to the ICU with septic shock were screened. 53 patients were excluded due to missing echocardiograms or inadequate image quality. The remaining 80 were analysed regarding RVSD, defined as Tricuspid Annular Plane Systolic Excursion (TAPSE) < 17 mm, RV:LV End Diastolic Area (EDA) ratio > 0.6, tricuspid S' by color tissue Doppler < 9.5 cm/s, Fractional Area Change (FAC) < 35% or Free Wall Strain (FWS) > -20%. The association of each parameter with myocardial injury, organ support free days (OSFD) and 30-day mortality was assessed using logistic and linear regression analysis.
Results: The incidence of RVSD was 74%. Myocardial injury was associated with FWS (OR 0.90, $p = 0.023$), TAPSE (OR 0.89, $p = 0.002$) and FAC (OR 0.96, $p = 0.045$). No parameter was significantly associated with OSFD or 30-day mortality.
Conclusion: In this cohort, RVSD was common in patients with septic shock admitted to the ICU. FWS, TAPSE and FAC was associated with myocardial injury, but not with OSFD or 30-day mortality.

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Acknowledgements This study was partly funded by grants from the Region Östergötland ALF grants and Linköping University (SC-2019-00155-12, LIO-935252, and LIO-900161).

001194

CLinical Efficacy of hemoperfusion with a Cytokine Adsorber in Norepinephrine-Resistant SEptic Shock (CLEANSE): A Preliminary report of a randomized controlled trialry

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Intensive Care Medicine Experimental 2022, **10(2)**: 001194

Introduction: Due to the pivotal role of inflammatory cytokines in sepsis, hemoperfusion with cytokine adsorber may lead to better outcomes. Although previous studies showed inconclusive results, proper patient selection and timing of hemoperfusion may lead to improved survival.
Objectives: To examine whether patients with septic shock requiring high-dose vasopressors undergoing add-on hemoperfusion with cytokine adsorber have better clinical outcomes than those treated with standard treatment alone.
Methods: This is a multi-center, randomized controlled study in 2 tertiary care centers. Patients with septic shock receiving norepinephrine of 0.2 mcg/kg/min or higher are randomized to receive either standard treatment combined with 3-h sessions of hemoperfusion with cytokine adsorber for two consecutive days (HP group) or standard treatment alone (ST group). The primary outcome is 28-d mortality. Secondary outcomes include hospital and ICU mortality, shock reversal, vasoactive-inotropic score (VIS), organ support-free days, interleukin-6 levels, as well as safety data.
Results: For the first interim analysis, 40 patients with age of 65.8 ± 13.0 years; and APACHE II score of 26.2 ± 6.44 were included. They were assigned to HP group (n = 19) or ST group (n = 21). Baseline characteristics were similar including median VIS of 32 vs 31 ($p = 0.89$) and median lactate of 4.6 vs 5.2 mmol/L ($p = 0.56$), in HP and ST groups, respectively. At 28 days, 8 (42.1%) in the HP group vs 13 (61.9%) in the ST group died (HR 0.53; 95% CI, 0.22–1.28; $p = 0.16$). At 6 h, 68.4% vs 57.1% achieved shock reversal (OR 1.63; 95%CI, 0.44–5.95; $p = 0.68$). There was no significant difference in ICU and hospital mortality, VIS, organ support-free days, and interleukin-6 levels. Adverse events were comparable, including dialysis catheter bleeding (5.3% in HP vs 0.0% in ST; $p = 0.48$) and dialysis catheter-related infection (15.8% in HP vs 9.5% ST; $p = 0.65$).
Conclusion: From this interim analysis, hemoperfusion in norepinephrine-resistant septic shock patients resulted in a trend towards lower 28-day mortality without increasing major complications.
Acknowledgements Grant funding is sponsored by the Faculty of Medicine Siriraj Hospital, Mahidol University.

001226

Peripheral microcirculatory alterations are associated with ICU-mortality in COVID-19 patients with ARDS. Preliminary results of the HEMOCOVID-19 multicenter study

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Introduction: We previously demonstrated that COVID-19 patients show altered peripheral microcirculation, measured by means of non-invasive near-infrared spectroscopy (NIRS) on skeletal muscle that are associated with the severity of ARDS [1].
Objectives: To evaluate the relationship between ICU-mortality and early systemic microcirculatory alterations of severe COVID-19 patients admitted to intensive care units (ICU).
Methods: Prospective observational study carried out in 10 intensive care units of Spain, Mexico, Brazil, Italy and USA (ClinicalTrials.gov NCT04689477). Severe COVID-19 patients admitted to the ICU with clinical diagnosis of ARDS were included. Respiratory, hemodynamic, and microcirculatory parameters were simultaneously evaluated within the first week of ICU admission. Local tissue oxygen saturation (StO_2), and local hemoglobin content (THC) were measured on the forearm (*brachioradialis* muscle) by means of NIRS (PortaMon, Artinis). A vascular occlusion test (VOT), consisting in a three-minute induced ischemia, was performed to obtain dynamic StO_2 parameters: deoxygenation rate (DeO_2), reoxygenation rate (ReO_2), and hyperemic response (AUCH). Patients were followed-up until ICU-discharge or death.
Results: Eighty-six COVID-19 patients were studied. Mean age was 57 ± 12, 67% male. Respiratory support at inclusion: 70% invasive mechanical ventilation (MV), and 28% high-flow nasal cannula (HFNC). ICU-mortality was 16% (14 patients). Non-survivors were older, had lower BMI, and lower PF ratio. Non-survivors showed impaired microcirculatory parameters, as compared to survivors (Table).
Table. Main characteristics of the studied COVID-19 critically ill patients at inclusion according to ICU-mortality. *$p < 0.05$.

	Survivors	Non-survivors
Age (years)	57 ± 13	65 ± 10*
Gender (male) (%)	75	57
BMI	30 ± 5	27 ± 5*
Days from hospital admission	6 ± 1	3 ± 1
Days from ICU admission	3 ± 1	3 ± 1
Pre-existing comorbidities (%)	36	43
· Hypertension	22	23
· Diabetes Mellitus	25	14
· Smoker		
MV at inclusion (%)	63	79
PF ratio (%) (n = 57)	195 ± 77	161 ± 47*
SF ratio (%)	203 ± 57	194 ± 53
D-dimer (ng/mL)	6702 ± 14,344	10,519 ± 17,858
Ferritin (ng/mL)	1449 ± 1025	854 ± 392*
C-reactive protein (mg/dL)	10.2 ± 10	8.5 ± 7
StO_2 (%)	66 ± 5	65 ± 6
THC (U)	48 ± 15	34 ± 12*
DeO_2 (%/min)	− 5.2 ± 1.9	− 5.1 ± 1.7
ReO_2 (%/min)	86 ± 40	72 ± 32
Hyperemia AUC (U)	9.7 ± 5.2	5.7 ± 3.9*

Conclusion: Microcirculatory alterations, measured by NIRS in the early course of ICU admission, are associated with ICU-mortality in COVID-19 patients with ARDS. Whether these alterations have therapeutic implications deserves to be further evaluated.

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001235

Cytokine hemadsorption for the treatment of severe postoperative systemic inflammatory response syndrome in cardiovascular intensive care unit

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Intensive Care Medicine Experimental 2022, **10(2)**: 001235

Introduction: Severe systemic inflammatory response and multiorgan dysfunction syndrome result in high mortality despite advances in intensive therapy. Although the etiology is different, pattern of deterioration is similar and leads to hypercytokinemia. This is believed to be harmful and reducing cytokine levels is considered beneficial.
Objectives: Cytokine removal by hemadsorption could control the overwhelming inflammatory response after heart and major vascular surgery and improve postoperative outcome.
Methods: In these retrospective case series of 22 critically ill patients we evaluated the effect of hemadsorption with Cytosorb® on IL-6 levels, hemodynamic and clinically relevant outcome parameters. Patients were treated in our 12-bed adult cardiovascular ICU at the University Medical Centre Ljubljana, Slovenia, in the period March 2017 to December 2021. They received hemadsorption with Cytosorb® as adjunctive treatment for postoperative severe hyperinflammatory state with rapid progressive organ dysfunction that developed after complicated heart or major vascular surgery. Indication for hemadsorption was a refractory shock with interleukin-6 value of more than 1000 ng/L, with increasing noradrenaline requirement (> 0,3 μg/kg/min) despite adding corticosteroids to maintain mean arterial pressure (MAP) ≥ 65 mmHg, serum lactate level ≥ 2 mmol/L despite adequate volume resuscitation (gold directed therapy completed in the previous 6 h) and multi-organ failure (at least 2 organs).
Results: Hemoadsorption with Cytosorb® was applied either during different regiments of renal replacement therapy or during extracorporeal membrane oxygenation. Patients received up to three CytoSorb® treatments (median two treatments) with total treatment durations ranging from 24 to 72 h (median 48 h). Filter was changed every 24 h. Results have shown effective reduction in IL-6 levels with corresponding clinical response including reduction in vasopressor therapy and increase in MAP (observed already from 6 h onward), as well as reduction of lactate levels (statistically significant at 48 h), suggesting efficacy of Cytosorb® treatment. Actual ICU mortality was 54% and in-hospital mortality was 59%. Predicted ICU-mortality, based on SOFA score, was 79% for our patients, which was significantly higher than the observed 54% ($p < 0,05$). No device-related adverse events were observed during treatment time.
Conclusion: CytoSorb® hemoadsorption resulted in control of hyperinflammatory response, rapid hemodynamic stabilization, restitution of deranged metabolic parameters and increased survival. Randomized controlled trials are needed to confirm this positive clinical experience and define the potential benefits of hemadsorption.

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Acknowledgements The authors thank all the staff of Cardiovascular ICU, as well as the staff from the Clinical Department of Nephrology and Dialysis at University Medical Centre Ljubljana, Slovenia.

001239

Influence of beta-lactam time and concentration above MIC on septic patients' outcome

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Introduction: The relationship between b-lactam concentrations and clinical response has not been well defined. The aim of this study was to determine whether adequate β-lactam exposure was associated with positive clinical outcome in this setting.
Methods: We studied 143 critically ill patients (2009–2012) with microbiological proven infection treated with intermittent infusion of broad-spectrum b-lactams including cephalosporins (CEF), piperacillin/tazobactam (TZP) and meropenem (MEM) in whom antibiotic concentration was measured. We excluded patients where isolates were not related to the infection or were resistant to the given antibiotic or when the antibiotic was administered for prophylaxis. Minimum drug concentrations were analyzed in relation to the minimal inhibitory concentration (Cmin/MIC) of the isolated strain, which was determined according to EUCAST clinical breakpoint. Insufficient Cmin/MIC were defined as < 1. Excessive drug levels were defined as > 64 mg/L for CEF, > 128 mg/L for TZP and > 16 mg/L for MEM. A positive clinical outcome was defined as a composite end-point of one of the following: a) completion of the treatment course or de-escalation; b) no escalation to another broader-spectrum drug; c) alive within 2 weeks from the diagnosis of infection.
Results: Patients were treated with CEF (n = 15), MEM (n = 68) or TZP (n = 60). Most infections were respiratory (n = 85) and abdominal (n = 28); the most common pathogens were *Escherichia coli* (n = 28), *Pseudomonas aeruginosa* (n = 26) and Klebsiella spp. (n = 26). A total of 86 (60%) patients had a positive clinical outcome. These patients had a significantly lower Cmin/MIC than the others (2.0 [1.0–5.7] vs. 4.0 [1.6–13.4]; p = 0.008). The proportion of patients with insufficient Cmin/MIC was similar in patients with positive clinical outcomes and the others (20/86 vs. 11/46; p = 0.17). However, patients with less excessive drug levels were more likely to have a positive clinical outcome (3/86 vs. 12/46; p = 0.01).
Conclusion: Positive clinical outcome was not associated with high β-lactam concentrations in critically ill patients. The impact of excessive drug levels on outcome deserves further investigations.

001256

Clinical outcomes of surgical sepsis and septic shock protocols in surgical intensive care unit

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Intensive Care Medicine Experimental 2022, **10(2)**: 001256

Introduction: Sepsis and septic shock are global public health problems that associated with high mortality. Factors related to mortality are delayed diagnosis, delayed antibiotic administration more than one hours, inadequate antibiotics dosage and multi-organ failure. Nowadays, Surviving Sepsis Campaign (SSC) have been developed guideline to decrease morbidity and mortality. Therefore these evidence-based protocols were adapted and applied to sepsis and septic shock management practice. However, its clinical outcomes are unknown. This study aims to compare medians survival time and outcome of treatment process before and after the sepsis and septic shock treatment protocol was implemented.
Methods: This study is interventional study. Data from all 401 patients were classified to 2 group, 195 in protocol group were retrieved during April 1st,2021 to January 31st, 2022 comparing with those of 206 patients in usual care during January 1st, 2018 to June 30th, 2021. Data collection comprised of patients' demographic data, treatment process in the first hours and outcomes of treatment.
Results: After the sepsis and septic shock treatment protocol was applied to practice; medians survival time was significantly increased in protocol group ($p = 0.016$, 95% CI 12.32–19.68), ICU length of stay significantly decreased from 11 to 4 days ($p < 0.001$), ventilator and vasopressor free day significantly increased from 2 to 6 days and 3 to 7 days ($p < 0.001$). Factors associated with mortality were delayed initial fluid resuscitation > 2 h, vasopressor > 2 h, culture sensitivity > 4 h and empirical antibiotics > 5 h ($p = 0.017$, 0.028, 0.008 and 0.008 respectively).
Conclusion: Sepsis and septic shock treatment protocol resulted increase medians survival time, ventilator and vasopressor free day. Consequently ICU length of stay is therefore decreased. Delayed initial fluid resuscitation > 2 h, vasopressor > 2 h, culture sensitivity > 4 h and empirical antibiotics > 5 h were associated with mortality.

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Acknowledgements My grateful thanks to Mrs Dollapas Panpanich for her helpful doing the data analysis, and extend to the staff of the surgical and medical intensive care unit of Phramongkutklao hospital for their help in offering me the resources in running the study.

001257

Endothelial prothrombotic and proinflammatory phenotype upregulation in an in vitro model of COVID-19 critical patients

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Introduction: Endothelial dysfunction has been appointed as a harbinger of COVID-19 complications, since circulating endothelial biomarkers in COVID-19 patients have shown to positively correlate with disease severity. However, the exact mechanisms of such endothelial dysfunction are yet to be unravelled.
Objectives: To characterise COVID-19 critical patient associated endothelial injury, using an in vitro approach based on endothelial cell culture.
Methods: Human microvascular endothelial cells (HMEC-1) were exposed to COVID-19 critically ill patient's sera, in order to evaluate modifications in: i) expression of adhesion receptors onto the endothelial cell monolayer and the extracellular matrix proteins, assessed by immunofluorescence; ii) extracellular matrix (ECM) reactivity to platelets after exposure to citrated blood under rheological conditions (800 s-1, 5 min); and iii) activation kinetics of intracellular signaling proteins involved in inflammation (p38MAPK) and cellular stress (Akt), using SDS-PAGE, immunoblot and chemiluminiscence analysis. Results were compared to those obtained in endothelial cells exposed to serum from healthy individuals (controls).
Results: Incubation of endothelial cells with patient serum resulted in a significant increase, compared to controls, of vascular cell adhesion protein 1 (VCAM-1) (2.5 ± 1.2 folds) and von Willebrand Factor (VWF) expression (9.6 ± 2.2 folds) ($p < 0.01$ both). Also, formation of platelet aggregates on ECM exposed to citrated blood flow was significantly superior on ECM obtained from endothelial cells grown with critically ill patient serum than on control ECM ($47 \pm 3\%$ vs $24 \pm 6\%$, respectively) ($p < 0.01$). Regarding the activation of intracellular signaling pathways, phosphorylation of protein p38MPAK was prompt (after 1 min of exposure), being more persistent (after 30 min of exposure) in those cells exposed to COVID-19 patient's sera. Activation of Akt was progressive, peaking after 30 min of exposure, and being superior in response to patient serum compared to controls.
Conclusion: We have established an in vitro model that allows research of the various mechanisms of activation and endothelial damage in COVID-19. Humoral mediators present in the serum of these patients are capable to induce a proinflammatory and prothrombotic phenotype in endothelial cells. Thus, the endothelium postulates as a potential therapeutic target to treat and/or prevent COVID-19 complications. The proposed in vitro model will allow future exploration of different therapeutic agents that could impact in the prognosis of critically ill COVID-19 patients.

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Acknowledgements
1. Instituto de Salud Carlos III, Gobierno de España (FIS PI19/00888)
2. Fundació La Marató de TV3 (202026)
3. Fundació Clínic, Barcelona (HCB/2020/0401)
4. Hospital Clínic de Barcelona, Contractes Clínic de Recerca "Emili Letang – Josep Font"

001181

Can PSP distinguish between infection and inflammation after enzymatic or surgical debridement in the critically ill burn patient?

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Intensive Care Medicine Experimental 2022, **10(2)**: 001181

Introduction: Burn patients are a challenge for all intensivists, presenting a high morbimortality. Secondary to the trauma and surgery involved in burn patients, there are alterations in the levels of certain proinflammatory markers that may pose a challenge when assessing their clinical usefulness. There is still insufficient data on PSP in these patients.
Objectives: to evaluate the response of the PSP in the critically ill burn patient both in the initial insult and in subsequent therapeutic insults, as well as to assess its ability to differentiate the inflammatory response from sepsis.
Methods: prospective, single-centre study, where 261 samples were collected from 20 patients in the Critical Burn Unit between November 2020 and September 2021. Plasma levels of PSP, C-reactive protein (CRP), procalcitonin (PCT), leukocytes and lactate were collected on a daily basis, in addition to other data on inflammation, infection and external aggressions (surgeries, enzymatic debridements and aggressive dressings), until discharge from the Critical Burn Unit (CBU). Ordinal and continuous variables were compared using the Kruskall Wallis test.
Results: 20 patients were included with a mean age of 51 ± 16 years, with a percentage of burnt body surface area (BSA) of 29 ± 16% and an Abbreviated Burn Severity Index (ABSI) of 7.5 ± 2.3, 80% of whom were men. In the first 3 days, considered the resuscitation phase, PSP levels were higher than the normal range, with the mean on day 1 being 135 ± 145 ng/ml, day 2 143 ± 187 ng/ml and day 3 137 ± 180 ng/ml, with higher levels found later (on day 9 PSP had a mean of 305 ± 229 ng/ml). PSP is higher in surgical debridements than in aggressive dressings and enzymatic debridement, but no significant differences were found in the measured PSP levels during these new therapeutic aggressions that would represent an inflammatory event (28 ± 208 ng/ml vs 36 ± 159 ng/ml vs 21 ± 193 ng/ml, respectively, p 0.9). PSP showed correlation with the other classical markers CRP, PCT, leukocytes and lactate, with $p < 0.05$ but with low significance. In contrast, a significant elevation of PSP was observed in patients who met infection criteria compared to those who did not, with a mean PSP of 360 ± 196 ng/ml vs. 149 ± 155 ng/ml (p 0.001), respectively. Thirty-five per cent of patients had at least one episode of infection, with mean day of onset being 15 ± 6.5; among infected patients, 85% met sepsis criteria in the burn patient on day 15 ± 7.1.

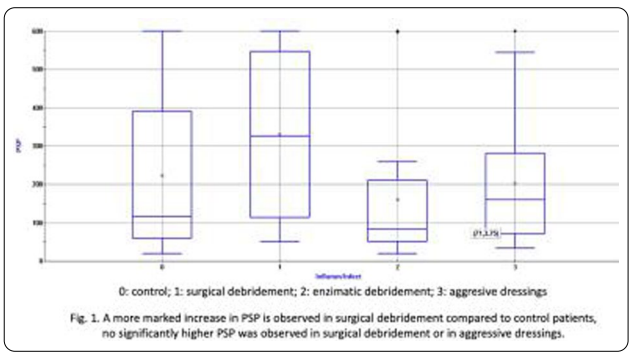

Fig. 1. A more marked increase in PSP is observed in surgical debridement compared to control patients, no significantly higher PSP was observed in surgical debridement or in aggressive dressings.

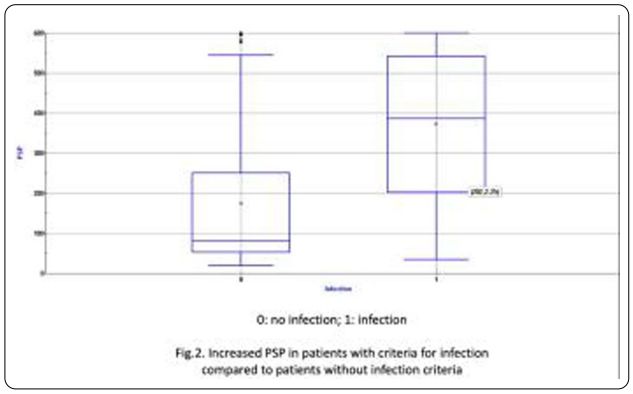

Fig.2. Increased PSP in patients with criteria for infection compared to patients without infection criteria

Conclusion: Our data suggest that during the resuscitation phase and the therapeutic aggressions, including enzymatic and surgical debridement, required by the critically ill burn patient, PSP is not as significantly elevated as in episodes of infection; therefore, we may conclude that PSP is useful in discriminating between inflammatory response and sepsis.

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Systemic Inflammation & Sepsis 10 + Health Services Research & Outcome 17

001433

Correlation between ICU prognostic models and in-hospital mortality in medical versus surgical patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 001433

Introduction: Predictive scoring systems are used in intensive care units (ICU) to evaluate the severity of disease and to predict in-hospital mortality. Two of the major scoring systems used are the Acute Physiologic and Chronic Health Evaluation (APACHE) scoring system and the Simplified Acute Physiologic Score (SAPS).
Objectives: Determine the local performance of the APACHE II, SAPS II, and SAPS 3, in medical versus surgical patients.
Methods: We included all patients hospitalized in a level two–three care district hospital ICU from January 2014 to June 2019. Readmissions into ICU were excluded. Predictive scores were calculated and registered manually by the attending physician. Patients were divided into three categories: medical, planned, and unplanned surgery. Performance was assessed by its ability in distinguishing between in-hospital outcomes (i.e., survived or dead). This was measured by the area under the receiver operating characteristic curve.
Results: Our sample included 3175 patients: 2116 medical patients, 435 planned surgical patients, and 580 urgent surgical patients. The results demonstrated a very good discrimination value (AUC 0.8–0.9) for in-hospital mortality, in both medical and surgical patients. In the medical patients' group: APACHE II, SAPS II, and SAPS 3 had AUC values of 0.828, 0.843, and 0.846 respectively; only between APACHE II and SAPS 3 there was there a statistically significant difference for a p-value < 0.05. In this same group, SAPS 3 had correctly classified 84,6% of in-hospital mortality. In the planned surgery group: APACHE II, SAPS II, and SAPS 3 had AUC values of 0.816, 0.813, and 0.850 respectively. In the unplanned surgery group: APACHE II, SAPS II, and SAPS 3 with AUC values of 0.821, 0.831, and 0.831 respectively. No statistically significant differences between the models in the surgery groups were observed. Parallel analysis showed lower AUC values (< 0.800) for lactate levels and Sequential Organ Failure Assessment (SOFA) at admission alone. As seen in the published literature, with time, these models have slowly run down in terms of prognosis.1 *"Uniformity of fit"* is questioned due to the heterogeneity within populations; patient demographics and an increase in chronic diseases and immunodeficiencies, and the availability of new therapies and tools in ICU. Subjectivity in scoring between physicians must also be considered and calibrated.

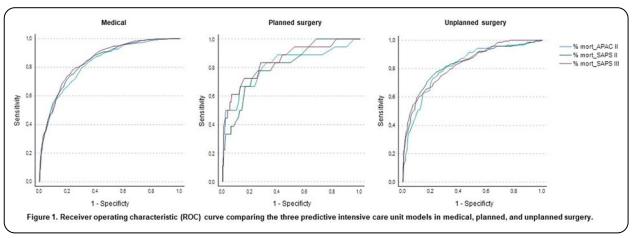

Figure 1. Receiver operating characteristic (ROC) curve comparing the three predictive intensive care unit models in medical, planned, and unplanned surgery.

Conclusion: APACHE II, SAPS II, and SAPS 3 are readily available prediction models and can be considered *very good* models to determine in-hospital death. From our sample, in medical patients, the SAPS 3 score appears to be a better discriminator of in-hospital death than APACHE II.

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001384

An in-situ/automated sustained improvement prototype: physiological targets setting in critical care

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Intensive Care Medicine Experimental 2022, **10(2)**: 001384

Introduction: Evidence based clinical guidelines suggest that setting and adhering to appropriate physiological targets can reduce patient morbidity and/or mortality, and improve patient safety in the critically ill [1, 2]. The medical team should set targets for each patient at least once every 24 h; the electronic health record (EHR) specifically considers eight targets (SpO_2, PaO_2, $PaCO_2$, mean arterial blood pressure, Richmond Agitation Sedation Score, pH, fluid balance and haemoglobin. Leveraging the EHR (*EPIC Systems Corp*) our institute acquired; our research group designed, built and implemented a 'shadow' live data warehouse of curated real-time clinical and operation data [3]. This provides data for the '*INFORM_us Hub*', bespoke software providing enhanced communication, education and a real-time quality improvement dashboard for critical care staff. One facet of this is a real-time display of target setting compliance, providing a floorplan highlighting deficits and presenting performance in time series. This improvement project aimed to evaluate the impact of a multifaceted intervention to improve target setting in a 35-bed Intensive Care Unit in a London University affiliated hospital. We aimed to improve the proportion of patients that had all targets set each day from a baseline of 73% to 90% within 30 days and to sustain at this level.
Methods: A multi-disciplinary Targets Improvement Working Group was formed to develop and implement the intervention. To inform tour PDSA cycles, we conducted staff interviews and process mapping about the barriers and levers to target setting using the Capability Opportunity Motivation Model of Behaviour (COM-B) [4]. We conducted PDSA cycles of: real-time feedback on the shop floor using a data dashboard that displayed unit real-time and weekly performance via Statistical Process Control (SPC) charts, targets education involving instruction on how to set targets in the EHRS and information about the clinical importance of target setting, weekly audit and feedback emails to doctors on their targets performance, and what's app prompts at the start of each shift. The proportion of patients with all targets set by 13:00 h each day was measured over 4 weeks using the data dashboard.
Results: The intervention improved the proportion of patients with eight targets set each day. We reached and exceeded our aim of 90% compliance with target setting. The SPC chart showed a statistically significant improvement (shift), which was sustained.

Conclusion: The implementation of a multifaceted intervention on physiological target setting for critically ill patients resulted in an improvement to the proportion of patients with targets set each day. The intervention may have been more successful because of the

preliminary work we did to explore barriers and levers to compliance, creating a nudge in behaviour change requiring minimal alteration of the working day as well as an easily accessible dashboard real-time updated data. Next steps include sustaining the behaviour change and developing further interventions to improve adherence to targets in the areas of mean arterial blood pressure, sedation, oxygenation and ventilation practice. We believe our model and prototype provide an opportunity for performing quality improvement in real-time, educating staff and enforcing learning at the time of an event, potentially beneficially affecting the outcome of the patients cared for at that time.

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Acknowledgements Funded by UCLH Charity.

001407

Evaluating the impact of the COVID-19 pandemic on obstetric intensive care unit (ICU) admissions in one UK District General Hospital (DGH)

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Intensive Care Medicine Experimental 2022, **10(2)**: 001407

Introduction: Severe COVID-19 in pregnancy increases the risk of adverse outcomes for both parturient and neonate. Pandemic planning included anticipation of reduced staffing levels (20–80%) and increased patient numbers. We anticipated that obstetric services would manage the majority of standard pathologies outside ICU and a higher proportion of obstetric ICU admissions would be complicated by COVID-19.
Objectives: To evaluate the impact of COVID-19 on the nature and acuity of obstetric ICU admissions in our UK DGH.
Methods: A single centre retrospective observational study was conducted between 19/02/2018 and 25/04/2020. This represents equal time periods before and after the first UK lockdown for COVID-19 on 23/3/2020. Our hospital cares for > 5000 pregnant patients per year. Case histories were reviewed for 44 patients who were pregnant or within 6 weeks of delivery on admission to ICU. Patients were grouped by primary reason for admission as either; direct obstetric (resulting from the complications of pregnancy), or indirect obstetric (from an existing disease, or one that developed during pregnancy which was aggravated by pregnancy).Two patients were excluded as, although recently post-partum, the admission was unrelated to pregnancy or delivery (e.g. anaphalaxis). Categorical data was examined using a Fisher's Exact test and continuous using a Mann–Whitney U with an alpha level of 0.05. Statistical analysis was performed using IBM SPSS Statistics for Windows (Version 27.0. Armonk, NY).
Results: Mean (SD) age was 32.3(6.1) years. Median (IQR) length of stay (LOS) was 1.35(0.7–2.45) days. Pre-pandemic, 20 admissions (83%) were due to direct obstetric causes compared to 6 (33%) from March 2020 onwards. Of the 12 indirect admissions since the beginning of the pandemic, 7 (58%) were for COVID-19. Where the primary reason for admission included post-partum haemorrhage (PPH), mean (SD) estimated blood loss was 4.35 (2.28) litres.

Direct and indirect obstetric admissions to our UK DGH ICU before and after the first UK lockdown for COVID-19

	Direct	Indirect	Total
Before March 2020	20	4	24
After March 2020	6	12	18
Total	26	16	42

Since the beginning of the Covid-19 pandemic significantly more obstetric patients have been admitted for indirect rather than direct obstetric causes ($p = 0.001$). There was no difference in the rate of intubation between admissions before and after the COVID-19 pandemic ($p = 0.622$) or between direct and indirect admissions ($p = 0.17$). There was no difference in APACHE-II scores ($p = 0.908$) or ICNARC scores ($p = 0.619$) highest Creatinine ($p = 0.052$), highest Lactate ($p = 0.750$) or unit LOS ($p = 0.118$) between admissions before and after March 2020.
Conclusion: Our small retrospective study suggests that ICU admissions due to indirect obstetric causes have increased since the start of the pandemic. However, severity of illness has not changed. Since the number obstetric complications (eg pre-eclampsia and PPH) has not decreased, and year-on-year our maternity unit sees more deliveries, it may be inferred that the pandemic has resulted in a higher volume and acuity of patients being cared for outside ICU. Further work is needed on the evaluation and delivery of a higher level of care beyond ICUs.

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001422

Management of profound hyponatraemia in ITU

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Intensive Care Medicine Experimental 2022, **10(2)**: 001422

Introduction: Hyponatraemia, defined as a serum sodium concentration < 135 mmol/L, is the most common disorder of body fluid and electrolyte balance encountered in clinical practice. It is present in 15–20% of emergency hospital admissions and up to 20% of critically ill patients. At levels < 125 mmol/L the likelihood of developing symptoms is increased. Despite high incidence management is often challenging. Prompt recognition of aetiology and appropriate management attenuate the likelihood of developing complications such as cerebral oedema or pontine demyelination from rapid correction.

Objectives: To assess management of patients with profound hyponatraemia admitted to critical care as per standards set in established ESICM guidelines (2014).
Methods: Retrospective observational single centre, non-specialist UK study of critical care patients admitted with sodium levels < 125 mmol/L over two years (2018–20). Excluding those with Pseudo hyponatraemia and those that passed away within 48 h of admission into ITU not related to hyponatraemia.
Results: Severe hyponatraemia at critical care admission was noted in 60 patients, giving an incidence of 4.6% of all admissions (1,302) over the study period. Urine Osmolarity and Urine sodium were checked 55% and 58%, respectively. Severe symptomatic cases with seizures were treated without waiting for diagnosis in 86% of patients. Appropriate correction was judged in 80%. Rapid correction was instituted in 25%. Prompt adjustment of active treatment in cases where sodium correction was occurring rapidly was noted in 6% of patients. Symptoms were severe in 25% of patients, moderate-severe in 35% of patients with hyponatraemia, with the remainder asymptomatic (no symptoms documented). Primary diagnoses in order of frequency were dehydration, sepsis, alcohol excess and/or alcoholic liver disease and related to a surgical procedure (prostate, laparotomy). In-patient mortality was 16%, though the cause of death was not thought directly related to the hyponatraemia.
Conclusion: In a case series of severe hyponatraemia when compared with standards, we observed that appropriate investigations were frequently not performed and appropriate treatment could be improved. Future study could look at longer-term outcomes including cognitive sequelae.

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001361

Neutrophil/Lymphocyte ratio may help to separate treatment responders in COVID-19

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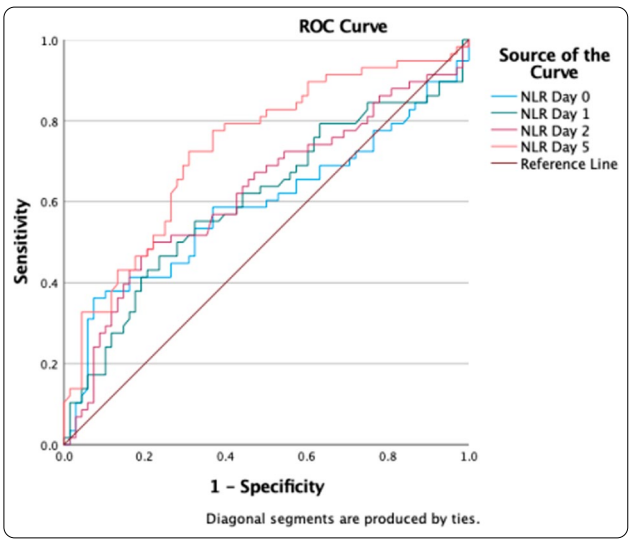
Intensive Care Medicine Experimental 2022, **10(2)**: 001361

Introduction: High neutrophil/lympphocyte ratio (NLR) has been shown to be associated with worse outcomes in hospitalised patients with COVID-19 early in the pandemic (1). There is little information on how this simple parameter can be used in critically ill patients infected by SARS-CoV-2 who are treated with immunomodulators.
Objectives: To establish the clinical course and usefulness of NLR in COVID-19 patients treated with contemporary evidenced-based therapies.
Methods: Retrospective observational study of patients admitted to a single ICU in the 2nd and 3rd UK wave of the pandemic. Basic demographic data and routinely performed blood test results were collected on admission (Day 0) then daily up until Day 7. Survivors and non-survivors were compared using Mann–Whitney U, Chi-square tests and ANOVA using Welch modification for non-parametric data. ROC analysis was performed to establish discriminatory power.
Results: 227 patients admitted to the ICU with median [IQR] age 58 [18] years, 71.2% male, 74.8% with at least one comorbidity, 47% mechanical ventilation on admission, all had dexamethasone and 65.3% had IL-6R inhibitors. ICU mortality was 41%. NLR was significantly higher in non-survivors throughout the first seven days of ICU stay (Table 1).

NLR differences between survivors and non-survivors, median [IQR]

	Survivors n = 134	Non-survivors n = 93	p-value
Day 0	11.14 [9.03]	14 [21.36]	< 0.001
Day 1	9.55 [7.90]	14.7 [17.30]	< 0.001
Day 2	8.82 [8.65]	15.20 [20.54]	< 0.001
Day 3	8.50 [8.93]	13.00 [18.21]	< 0.001
Day 4	9.96 [8.40]	15.13 [17.36]	< 0.001
Day 5	8.03 [7.68]	14.98 [15.21]	< 0.001
Day 6	8.75 [7.33]	15.17 [16.32]	< 0.001
Day 7	9.78 [10.30]	19.92 [20.96]	< 0.001

ROC analysis revealed that NLR had a moderate abilty to distinguish between survivors and non-survivors on Day 1, 2 and 5. The best ROC was found at Day 5 0.732 (95%CI 0.643–0.820) p < 0.001. Best cut-off was at 12.00 with sensitivity of 72% and specificity of 73%.



Conclusion: NLR was elevated in ICU patients with COVID-19 in line with previous reports earlier in the pandemic (1). ICU non-survivors had even higher NLR throughout their ICU stay than reported previousy. NLR doesn't appeared to be affected by steroid and IL-6R antagonist treatment and did not show significant change over time. As all eligible patients had received immonumodulatory treatment by Day 5 of ICU admission, at this point it might be used as marker of therapeutic response even in the contemporary ICU cohorts. Further validation of the optimal cut-off in larger ICU populations is warranted.

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001370

The use of corticosteroid and IL-6R blocking agents are associated with significant drop in CRP, but not in PCT and white cell count levels in COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**: 001370

Introduction: We have previously demonstrated that inflammatory markers were significantly lower after corticosteroid treatment became usual care in COVID-19 ICU patients (1). It's unknown if further drop in these markers can be attributed to IL-6R antagonist treatment.
Objectives: To evaluate the longitudinal course of CRP, PCT and white cell count (WCC) and compare the response of the patients admitted to the ICU in the 2nd and 3rd wave of the pandemic.
Methods: Retrospective observational study of patients admitted to a single ICU in Wales, UK. Patients in the 2nd and 3rd wave were compared. Basic demographic data and daily inflammatory marker changes (CRP, PCT and WCC) were evaluated during the first week of ICU admission. For statistical analysis Mann–Whitney-U, Chi-square tests and ANOVA with Welch modification was used for non-parametric data. Data is presented as % or median [IQR].
Results: There were 234 patients admitted in the two waves, 116 in the 2nd wave and 118 in the 3rd wave. There was no signifcant difference in male/female distribution (30% female) or length of ICU stay in the 2nd wave 8.3 [12.4] days vs 3rd wave 7.0 [8.5] days, respectively. Patients in the 3rd wave were significantly younger 54 [23] years vs 61 [16] years, $p < 0.05$. Mortality was significantly lower in the 3rd wave 31.4% vs 48.3%. Significantly more patients received IL-6R inhibitors in the 3rd wave 65.2% vs 34.5%. Every patient received dexamethasone. CRP, PCT and WCC levels were similar on ICU admission, but CRP levels dropped significantly lower by Day 2 in the 3rd wave (Table 1). There were no signifcant differences in PCT levels and WCC between the two groups.

CRP, PCT and WCC levels in the 2nd and 3rd wave

	2nd wave (n = 116)	3rd wave (n = 118)	p-value
CRP mg/dL Day 0	128 [140]	108 [113]	0.588
Day 1	117 [152]	81 [105]	0.052
Day 2	89 [118]	48 [59]	< 0.001
Day 3	63 [92]	26 [33]	< 0.001
Day 4	41 [94]	16 [25]	< 0.001
Day 5	38 [120]	13 [21]	< 0.001
Day 6	41 [132]	10 [19]	0.005
Day 7	39 [155]	16 [92]	0.062
PCT ng/mL Day 0	0.24 [1.10]	0.18 [0.39]	0.332
Day 1	0.29 [1.35]	0.14 [0.53]	0.804
Day 2	0.24 [2.03]	0.19 [0.31]	0.970
Day 3	0.21 [1.15]	0.09 [0.16]	0.408
Day 4	0.18 [0.41]	0.12 [0.39]	0.279
Day 5	0.12 [0.78]	0.10 [0.16]	0.642
Day 6	0.12 [0.6]	0.12 [0.53]	0.182
Day 7	0.18 [1.19]	0.11 [0.38]	0.997

CRP, PCT and WCC levels in the 2nd and 3rd wave

	2nd wave (n = 116)	3rd wave (n = 118)	p-value
WCC 10 × 9/L Day 0	11.7 [7.1]	9.1 [6.9]	0.870
Day 1	10.3 [5.8]	7.9 [6.1]	0.843
Day 2	9.5 [5.5]	8.1 [5.9]	0.770
Day 3	9.6 [4.9]	7.6 [5.6]	0.763
Day 4	10.4 [5.8]	8.4 [5.4]	0.973
Day 5	10.7 [6.7]	9.7 [6.4]	0.820
Day 6	11.5 [7.0]	11.2 [5.9]	0.756
Day 7	11.6 [6.9]	11.4 6.5]	0.768

Conclusion: As expected more frequent use of IL-6R inhibitors was assoicated with significant drop in the CRP levels in the 3rd wave of the pandemic. Due to the inflammatory pathway mechanisms this artifically lowered CRP persisted during the first week of ICU stay. PCT and WCC levels remained static. Further investigation is needed to establish if PCT kinetics could be used to predict new onset bacterial infection as we have observed in the first wave (2).

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001387

Clinical cure rate and mortality for complicated intra-abdominal infections: a systematic review, meta-analysis and trial sequential analysis of randomised controlled trials comparing bactericidal and bacteriostatic antibiotic treatment

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Intensive Care Medicine Experimental 2022, **10(2)**: 001387

Introduction: The mainstay therapies for treating complicated intra-abdominal infections are source control, organ support on Intensive Care, and antibiotics [1, 2]. Bactericidal antibiotics are favoured as first line therapy over bacteriostatic antibiotics because it is assumed they have a better treatment profile. However, evidence supporting this assumption is lacking and increasing rates of anti-microbial resistance have led to the need to consider alternative antibiotic classes [3, 4].
Objectives: We performed a systematic review, meta-analysis and trial sequential analysis (TSA) of randomized controlled trials of comparing the efficacy of bactericidal versus bacteriostatic antibiotics on clinical cure rate (primary outcome), mortality and microbiological eradication (secondary outcomes).
Methods: A literature search was conducted and all randomized control trials (RCTs) comparing bactericidal and bacteriostatic antibiotics in the treatment of complicated intra-abdominal infections were included. Data were extracted by two authors independently and analysed using RevMan version 5.4 and trial sequential analysis version 0.9.5.10. Data are presented as risk ratios (RR), 95% confidence intervals (CI) and heterogeneity *I2*.

Results: Eleven RCTs (4078 patients) met the eligibility criteria. Bactericidal antibiotics were not superior over bacteriostatic antibiotics at improving clinical cure rates [RR 0.99 (95%CI 0.96–1.02); $I2 = 13\%$; TSA adjusted CI 0.93–1.05. In addition there was no difference in mortality [1.36 (0.90–2.06); $I2 = 0\%$] or microbiological eradication [0.99 (0.97–1.02); $I2 = 0\%$] between bactericidal and bacteriostatic antibiotics. Most studies had high risk of bias.
Conclusion: This meta-analysis did not demonstrate any difference in clinical cure rate, mortality, or microbiological eradication between bactericidal and bacteriostatic antibiotics in treatment for complicated intra-abdominal infections.

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Acknowledgements ESICM Next Start Up (2018).

001414

Commonly used antibiotics may worsen sepsis-induced lymphocyte dysfunction- an ex vivo model

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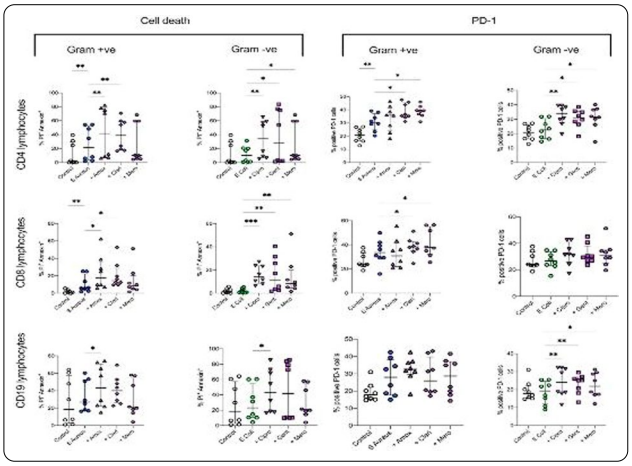
Intensive Care Medicine Experimental 2022, **10(2)**: 001414

Introduction: Many patients with sepsis survive their initial insult but die several days following initial presentation. Persistent and secondary infections are commonplace and often associated with impaired immune cell function (sepsis- induced immunosuppression).
Objectives: To ascertain if commonly used antibiotics contributed to features associated with sepsis-induced lymphocyte dysfunction.
Methods: Whole blood samples were collected from healthy volunteers. Peripheral blood mononuclear cells (PBMCs) were isolated and incubated with heat killed bacteria (HKB) ± antibiotics (15mcg/ml) for 5 days. We assessed levels of intracellular cytokines, cell surface markers and cell death using flow cytometry.
Results: Compared to incubation with HKB alone, amoxicillin was associated with an increase in CD4 + ($p = 0.007$), CD8 + ($p = 0.03$) and CD19 + ($p = 0.02$) lymphocyte death. Clarithromycin was associated with an increase in CD4 + ($p = 0.007$) and CD8 + ($p = 0.03$) cell death, and PD-1 in CD4 + ($p = 0.02$) and CD8 + cells ($p = 0.048$). Ciprofloxacin was associated with greater CD4 + ($p = 0.004$), CD8 + ($p = 0.003$) and CD19 + ($p = 0.01$) death, with increased PD-1 in CD4 + ($p = 0.002$) and CD19 + ($p = 0.003$) cells. Gentamicin was associated with an increase in CD4 + ($p = 0.01$) and CD8 + ($p = 0.004$) cell death as well as an increase in PD-1 in CD4 + ($p = 0.03$) and CD19 + ($p = 0.04$) cells.
Meropenem was associated with an increase in CD4 + ($p = 0.02$), CD8 + ($p = 0.004$) and CD19 + ($p = 0.04$) lymphocyte death. Meropenem was also associated with an increase in PD-1 in different cells depending on the microbial stimulus; it was higher in CD4 + ($p = 0.01$) and CD8 + ($p = 0.02$) cells with gram + ve stimulus or in CD4 + ($p = 0.02$) and CD19 + ($p = 0.02$) cells with gram –ve stimulus.



Conclusion: At clinically relevant levels of antibiotics, a number of commonly used antibiotics amplify features of sepsis- induced lymphocyte dysfunction. This makes a strong argument for proactive prompt antibiotic cessation when clinically appropriate.

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Acknowledgements

1. UCLH National Institute of Health Research (NIHR) Biomedical research centre (BRC)- Precision AMR grant (2021)
2. ESICM NEXT start up grant (2018)

001201

Documentation of Microbiology Ward Round Pre and Post Proforma Implementation on the ICU at Buckinghamshire Healthcare Trust

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Introduction: According to the Faculty of Intensive Care Medicine guidelines for the provision of ICU services, a daily interaction with a microbiologist is the number one standard with regards to the multidisciplinary team approach to the care of a patient. This should be a standardised and sufficiently documented interaction with the microbiology team regarding a patient's antimicrobial regimen if ICU is to comply with GPICS standards and recommendations. Direct input from microbiology is essential in the management of many critically ill patients especially in sepsis with regards to early broad-spectrum antibiotics. In contrast, inappropriate use of antimicrobials leads to development of antimicrobial resistance and nosocomial infections such as *C. difficile* (DOH 2011). Despite the factors primarily stated, there is still a high variability regarding the frequency of documented daily microbiology interactions within the ICU to which the Proforma implemented on the ward should address.

Objectives: Evaluate the effectiveness of a proforma on the documentation of the daily microbiology ward rounds on the intensive care unit.

Methods: Although daily microbiology ward rounds take place and form part of the trust's guidelines on critical care management, the advice provided by the microbiology team is not always documented. It is therefore crucial to analyse the effectiveness of any measures implemented to improve this. Records were accessed retrospectively using 'Evolve', an electronic database of medical records used by the trust, and we inspected patients notes thoughout their admission and documented any mention of a microbiology ward round. Inclusion criteria included detailed mention of a "microbiology ward round" taking place each day regardless of what the patient's treatment was as well as a minimum length of stay of one week excluding admission within the ICU. Exclusion criteria included copying the notes from the day prior, whether they had Covid, length of stay shorter than week. Ten patients from 2016, prior to CareFlow implementation, and patients from 2020, post CareFlow implementation, were selected and 10 days post ICU admission were analysed. The presence of these ward round documentations were analysed.

Results:

Patient	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Total
10719385	0	0	0	1	0	1	0	2
11081344	0	0	0	1	0	1	0	2
10561608	1	0	0	0	0	1	0	2
11028042	0	1	0	0	1	0	0	2
11619378	0	0	0	0	0	0	1	1
30115806	0	0	1	0	0	1	1	3
11073944	0	0	0	1	0	0	0	1
11059575	0	0	0	0	0	0	0	0
10557172	0	0	0	0	0	1	1	2
20190518	0	0	0	0	0	0	0	0

Table 1: Documentation of ward round in 10 patients over a week period pre proforma.

Patient	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Total
10873570	0	1	0	0	1	0	0	2
31036476	1	0	0	0	1	0	0	2
11432082	1	0	0	1	1	0	0	3
31087083	0	1	1	0	1	0	0	3
10758694	0	0	0	0	0	0	0	0
11028808	1	0	0	0	0	1	0	2
10101435	0	0	1	1	1	0	1	4
31132415	0	1	1	1	0	1	0	4
10119974	1	1	0	0	0	0	1	3
10656331	1	0	1	1	1	1	0	5

Table 2: Documentation of ward round in 10 patients over a week period post proforma.

Conclusion: Prior to the Proforma regarding a microbiology ward round being documented in 2016, there is a significant number of undocumented interactions in comparison to after the Proforma has been initiated. This shows that the requirements set out by QPICS guidelines were not being met and the use of the standardised Proforma has increased compliance. However, there is still a proportion of undocumented microbiology ward round interactions globally throughout both ICU sites. We recommend the following actions:
Compare and contrast the documented microbiology ward round using the Proforma and the Careflow system that has been implemented as a technological platform for patient notes. Ensure all new doctors are aware of the proforma and how to complete this during induction. Regular audits of documentation and following trends of weeks with minimal documented microbiology ward rounds to address this with the appropriate doctor that week.

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000070

Representation of Cancer Patients in Sepsis Studies: A Review of the Most-Cited Randomised Controlled Trials

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Intensive Care Medicine Experimental 2022, **10(2)**: 000070

Introduction: Cancer patients represent an important cohort of patients admitted to hospital with sepsis with up to 21% of sepsis cases related to cancer. Cancer patients are thus an important cohort to be represented and characterised amongst sepsis trials. However, evidence suggests cancer patients are commonly excluded from trials with a recent study of randomised controlled trials across all fields published in high-impact journals demonstrating approximately 16% of trials excluding cancer patients.The extent to which cancer patients are excluded from sepsis trials is unknown and provides impetus for this study.
Objectives: The aim of this study was to quantify the degree of exclusion of cancer patients amongst the most frequently cited randomised controlled trials in sepsis.
Methods: We performed a search of all Web of Science databases to identify the 500 most highly cited randomised controlled trials in sepsis. Of these, 177 met our criteria of being in English, involving human participants aged 16 or older, randomised controlled trials on sepsis and stated eligibility criteria. We then assessed whether cancer was listed as an exclusion criterion in these trials. Cancer exclusion was subdivided into three tiers: tier 1 excluding all cancer patients, tier 2 excluding subsets of cancer patients and tier 3 excluding features pertaining to cancer patients (e.g., chemotherapy).
Results: Only 3/177 trials excluded all cancer patients (tier 1) with a further 42/177 excluding subsets of cancer patients (tier 2). Together these represented 25% (45/177) of the trials. Out of the remaining 132 trials 42 contained exclusion criteria pertaining to cancer patients (tier 3). Altogether, approximately half (49%, 87/177) of the trials in this study excluded cancer in some form. Trials of immune modulators (36/44, 82%) were most likely to exclude cancer (in all tiers) and fluid-related trials (1/8, 12.5%), were least likely. Of the 174 sepsis trials not excluding all cancer patients (tier 1), 41 stated the number of cancer patients recruited. In these trials a total of 2786/16033 (17%) were cancer patients. Such a figure is similar but lower than prior estimates of cancer-related cases of sepsis (up to 21%).
Conclusion: Our results show that a significant proportion of sepsis trials (49%) exclude cancer patients in some form. This suggests an important cohort of patients most at risk of sepsis are likely

under-represented in sepsis trials, often with an unclear rationale. As the number of people living with cancer increases, this lack of representation may increase unless a shift for wider inclusion of cancer patients is made. This would bridge the knowledge gap in sepsis management for cancer patients, in an era focused on characterising sepsis heterogeneity to develop more personalised therapies.

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Trauma & Emergency Medicine 1

000025

Rib Fractures: A major problem in minor centres

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Intensive Care Medicine Experimental 2022, **10(2)**: 000025

Introduction: Rib fractures occur in 10% of patients following significant trauma1. Patterns of injury differ between age groups. Younger patients more commonly sustain high impact blows, whereas elderly patients are more likely to suffer fragility fractures2. Both patterns create significant morbidity and mortality due to pain-related hypoventilation, impaired gas exchange and altered breathing mechanics. Rib pain reduces tidal volume and risks significant atelectasis and pneumonia even in the context of isolated minor rib fractures: occurring in approximately 1.6% of cases3. Complication rates rise with increasing numbers of rib fractures and a significant proportion of these patients require level 2 or 3 care. Effective multi-modal analgesic strategies improve patient experience, prevent atelectasis and allow secretion clearance. Thus, analgesia may reduce the incidence of pneumonia, rib fracture mortality and ITU admissions4. Owing to large patient numbers, major trauma centres often have formal policies for rib fracture management. By contrast, smaller centres that see fewer fractures may struggle to justify local policy development and rely on guidelines from other centres, risking variance in management. We investigate management of rib fractures in a large DGH which follows guidance from a local major trauma centre.
Objectives: To determine whether non-internal policy leads to significant variance in rib fracture management and whether sufficient patients present to a local district general hospital with rib fractures to warrant local guidance development.
Methods: Data was collected for all patients > 18 presenting with rib fractures over an 8-month period. Data was collected on pain scores and analgesic strategy compared with the Coventry Rib Fracture Management Pathway (2016), used by the hospital. Patients discharged from A&E were excluded.
Results: 80 patients presented with rib fractures (median age 74, IQR 58.5–81.25) with a mean of 5.95 breaks. 77.5% were fragility fractures following a mechanical fall. 16% of patients received appropriate analgesia (n = 13). 28% of patients were under-analgesed (n = 22) and 10% (n = 8) were over-analgesed. An additional 47% of patients (n = 37) has analgesic agents omitted from their management with no clinical justification. Pain scores were only recorded in up to 21% of patients (n = 17).
Conclusion: This study demonstrates that a significant number of patients present to non-trauma centres with rib fractures. In a centre which adopts non-local policy without formalising it into a local guideline, adherence is poor, putting patients at risk of complications and requiring critical care support. These findings support the development of local guidelines for the management of rib fractures in smaller hospitals outside of the major trauma centre setting. This would likely improve adherence to management standards and allow adaptation of established guidance to more closely reflect smaller centre resources and capabilities.

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000033

Predicting Survival and Neurological Outcome in Out-of-Hospital Cardiac Arrest Using Machine Learning: The SCARS Model

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Introduction: There are no prediction models that estimate survival and neurological outcomes during on-going cardiac arrest. Such models may have the potential to facilitate clinical management in emergency rooms worldwide.
Objectives: To develop a clinically relevant prediction model to be used in the emergency department to predict survival and neurological outcome following out-of-hospital cardiac arrest.
Methods: We used the Swedish Registry for Cardiopulmonary Resuscitation to study all cases of out-of-hospital cardiac arrest (OHCA) in Sweden during 2010 to 2020. The registry was linked to several sources with individual-level data (e.g. the Inpatient Registry). After data merger, we had 474 candidate predictors describing the circumstances at cardiac arrest, critical time intervals during arrest, patient demographics, initial presentation at EMS arrival, area of residence, spatiotemporal data during arrest, socioeconomic status, medications and comorbidities. We assessed 30 days survival and cerebral performance score. We created training, evaluation and test data, with five-fold cross validation driving model selection. We evaluated several frameworks (e.g. neural networks, random forest, logistic regression). Hyperparameter tuning was done using grid search for model with tuning parameters. A parsimonious model with 1 to 20 predictors was tested. We calibrated the decision threshold to assess the cut-off yielding 95% sensitivity. The final model was deployed as a web application.
Results: A total of 55,615 cases of OHCA were included. Extreme gradient boosting was the best model. Variables that contained information on initial presentation, prehospital interventions and critical time intervals completely dominated variable importance. The standard decision cut-off (50%) had sensitivity 77.2%, specificity 98.4%, positive predictive value (PPV) 86.0%, negative predictive value (NPV) 97.2%. Maximizing Youden index suggested a decision threshold at 7.9% (sensitivity 92.4%, specificity 92.3, PPV 60.3%, NPV 99.1%). To achieve sensitivity at 95%, the decision threshold was set at 4.6% probability of survival, resulting in sensitivity 95.1%, specificity 89.1%, PPV 52.2% and NPV 99.3% in test data. Refitting the final model with the top 1 to top 20 predictors showed that there was no difference between the top 10 predictors and all 474 predictors with regards to AUC ROC (p = 0.20). The final model showed excellent calibration across all probabilities.

Conclusion: Survival in OHCA can be estimated reliably using a machine learning model incorporating variables available in most health care settings worldwide.
Acknowledgements This work was funded by the Swedish Research Council [2019-02019].

000055

Decision support system for the prognostication of neurological outcome in the successfully resuscitated OHCA patient: Machine learning analysis using multi-center registry data

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Intensive Care Medicine Experimental 2022, **10(2)**: 000055

Introduction: This study uses machine learning and multi-center registry data for analyzing the determinants of favorable neurological outcome in the out-of-hospital cardiac arrest (OHCA) patient and developing its decision support systems for various subgroups.
Methods: Data came from Korean Cardiac Arrest Research Consortium registry with 2679 OHCA patients aged 18 or more with the return of spontaneous circulation (ROSC). The dependent variable was favorable neurological outcome (Cerebral Performance Category scores 1–2) and 68 independent variables were included, e.g., first monitored rhythm, in-hospital cardiopulmonary resuscitation (CPR) duration and post-ROSC pH. The random forest was used for identifying major determinants of favorable neurological outcome and developing its decision support systems for various subgroups stratified by major variables.
Results: Based on random forest variable importance, major determinants of OHCA outcome were in-hospital CPR duration (0.0824), in-hospital electrocardiogram on emergency room arrival (0.0692), post-ROSC pH (0.0579), prehospital ROSC before emergency room arrival (0.0565), coronary angiography (0.0527), age (0.0415), first monitored rhythm (EMS) (0.0402), first monitored rhythm (community) (0.0401), early coronary angiography within 24 h (0.0304) and scene arrival to CPR stop (0.0301). It was also found that patients can be divided to 6 subgroups in terms of prehospital ROSC and first monitored rhythm (EMS) and that a decision tree can be developed as a decision support system for each subgroup to find its effective cut-off points regarding in-hospital CPR duration, post-ROSC pH, age and hemoglobin.
Conclusion: We identified the major determinants of favorable neurological outcome in successfully resuscitated OHCA patients using machine learning. This study demonstrated the strengths of the random forest as an effective decision support system for each stratified subgroup (prehospital ROSC and first monitored rhythm by EMS) to find its own optimal cut-off points for major in-hospital variables (in-hospital CPR duration, post-ROSC pH, age and hemoglobin).

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Acknowledgements This work was supported by the Ministry of Science and ICT of South Korea under the National Research Foundation of Korea grant (No. 2019R1A2C1007110).

000060

The relationship between cooling rate and neurological outcome at targeted temperature management at 33 °C after cardiac arrest

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Intensive Care Medicine Experimental 2022, **10(2)**: 000060

Introduction: It is inconclusive if the early achievement of target body temperature (BT) during targeted temperature management (TTM) in comatose cardiac arrest survivors is associated with neurologic outcome.
Objectives: We examined the association between cooling rate at induction phase and 6-month neurologic outcome in out-of-hospital cardiac arrest (OHCA) survivors who underwent TTM.
Methods: This retrospective observational study used data prospectively collected from adult comatose OHCA survivors treated with TTM at Chonnam National University Hospital in Gwangju, Korea, between October 2015 and December 2020. We measured core BT via esophageal probe and recorded at every 5 min throughout TTM. We defined the induction time as the elapsed time between the initiation of TTM and the achievement of target temperature of 33 ℃. We calculated the cooling rate as the change of BT divided by induction time. The primary outcome was a poor neurologic outcome at 6-month, defined as cerebral performance category 3–5.
Results: Of the OHCA survivors, 218 patients were included, and 137 (62.8%) patients had poor neurologic outcome. Patients with poor neurologic outcome had lower BT at initiation of TTM and shorter induction time, and higher cooling rate than those with good neurologic outcome. After adjusting for confounders, induction time (odds ratios [OR] 0.995; 95% confidence intervals [CI], 0.992–0.999) and cooling rate (OR 2.362; 95% CI, 1.1784.734) were independently associated with poor neurologic outcome.
Conclusion: In the present study, cooling rate was independently associated with poor neurologic outcome in OHCA survivors who underwent TTM at 33 °C.

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000067

The associations between electrocardiogram findings and mortality in patients with traumatic brain injury

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Intensive Care Medicine Experimental 2022, **10(2)**: 000067

Introduction: Electrocardiogram (ECG) patterns can change, especially in patients withcentral nervous system disorders such as spontaneous subarachnoid hemorrhage.However, the association between the prognosis of traumatic brain injury (TBI) andECG findings is unknown.
Objectives: This study aimed to compare and to analyze ECGfindings to predict early mortality in patients with TBI.
Methods: This retrospectiveobservational study included patients with severe trauma and TBI who were admittedto the emergency department (ED) between January 2018 and December 2020. TBIwas defined as an abbreviated injury scale score of the head of ≥ 3. We examinedECG findings, including PR prolongation (≥ 200 ms), QRS complex widening (≥ 120 ms), corrected QT interval prolongation

(QTP, ≥ 480 ms), ST-segment elevation, andST-segment depression (STD) at ED arrival. The primary outcome was 48-h mortality.
Results: Of the total patients with TBI, 1024 patients were included in this study and48-h mortality occurred in 89 patients (8.7%). In multivariate analysis, QTP (odds ratio[OR], 1.934; confidence interval [CI], 1.164–3.124) and STD (OR, 8.387; 95% CI,5.038–13.962) were independently associated with 48-h mortality in patients with TBI.The areas under the curve (AUCs) of the revised trauma score (RTS), injury severityscore (ISS), QTP, STD, and the combination of QTP and STD were 0.790 (95% CI,0.764–0.815), 0.632 (95% CI, 0.602–0.662), 0.605 (95% CI, 0.574–0.635), 0.723 (95%CI, 0.695–0.750), and 0.786 (95% CI, 0.759–0.811), respectively. The AUC of thecombination of QTP and STD significantly differed from that of ISS, QTP, and STD, butnot RTS.
Conclusion: ECG findings, including QTP and STD, may help predict 48-hmortality in patients with TBI.

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000091

Association between insulin administration method and six-month neurological outcome in survivors of out-of-hospital cardiac arrest who underwent targeted temperature management

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Introduction: Conventional glucose control (< 180 mg/dL) rather than intensive glucose control (81 to 108 mg/dL) is proper method to control hyperglycemia and continuous insulin infusion is preferred route in critically ill patients. However, the optimal glucose control range is unclear and clinical difference according to the insulin administration in cardiac arrest survivors had not been examined.
Objectives: We investigated the association between insulin treatment method and 6-month neurological outcomes in out-of-hospital cardiac arrest (OHCA) survivors who had hyperglycemia after the return of spontaneous circulation (ROSC).
Methods: We extracted the data of comatose adult OHCA survivors who underwent targeted temperature management (TTM) between 2015 and 2018 from a multicenter prospective registry. Blood glucose levels after ROSC and every 4 h after the initiation of TTM were obtained for 72 h. The insulin treatment method was divided into three categories: subcutaneous (SQI), intravenous bolus (IBI), and continuous intravenous (CII). We calculated glucose characteristics, including the maximum, mean, minimum glucose, and standard deviation (SD) of glucose and defined moderate (< 70 mg/dL) and severe (< 40 mg/dL) hypoglycemia. The primary outcome was the 6-month neurological outcome based on the Cerebral Performance Category (CPC) scale (good, CPC 1–2; poor, CPC 3–5). The secondary outcome was glucose characteristics.
Results: Of the 549 patients, 438 (79.8%) had poor neurological outcomes, 134 (24.4%), 132 (24.0), and 283 (51.5%) were in the SQI, IBI, and CII groups, respectively. Compared to the CII group, the SQI (adjusted odds ratio [aOR], 0.660; 95% confidence intervals [CIs], 0.335–1.301) and IBI (aOR, 1.757; 95% CIs, 0.867–3.560) groups were not independently associated with poor neurological outcomes. The CII (168 mg/dL [147–202]) group had the lowest mean glucose than the SQI (181 mg/dL [156–218]) and IBI (184 mg/dL [162–216]) groups. The IBI (50.8 [39.1–72.0]) group had higher SD than the SQI (47.0 [33.2–61.1]) and CII (45.0[33.9–63.5]) groups. IBI and CII groups had severe hypoglycemia in 8 (6.1%) and 9 (3.2%), respectively. Moderate hypoglycemia was not different among groups.
Conclusion: Insulin treatment method was not associated with the 6-month neurological outcomes. However, CII group had better glucose characteristics regarding lower mean glucose and lower SD than the SQI and IBI groups.

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000122

Accuracy of diagnosis of drug overdose in emergency room

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Intensive Care Medicine Experimental 2022, **10(2)**: 000122

Introduction: The number of drug overdose visits to emergency department is increasing every year. In previous studies, they found that self-reported drug ingestion histories are often inaccurate. Besides, in many cases, patients with acute intoxication present to ED with impaired consciousness, some may be uncooperative and violent. Inaccurate and insufficient medical information can lead to misdiagnoses and diagnostic delays, which make patients more susceptible to many complications and sometimes even fatal consequences. Thus, there is an increasing need to construct reliable diagnostic tool for drug overdose patients.
Objectives: In patients with acute drug overdose, identification of drugs ingested is crucial to make precise diagnosis. In most cases, the initial diagnoses are made on the basis of medical signs and reported information rather than diagnostic tests. In this study, we aim to evaluate the accuracy of diagnosis made based on the history taking by comparing with the results from urine toxicology test, and investigate clinical factors that affect to diagnostic errors.
Methods: We performed a retrospective study of drug overdosed patients over 18-year-old who presented to the emergency center from 2017 to 2019. Specimens from urine were tested using ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-TMS). The test results were compared with information obtained from patients. Diagnostic accuracies for drug detection in intoxicated patients were calculated. Logistic regression analysis was used to examine the association of clinical characteristics and diagnostic accuracy.
Results: In total, 370 patients were included in the analysis. Overall, 66 types of drugs were detected by UPLC-TMS and the most frequently detected drugs were zolpidem (104, 27.8%), citalopram (70, 18.7%), and paracetamol (66, 17.6%). The diagnostic accuracy was 100% in 131 (35.4%) patients and 0% in 113 (30.5%) patients. In univariate analysis, there were significant differences between the two groups in the following clinical parameters; underlying depression or other psychiatric disease, heart rate, mean arterial pressure, number of overdosed and detected drugs. The logistic regression analysis showed significantly lower diagnostic accuracy in patients with underlying depression (OR 3.14; P = 0.000) and patients with multidrug intoxication (OR 1.72; P = 0.000).

Conclusion: In ED patients with acute drug overdose, the diagnoses made on history alone were often inaccurate. The urine toxicology test such as UPLC-TMS should be performed as a confirmatory instrument to improve accuracy for evaluating patients with drug intoxication.

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Acknowledgements The author(s) received no financial support for the research and authorship of this article.

000168

Factors Affecting Survival to Hospital Discharge Following Extracorporeal Cardiopulmonary Resuscitation in Patients Who Underwent In-hospital Cardiac Arrest in General Ward

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Introduction: Extracorporeal cardiopulmonary resuscitation[ECPR] refers to emergent initiation of veno-arterial(VA) extracorporeal membrane oxygenation[ECMO] in cardiopulmonary arrest. ECPR has shown encouraging outcome in survival rate by recent study, and It is becoming more common. However, since ECMO requires specially trained teams and expensive equipments, most of the studies have been conducted on intensive care unit or cardiac catheterization labaratory cases. Only a few studies have reported ECPR for general ward patients.
Objectives: The purpose of this study was to identify the factors affecting survival to hospital discharge in adults resuscitated with ECPR following In-hospital cardiac arrest[IHCA] at general wards.
Methods: This was a single-tertiary hospital retrospective cohort study of ECPR patients between January 2015 and December 2021. Multiple logistic regression analysis was used to identify independent factors of survival to hospital discharge. Then, we investigated the trend of the time form cardiac arrest to initiation ECMO over the study period.
Results: From 811 IHCA treated in general wards over 7 years, 70 ECPR patients(8.6%) were identified. Median age was 64[56–73]years and 55 men(78.6%). Cardiac etiology was verified in 51 patients(83%). Overall, 20 patients(29%) survived after their hospitalization. In the multivariate logistic regression, total cardiac arrest time (odds ratio[OR] = 0.96; 95% confidence interval[CI], 0.92–0.99; P = 0.026) and prior history of cardiac arrhythmia(OR = 3.47; 95% CI, 1.05–11.18; P = 0.037) were independently associated with survival to hospital discharge. The time from cardiac arrest to initiation of ECMO decreased over the time during the study period(B = − 4.90[min/year], P < 0.001).
Table. Factors independently related to survival to hospital discharge

Variable	OR	Lower	Upper	P value
Total cardiac arrest time	0.96	0.92	0.99	0.026
History of arrhythmia	3.47	1.05	11.18	0.037

Conclusion: Prior history of cardiac arrhythmia and total cardiac arrest time are independent factors associated with survival to hospital discharge for ECPR at general wards. And the time from cardiac arrest to initiation of ECMO shortened over the years.

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001163

Characteristics of Motorcycle and Non-Motorcycle Crash Patients with Traumatic Brain Injury: A 10-year Retrospective Study at a Level One Urban Trauma Center

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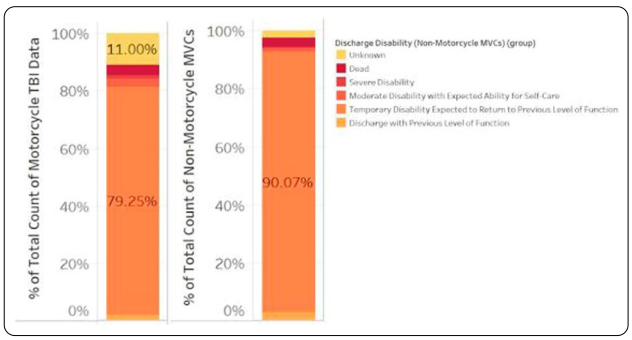
Introduction: Traumatic brain injuries (TBIs) are a contributing factor in over one-third of all injury-related deaths and a leading cause of mortality in motor vehicle crashes (MVCs). Given the high velocity mechanism of injury, understanding the difference between TBI in motorcycle MVCs (mMVCs) versus non-motorcycle MVCs (nmMVCs) is vital. Moreover, a better understanding of the patient demographics is essential for designing effective prevention methods and treatments.
Objectives: To describe the demographics of the patient population diagnosed with TBI after mMVCs, and to distinguish the ways in which outcomes may differ between patients diagnosed with TBI after mMVCs compared to nmMVCs.
Methods: We performed a retrospective review of all patients admitted with a diagnosis of TBI to an urban level 1 trauma center from January 1st, 2010 to December 31st, 2019. Patients who were injured in MVCs were identified and were split into two groups- those injured in mMVCs, and those injured in nmMVCs. TBI severity was determined using the admission Glasgow Coma Scale (GCS). A GCS of 3–8 was defined as severe, 9–12 was moderate, and 13–15 was mild TBI.
Results: Of the 2,908 patients presenting with TBI caused by MVCs, 408 patients were involved in mMVCs with the remaining 2,500 patients involved in nmMVCs. 37.75% (154) of the mMVC patients were white and 37.25% (152) were black. 91.18% (372) of the patients were male. 19.49% (30) of white mMVC patients were admitted with severe TBI, compared to only 6.58% (10) of black patients. In the severe TBI group, there were significantly more black patients discharged with temporary disability than whites, whereas death and severe disability were more prevalent in white patients than in black patients. Demographics of nmMVC patients showed that 23.48% of the patients were female, 52.64% were male, and the remaining 23.88% were not

recorded. The distribution of the GCS on admission was very similar between the mMVC and nmMVC patients, with 71.32% and 75.32% (respectively) coming in with a GCS of 15. 12.99% (53) of the mMVC patients and 10.04% (251) of the nmMVC patients had an admission GCS between 3 to 8. Overall, 3.68% (15) mMVC patients and 4.52% (113) nmMVC patients died, and 93.3% (14) and 83.19% (94) of those patients were classified as severe TBI patients, respectively.



Conclusion: In our cohort, severe TBI was slightly higher in mMVC than nmMVC patients. The admission GCS seems to be a good predictor of survival; As majority of patients who died in both groups had an admission GCS of 3–8. The age distributions between the mMVC and nmMVC patients were similar, with the majority being between 18 and 29. Comparatively, more white mMVC patients presented with severe TBI injuries, leading to worse discharge outcomes than black mMVC patients. Despite assumptions that motorcycle accident patients do worse than nmMVC patients, our study shows that with proper hospital care, patients with the same TBI severity levels from mMVCs and nmMVCs have similar outcomes.

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Trauma & Emergency Medicine 2

000245

The differences in effectiveness of public access defibrillation with automated external defibrillators for out-of-hospital cardiac arrest according to the cause of cardiac arrest

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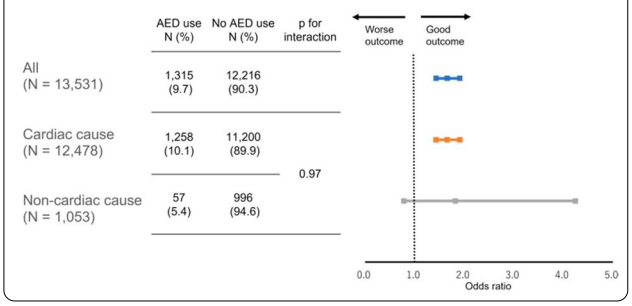
Intensive Care Medicine Experimental 2022, **10(2)**: 000245

Introduction: Early defibrillation in out-of-hospital cardiac arrest (OHCA) is associated with better outcomes. The effectiveness of early defibrillation may differ according to the etiology of ventricular fibrillation, as the prognosis of OHCA differs according to the etiology of cardiac arrest.
Objectives: We aimed to investigate the differences in effectiveness of public access defibrillation with automated external defibrillators (AEDs) according to cause of cardiac arrest in adult OHCA patients.
Methods: This was a retrospective cohort study using the All-Japan Utstein registry between 2013 and 2017. We included adult OHCA patients with initial shockable rhythm. They received witnessed bystander cardiopulmonary resuscitation (CPR). We dichotomized study participants by cause of cardiac arrest: cardiac or non-cardiac. Characteristics and treatment were compared between the two groups. Then logistic regression analyses were conducted to investigate interaction between effectiveness of public access defibrillation and cause of cardiac arrest. The primary outcome was favorable neurological outcome (CPC score of 1 or 2) at one month.
Results: Among 625,068 patients, a total of 13,531 patients were eligible for this study. Of those, 12,478 patients with cardiac cause and 1,053 patients with non-cardiac cause were identified. Patients with cardiac cause were younger than those with non-cardiac cause [65 (55–76) vs. 72 (57–82) years, $p < 0.01$]. AED was used more frequently in patients with cardiac cause than in those with non-cardiac cause (10.1% vs. 5.4%, $p < 0.01$). All patients received at least one more defibrillation by emergency medical service (EMS) personnel. Patients with cardiac cause had shorter time periods from witness to first defibrillation by EMS personnel [11 (7–13) vs. 13 (9–15) min., $p < 0.01$] and witness to hospital arrival [32 (26–39) vs. 32 (28–42) min., $p = 0.048$]. There was no difference in witness-to-bystander-CPR time between patients with cardiac and non-cardiac cause. Favorable neurological outcome was more frequent in patients with cardiac cause than in those with non-cardiac cause (28.6% vs. 11.2%, $p < 0.01$). The logistic regression analysis adjusting patients' characteristics, treatment, and time courses of CPR showed that AED use was associated with favorable neurological outcome in patients with cardiac cause [OR (95% CI): 1.65 (1.43–1.91), $p < 0.01$] whereas it was not associated in patients with non-cardiac cause [OR (95% CI): 1.82 (0.78–4.24), $p < 0.01$]. The interaction between AED use and cause of cardiac arrest was not observed (p for interaction = 0.97) in the outcome.

Figure: The association between automated external defibrillator (AED) use and favorable neurological outcomes stratified by cause of cardiac arrest.



Conclusion: The effectiveness of earlier defibrillation by lay-persons for OHCA did not significantly differ according to cause of cardiac arrest. In addition, it was not found in patients with non-cardiac cause. Strategy of CPR for OHCA patients with non-cardiac cause could be reconsidered, such as adding earlier treatments specific to cause.

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Acknowledgements None.

000270

Impact of trained intensivist coverage on survival outcomes after in-hospital cardiopulmonary resuscitation: A nationwide cohort study in South Korea

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Intensive Care Medicine Experimental 2022, **10(2)**: 000270

Introduction: The physician staffing pattern in the intensive care unit (ICU) has been an important issue in critical care.

Objectives: We aimed to investigate whether trained intensivist coverage affects survival outcomes following in-hospital cardiopulmonary resuscitation (ICPR) for in-hospital cardiac arrest (IHCA).
Methods: All adult patients who received ICPR for IHCA between January 1, 2016, and December 31, 2019, in South Korea, were included. The study population consisted of two groups (patients who received ICPR during ICU stay and patients who received ICPR in the ward and received post-ICPR care in the ICU). Patients who received ICPR in hospitals with trained intensivist coverage for ICU staffing were defined as the intensivist group, whereas other patients were considered as the non-intensivist group.
Results: In total, 68,286 adult patients (36,025 [52.8%] in the intensivist group and 32,261 [47.2%] in the non-intensivist group) were included in the analysis. After propensity score (PS) matching, 40,058 patients (20,029 in each group) were included. In logistic regression after PS matching, the intensivist group showed a 1.20-fold (odds ratio: 1.20; 95% confidence interval [CI]: (1.15 to 1.25); $P < 0.001$) higher live discharge rate after ICPR than the non-intensivist group. In Cox regression after PS matching, the 6-month and 1-year mortality rates in the intensivist group after ICPR were 12% (hazard ratio [HR]: 0.88; 95% CI: (0.86 to 0.90); $P < 0.001$) and 11% (HR: 0.89; 95% CI: (0.87 to 0.90); $P < 0.001$) lower than those in the non-intensivist group, respectively.
Conclusion: Trained intensivist coverage in the ICU was associated with both short- and long-term survival outcomes after ICPR for IHCA in South Korea. This suggests that employing a trained intensivist in the ICU might improve outcomes of ICPR. Future studies are needed to confirm our findings considering the importance of acute-phase care and post-resuscitation care.

000303

Coagulation measures after cardiac arrest (CMACA)

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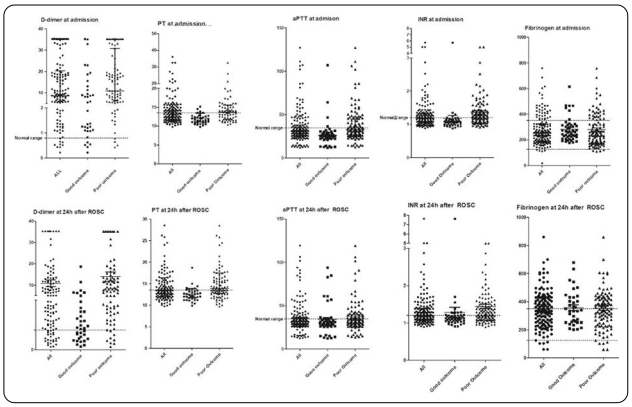
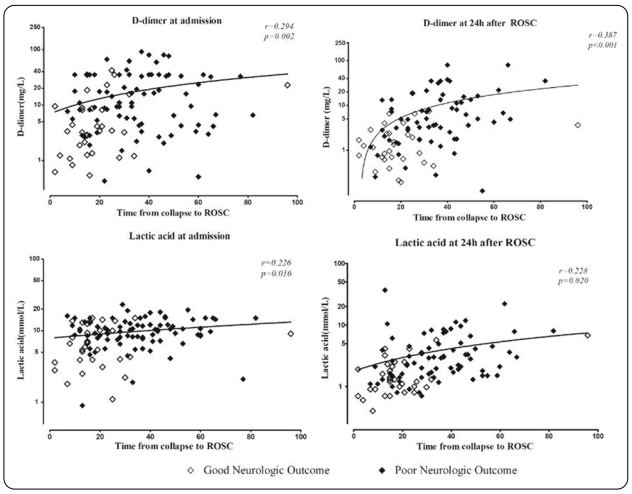
Intensive Care Medicine Experimental 2022, **10(2)**: 000303

Introduction: During cardiac arrest and after cardiopulmonary resuscitation, activation of blood coagulation occurs, with a lack of adequate endogenous fibrinolysis. The aim of the present study was to describe the time course of coagulation related factors and its association with neurologic outcomes in patients undergoing targeted temperature management after out-of hospital cardiac arrest.
Methods: This prospective, multicenter, observational cohort was performed eight emergency departments in the Korean Hypothermia Network between September 2018 and September 2019. Laboratory findings were measured at hospital admission and 24 h after ROSC. Primary outcome was CPC at discharge and secondary outcome was survival at hospital discharge. Logistic regression was used for both univariable and multivariable analysis.
Results: A total 170 patients were included in this study. Except for D-dimer, the total median values of coagulation factors were within the normal range. However, when divided by neurological outcomes, except for fibrinogen, other coagulation factors showed a difference between good and poor neurological outcomes. D-dimer were higher in poor neurologic outcome group at admission (median 3.54, IQR = 1.24–9.98 vs median 10.95, IQR = 4.144–32.33) and 24 h after ROSC (median 1.16, IQR = 0.46–3.65 vs median 3.96, IQR = 1.80–28.14). In multivariate logistic regression analysis, only D-dimer at 24 h after ROSC was associated with poor neurologic outcome at hospital discharge after adjusting confounding factors. (OR = 1.207, 95% CI = 1.043–1.396).





Conclusion: These results shows that D-dimer at 24 h after ROSC is associated with poor neurologic outcomes.

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000312

Plasma and urine pharmacokinetics of linezolid in critically ill septic patients with renal failure: are standard doses excessive or necessary to treat urinary tract infections?

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Intensive Care Medicine Experimental 2022, **10(2)**: 000312

Introduction: Recent studies have suggested a reduced linezolid (LNZ) dose in patients with renal failure, but no data are available about the urinary concentrations achieved in those patients and if they may be enough for the treatment of urinary tract infections (UTI).
Objectives: To describe plasma and urine concentrations of LNZ in critically ill patients with renal dysfunction and to evaluate the urinary recovery and the achievement of a pharmacokinetic/pharmacodynamic (PK/PD) target for UTI.
Methods: Single center, prospective PK study in 20 adult critically ill patients with renal failure (baseline estimated GFR < 60 ml/min) treated with LNZ (600 mg/12 h iv) for > 72 h. Blood and urine samples were drawn on day 3 of treatment at start (Cmin) and after 1 (Cmax), 4, 8 and 12 h. LNZ plasma and urine concentrations were measured by HPLC. Therapeutic range for LNZ in plasma was defined as 2–8 mg/L. PK parameters and LNZ urinary recovery 0–12 h (% dose) were calculated. Data are described as frequencies (%) and median (range).
Results: Twenty patients were included: 11(55%) males, 85(63–93) years old, APACHE-II: 20(15–36); SOFA: 9(5–14). Seven (35%) patients presented an UTI caused by *E. faecium and E.faecalis* (MIC: 1–2 µg/mL). Clinical parameters: LNZ dose: 16.6(12.9–23.1) mg/kg/day, estimated GFR: 30(9–24) mL/min. Clinical cure 65% and 30-day all-cause mortality 35%. Clinical and microbiological cure among patients with UTI caused by LNZ-sensible microorganisms was 100%. PK parameters in plasma: median Cmin 9.4 (0.4–18.7) mg/L, patients with Cmin 2–8 mg/L: 3/18 (16.7%), Cmin < 2 mg/L: 5/18 (27.8%), Cmin > 8 mg/L: 10/18 (55.6%), Cmax 18.5 (8.1–60.8) mg/L, AUC0-12 h 133.5 (29.6–398.1) mg*h/L, Clearance 2.7 (0.8–17.8) L/h, half-time 6.6 (2.0–12.3) h and volume of distribution 0.4 (0.2–0.9) L/kg. Urinary recovery in 12 h: 4% (0.2–30.9) of the dose, volume of urine in 24 h: 1300 (162–2520).

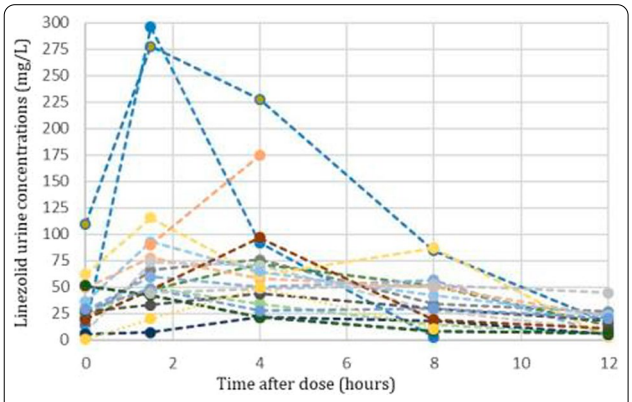

Fig. 1 Individual urine linezolid concentrations

Conclusion: This is the first study evaluating the urine concentrations of LNZ in critically ill patients with renal failure. LNZ urinary recovery was much lower than previously described for healthy volunteers, but urine concentrations remained much above the most common MICs.

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Acknowledgements This research received no funding.

000340

The use of a cooling protocol in patients admitted to the ICU following cardiac arrest and the care delivered: a review of targeted temperature management and patient outcomes

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Intensive Care Medicine Experimental 2022, **10(2)**: 000340

Introduction: In Scotland, there are approximately 3200 annual out-of-hospital cardiac arrests (OHCAs) with 10% surviving until hospital discharge (British Heart Foundation 2022). The Scottish Government has published a national cardiac arrest strategy which seeks to increase the OHCA survival rate to 15% by 2026 (Scottish Government 2021). Targeted temperature management (TTM) is the recommended treatment after cardiac arrest for those who remain unresponsive following return of spontaneous circulation (ROSC). Patients are actively cooled to a constant core temperature between 32 and 36C for 24 h, with fever avoided for up to 72 h after ROSC (Nolan et al. 2021). Cooling is a neuroprotective therapy to reduce secondary brain injury and optimise neurological recovery after cardiac arrest (McDonnell 2018).
Objectives: This study aims to compare clinical management of TTM in cardiac arrest patients who were admitted to an ICU and any impact on neurological recovery and mortality.
Methods: A clinical audit was conducted to measure practice against a published protocol for management of TTM. Quantitative study involving retrospective data from routinely collected clinical information which was obtained from ICCA and WardWatcher. Patients ≥ 18 years who were admitted to ICU with cardiac arrest between 1st January 2020 to 31st December 2021 were included. Neurological recovery was assessed using the Cerebral Performance Category (CPC) Scale, where good neurological recovery was defined as a CPC of 1–2 and poor neurological recovery was defined as a CPC of 3–5. Data were analysed using descriptive statistics.
Results: A total of 113 patients were identified. 51 patients met the inclusion criteria and were included in the data analysis. 78% of patients (n = 40) developed a fever within 72 h of ICU admission. Fever most commonly occurred whilst patients were not being actively cooled (52%, n = 26), and in reduced or no sedation (82%, n = 41). Patients with a good neurological recovery spent less time on average with a recorded temperature ≥ 37.5C than those with a poorer neurological recovery (8 h (SD = 8.65) VS 11 h (SD = 11.72)). Patients with a good neurological outcome had less temperature variation from the set targets of the ICU cooling protocol than patients with poor neurological outcomes (SD to the mean of patients' hourly recorded temperatures was 0.531 to 0.842 VS 0.256 to 3.639, respectively).
Conclusion: This clinical audit suggests inconsistent clinical practice may be related to poor temperature control in patients admitted to the ICU for TTM, resulting in greater variations in core temperatures and poorer neurological outcomes/mortality. Inconsistencies reported include the length of time patients received active cooling, fever prevention and shivering management. It became apparent from conducting this audit that the approach to care delivery within the study population was often unstandardised. There is a strong requirement to improve the quality of TTM delivered for this patient group.

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Acknowledgements
1. NHS Grampian, Practice Education.
2. Helen Paddon (Nurse Manager), Critical Care.

000348

Therapeutic drug monitoring of β-lactam antibiotics in a mixed population of critically ill patients: a single-centre experience

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Intensive Care Medicine Experimental 2022, **10(2)**: 000348

Introduction: Pathophysiological derangements in critical care patients are responsible for major alterations in the pharmacokinetic (PK) profile of drugs. Commonly used antibiotics, such as the β-lactam antibiotics (βLA), are therefore highly susceptible to PK variability (1). This could result in inadequate antibiotic dosing leading to either therapy failure or toxicity. Therapeutic drug monitoring (TDM) of βLA is a useful tool to measure antibiotic plasma concentrations in critically ill patients treated with βLA (2).
Objectives: To analyse patient characteristics and main indications for TDM of βLA in the intensive care unit (ICU). Furthermore, we analysed the incidence of correct pharmacokinetic/pharmacodynamic (PK/PD) target achievement and dose adjustments following the interpretation of the TDM result.
Methods: Retrospective, observational review of all βLA TDM results (n = 91) (piperacillin, meropenem, ceftazidim, ceftriaxon and flucloxacillin) of 57 patients who were admitted at the ICU of AZ Sint-Jan hospital (Bruges, Belgium) between 2018 and 2021. βLA free plasma concentrations were measured using a validated sample preparation by ultrafiltration and subsequently measured by Liquid Chromatography-Diode Array Detection (LC-DAD). PK/PD target attainment was defined as βLA free concentration above the MIC 100% of the time (fT > 1xMIC) or 100% fT > 4xMIC and toxicity risk as free plasma concentrations exceeding 10-times the breakpoint for resistance (BP-R). PK/PD targets were calculated using the measured MIC and if MIC was unknown, using the epidemiological cutoff value (ECOFF) or EUCAST BP-R.
Results: The main reasons for TDM of βLA in the ICU were renal replacement therapy (RRT) and veno-venous extracorporeal membrane oxygenation (VV-ECMO) (33%), high MIC values (18%), therapy failure (15%), suspicion of toxicity (12%), and acute kidney injury (AKI) without need for RRT (11%). Adequate PK/PD targets were achieved in 66/91 (73%) cases. Antibiotic underdosing and overdosing resulted in dose adjustments in 2/5 (40%) and 25/30 (75%) cases, respectively.
Conclusion: Using standard dosing regimens, βLA free plasma concentrations were predominantly adequate despite the frequent presence of major PK influencers. The use of βLA-TDM in the ICU facilitates a more effective and individualised antimicrobial therapy and may avoid potential toxic side effects. However, standardisation of our βLA-TDM protocol was necessitated, since dose adjustments were only done in less than half of subtherapeutic and in three quarters of supratherapeutic βLA concentrations. Finally, it's our opinion that a multidisciplinary cooperation involving clinical pharmacists, clinical microbiologists and intensive care specialists is paramount for a successful antibiotic stewardship in the ICU.

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Acknowledgements No funding to declare.

000351

Angiography after Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation: A systematic review and Meta-analysis of randomized trials

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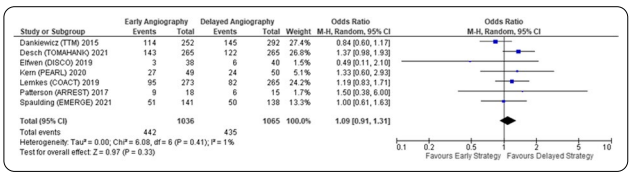
Intensive Care Medicine Experimental 2022, **10(2)**: 000351

Introduction: Out-of-hospital cardiac arrest (OHCA) has a poor prognosis. The timing and role of early coronary angiography (CAG) in OHCA patients without ST elevation remains unclear.
Objectives: To compare early CAG versus delayed CAG strategy in OHCA patients without ST elevation.
Methods: We systematically searched PubMed, Embase and Cochrane databases, in March 2021, for randomized controlled trials (RCTs) comparing.
Results: A total of 7 RCTs were included, providing a total 2101 patients, 1036 in early strategy and 1065 in delayed strategy. In terms of outcomes assesed, our meta-analysis revealed similar rate of all-cause mortality (pooled OR 1.09 [0.91, 1.31], P = 0.33, I2 = 1%), neurological status (pooled OR 0.85 [0.64, 1.14], P = 0.28, I2 = 0%), acute renal worsening (pooled OR 1.06 [0.75, 1.50], P = 0.33, I2 = 1%) and bleeding events (pooled OR 1.14 [0.80, 1.64], P = 0.47, I2 = 0%).



Conclusion: According to our meta-analysis, in patients suffering OHCA without ST-elevation, early CAG is not associated with reduced mortality or neurological status.

000368

Antithrombotic therapy and outcomes in older than 65 years with major trauma

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Intensive Care Medicine Experimental 2022, **10(2)**: 000368

Introduction: The demographic changes in the high income countries have induced that people over 65 are a vulnerable population to trauma (1). Antiplatelet and anticoagulant therapy are frequently prescribed to this group of patients, which may influence the result on patients with major trauma (2).
Objectives: To determine the impact of antiplatelet or anticoagulation therapy on the outcomes of trauma patients older than 65 years old.
Methods: An observational, retrospective cohort study of patients admitted during the period between January 2020 and October 2021 in the trauma and neurocritical unit of a level II hospital of trauma. Demographic variables, type and severity of trauma, and results of the cohort of patients older than 65 years with and without antiplatelet or anticoagulant treatment prior to trauma were included. Continuous variables are described as median and interquartile range (IQR) and were compared with Kruskal–Wallis test; categorical variables

are expressed as frequency and percentages and are contrasted with Fisher's exact test. A significance level of 5% (2-sided) was used. The analysis was performed using STATA version 13® (StataCorp LCC).
Results: There were a total of 248 admissions with major trauma. 67 (27%) were older than 65 years. 38/67 (57%) did not receive any type of antithrombotic treatment, 16 (24%) received antiplatelet treatment and 13 (19%) anticoagulants. 71.6% (48/67) were male and had a median age of 74 (70–78) years old without differences between the groups (Table 1). Frailty and comorbidity did not present differences between the groups. Falls from own height was the main mechanism of injury 45/67 (67.16%). Patients presented similar functional outcomes at discharge from the ICU and at 6 months (Fig. 1 and Table 2). In-ICU mortality was lower in patients without antithrombotic therapy (7.89%) compared to those who received antiplatelet therapy (37.5%) and anticoagulant therapy (30.7%), p = 0.015. At-6 months mortality did not present statistically significant differences (p = 0.536).

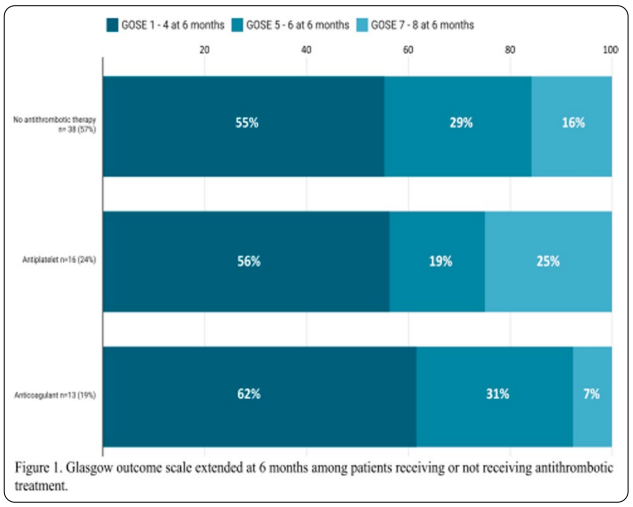

Figure 1. Glasgow outcome scale extended at 6 months among patients receiving or not receiving antithrombotic treatment.

Conclusion: Antithrombotic treatment contributed to higher in-ICU mortality in patients older than 65 years. However, mortality did not vary at 6 months of admission, nor were there differences in the functional outcomes at-6 months. These results occurred despite the fact that the main mechanism of injury was low energy. The sample size is an important limitation of the study; more clinical studies are needed.

000405

Airway Management during out-of-hospital cardiac arrest: A meta-analysis of randomized controlled trials (Effects of advanced airway on ROSC in OHCA)

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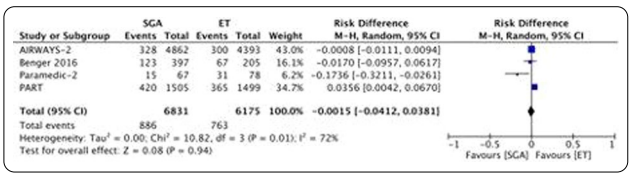
Intensive Care Medicine Experimental 2022, **10(2)**: 000405

Introduction: Out-of-hospital cardiac arrest (OHCA) represents a life-threatening condition requiring immediate treatment. During the last decade, improved treatment strategies have led to improved survival and neurological outcomes. Optimum airway strategies have changed, leading to frequent use of supraglottic airways when compared to endotracheal intubation, which was recognized as the previous gold standard. Based on the setting of OHCA, valid data on prospective controlled studies are lacking and the optimum airway strategy remains controversial.
Objectives: We aimed to evaluate the evidence on potential effects of supraglottic airway versus endotracheal intubation treatment on return of spontaneous circulation in adult patients suffering from OHCA by summarizing available randomized controlled trials.
Methods: We searched for all potentially relevant studies using the term "(Reanimat* OR resuscitat* OR CPR OR cardiopulmonary resuscitation OR cardio-pulmonary resuscitation) AND (Airway OR bag OR mask OR intubation OR endotracheal intubation OR tracheal intubation OR orotracheal intubation OR oro-tracheal intubation OR nasotracheal intubation OR naso-tracheal intubation OR laryng* OR supraglottic OR supra-glottic OR glottic OR IGEL OR I-gel OR combitub* OR Fastrach OR extraglottic OR extra-glottic OR face-mask-ventilation)". Exclusion and inclusion criteria were defined based on a study protocol. Data search included the databases PubMed, Web of Science and the Cochrane Library. Subsequently, a meta-analysis of randomized controlled studies was performed in accordance with the PRISMA statement.
Results: We identified 7,063 studies. After removing duplicates and based on the criteria valid airway assessment, age 18 years or higher, OHCA and cardiopulmonary resuscitation, 269 studies were assessed for eligibility. After exclusion due to study protocol, invalid outcome data or study population, five randomized controlled studies were included in the quantitative meta-analysis fulfilling our predefined criteria, in which 13,006 patients were analyzed. Pooled analysis indicated no mortality reduction in patients treated with a supraglottic airway device when compared to endotracheal intubation (Risk difference, − 0.0015 [95% CI, − 0.041 to 0.067]; p = 0.08; p for Cochran Q = 0.002; I2 = 56%). The assessment of bias indicates presence of significant bias based on the ROBINS-I criteria. Additionally, there was evidence for significant statistical heterogeneity.



Conclusion: The type of advanced airway (supraglottic airway versus endotracheal intubation) did not impact mortality based on current randomized controlled studies. Hence, further randomized studies are mandatory.

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000464

Analysis of the impact of the COVID-19 pandemic on trends in critical care admissions for self-harm in one UK District General Hospital

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Intensive Care Medicine Experimental 2022, **10(2)**: 000464

Introduction: There is evidence that the COVID-19 pandemic has had a significant negative impact on mental health. Studies observing the psychological effects of war and the SARS pandemic have shown that a decrease in suicide can occur initially, possibly due to a "honeymoon period" or "pulling together" phenomenon, followed by a rebound effect. However, a large UK panel survey has shown that rates of self-harm have remained constant throughout the pandemic.
Objectives: To evaluate whether there was a change in the rate and acuity of admissions to a UK District General Hospital (DGH) critical care unit for self-harm before, during and following the peaks of the COVID-19 pandemic.
Methods: We examined complete anonymised data of patients admitted for self-harm. The first epoch has 49 patients and comprised five time periods: before COVID-19, during first wave, between waves, during second wave and after the second wave. For comparison, a second epoch containing 35 patients was examined using the same dates but two years prior. Frequency analysis was performed using a Fisher's

Exact test. To assess severity, we performed a linear mixed-effects model fit by maximum likelihood using a penalised quasilikelihood (PQL) method. The fixed effects assessed were gender, highest creatinine and lactate within the first 24 h, age on admission, intubation requirement, and APACHE II scores. The random effects were epoch and time periods selected. Analysis was performed using R (version 4.1.3, Austria, Vienna) using an alpha level of 0.05.
Results: The average age (SD) of the first and second epochs were 44.3 (12.9) years and 44.9 (12.5) years respectively. There was no significant difference observed in the frequency of admissions between the epochs and COVID-19 time periods ($p = 0.34$). The linear mixed-effects model suggests that highest creatinine in the first 24 h is more likely to result in an increased length of stay (LOS) ($p = 0.0005$). The average (SD) creatinine serum concentrations were 89.4 (54.7) mmol/L and 79.6 (29.2) mmol/L respectively. Mechanical ventilation was associated with increased LOS ($p = 0.047$). The time frames and COVID-19 waves do not appear to influence LOS.
Conclusion: There was no effect on the frequency of critical care admissions for self-harm to our UK DGH before, during and after the waves of the COVID-19 pandemic. A prolonged LOS after an admission for self-harm is associated with a higher admission creatinine and need for intubation. There is no association between COVID-19 waves and severity or LOS of self-harm admissions. Our data is in line with other studies from the UK and worldwide that suggest that the COVID-19 pandemic has not led to an increase in self-harm. Thus, critical care admissions likely act as a surrogate marker for severity in real world terms. Of interest, the anecdotal evidence which informs a belief that the pandemic has caused an increase in self-harm likely represents a cognitive bias in clinicians which would be of interest to investigate further.

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000422

Delayed deterioration of electroencephalogram in cardiac arrest patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000422

Introduction: In patients with cardiac arrest (CA), highly malignant patterns (HMPs) at electroencephalography (EEG) showed a high specificity to prognosticate unfavorable outcome (UO) [1]. Patients without HMPs on initial EEG may show delayed deterioration of EEG, either for epileptic features or for background abnormalities.
Objectives: The aim of this study was to assess the prevalence of delayed deterioration on EEG in this setting and to determine their associations with clinical and biological findings.
Methods: Retrospective monocentric cohort study of adult CA patients admitted between January 2012 and December 2020 to the Intensive Care Unit (ICU) of a University hospital. We included all CA patients who had a normal voltage EEG, no more than 10% discontinuity and absence of epileptiform discharges. Delayed deterioration was classified as: a) epileptic deterioration (ED), defined as the appearance, at least 24 h after CA, of sporadic epileptic discharges (SED), any PDs (i.e., lateralized PDs [LPDs], bilateral independent PDs [BIPDs], multifocal PDs [MfPDs] and generalized PDs [GPDs]), or electrographic seizures, including status epilepticus (SE), or b) background deterioration (BD), defined as increasing discontinuity (> 10%) or progressive attenuation (< 20 μV) background 24 h after CA. To assess organ dysfunction, we used a modified SOFA (mSOFA) score, excluding data on neurologic function. The primary outcome was the incidence of EEG deteriorations. Secondary endpoints included association of the two subtypes of deterioration with clinical or biological features, ICU mortality and unfavorable neurological outcome (UO, defined as a CPC score 3–5) at 3 months.
Results: We enrolled 188 patients; ICU mortality was 46%, and 99 (53%) patients presented UO. Overall, 30 (16%) patients presented ED and 10 (5%) patients BD; of those, two patients presented both deteriorations. Among the 30 patients with ED, 14 (7%) presented SED, 24 (13%) GPDs, 1 (< 1%) LPDs and 1 (< 1%) BIPDs. Patients with ED more frequently had out-of-hospital CA (90% vs 63%; $p < 0.01$) and less frequently bystander resuscitation (37% vs. 67%; $p < 0.01$) than others. Nine (5%) had electrographic seizures with criteria of SE. Of the nine patients with BD, eight presented with progressive attenuation and one with increased discontinuity. Patients with BD showed a predominantly non-cardiac etiology (67% vs. 24%; $p < 0.01$), more frequently developed post-ROSC shock (100% vs. 48%, $p < 0.01$), multiple organ failure (mSOFA at 24 h: 11 [10–13] vs. 8 [6–9]; $p < 0.01$ – at 48 h: 12 [10–13] vs. 7 [6–9]; $p < 0.01$) and required more frequently ECMO (56% vs. 16%; $p < 0.01$) than others. Patients with ED presented a higher ICU mortality (77% vs. 41%; $p < 0.01$) and more frequently UO (90% vs 46%; $p < 0.01$) than others, while all patients with BD died in the ICU.
Conclusion: Delayed EEG deterioration occurred in 15% and was associated with high mortality rate. ED was associated with worse characteristics of CA, while BD was associated with shock and multiple organ failure.

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000423

Clinical significance of quantitative left ventricular function during in and out of hospital cardiac arrest

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Intensive Care Medicine Experimental 2022, **10(2)**: 000423

Introduction: Previous studies have shown that echocardiographic evidence of myocardial activity during cardiac arrest is a prognostic indicator of mortality. Impaired left ventricular ejection function (LVEF) is common after sustained return of spontaneous circulation (ROSC); however, its clinical significance has not been extensively studied.
Objectives: The purpose of this study was to retrospectively assess the association between LVEF and outcomes in patients with cardiac arrest.

Methods: We retrospectively analysed 857 patients' case notes, and focused transthoracic echocardiographic (TTE) findings during cardiopulmonary resuscitation (CPR), from both in-hospital (IHCA) and out-of-hospital cardiac arrests (OHCA). Data were obtained from the Cardiac Arrest Registry from 2017 to March 2021. LVEF quantification was determined via Simpson biplane method. Patients were classified in two groups: Grp1 (LVEF < 35%) and Grp2 (LVEF > 35%). Regression analyses were performed independently to evaluate for relationships between LVEF and outcome of interest, including sustained ROSC, survival to hospital admission (STHA) and survival to hospital discharge (STHD).
Results: A total of 857 patients, with a mean age of 67.78 ± 10.69 years, were included in this study; 497 patients had an IHCA, while 360 patients had an OHCA. TTE was performed on 397 out of the 857 patients, with 327 (82.37%) demonstrating cardiac activity on initial TTE. 213 of these patients (53.65%) achieved ROSC, 188 (47.35%) survived to admission and 139 (35.01%) survived to hospital discharge. A positive association between LVEF and the primary outcome of ROSC (OR 1.11, 95%CI 1.12–3.99) was observed, as well as secondary outcome of STHA (OR 1.67, 95%CI 1.79–4.97) and STHD (OR 1.81, 95%CI 3.22–8.89). In addition, a threshold effect was observed between LVEF, and primary and secondary outcomes. Grp1 is associated with lower probability for sustained ROSC (41.88%), survival to hospital admission (OR: 11.22, 95%CI: 8.77–12.25; p < 0.001), and survival to hospital discharge (OR: 13.79, 95%CI: 7.88–14.66; p < 0.001), compared with Grp2, having sustained ROSC probability of 65.42%, increased STHA (OR: 3.38, 95%CI: 3.11–5.49; p < 0.001) and STHD (OR: 2.23, 95%CI: 1.19–4.97; p < 0.001).
Conclusion: LVEF of > 35% on initial TTE is associated with sustained ROSC, STHA and STHD. We strongly recommend that TTE to be considered as core aspect of resuscitation protocol, as well as a prognostic adjunct in cardiac arrest.

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000427

Who should be treated with targeted temperature management among resuscitated cardiac arrest patients with non-shockable rhythms?

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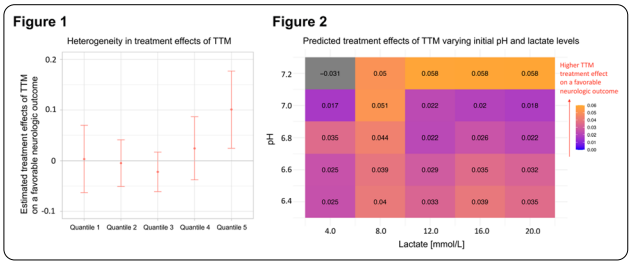
Intensive Care Medicine Experimental 2022, **10(2)**: 000427

Introduction: International guidelines recommend targeted temperature management (TTM) for all comatose patients after successful resuscitation from cardiac arrest, regardless of the initial cardiac rhythm [1–2]. However, some studies showed conflicting findings on the effects of TTM among patients with non-shockable rhythms. As such, optimal targets of TTM are still unknown [3–6]. Therefore, we aimed to evaluate heterogeneity in treatment effects of TTM and identify the optimal target of TTM among resuscitated comatose patients after out-of-hospital cardiac arrest (OHCA) with non-shockable rhythms.
Methods: This was a retrospective cohort study using a nationwide registry of OHCA patients from 93 hospitals in Japan, 2014–2019 [7]. We identified 591 patients treated with TTM from 4,235 comatose patients (score ≤ 8 on the Glasgow Coma Scale) without extracorporeal membrane oxygenation who had been resuscitated from non-traumatic and non-stroke OHCA with non-shockable rhythms. The causal forest—a machine learning-based approach to estimate heterogeneous treatment effects [8]—was applied to all comatose patients to estimate individual treatment effects (ITEs) of TTM on a favorable day-30 neurologic outcome (the Cerebral Performance Category [CPC] scale of 1 or 2) adjusted for potential confounders (e.g., age, sex, initial pH and lactate levels). After ranking patients into quintiles of estimated ITEs, we estimated the average treatment effect in each group to evaluate heterogeneity in treatment effects of TTM and attempted to explain the heterogeneity using initial pH and lactate levels, representative prognostic markers of OHCA [9]. Finally, we used the policytree algorithm [10] to choose the best criteria for TTM indication among comatose OHCA patients who initially had non-shockable rhythms, using covariates measured prior to TTM initiation.
Results: We found heterogeneity in treatment effects of TTM on a favorable neurologic outcome (Fig. 1). Initial pH and lactate levels contributed to the heterogeneity in the treatment effects, and it was suggested that patients with moderately elevated lactate levels (e.g., 8 mmol/L) and slightly decreased pH levels (e.g., 7.2) may benefit the most from TTM (Fig. 2). On the other hand, the policytree algorithm determined that targeting patients with pH < 7.0 or those with pH ≥ 7.0 and Lac > 5 mmol/L likely maximizes overall patient benefit. Indeed, based on the causal forest estimator, TTM use in this targeted subpopulation was significantly associated with a more favorable neurologic outcome (adjusted treatment effect 3.8%; 95%CI 1.6 to 5.9%), but was associated with a worse outcome in individuals not in the targeted subpopulation (adjusted treatment effect − 23.2%; 95%CI − 46.0 to − 0.3%).



Conclusion: We found that initial pH and lactate levels could effectively identify potential targets of TTM among comatose patients after resuscitated OHCA with non-shockable rhythms. Our findings could serve as a milestone for future intervention trials.

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Acknowledgements All authors have no conflicts of interest to declare.

000472

A review of thromboprophylaxis therapy in critically injured-burn patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000472

Introduction: Venous thromboembolism (VTE) is a leading cause of death and disability in the U.K and worldwide. The risk of VTE in the burn-injured patient is higher than that of the general hospital patient. The burn-injured patients display all three characteristics of Virchow's triad: endothelial damage, stasis of blood flow, and hypercoagulability. The occurrence of VTE in the burn-injured patient despite routine thromboprophylaxis therapy has spawned a whole body of research. Treatment regimens and monitoring with the use of Anti-FXa levels have played important role in helping to achieve adequate thromboprophylaxis in the burn-injured population.
Objectives: Aim To assess current thromboprophylaxis therapy in critically injured burn patients.
Hypothesis: Burn-injured patients are inadequately anti-coagulated. Therefore, at an increased risk of VTE.
Primary objective: To review if adequate thromboprophylaxis was achieved in line with Anti-FXa level monitoring.

Secondary objectives: Identify the incidence of VTE events and cross-Reference patient demographics, burn severity, and known risk factors to help identify patient-specific groups that are more at risk of inadequate thromboprophylaxis and thereby VTE.
Methods: A retrospective single-centre cohort study was conducted over a three-year between January 2018 – January 2021. All adult patients (18 yr and over) admitted with burn injuries to the critical care with at least one Anti-FXa level result were included. The first Anti-FXa level was reviewed against the pre-defined prophylactic range of 0.1–0.3 IU/ml as per the local guideline. Anti-FXa levels for the total sample population were non-normally distributed and so were divided into prophylactic (0.1 IU/ml and over) and sub-prophylactic (< 0.1 IU/ml) groups. To assess the correlation of clinical parameters with ITU mortality and length of stay, univariate and multivariate binary logistic regression models were used. Covariates included age, gender, BMI, inhalational injury, burn severity and frailty scores.
Results: Two patients were found to have confirmed VTE, which translated to an overall VTE incidence of 4.65%. From the sample population n = 43, 24 (56%) patients first Anti-FXa level was within prophylactic range (0.1 IU/ml or more), with the remaining 19 (44%) patients classified as sub-prophylactic (< 0.1 IU/ml).
The mean Anti-FXa level for the prophylactic group was 0.19 ± SD 0.10 IU/ml, compared with the mean Anti-FXa level of the sub-prophylactic group 0.04 ± SD 0.02 IU/ml. Subgroup analysis found no statistical significance associated with VTE or sub-prophylactic Anti-FXa levels. There were inconsistencies in both administration and monitoring of thromboprophylaxis with a total of 35 LMWH dose omissions and the mean number of LMWH doses received at sampling the first Anti-FXa was 4.3 (SD 7.7). This was above the recommended 3rd dose.
Conclusion: This study adds to the body of research examining thromboprophylaxis in critically injured burn patients. Data from this study does not show any statistically significant risk in VTE for the overall sample population and sub-group analysis. A more comprehensive study is required with larger sample size. Further research should focus on examining how Anti-FXa levels change over time. Performing a pharmacokinetic analysis of serial Anti-FXa levels would provide a more accurate representation of VTE risk in burn-injured patients receiving routine thromboprophylaxis.

000479

COVID-19 has a devastating effect on observational research: how the pandemic has affected inclusions in an observational study about the prognosis of ICU patients with acute intoxications (the INTOXICATE study)

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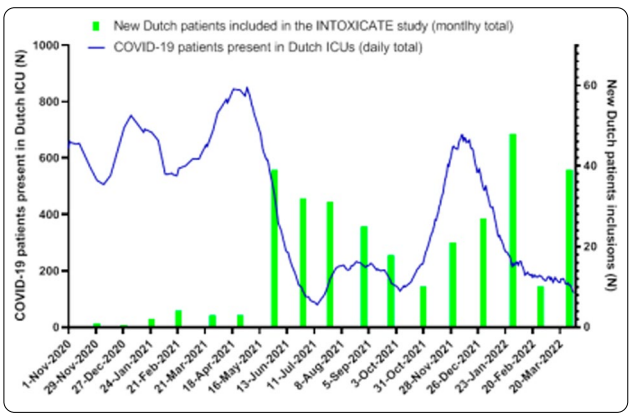
Intensive Care Medicine Experimental 2022, **10(2)**: 000479

Introduction: Since March 2020 the COVID-19 outbreak was acknowledged as a pandemic by the WHO. Previous studies have shown a decrease in COVID-19 unrelated patient visits during surges of the pandemic at the emergency department (ED) and Intensive Care Unit (ICU). The INTOXICATE study for prognosis assessment of acutely intoxicated patients at the ICU started during the pandemic. We aimed to study the relationship between the prevalence of COVID-19 patients at Dutch ICUs and patient inclusion rates in the INTOXICATE study.
Objectives: The objective of this study is to display time-series data of daily COVID-19 patient ICU prevalence and monthly inclusion rate of intoxicated ICU patients in the INTOXICATE study.
Methods: The INTOXICATE study started on 1 November 2020. Adult patients were prospectively collected in Castor Electronic Data Capture according to the declaration of Helsinki and GDPR regulations. Data from Dutch ICUs participating in the INTOXICATE study, registered between 2 November 2020 and 1 April 2022 were used. Data of COVID-19 patient admissions at Dutch ICUs are derived from the National Intensive Care Evaluation (NICE).
Results: Wthin 2 months (January 2021), 13 of the 15 participating Dutch ICUs were recruited. Two extra Dutch ICUs were recruited in March and April 2021. During the first 6 months (November 2020 – May 2021), the average monthly inclusion rate was only 2 whereas the ICU prevalence of COVID-19 patients was huge, with a peak in May 2021 at 850 COVID-19 patients admitted in Dutch ICUs. In July 2021, the number of COVID-19 patients dropped to 80 while the monthly inclusion rate in the INTOXICATE study increased to 36. The next month when the COVID-19 prevalence increased again to 233 on August 23rd the inclusion rate reduced to 31. The inclusion rate declined further to 22 during another increase in COVID-19 prevalence to 686 on the 10th of December. During the last drop in ICU COVID-19 prevalence the monthly inclusion rate increased again to 30 (Fig. 1).
Fig. 1 Number of COVID-19 patients in Dutch ICUs (blue line, left-hand y-axis) and new Dutch patient inclusions in the INTOXICATE study (green bars, right-hand y-axis)



Conclusion: The inclusions in our observational study are inversely correlated with the national COVID-19 pandemic pressure in the

Dutch ICUs during the period from November 2020 to March 2022. The immediate consequence is that the duration of the INTOXICATE study—initially planned for one year- must be extended to reach its predetermined sample size. This has major consequences for research management, finances and research ethics.

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Acknowledgements

1. This study is endorsed by the ESICM.
2. This study is endorsed by the EAPCCT.

000504

Low Kallistatin expression exacerbates post-ischemic injury in human neuronal cells and cardiac arrest survivors with poor neurological outcome

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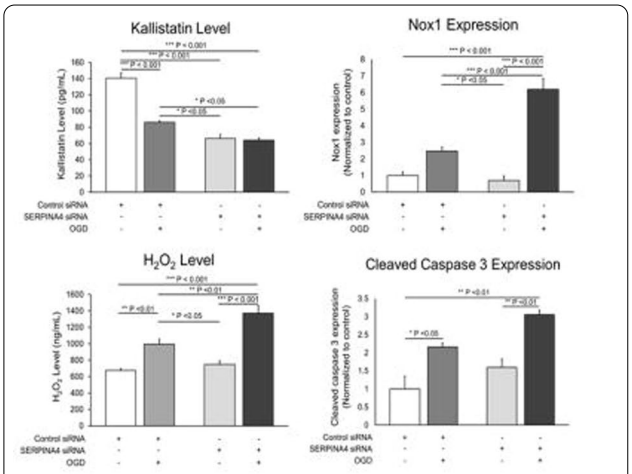
Intensive Care Medicine Experimental 2022, **10(2)**: 000504

Introduction: The neurological outcomes after cardiac arrest are still poor, and the main mechanism of brain injury after cardiac arrest is ischemia–reperfusion injury. According to a recent study, low serum levels of kallistatin are associated with poor neurological outcomes in cardiac arrest survivors. Kallistatin is encoded by the SERPINA4 gene and known to contribute to antioxidant effects by inhibiting NADPH oxidase activity. Therefore, the purpose of this study was to show that low expression of kallistatin causes excessive reactive oxygen species production and exacerbates oxidative damage in human neuronal cells and cardiac arrest survivors with poor neurological outcome.

Methods: For experimental research, SERPINA4-targeting siRNA was transfected into human neuronal cells to produce kallistatin knockdown neuronal cells. To induce ischemia–reperfusion injury, SERPINA4 knockdown and control cells were exposed to 60 min of oxygen–glucose deprivation followed by 23 h of reoxygenation, and the cell viability was measured. The levels of oxidative stress and apoptosis were compared by measuring the levels of kallistatin, NADPH oxidase (Nox-1), H_2O_2, and caspase-3 in the kallistatin knockdown cells and control cells following the treatment of each group with OGD/Reoxy. For clinical investigation, 62 cardiac arrest survivors admitted to the ICU were divided into the good (CPC 1–2) and poor (CPC 3–5) 6-month neurological outcome groups. Serum levels of kallistatin, Nox-1, H_2O_2 were measured using blood samples obtained at admission, 24 h, and 72 h after admission to the ICU.

Results: Transfection with SERPINA4 siRNA decreased the expression of kallistatin. OGD/Reoxy reduced cell viability in both the SERPINA4 knockdown cells and control siRNA cells. Nox-1 expression and H_2O_2 levels were increased in the kallistatin knockdown cells that were subjected to OGD/Reoxy. When the control siRNA group and kallistatin knockdown group were subjected to OGD/Reoxy, caspase-3 expression was elevated and apoptosis was promoted. 16 good outcome groups, 46 poor outcome groups were enrolled for the clinical investigation. Compared with good outcome groups, serum kallistatin levels were lower in poor outcome groups at all time points. Serum Nox-1 levels were higher in poor outcome groups at admission compared with good outcome groups, while H_2O_2 showed no difference at admission. At 24 h, 72 h, serum Nox-1 and H_2O_2 levels were higher in poor outcome groups compared with good outcome groups.



Comparison of serum levels of Kallistatin, Nox-1, H_2O_2 among 6-month good CPC(CPC 1-2) and poor CPC(CPC 3-5)

	Good CPC (CPC 1-2) (N=16)	Poor CPC (CPC 3-5) (N=46)	P value
At admission			
Kallistatin, μg/mL	1.01 (0.93-1.11)	0.84 (0.57-1.00)	0.011
Nox-1, μg/L	0.60 (0.16-2.02)	2.41 (0.76-3.61)	0.013
H_2O_2, μmol/L	7.91 (6.63-9.10)	8.83 (6.90-10.30)	0.21
At 24h			
Kallistatin, μg/mL	0.91 (0.70-0.98)	0.67 (0.49-0.89)	0.034
Nox-1, μg/L	1.08 (0.62-1.43)	2.27 (1.08-4.09)	0.02
H_2O_2, μmol/L	7.05 (6.45-7.64)	7.29 (6.51-8.90)	0.247
At 72h			
Kallistatin, μg/mL	0.77 (0.64-1.02)	0.62 (0.43-0.70)	0.001
Nox-1, μg/L	1.17 (0.82-1.78)	2.67 (1.30-4.62)	0.011
H_2O_2, μmol/L	6.82 (5.83-7.07)	7.27 (6.23-8.69)	0.038

Conclusion: The inhibition of kallistatin expression did not inhibit the activity of NADPH oxidase. As a result, more free radicals were generated, more H_2O_2 was produced, and more caspase-3 was expressed, thereby promoting apoptosis. Low serum kallistatin level was associated with poor neurological outcome of cardiac arrest survivors. In relation to kallistatin expression, Nox-1 and H_2O_2 were higher in the poor outcome groups, suggesting that low kallistatin expression exacerbated post ischemic injury.

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Acknowledgements None.

000525

Comparison of energy expenditure using Indirect calorimetry and Predictive equations in Trauma Patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000525

Introduction: Appropriate nutritional support for critically ill patients is now accepted as an essential element of patient care in intensive care unit. For patients with severe trauma, it is difficult to adequately assess the nutritional requirements due to hypermetabolic changes. Failure to provide adequate nutritional support can result in undernutrition or overnutrition.
Currently, indirect calorimetry is considered gold standard for measuring resting energy expenditure (REE). Several studies have reported that indirect calorimetry is more accurate than predictive equations in determining patient energy requirements. However, measuring REE by indirect calorimetry is limited in that expensive equipment and skilled personnel are required. So, medical staff treating patients with severe trauma still rely on various predictive equations to predict a patient's caloric needs.
Objectives: The aim of this study was to compare REE measured by indirect calorimetry with REE calculated by predictive equations.
Methods: This study was a retrospective study of patients admitted to the Regional Trauma Center from July 2019 to July 2020. Among adult patients (age > 18) admitted to the intensive care unit due to severe trauma (Injury Severity Score > 15), patients on mechanical ventilation were included. REE measured by indirect calorimetry within 48–72 h after admission was investigated. Experienced nutrition support team measured REE for more than 15 min. The measured REE and various prediction equations (Harris and Benedict, Faisy, Fusco, Ireton-Jones, Mifflin-St.Jeor, ESPEN) were compared and analyzed.
Results: Seventy-one patients were included in the study, 57 men (80.3%), with an average age of 57 years. The ISS mean score of the patients was 26.1 ± 9.3. The mean REE measured by indirect calorimetry was 2146.2 ± 539.7(kcal/day). The pearson correlation coefficient values between the measured REE and the calculated REE showed moderate correlation (r = 0.390–0.568). among them, the Faisy equation(r = 0.568) and the Harris-Benedict equation(r = 0.525) were found to be most related with REE measured by indirect calorimetry.
Conclusion: In severe trauma patients, predictive equations do not reflect sufficient nutritional requirements. When evaluating the nutritional requirements of trauma patients, medical staff are aware of the limitations of the equations, and efforts are needed for accurate evaluation.

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000530

Short-term outcomes of ECPR in septuagenarians and octogenarians

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Intensive Care Medicine Experimental 2022, **10(2)**: 000530

Introduction: It is widely supposed that old age is a risk factor of Extracorporeal cardiopulmonary resuscitation (ECPR). However, it has not yet been known much about effectiveness of ECPR in elderly patients. Therefore we compared short-term outcomes of ECPR in septuagenarians versus octogenarians to understand the risk of ECPR in elderly patients.
Methods: We retrospectively collected clinical data at single center. From January 2015 to December 2021, 91 septuagenarian and 27 octogenarians received out-of-hospital and in-hospital ECPR. The primary outcome was weaning success, survival to discharge and neurologic outcome after ECMO weaning.
Results: The rate of weaning success was 31.9% versus 51.9% (P = 0.09) in septuagenarians and octogenarians, respectively. Survival to discharge was 23.1% versus 37% (P = 0.23). The rate of good neurologic outcomes (cerebral performance categories scale = 1, 2) after ECMO weaning was 55.2% versus 57.1% (P = 1.0). There was no statistically significant difference in short-term outcomes between septuagenarians and octogenarians who received ECPR.
Conclusion: There was no statistically significant difference in weaning success, survival to discharge and neurologic outcome between septuagenarians and octogenarians who received ECPR. The short-term outcomes of octogenarians is also acceptable compared to ELSO registry results. Therefore, ECPR in elderly patients also needs to be carefully considered and applied.

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000328
Clinical Survey and Predictors of Outcomes of Paediatric Cardiac Arrest Admitted to Non Tertiary Centre

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Intensive Care Medicine Experimental 2022, **10(2)**: 000328

Introduction: Paediatric cardiac arrest is a relatively rare but devastating presentation with high mortality. Despite on-going efforts to improve the quality of paediatric resuscitation, it remains unknown whether survival in children with both in (IHCA) and out of hospital cardiac arrest (OHCA) has improved.
Objectives: To describe the epidemiology and outcomes of paediatric cardiac arrest in non-tertiary centres and to identify factors associated with favorable outcomes.
Methods: Case notes from the Cardiac Arrest Registry dated from 2011 to March 2022 were reviewed for patients younger than 16 years in this non-tertiary multicenter retrospective study. Data collected included demographic and etiology of cardiac arrest, initial cardiac rhythm, time of commencing resuscitation protocol and mean arterial pressure (MAP) after achieving return of spontaneous circulation (ROSC). Targeted outcomes of interest were ROSC and survival to hospital discharge (STHD).
Results: There were 103 patients [(35.9% female), 34 (33.0%) infants 11 (10.7%) neonates] in the study. The most common initial cardiac arrest rhythm was pulseless electrical activity (PEA) (71 children, 68.9%) with an increase in cardiac arrests due to PEA over time (P for trend < 0.001). OHCA was identified by bystanders in 66 cases with bystander cardiopulmonary resuscitation (CPR) was provided in only 13(19.7%) cases [Table 1]. However, all IHCA were witnessed. Most common aetiology of cardiac arrest was respiratory diseases (n = 50, 48.5%) followed by infectious diseases (n = 21, 20.4%) and cardiovascular causes (n = 11, 10.7%). Total mortality was observed at 76.6%(n = 79). Bystander CPR (OR 42.7; [95% CI], 39.3–48.7; P < 0.005), ROSC within 30 min (OR 90.0; 95% CI, 37.9–51.3; P < 0.005) and post ROSC MAP > 65 mmHg (OR 90.0; 95% CI, 23.3–57.7; P < 0.005) were good prognostic indicator for STHD.
Table 1: Patient's demographic and factors associated with favorable outcome

	All (n = 103)	Return to Spontaneous Circulation		Survival to Hospital Discharge	
		YES	NO	YES	NO
Age < 28 weeks/ < 1 years old/ > 1 years old	11/34/58	1/8/18	10/26/40	1/6/10	0/2/8
IHCA/Witnessed OHCA/ Bystander CPR	66/15/13	29/9/10	37/6/3	19/5/9	10/4/4
Time to CPR/1st Adrenaline from CPR (min)		19.7 ± 3.5/ 3.1 ± 1.9	33.3 ± 7.8/ 3.8 ± 2.4	19.9 ± 4.3/ 1.9 ± 3.9	24.8 ± 2.6/ 2.9 ± 1.5
Cardiac Etiology	11	8	3	6	2
Respiratory Etiology	50	11	39	5	6
Infectious Diseases	21	4	17	2	2
External (e.g. Hanging)	21	4	17	2	2
Cardiac Rhythm Shockable/PEA/Asystole	21/71/11	15/12/0	6/9/11	12/5/0	3/7/0

Conclusion: Outcomes for pediatric cardiac arrest continue to be poor. Witnessed arrest status, fewer adrenaline doses, ROSC within 30 min and post ROSC MAP > 65 mmHg remains associated with improved survival.

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000539 Epidemiology of cardiac arrest care and outcome: A single-center study over 18 years

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Intensive Care Medicine Experimental 2022, **10(2)**: 000539

Introduction: Sudden cardiac arrest (CA) is the third leading cause of death in Europe[1]. At least half of the patients who are resuscitated, eventually experience unfavorable long-term neurological outcome (UO)[2]. Post-resuscitation care following cardiac arrest has progressively improved over the years, aiming at improving the outcome of these patients.
Objectives: The purpose of this study was to evaluate the temporal changes in mortality and neurologic outcome in CA patients in a large database over the last 18 years.
Methods: This was a retrospective study including adult (> 18 years) CA patients who were admitted after successful resuscitation from January 2004 to December 2021 to the Intensive Care Unit (ICU) at Erasme Hospital (Brussels, Belgium). Time course was analyzed into six groups according to the years of admission (I = 2004–2006; II = 2007–2009; III = 2010–2012; IV = 2013–2015; V = 2016–2018; VI = 2019–2021). A multivariable logistic regression analysis (including age, location of arrest, time to return of spontaneous circulation—ROSC—and initial rhythm) was performed to assess whether hospital mortality and UO (defined as a Cerebral Performance Category of 3–5 at 3 months after CA) significantly changed over time, when the period I was considered as Reference. Subgroup analyses were performed according to location of arrest (out-of-hospital vs. in-hospital CA) and initial rhythm (shockable vs. non-shockable).
Results: A total of 1116 patients were included in this study: 746 patients (66.8%) died and 784 (70.2%) had a poor outcome. Over the years, there was an unadjusted significant increase of hospital mortality and UO; however, the severity of patients' population also increased over time (i.e. higher incidence of non-witnessed CA, higher incidence of non-shockable rhythm, longer time to ROSC, higher percentage of patients with shock on admission). In the multivariable analysis, period VI was associated with a significantly higher risk of mortality (OR 1.72 [95% CI 1.05–2.83]; p = 0.03) but not of UO (OR 1.54 [95% CI 0.93–2.54; p = 0.1) when compared to period I. No differences in mortality and UO was observed among different time periods in the subgroup analyses.
Conclusion: In our cohort of patients, the occurrence of mortality and UO increased over time. In particular, the last time-period had a significantly higher mortality rate than the first time period, even after correction for confounders.

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000572

Visual inspection of brain computed tomography as a practical way to predict neurological outcomes in post-cardiac arrest survivors

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Intensive Care Medicine Experimental 2022, **10(2)**: 000572

Introduction: Assessment of ischemic changes in brain computed tomography (CT) images by determining grey-white matter ratios (GWR) has become an accurate tool to predict neurological outcome in post-cardiac arrest survivors. However, the determination of GWR has limitedly been used in clinical settings due to the detailed standard protocol.
Objectives: We thus aimed to evaluate whether a visual inspection of ischemic changes in brain CT images, which is very practical in clinical settings, could predict neurological outcomes in such patients.
Methods: We retrospectively reviewed medical records and brain CT images of 62 patients who remained comatose after surviving from cardiac arrest and had a CT scan done within 24 h to 7 days. Neurological outcomes at 1 month were assessed using the Cerebral Performance Category (CPC). CPC 1–2 and 3–5 referred to good and poor neurological outcomes, respectively. Simple visual inspection of brain CT images was focused on the basal ganglia and the cerebral cortex levels. Findings from the inspection of the images were graded into grade 1, absence of ischemic change; grade 2, decreased attenuation of grey matter in some brain region(s); and grade 3, diffused loss of grey-white matter differentiation or apparent brain swelling. An experienced neurologist and a consensus group of four preclinical medical students, blinded to the neurological outcomes, evaluated the grades of ischemic changes in CT images.
Results: Positive correlations were observed between the CPC and the CT grading by both neurologist ($\rho = 0.76$, 95%CI [0.63–0.90], $p < 0.001$) and medical students ($\rho = 0.57$, 95%CI [0.38–0.77], $p < 0.001$). The CT grading of ≥ 2 by the neurologist could well predict poor neurological outcomes with a specificity of 1.00, a sensitivity of 0.89, and a receiver operating characteristic (ROC) AUC of 0.94 (95%CI [0.89–1.00]). The evaluation by medical students showed an ROC AUC of 0.80 (95%CI [0.64–0.96]). Grades of ischemic changes evaluated by neurologist and medical students were moderately correlated ($\rho = 0.61$, $p < 0.001$).
Conclusion: Visual inspection of ischemic changes in brain CT images showed a high diagnostic accuracy and could probably be considered a practical method for predicting neurological outcomes in post-cardiac arrest survivors.

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Acknowledgements Brain imaging in this study was performed at the Department of Radiology, King Chulalongkorn Memorial Hospital, Thailand.

000635

Factors Affecting Mortality and The Prognostic Value Of Scoring Systems in Traumatic Brain Injury

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Intensive Care Medicine Experimental 2022, **10(2)**: 000635

Introduction: Traumatic brain injury (TBI) is an important public health problem and is the leading cause of post-traumatic death (1). TBI patients of different severity have been followed and treated in ICUs with combined medical-surgical approaches which has changed little in the last 20 years (2). The aim of this study is to investigate the factors affecting mortality and the prognostic value of scoring systems in TBI.
Methods: After obtaining ethics approval, in this single center retrospective study, electronic files of TBI patients admitted to ICU between October 2018 and October 2019 were reviewed. The patient's age, gender, medical history, mechanism of injury, GCS at admission, imaging and laboratory results, length of hospital stay and survival were recorded. The severity of TBI was classified according to GCS as mild (GCS 13–15), moderate (GCS 9–12) and severe (GCS 3–8). Data were also collected for ISS and all CT scans were reviewed for Marshall scoring. The patient data were evaluated in terms of factors affecting mortality, scoring systems and TBI mechanisms (traffic accidents (TA), falls, violent injury and others).
Results: 102 patients were included and 27 (26.4%) of them died during their ICU follow-up. The mean age was 47.5 (±18.45) years. Mortality assessment of TBI patients according to demographic, clinical information and severity scores are present in Table 1. Comparison of patients' age, GCS, ISS and mortality according to TBI formation mechanism are shown in Table 2. The use of anticoagulants and antiaggregants and age were significantly related with mortality.
Table 1 Mortality assessment of TBI patients according to demographic, clinical information and severity scores

	Survived (n = 75)	**Deceased (n = 27)**	**Total (n = 102)**	***p***
Male/ female	59/16	19/8	78/24	0,386
Age (mean ± SD)	45.3 ± 18.45	53.7 ± 19.11	47.5 ± 18.45	0,042
Chronic disease (%)	27 (36.0)	12 (48.1)	39 (38.2)	0,485
Use of anticoagulant/ antiaggregant n (%)	8 (10.6)	8 (29.6)	16 (15.6)	0,013
GCS (severe/ moderate/ mild) (n)	23/9/43	20/2/5	43/11/48	
ISS (mean ± SD)	26.4 ± 9.7	32.3 ± 14.3	27.9 ± 11.3	0,133
Marshall score (median)	2	4	3	
ICU stay (days)	16.7 ± 19.6	20.4 ± 38.2	17.7 ± 25.7	0,322

Table 2 Comparison of patients' age, GCS, ISS and mortality according to TBI formation mechanism

	TA n = 54	Falls n = 41	Violent injury n = 2	Other n = 5	p value
Mean age (years ± SD)	42,3 ± 15.6	57,1 ± 19.3	47.0 ± 24.0	24.4 ± 8.7	> 0.05
GCS (n) severe/ moderate/ mild	24/6/24	16/5/20	0/0/2	3/0/2	> 0.05
ISS (mean ± SD)	30.0 ± 9.7	25.4 ± 12.2	19 ± 4.2	28.8 ± 17.4	> 0.05

Conclusion: Advanced age and anticoagulant/antiaggregant use is found to be corralated with mortality but when evaluated in multivariate cox regression analysis, it was found that the significance due to anticoagulant/antiaggregant use was age-related. We speculate that, after confirmation of these results by prospective trials, anticoagulant/antiaggregant use may be incorporated into trauma/injury scoring systems.

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000649

Input/Output ratio can improve current resuscitation regimes in burned patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000649

Introduction: Resuscitation fluid rates following burn injury are guided by a weight/burn size formula (Parkland formula) and then are titrated to urine output and in all the studies resuscitation is reported only as of the volume of resuscitation. Many burn centers have advocated the utilization of an intake and output ratio (I/O) as means of more effectively assessing circulation than simple volume alone.
Objectives: The aim of this study is to present data for resuscitation of a cohort group of patients in the 48 h after the burn injury by applying this ratio which takes into consideration not only the volume received but also the physiologic response.
Methods: A prospective cohort study was performed among 50 patients admitted to the ICU, with major and moderate burns. The inclusion criteria were burned patients admitted within 24 h of burn-in ICU of the Service of Burns in UHC" Mother Teresa" and survived on the first two days. Patients were divided into groups according to I/O rate in the Expected group (I/O between 0.166–0.334), Over-responders group (I/O < 0.166), and Under-responders ((I/O > 0.334).ANOVA and t-test were used for analyzing variables.
Results: After 24 h we calculated the rate and noticed that in the expected group there were 7 patients (14%), in the over-responders group there were 43 patients(86%), while there were no present patients with an under-responding ratio. Regarding burn characteristics, there were no significant differences between groups for age, gender, presence of full-thickness, and inhalation burn. There were statistical difference for TBSA burn(%) especially for patients with burn size > 40% TBSA($p = 0.02$;$p = 0.009$).In the first 24 h of comparing Input(I) values in two groups, there is a statistical significance ($p = 0.001$), while there is no significance for O(Output). Regression of I by O for two groups was with strong R2 and with statistical significance. After 48 h all the patients were over-responders (I/O rate < 0.166) and follows a normal distribution. Also, regression of the I/O ratio of the 24 h by regression of the I/O ratio of the 48 h revealed an adjusted R2 of 0.169 indicating not a strong correlation but statistical significance ($p = 0.003$). Variability in I/O ratio in 48 h increases with increasing I/O ratio in 24 h If we perform a comparison of two distributions with the Kolmogorov Smirnov test, we saw that the two distributions have significant differences $p < 0.0001$ and we can still draw important conclusions about how changes in the predictor values (I/O ratio 24 h) are associated with changes in the response value (I/O ratio 48 h).
Conclusion: I/O ratio as a novel calculation identifies three unique groups of patients and helps for the prediction of fluids in the second 24 h after burning.It should be used as another tool in the armamentarium of burn physicians in assessing the adequacy of resuscitation.

000656

Evidence of hyponatremia in patients with burns after fluid resuscitation in the first 24–48 h

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Intensive Care Medicine Experimental 2022, **10(2)**: 000656

Introduction: Generally, in critical patients, including the burned one, the irregular sodium concentrations emerge from crystalloid treatment, certain medicines, or renal function disturbance. Most resuscitation liquids are given intravenously, and the osmotic concentration of the sodium-containing liquids can contribute to modified plasma sodium concentration. The different formulae for calculation of resuscitation therapy after thermal damage recommend 0.5–0.6 mmol sodium for each % of Total Body Surface Area (TBSA) burned, suggesting fluid requirements between two to four ml/kg/% burn because of sodium loss in the burned and unburned tissues.
Objectives: The aim of the study was to examine sodium balance (sodium deficit, received, excreted, and retained) after burns.
Methods: An observational study was conducted on 150 patients hospitalized in the ICU of the Service of Burns at the University Hospital Center "Mother Teresa" in Tirana, Albania, in 2016. Of these, 50 patients were diagnosed with severe burns and, in this way, satisfied the incorporation criteria for our study. From fluid load, urine output, blood, and urine analyses, we calculated: Sodium deficit, Sodium received, Sodium excreted and Sodium retained.
Results: On admission, the mean sodium deficit of all patients was 163.1 ± 130.7 mmol, after 24 h 193.1 ± 141.3 mmol, and after 48 h 195.6 ± 144.4 mmol. Sodium deficit improved in a quarter of patients after the first 24 h and in half of the patients after the second 24 h. The mean sodium received for all patients in the first 24 h was 0.51 ± 0.17 mmol/kg/%. The mean sodium excreted for all patients in the first 24 h was lower (0.3 ± 0.2 mmol/kg/%) compared with the second 24 h (0.30 ± 0.3 mmol/kg/%). In the case of sodium retained, the values were higher in the first 24 h (0.2 ± 0.2 mmol /kg/%) vs the second 24 h (0.04 ± 0.21 mmol /kg/%). The sodium deficit (derived from blood analysis of plasma sodium after the first 24 h and the second 48 h) with respect to corresponding time has been presented in Fig. 1. We observed that sodium retained, and sodium deficit had a close relationship with each other. In situations where the retaining sodium increased, the plasma sodium deficit was reduced and vice versa. Furthermore, to see if there was a correlation of sodium retained with sodium excreted, we performed a linear regression. With linear regression, it was seen that sodium excreted was responsible for sodium retained in 43% of the variance in the first 24 h and for 83% of the variance in the second 24 h. Concretely, for the first 24 h, $F(1,49) = 36.3$, $p < 0.001$, $R2 = 0.431$ and for the second 24 h, $F(1,49) = 237.8$, $p < 0.001$, $R2 = 0.832$. The correlation was stronger, especially in the second 24 h.
Conclusion: Resuscitation with LR did not correct hypoosmolality hyponatremia, which persisted even after the first 24 h, especially in patients with burns > 60%. In critical burns, the restoration of sodium

losses in the burn tissue is essential. By keeping diuresis under strict control (considering the risk of acute kidney injury), it is possible to deliver a proper supply of fluids, not eliminate sodium from the urine, ensure better sodium retention in the body, and less sodium deficit. We agree with the burn experts regarding the fluid load of 2 ml/kg/% TBSA burned for 24 h. If we give more than these amounts of fluids during resuscitation, we will introduce a higher sodium load above the normal values, which would lead to increased urinary output, elevated sodium excretion, and non-correction of plasma sodium at the end of resuscitation.

000700

Convective and diffusive cerebral oxygen delivery is impaired in post-cardiac arrest patients with persistent brain hypoxia

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Intensive Care Medicine Experimental 2022, **10(2)**: 000700

Introduction: Following cardiac arrest and return of spontaneous circulation, persistent brain hypoxia leads to ongoing hypoxic-ischemic brain injury (HIBI). To date, clinical trials have not identified an effective strategy to optimize cerebral oxygen delivery in the post resuscitation phase in these HIBI patients.
Objectives: To determine at which stages of the oxygen cascade impairments in cerebral oxygen transport arise in post-cardiac arrest HIBI patients.
Methods: We conducted a prospective interventional study assessing cerebrovascular physiology in 17 patients with HIBI. Patients were instrumented with radial artery and jugular bulb catheters (blood gases), as well as a quadruple lumen cranial access bolt for the measurement of intracranial pressure (ICP), brain tissue partial pressure of oxygen ($PbtO_2$), cerebral blood flow (CBF), and collection of microdialysate. Cerebral perfusion pressure (CPP) was calculated as the difference between mean arterial pressure (MAP) and ICP. Patients were identified as exhibiting brain normoxia (NX HIBI; $PbtO_2 \geq 20$ mmHg) or hypoxia (HX HIBI; $PbtO_2 < 20$ mmHg) based upon mean $PbtO_2$ over the first 24 h of monitoring. For control comparisons, 15 healthy volunteers were instrumented with a radial artery and jugular bulb catheter (blood gases). In controls, Duplex ultrasound was used to measure CBF, while CPP was calculated as the difference between MAP and jugular venous pressure. White matter CBF was estimated to facilitate CBF comparisons to patients, wherein the CBF catheter is situated in subcortical white matter. We employed a hypocapnic challenge to reduce CBF and determine the resulting increase in oxygen extraction fraction (OEF) as an index of the capacity for cerebrovascular-to-parenchymal oxygen diffusion.
Results: The CPP was similar between the controls (83 [78–86] mmHg) and both NX HIBI (80 [69–88] mmHg; $P > 0.99$) and HX HIBI patients (79 [73–86] mmHg; $P > 0.99$). While CBF was similar between controls (27 [24–34] mL/100 g/min) and NX HIBI patients (25 [23–31] mL/100 g/min; $P > 0.99$), CBF was lower in HX HIBI patients (20 [10–27] mL/100 g/min; $P = 0.023$). During hypocapnia, cerebral OEF increased similarly in controls (+ 18 [14–22] %) and NX HIBI patients (+ 10 [6–18] %; $P = 0.59$), but this response was reduced in HX HIBI patients (+ 5 [4–6] %; $P = 0.00038$). We further scaled the changes in OEF to each mL/100 g/min reduction in CBF. Nonetheless, the change in OEF per unit reduction in CBF was similar between controls (− 0.60 [− 0.75 to − 0.39] %/mL/100 g/min) and NX HIBI patients (− 0.57 [− 1.40 to − 0.36] %/mL/100 g/min; $P > 0.99$), but again lower in HX HIBI patients (− 0.19 [− 0.26 to − 0.11] %/mL/100 g/min; $P = 0.018$).
Conclusion: Lower CBF, and a smaller change in OEF during hypocapnia indicate that patients with brain hypoxia exhibit impaired convective and diffusive oxygen delivery. Future therapeutic studies must aim to target both the convective and diffusive stages of oxygen transport to alleviate brain hypoxia in HIBI patients.
Acknowledgements This study was funded by the Canadian Institutes of Health Research (#437644) and the Vancouver General Hospital Foundation.

000758

Pharmacokinetic/pharmacodynamic of ceftobiprole in patients on ECMO

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Intensive Care Medicine Experimental 2022, **10(2)**: 000758

Introduction: The use of extracorporeal membrane oxygenation (ECMO) exposes patients to cannula infection and local cellulitis. Due to a large antimicrobial spectrum, ceftobiprole may represent the drug of choice for empiric or definite treatment for these infections. However, no data exists on pharmacokinetic/pharmacodynamic (PK/PD) of ceftobiprole in ECMO patients.
Methods: Data from patients suspected of having developed ECMO-related cannula infection (during ECMO support or after its removal) who received ceftobiprole (500 mg every 8 h, dose adjusted in case of renal failure) as empiric treatment for at least 48 h and had ceftobiprole blood level measurements for standard of care, were retrospectively analysed. Patients whose infection occurred after ECMO withdrawal were considered as control-patients. Ceftobiprole plasma concentrations were determined 48 h after start of antibiotic treatment. Trough, CT50 and peak ceftobiprole serum levels were obtained before (Cmin), 30 min (peak) and 2 h (CT50) after the end of ceftobiprole infusion, respectively.
Results: Thirty-five patients were included in the study: 28 patients on ECMO (11 veno-venous and 9 veno-arterial) and 7 patients without ECMO. Ceftobiprole serum levels were similar in the ECMO and non ECMO groups: the median [IQR] values were respectively: 5.65 µg/mL [3.75–9.25] and 3.2 µg/mL [2.7–13.7] for trough level ($p = 0.52$); 13.4 µg/mL [12.125–19.6] and 16.4 µg/mL [12.9–22.7] for peak level ($p = 0.2$); 9.95 µg/mL [8.07–14.46] and 9.4 µg/mL [8.7–13.275] for CT50 ($p = 0.42$) (Fig. 1). The 0–8 h areas under the curves AUC0-8 h of ceftobiprole were 66 µg.h/mL [56.25–106.75] and 59 µg.h/mL [51–109] for ECMO and non ECMO patients, respectively ($p = 0.45$). Forty-eight pathogens were retrieved in 29 patients, among which 6 were resistant to ceftobiprole. In 23 patients with pathogens susceptible to ceftobiprole, MIC was determined in 19, and trough levels were above ceftobiprole MIC for 94% of them, without any difference between ECMO and non ECMO patients ($p = 0.79$). Patients requiring renal replacement therapy had lower trough ceftobiprole levels than those not requiring RRT (mean difference: − 3.17 (− 5.7; − 0.6), $p = 0.009$ for between groups comparison). Patients with augmented renal clearance (defined as a creatinine clearance > 130 mL/min) had also lower trough ceftobiprole levels than patients with normal clearance (creatinine clearance 60–130 mL/min): the mean difference was − 2.07, $p = 0.04$ for between groups comparison.

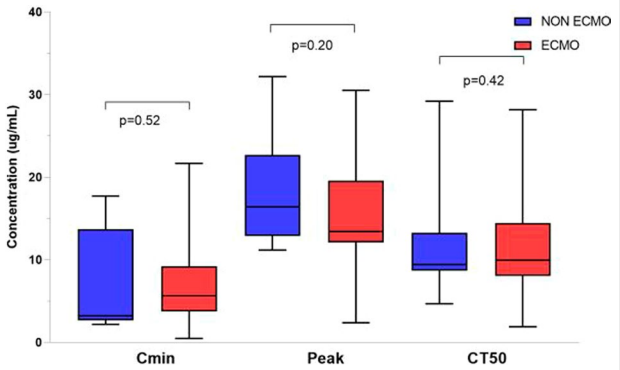

Fig. 1 Ceftobiprole serum measurements for 35 patients, 7 in the non-ECMO group and 28 in the ECMO group. The data distribution was depicted with the use of boxplots expressing median, interquartile range and extreme values

Conclusion: In our study, PK/PD of ceftobiprole was not modified in patients on ECMO and the dose of 500 mg, administered 3 times a day, allowed to obtain a trough level higher than the ceftobiprole MIC for 94% of them. Situations associated with under-dosing were renal replacement therapy and augmented renal clearance.

000795

A comparison of SAPS-II and SOFA score for prediction of hospital mortality in Intensive-Care-Unit cardiac arrest

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Introduction: Cardiac arrest on Intensive-Care-Unit (ICUCA) is a rare but significant complication of intensive care therapy.
Objectives: The present study investigates the predictive value of the established intensive care scores Sepsis-related Organ Failure Assessment (SOFA) score and Simplified Acute Physiology Score (SAPS)-II with regard to prognosis in ICUCA.
Methods: The ICU database of a German university hospital with a total of five ICU was screened for all ICUCA, defined according to the Utstein criteria as the need to perform chest compressions and/or defibrillation between 2016–2019. The primary endpoint was the occurrence of ICUCA. Secondary endpoints included SOFA and SAPS scores, and the outcome of ICUCA. For statistical evaluation, the exact Mann–Whitney-U-test for two independent groups (died vs. survived) was used. In addition, Hedges' g was calculated as effect size measure. Receiver operating characteristic curves (ROC) were performed for the SAPS and SOFA scores for the outcome hospital mortality, the area-under-the ROC (AUROC) and confidence limits of the AUROC were calculated and the zero hypothesis (true area = 0.5) was tested. Sensitivity, specificity, positive and negative predictive values were calculated for cut-off values determined by Youden-Index.
Results: A total of 114 (f = 36; mean age:72.8 ± 12.5 years) Intensive-Care-Unit-cardiac-arrests were observed out of 14,264 Intensive-Care-Unit-admissions (incidence: 0.8%; 95%CI:0.7–1.0). 29.8% (n = 34;CI95:21.6–39.1) had no return of spontaneous circulation. Hospital-mortality was 78.1% (n = 89; CI95:69.3–85.3). 1-year-survival-rate was 10.5% (95%CI:5.5–17.7). Table 1 indicates that the SAPS scores (recorded before and after ICUCA) showed a better discrimination between survival and death during hospital stay than the SOFA scores. The receiver operating characteristic curve (ROC) indicates that a cut-off value of the SAPS-II after ICUCA of 43.5 seems to be suitable for prognosis of hospital mortality (area-under the curve 0.81 [CI95:0.70–0.92], specificity 87.5%, sensitivity 65.6%; SAPS-II > 43.5: 87.5% died in hospital; SAPS-II < 43.5: 65.6% survived).
Table 1: Comparison of SOFA and SAPS-values in the group of patients with survival vs. death during hospital stay

	Survived (N = 25)	Died (N = 89)	Effect size (Hedges' g)	p
SAPS-II before ICUCA	36.9 ± 14.8	45.3 ± 14.4	0.57	0.006
SAPS-II after ICUCA	34.3 ± 9.2	46.5 ± 11.8	1.12	< 0.001
SOFA before ICUCA	6.3 ± 4.2	8.1 ± 4.9	0.38	> 0.10
SOFA after ICUCA	8.7 ± 5.2	11.9 ± 3.6	0.77	0.003

Legend: ICUCA = Intensive-Care-unit-Cardiac arrest; SAPS = Simplified Acute Physiology score; SOFA = Sepsis-related Organ Failure Assessment score.
p = p values according Mann–Whitney-U-test (effect size Hedges'g > 0.5 moderate effect, > 0.8 strong effect).
Conclusion: ICUCA is a significant complication of intensive care medicine. In contrast to the SOFA score, the SAPS-II seems to be more suitable for prediction of hospital mortality after ICUCA. This may therefore be used in future prognostic calculators for ICUCA.

000923

Prediction of respiratory complications by quantifying lung contusion volume using chest CT in patients with chest trauma

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Intensive Care Medicine Experimental 2022, **10(2)**: 000923

Introduction: In trauma patients, pulmonary contusion is an important risk factor for respiratory complications such as pneumonia and acute respiratory distress syndrome (ARDS). We aimed to determine the relationship between pulmonary contusion volume and patient outcome and the predictability of respiratory complications.
Methods: Among 800 patients with chest trauma admitted to our trauma center between January 2019 and January 2020, 73 patients with pulmonary contusion on the chest computed tomography (CT) were retrospectively included. The chest injury severity was expressed as the ratio of the uninjured lung volume to total lung volume by quantifying pulmonary contusion volume based on chest multi-detector CT. The cut-off value was 80%. Data included patient demographics, injury severity score, respiratory complications, and mortality.
Results: A total of 73 patients with pulmonary contusion were identified (77% men, mean age 45.3 years). Among 73 patients, the mean injury severity score was 22.3, 28 patients had pneumonia, and 5 patients had ARDS. The number of patients in the severe risk group with less than 80% of uninjured lung volume was 39, among which 24 had pneumonia. In predicting pneumonia, the area under the ROC curves for the ratio of the uninjured lung volume to total lung volume was 0.85 (95% CI 0.76–0.95, p = 0.008), and the optimal threshold was 70.4%.
Conclusion: Quantifying pulmonary contusion volume using initial CT in patients with chest trauma allows for identifying patients at high risk for delayed respiratory complications such as pneumonia.

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1. Automatic Segmentation of Lung, Airway and Pulmonary Vessels using Morphology Information and Advanced Rolling Ball Algorithm

2. Clinical Significance and Prognostic Implications of Quantifying Pulmonary Contusion Volume in Patients with Blunt Chest Trauma
3. Thoracic Trauma Severity score on admission allows to determine the risk of delayed ARDS in trauma patients with pulmonary contusion

Acknowledgements None.

000942

Self-assessment and willingness for lifelong training in adult and pediatric emergency algorithms of doctors, nurses, and paramedics of the prefecture of Lasithi in Crete

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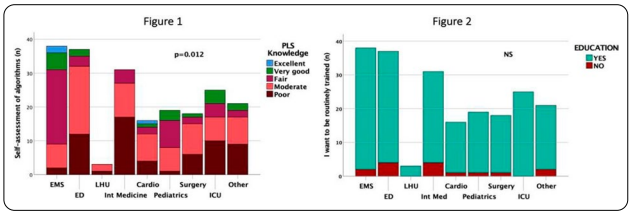
Introduction: For emergencies, the medical and nursing staff, using the appropriate updated algorithms and their acquired skills, follow a structural approach of initial assessment, resuscitation, and emergency treatment. Adult and pediatric emergency medicine includes education and training in recognizing a life-threatening condition and treating it appropriately.
Objectives: To assess the knowledge and the need for training of the healthcare personnel in the management of emergencies in adults and children. Also, to demonstrate the need for better organization and continuing education in the field of life support. The health structures involved were the Emergency Departments (EDs) and Clinics of three General Hospitals, the Emergency Medical Service (EMS), and the Health Centers and Local Health Units (LHU) in the prefecture of Lasithi, Crete.
Methods: This is a cross-sectional study using a multiple-choice questionnaire, which assessed knowledge of the latest Advanced Life Support (ALS), Advanced Paediatric Life Support (APLS), Basic Life Support (BLS), Paediatric Life Support (PLS) guidelines, self-assessment of knowledge and perception of participants on the importance and necessity of lifelong education. The sample consisted of doctors, nurses, and paramedics of the prefecture of Lasithi, and their responses collection took place from July to December 2021.
Results: Three-hundred-and-seven questionnaires were disseminated and 208 were returned completed (response rate 67.7%). Regarding the various skills used by health professionals, the most used procedures were cardiopulmonary resuscitation (CPR), defibrillation, and foreign body removal, while none of the participants had ever attempted an intraosseous needle insertion. Less than 40 questions were answered correctly by all health professionals who participated in the study (17.6 ± 4.6) with the average value of correct answers falling below 50% ($47.5 \pm 19.8\%$). Overall, physicians answered more than half of the 40 questions (21.9 ± 4.9) correctly compared to nurses (16.9 ± 4.2) and paramedics (15.5 ± 2.2) ($p < 0.001$). The percentages of correct answers per workplace department also differed significantly. Training in various basic or advanced adult life support seminars was reported by 72.1% ($n = 150$) of participants, while 10.5% of physicians and 39.4% of nurses had never been trained in a basic or advanced life support seminar. Healthcare providers in all structures, but EMS, characterized their BLS/PLS knowledge as inadequate (Fig. 1). Most participants stated that they want to receive lifelong learning (87.1–100%) regardless of their workplace (Fig. 2).
Conclusion: The present study demonstrates that the healthcare personnel's knowledge is not of the required level to deal with emergencies. It is possible to provide lifelong training to doctors and nurses through appropriate, integrated, and repetitive training programs, as desired and proposed by most healthcare professionals.



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000952

Midregional-ProAdrenomedullin (MR-ProADM) as a mortality predictor in critical burned patients

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Introduction: Burn injuries are one of most devastating forms of trauma and result in high morbidity and mortality. Several specific burn outcome prediction scores and biomarkers have been suggested and used to predict the outcome in critically burn patients. High levels of MR-proADM on admission in critically ill and septic patients have been associated with greater organ dysfunction and higher mortality. MR-ProADM has been poorly studied in these patients.
Objectives: To evaluate the relationship between MR-proADM levels, severity scales used in burned patients and mortality.
Methods: Prospective observational cohort, enrolling critical burned patients admitted in Burn Intensive Care Unit during 3 years. Data Collected: Baux Index, ABSI (Abbreviated Burn Severity Index), APACHE II (Acute Physiology and Chronic Health Evaluation) and SOFA scale (Sequential Organ Failure Assessment Score). C-Reactive Protein (C-RP), procalcitonin and MR-ProADM were measured during resuscitation phase at different times and daily during 15 days. Data was analyzed with receiver-operating characteristic (ROC) curve analysis.
Results: 27 patients with $41 \pm 18\%$ TBSA were studied. The mean ABSI was $9,74 \pm 2,96$, mean APACHE II: 17 ± 7, and mean Baux Index 92 ± 20. Mean SOFA scale at admission: $3,2 \pm 2,7$, day 1: $6,0 \pm 3,7$, day 2: $6,4 \pm 3,1$, day 3: $6,7 \pm 3,7$, and day 7: $4,6 \pm 4,2$. The highest levels of MR-proADM correspond to greater severity measured by the SOFA score. The mean MR-ProADM levels in the patients who died was 3.51 ± 2.30 nmol/l versus 1.28 ± 1.10 nmol/l (p 0.0001) in survivors. Elevation of MR-proADM was associated with higher mortality. At ROC curve analysis, MR-ProADM showed the highest area under the curve: ROC 0.822 compared with Procalcitonin (0,714) and C-RP (0,452).
Conclusion: Higher levels of MR-proADM are associated with greater organ dysfunction and higher mortality in burn patients.

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000945

The practice of algorithms and the lifelong pediatric and adult basic and advanced life support training of doctors, nurses, and paramedics of the prefecture of Heraklion

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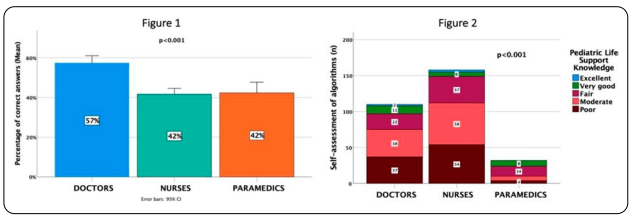
Intensive Care Medicine Experimental 2022, **10(2)**: 000945

Introduction: Immediate and effective treatment of life-threatening conditions and cardiac arrest is probably the biggest challenge for healthcare systems. Severe disease and trauma situations in children and adults are potentially reversible if timely and properly managed. Studies have highlighted the importance of education in emergencies and the need for lifelong training of first responders, in line with the current guidelines.
Objectives: To study the theoretical approach of the healthcare personnel to the management of emergencies in adults and children. The health structures involved were the Emergency Departments (EDs) and Clinics of two General Hospitals, the Emergency Medical Service (EMS), and the Health Centers and Local Health Units in Heraklion, Crete. Also, to encourage self-assessment and formulation of proposals by the participants.
Methods: A 6-month cross-sectional study was conducted using an anonymous questionnaire based on the latest Advanced Life Support (ALS), Advanced Paediatric Life Support (APLS), Basic Life Support (BLS), Paediatric Life Support (PLS) guidelines, to doctors, nurses, and paramedics of all participated health structures.
Results: A total of 500 questionnaires were distributed, of which 300 were completed (60%). Out of the participants, 36,7% were doctors, 52,7% nurses and 10,7% paramedics. Education in BLS or ALS was reported in 70,7% (n = 212), in APLS 0,7% (n = 2), in two different pediatric and adult seminars 17% (n = 51), while 11,7% (n = 35) had never been trained in any kind of BLS or ALS seminar. More than half of the physicians answered the questions correctly (57.5 ± 19.2%) compared to nurses (41.7 ± 18.5%) and paramedics (42.3 ± 14.9%, $p < 0.001$) (Fig. 1). Significantly different rates of correct responses per workplace were recorded, with higher rates of > 50% recorded in the ICUs, Pediatric and Cardiology Departments and lower < 50% in Surgery and Pulmonary Departments, and Healthcare Centers ($p = 0.004$). The rates of a theoretically complete emergency education covering adult and pediatric cases were very low in total (17%) with statistically significant differences ($p < 0.001$) in the individual occupational groups and between workplaces. Lower rates of workplace education were reported by physicians (33.6%). Apart from EMS (61.5%) and ED (68.8%), other workplace education was below 50% (4—47.1%) ($p < 0.001$). Higher rates of physicians and nurses (almost 50%) described their BLS or PLS knowledge as moderate or below average compared to paramedics (28.2%, $p = 0.04$) (Fig. 2). Most healthcare workers from all structures (93.8—95.5%) reported that they wish to undertake continued lifelong education (84.6 – 100%).
Conclusion: It is desirable and necessary for healthcare personnel from all healthcare service structures to be systematically trained in updated adult and pediatric emergency algorithms (best practice). Hospital managers and health heads should ensure and provide appropriate support.



000976

Metformin pharmacodynamics in the ICU patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000976

Introduction: Profound insulin resistance in critically ill patients may result in poor glucose control, which is associated with a worse outcome. In non-ICU patients the biguanide metformin is effective in reducing insulin resistance. Impaired renal function and potential lactic acidosis are important concerns during metformin treatment. More than 5 years ago, we implemented a "6 × 6" guideline for enteral metformin administration that takes these concerns into account. Metformin use in the ICU has been reported [1], but not in the context of computerized glucose control and lactate monitoring.
Objectives: Assess the added value of metformin to computerized glucose control in the ICU and its effect on insulin resistance as well as its potential side effects.

Methods: All metformin administrations in adult ICU patients since the implementation of a new hospital information system were evaluated. Glycemic control was performed with our glucose regulation for ICU patients (GRIP) computer program, that only prescribes continuous insulin [2]. If the insulin rate is ≥ 6 IU/h for ≥ 6 h, the "6×6" metformin guideline advises to consider a metformin loading dose of 500 or 1000 mg followed by 500 mg every 8 h, provided the creatinine clearance is > 30 ml/min and lactate < 2.5 mmol/L. GRIP was 'blinded' for metformin initiation. Insulin resistance (IR) was continuously estimated as IR = (Glu -3.5)·(Ins + 1), with Glu in mmol/L and Ins in IU/h. Comparisons were assessed with the paired Student's t-test.
Results: In 55 ICU patients metformin was given at high sustained insulin administration rates with hyperglycemia. Mean insulin administration rate, glucose and lactate at metformin initiation were 8.1 ± 3.4 IU/h, 8.7 ± 2.0 mmol/L, and 1.3 ± 0.4 mmol/L, respectively. In most cases a metformin loading dose of 500 mg was given. We saw a rapid response, and after 8 h a decrease of insulin administration to 5.6 ± 3.0 IU/h, a decrease of glucose to 7.2 ± 1.7 mmol/L and a mild increase of lactate to 1.5 ± 0.5 mmol/L respectively (all P < 0.001). Over the same period IR halved from 48 ± 28 to 24 ± 16 mmol·IU/(h·L) (P < 0.001). Metformin was continued for a median duration of 65 h. During the first 5 days after metformin use, creatinine levels remained stable, and lactate levels > 2.5 mmol/L occurred in 8% of the measurements, with 0.9% > 4 mmol/L.
Conclusion: Metformin administration in strongly insulin-resistant ICU patients resulted within hours in a significant reduction of glucose levels and insulin needs. We believe that, provided lactate monitoring is available, metformin use can be well integrated into glucose control for highly insulin resistant patients.

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Acknowledgements None.

001028

Readjusting mechanical compression device benefits circulation in porcine model of CPR

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Intensive Care Medicine Experimental 2022, **10(2)**: 001028

Introduction: In a shock resistant out-of-hospital cardiac arrest (OHCA), the patient is transported to hospital for invasive procedures using mechanical CPR and ventilation with 100% oxygen through a secured airway. Still, many patients have severe hypercapnia and hypoxia when arriving to hospital. One possible reason for this is impaired ventilation due to the counterpressure caused by the continuous chest compressions (CCC).
Objectives: We hypothesized that interrupted chest compression (ICC) in a 30:2 compression / ventilation ratio would provide better ventilation and arterial gas exchange compared to CCC.
Methods: We randomized 31 anaesthetized domestic swine (weight approximately 50 kg) with electrically induced ventricular fibrillation to CCC or ICC group. The experimental setup is described in Fig. 1.

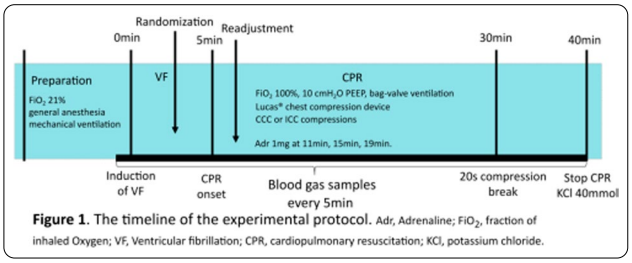

Figure 1. The timeline of the experimental protocol. Adr, Adrenaline; FiO_2, fraction of inhaled Oxygen; VF, Ventricular fibrillation; CPR, cardiopulmonary resuscitation; KCl, potassium chloride.

With both experimental groups we often lost efficient blood perfusion early in the setting. We realized late in the study, that a readjustment manouver with the compression device has an instant positive effect on mean arterial pressure levels. It was performed with the last 8 pigs by pushing the suction cup firmly against the sunken thoracic cage. We compared PaO_2, $PaCO_2$, end tidal CO_2 ($EtCO_2$) and MAP levels over time using a mixed linear model.
Results: There were no statistically significant differences in PaO_2, $PaCO_2$, MAP or $EtCO_2$ between CCC and ICC groups compared with a linear mixed model. The effects of the readjustment maneuver are reported in Fig. 2.

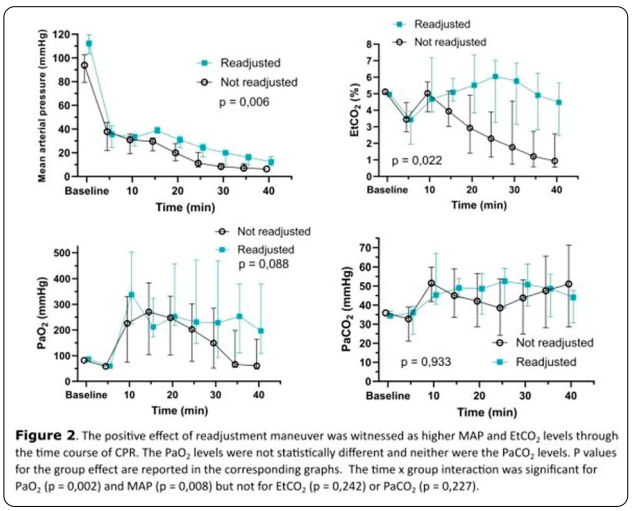

Figure 2. The positive effect of readjustment maneuver was witnessed as higher MAP and $EtCO_2$ levels through the time course of CPR. The PaO_2 levels were not statistically different and neither were the $PaCO_2$ levels. P values for the group effect are reported in the corresponding graphs. The time x group interaction was significant for PaO_2 (p = 0,002) and MAP (p = 0,008) but not for $EtCO_2$ (p = 0,242) or $PaCO_2$ (p = 0,227).

Conclusion: The readjustment maneuver seems to be a major improvement to our experimental setup. It might also be clinically relevant especially with patients with a barrel shaped chest. This needs to be confirmed with further studies preferably in a randomized fashion.

001134

New problems in critical care: migration is coming

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Intensive Care Medicine Experimental 2022, **10(2)**: 001134

Introduction: The migrant crisis has been an important challenge for the Western countries of Europe in the past two years, especially in social and health care terms. During 2020 almost 17,000 African migrants have reached the coasts of the Canary Islands, six more times than the year before. As a consequence of embarking on a long journey during which they are many days exposed to extreme climatic

conditions, they arrive in very poor condition and some of them critically ill. Many of them pass away along the sea crossing.
Objectives: The purpose of this study is to describe the main characteristics of the African migrant population that arrives critically ill to our coast and create new strategies to improve the management and clinical outcome.
Methods: A prospective observational study was performed. This study included the African migrants admitted to the Intensive Care Unit during a period of 14 months, since October 2020 to December 2021. Anthropometry data, vital signs, laboratory tests and severity scales at admission were collected. Complications during hospitalization and mortality were studied.
Results: This study included 30 African migrants. Most patients were males (83.3%) and came from Western Africa (60%). The median age was 25 and the anthropometry measurements were weight 68,8 kg ± 10,4 and height 176,6 cm ± 6,8 (BMI 22,2 ± 3,1). At the admission in the Intensive Care Unit (ICU), the mean temperature measured was 33,7 ºC ± 2,7 and a punctuation in the Glasgow Coma Scale of 8,5 ± 4,5. We collected the severity scales at admission as APACHE II (19 ± 8) and SOFA (8 ± 4). A total of 20 patients required orotracheal intubation (66.7%), and from these, 10 (36,7%) were intubated at the port of arrival. A 69,3% of migrants were on noradrenaline at admission, 76.7% (n = 23) presented acute kidney injury and 30% (n = 9) required continuous venous-venous hemodiafiltration. 90% of patients suffered from skin lesions (n = 27) because of the long trip in bad conditions. Pneumothorax was presented in 23, 3% of the migrants and cardiorespiratory arrest in 20%. The most important metabolic alterations at admission were sodium levels (156,4 mmol/l ± 13), osmolarity (352,4 mOsm/Kg H_2O ± 39,4) and acidosis (pH 7,26 ± 0,12). From all the migrants admitted to ICU, only 4 (13,3%) were positive to SARS-COV2 PCR. The mortality was 23.3% (n = 7).
Conclusion: Our study reveals the critically ill migrants who arrive to our coast are young males from Western Africa. They present signs of severe hypothermia, hypernatremia and dehydration, alteration of the level of consciousness, acidosis and multiorgan failure. The treatment requires controlled warming, a large amount of intravenous fluids, close hydroelectrolyte monitorization and high dose of catecolamines. The migrants present higher mortality than patients admitted to the ICU with SARS-COV2 (23, 3% vs 16%). The early recognition of severity and prompt management is essential to improve outcome and survival of African migrants in Europe.

001135

Comparison of neuron-specific enolase, tau-protein and neuro-filament light chain values for early outcome prediction in cardiac arrest survivors

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Intensive Care Medicine Experimental 2022, **10(2)**: 001135

Introduction: Early and precise prognosis determination in cardiac arrest survivors remains challenging despite multimodal approach. Currently, the only guidelines-recommended biomarker for early prognostication is neuron-specific enolase (NSE).
Objectives: The aim of our study was to compare prognostic values of NSE with novel biomarkers serum tau protein (Tau) and neuro-filament light chain (Nfl) at different timepoints after cardiac arrest.
Methods: Eligible subjects for this single-center prospective study were out-of-hospital cardiac arrest survivors. All patients were treated with targeted temperature management (33 °C for 24 h) using an endovascular device. Blood samples for the measurements of NSE, Tau and Nfl levels were drawn at 24 h (D1), 48 h (D2), 72 h (D3), and 96 h (D4) after hospital admission. Thirty-day neurological outcomes according to the Modified Rankin Scale (mRS) were evaluated as clinical endpoints, poor outcome was defined as mRS 4–6. Prognostic values of NSE, Tau and Nfl for the prediction of poor outcomes were determined using ROC analysis.
Results: A total of 43 cardiac arrest survivors (mean age 64.1 years) were enrolled in the present study. The area under the ROC curve (AUC) for NSE was 0.776, P < 0.001 at D1, 0.911, P < 0.001 at D2, 0.982, P < 0.001 at D3, and 1.0, P < 0.001 at D4. The AUC for Tau was 0.823, P < 0.001 at D1, 0.893, P < 0.001 at D2, 0.938, P < 0.001 at D3, and 0.980, P < 0.001 at D4. The AUC for Nfl was 0.614, P = 0.232 at D1, 0.782, P = 0.001 at D2, 0.969, P < 0.001 at D3, and 0.990, P < 0.001 at D4. The comparison of ROC curves revealed trend to lower AUC for Nfl at D1 in comparison to NSE (P = 0.151) and Tau (P = 0.077) with comparable values at D2, D3 and D4. Numerically, the highest AUC at D1 was observed for Tau and at D2, D3 and D4 for NSE. The highest sensitivity for the prediction of poor prognosis with 100% specificity was detected for Tau values at D1 (33.3%) or D2 (70.0%) and for NSE values at D3 (92.9%) or D4 (100%).
Conclusion: Our results indicate that the novel biomarkers Tau and Nfl have comparable predictive value for clinical outcomes as NSE at 48 to 96 h after cardiac arrest. At the first day after admission the highest predictive value has Tau followed by NSE, whereas Nfl is not significantly associated with outcomes at this timepoint. It can be speculated that combination of different biomarkers could improve prognosis prediction.

001137

Another pandemic during the SARS-COV 2 outbreak: Migration Crisis

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Introduction: During the past two years, the number of African migrants critically ill arriving at the Canary Islands has increased. Because of bad conditions during the trip, the poor outcomes and mortality of these patients has become an important challenge for Intensive Care Units in Canary Islands. These critically ill patients present poor outcome and high risk of death.
Objectives: The purpose of this study was to analyze which parameters can predict poor outcome and mortality in the African migrant population arriving at Canary Islands.
Methods: A prospective observational study was carried out between October 2020 and December 2021. The study included all the migrants admitted to Intensive Care Unit (ICU). Data were collected from medical records as Drago AE and Critical Care Management and incorporated on a database designed for the purpose of this study. Two groups were compared, the dead patients (Group1) and the survivors (Group 2). Different variables at the first 24 h at the admission in the ICU were compared: epidemiological characteristics, laboratory results, complications and severity scales. Poor outcome was determined by duration of mechanical ventilation, days of stay in ICU, days of stay in hospital and mortality.
Results: 30 African migrants were included in this study. A low punctuation in the Glasglow Coma Scale (GCS) in the first medical assistance (Group 1: 5 ± 3, Group 2: 10 ± 4, p < 0.015) and the need for orotracheal intubation and mechanical ventilation at the arrival were associated to poor outcome (p < 0.03). A low temperature at the moment of reaching land is related to higher mortality (31 ± 2,6, p < 0.018). There was significant difference between mortality and complications as cerebral edema (p < 0.007) and the use of continuous venous-venous hemodiafiltration (p < 0.05). Laboratory results in the first 24 h related to higher mortality were lactate, D-dimer levels and INR. We found differences between both groups regarding to the metabolic alterations as sodium levels at the ICU discharge (161 mmol/l ± 16.6 vs 147.6 mmol/l ± 13.10, p < 0.001) and osmolarity (286.57 mOsm/Kg H_2O ± 39 VS 341.6 mOsm/Kg H_2O ± 33.6). Higher punctuation in the Severity scales at admission showed poor outcome (SOFA 12.6 ± 2 vs 6.6 ± 3.6, p < 0.00; APACHE II: 25.8 ± 6.5 vs 17 ± 8.2, p < 0.014).

Conclusion: Our study reveals the poor condition and the challenge in the management of African migrants who arrive at the coasts of Canary Islands. The serious clinical condition of these patients at the arrival is a trial for first medical assistance, and also involves a high risk of complications and a worse prognosis. Severity of hypothermia, impaired level of consciousness, coagulopathy and the need for mechanical ventilation are parameters to consider especially in the management of African migrants to improve their survival.

001142

Can the effectiveness of cardiopulmonary resuscitation performed by non-health care providers be improved by a Glove-Coach technology? A controlled study

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Intensive Care Medicine Experimental 2022, **10(2)**: 001142

Introduction: Cardiovascular accidents are the leading cause of death worldwide. Good quality cardiopulmonary resuscitation (CPR) can reduce mortality associated with cardiac arrest. Cardiovascular accidents are the leading cause of death worldwide, with the incidence of cardiac arrest steadily increasing in the out-of-hospital setting. The quality of cardiopulmonary resuscitation (CPR) has been reaffirmed by the American Heart Association as the major component in influencing survival from cardiac arrest. The survival rate after cardiac arrest has not changed significantly over the years, remaining below 11% despite the introduction of early treatment through BLS techniques to an increasing number of lay persons. The reasons behind these data remain unclear.
Objectives: his study aims to test a wearable glove coaching system that provides instruction during out-of-hospital CPR.
Methods: We performed a blinded, parallel-group controlled study to test non-health care providers volunteers during a CPR simulation performed on an electronic manikin. Volunteers were recruited and randomized in a 1:1 ratio in both groups. The glove group and the control group, how performed CPR without glove. A brief explanation and demonstration of CPR was provided before the collection of study data. All data collected were recorded electronically during the CPR simulation from AMBU manikin software. The primary outcome was to compare the accuracy of simulated CPR sessions performed by lay volunteers from both groups in terms of frequency and depth of chest compressions. The secondary outcomes were to report the decay in performance between the two groups in terms of the evolution of the depth of chest compressions over time and the percentage of time the candidate performed accurate CPR.
Results: 600 chest compressions were performed; 571 were analyzed. The mean frequency in the glove group was 117.67 versus 103.02 cycles in the control group ($p < 0.001$). The appropriate frequency of cycles was 92.4% in the glove group versus 71% in the control group, a difference of 21.4% ($p < 0.001$). The mean compression depth in the glove group was 52.11 versus 55.17 mm in the control group ($p < 0.001$). A mean reduction in compression depth over time of 5.3 mm was observed in the control group versus a reduction of 0.83 mm in the glove group ($p = 0.018$).
Conclusion: A wearable device, such as a glove that can provide laymen with real-time feedback through a training system could aid in the execution of an appropriate CPR maneuver. Although technical improvements and further studies are needed to confirm these promising results, this innovative approach could potentially improve the effectiveness of lay-provided CPR, thereby improving clinical outcomes for victims of sudden cardiac arrest.

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Acknowledgements

1. Prize as «Best scientific contribution» at the national congress «Emergenza, urgenza, accettazione», 5 april 2019, Riccione (Italy).
2. Second Prize "Young Investigator" at the "Réunion annuelle commune 2019 SSMI, SSInf, SSHH", 18–20 September 2019, Lausanne

001174

Characteristics of in-hospital emergency calls in a tertiary care teaching hospital in the United Kingdom

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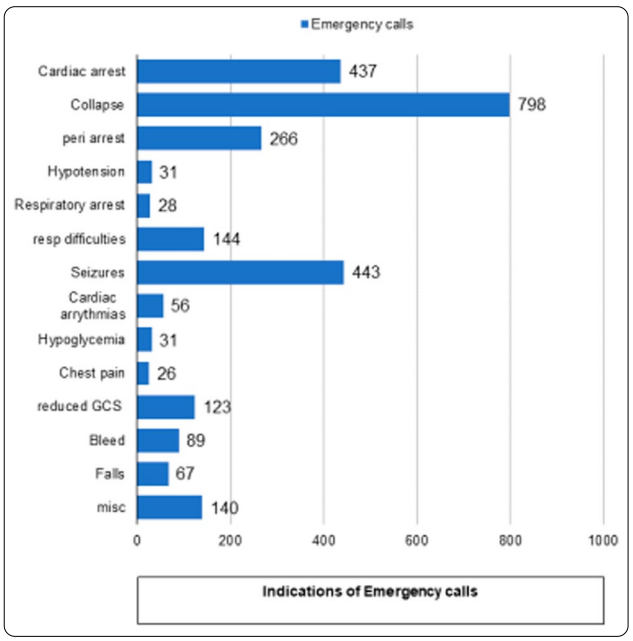
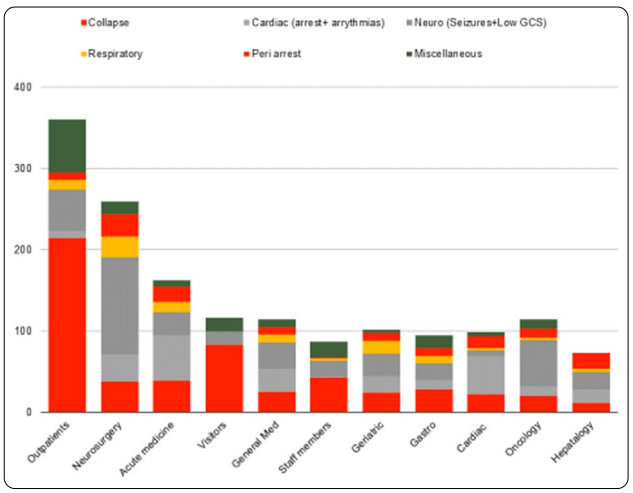
Introduction: Emergency calls or crash calls alert and summon the emergency care team to the location of a clinical emergency. Their nature, frequency and outcome depend on the patients involved and also clinical specialities the patients belong to. Considering the variability in definitions and the factors involved, the effectiveness of in-hospital resuscitation is difficult to measure[1]. Knowledge of the location, frequency, RESPECT status and clinical speciality of these calls can help effective allocation of precious resources[2].

Methods: We collected retrospective resuscitation services data in a 1100 bedded, tertiary care teaching hospital from 2018 to 2021. We excluded the paediatric emergency calls.
Results: Our analysis showed that there were 2740 call with an average 685 emergency calls per year (~14 per week or ~2 per day). The busiest year was 2019 with 783 calls. Throughout the week, Wednesday was busiest with 113 calls per year and Sunday was the least busy day (73 calls per year). With 1384 male and 1353 female patients, there was no significant difference in gender distribution. The outpatient department was the busiest clinical area (396) for emergency calls. Overall, collapse of a patient (798) was the commonest reason for the emergency calls followed by seizures (443) and cardiac arrest (437). Considering different specialty services, the clinical specialty with most number of emergency calls was neurosurgery (259) where seizures and low GCS constituted the commonest reasons for these calls. Collapse was the commonest indication of an emergency call in outpatients, for visitors or staff members and in geriatric medicine and gastroenterology. Cardiac arrest or cardiac arrhythmia was the commonest indication for emergency calls in acute medicine, general medicine and cardiology. DNACPR ("Do not attempt CPR") was documented for 353 patients. Collapse (78), cardiac arrest (68) followed by peri-arrest (53) were the commonest indications for cardiac arrest calls in patients with documented DNACPR. Active treatment plans were verified for 825 patients and assumed for 863 patients that received it. Of the patients

with caridac arrest 44% (192) survived the event, with 142 surviving the first 24 h after the arrest and only 89 surviving to discharge.





Conclusion: Prevention and timely management of seizures in neurosurgery can potentially help reducing their burden of emergencies. Further investigation into reasons for collapse, awareness of RESPECT status of a patient and treatment of preventable causes of cardiac arrest is planned and will reveal potential improvement targets.

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Acknowledgements KK is supported by an AMS Clinical Lecturer Starter Grant (AMS/SGL023/1048).

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001195

Comparison of the Sequential Organ Failure Assessment, Simplified Acute Physiology Score II, and Trauma and Injury Severity Score method for predicting the outcomes of intensive care unit trauma patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 001195

Introduction: Many scoring systems have been published for classification of trauma patients in the field,emergency room, and intensive care settings, so far. The present study aimed to compare theability of Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology ScoreII (SAPS II), and Trauma and Injury Severity Score method (TRISS) in predicting mortalityof intensive care unit (ICU) admitted trauma patients.
Objectives: The aim of this study was to assess the ability of the Sequential Organ Failure Assessment(SOFA), Simplified Acute Physiology Score II (SAPS II) scoring system,and Trauma and Injury Severity Score (TRISS) method to predict group mortalityfor intensive care unit (ICU) trauma patients.
Methods: The medical records of 1730 consecutive major trauma patients admitted to the ICU of HabibBourguiba Hospital were retrospectively examined. The SOFA and the SAPS II scores werecalculated based on data from the first 24 h of ICU admission, and the TRISS wascalculated using initial laboratory data from the emergency department and operative data.The probability of death was calculated for each patient based on the SOFA score,SAPS II score, and TRISS equations. The ability to predict group mortality for theSOFA score, SAPS II score, and TRISS method was assessed by using 2-by-2 decisionmatrices and receiver operating characteristic curve analysis. The areas under the ROC curvesand the standard errors were calculated and the 95% confidence intervals are reportedaccording the De Long's method.
Results: In 2-by-2 decision matrices with a decision criterion of 0.5, the sensitivities, and specificities,were 81.6%, and 73.8%, respectively, for the SOFA score; 71.7% and 79.5%, respectively,for the SAPS II scoring system; 69.5% and 82.3%, respectively, for the TRISS method.In the receiver operating characteristic curve analysis, the areas under the curve for theSOFA score, SAPS II scoring system, and TRISS method were 0.839, 0.828, and 0.828,respectively.
Conclusion: The results from the present study showed that the SOFA score was not different fromSAPS II scoring system and TRISS in predicting the outcomes for ICU trauma patients.However, the method for calculating SOFA scores is easier and simpler than SAPS II andTRISS.

001206

Animal Experiments of A New Temporary Embolic Agent: Transarterial hepatic embolization using a bio-inspired hemostatic materials in rabbit Model

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Intensive Care Medicine Experimental 2022, **10(2)**: 001206

Introduction: Trans-arterial embolization is used as an effective treatment in various clinical fields. Various embolic materials have been developed for this procedure, but temporary embolic materials are not diverse.
Objectives: The purpose of this study was to confirm the efficacy of InnoSEAL Plus, a hemostatic agent with a new mechanism, as a temporary embolic material.
Methods: This study is an animal experiment using rabbits. After liver embolization using InnoSEAL Plus the macroscopic findings and histopathological findings were examined on the 1st, 3rd, 7th, 14th, 21st,

and 28th days. A total of 16 New Zealand white rabbits were included in this study. A total of 6 were excluded, 3 with vascular malformation and 3 with embolization of non-targeted organ. Hepatic artery embolization was performed through the ear artery. A part of the hepatic artery was confirmed by angiography and embolized by mixing InnoSEAL Plus and a contrast agent.
Results: Hepatic ischemia and necrosis of the embolic region were observed in subjects sacrificed on days 1, 3, 7, and 14, and only partial hepatic ischemia was observed in subjects sacrificed on days 21 and 28. According to histopathological findings, it was confirmed that partial liver tissue necrosis and inflammatory reaction remained in all rabbits sacrificed on day 28.
Conclusion: As a result of this study, it was found that InnoSEAL Plus was able to recanalize blood vessels between 14 and 21 days after hepatic artery embolism and demonstrated to be the potential for use as a temporary embolic material.

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001215

Combined use of ECMO and CYTOSORB in an experimental model of post-cardiac arrest syndrome

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Introduction: Increasing number of patients with end-stage organ failure (including heart failure under implantable mechanical circulatory support devices) has further increased the transplant waitlist and the availability of donor organs from the standard pathway of donation after brain death. An alternative strategy to increase the number of available organs is to permit organ donation after circulatory determination of death (DCDD) following the withdrawal of life-sustaining therapies. However, the clinical use of donation after DCDD requires a better understanding of the pathophysiological consequences of a 'no touch' 5 min period on cardiac function and tissue perfusion. Indeed, pathophysiological disturbances during this period are described as a combination of cardiogenic and vasodilatory shocks (1). Veno-arterial extracorporeal membrane oxygenation (VA ECMO) allows to restore adequate perfusion but little is known about its direct effect on left ventricular (LV) function and tissue perfusion and about the role of cytokines in this setting.
Objectives: The aim of this study was to assess combined effects of ECMO and CYTOSORB (extracorporeal blood purification therapy designed to reduce excessive levels of inflammatory mediators such as cytokines) on LV function and tissue perfusion after circulatory death.
Methods: This study was performed in an experimental model of cardiac arrest performed in 3 groups of 3 anesthetized and mechanically ventilated pigs. Cardiac arrest was obtained by application of electrical current to the epicardium inducing ventricular fibrillation. After a no-flow period of 5 min, medical resuscitation with catecholamines and vasopressors was performed in "CONTROL" group while VA ECMO was started in "ECMO" group and VA ECMO in combination with CYTOSORB was started in "ECMO-CYTO" group. LV function was assessed with transthoracic echocardiography and arterial pressure with aortic pressure catheter.
Results: Hemodynamic stability (mean arterial pressure above 65 mmHg) was obtained after 23 ± 6 and 26 ± 7 min in ECMO and ECMO-CYTO groups, respectively. No return of spontaneous circulation (ROSC) was observed in CONTROL group and all pigs in this group died. At 15 min following cardiac arrest, LV area fractional change on short axis was normalized in ECMO and ECMO-CYTO groups (31 ± 3 and 34 ± 4%, respectively). Vasopressor requirements were significantly lower in ECMO-CYTO group than in ECMO group (norepinephrine $0{,}10 \pm 0{,}03$ vs. $0{,}17 \pm 0{,}06$ µg/kg/min, $p < 0{,}05$). During 30 min following cardiac arrest, IL 6 significantly increased by 5% in ECMO group while it decreased by 6% in ECMO-CYTO group.
Conclusion: After cardiac arrest (no flow) of 5 min duration, VA ECMO allowed complete LV recovery and hemodynamic stability within 30 min of post-cardiac arrest syndrome. CYTOSORB added to VA ECMO could contribute to improve tissue perfusion after circulatory death by reducing norepinephrine requirements and decreased circulating levels of pro-inflammatory cytokines.

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Acknowledgements Funding: Leon Fredericq Foundation, University of Liège.

001282

Machine-Learning Models to Predict Tacrolimus Concentration in Liver Transplant Recipients

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Introduction: Tacrolimus is a major immunosuppressant in liver transplantation patients. However, titration of the tacrolimus dose during the postoperative period requires several trials and errors under therapeutic drug monitoring because it has large inter-individual variability and there are rapid changes in organ functions. We aimed to develop and validate the machine learning models to aid the initial titration of the tacrolimus by predicting concentrations.
Methods: Data from 434 patients at a tertiary hospital was collected from electric medical records for developing a model. A long short-term memory (LSTM) model and the gradient boosting machine (GBM) for predicting the tacrolimus concentration were developed using the patient's age, sex, weight, height, time-series inputs of the previous doses and concentrations of tacrolimus, serum creatinine, and liver enzymes. The performance of the models was evaluated using root-mean-squared error (RMSE), median performance error (MDPE), and median absolute performance error (MDAPE) and compared to the linear regression (LR) model. External validation was performed on the Massachusetts Institute of Technology electronic intensive care unit (MIT eICU) dataset.
Results: The LSTM model showed the better performance than the GBM and LR model in terms of RMSE (1.61, 3.29, and 2.83 ng/ml;

$p < 0.05$), MDPE (0.73%, 9.36%, and 7.89%; All $p < 0.001$) and MDAPE (16.6%, 21.5%, and 19.3%; All $p < 0.001$). The outstanding performance of the LSTM model was maintained in external validation; RMSE (1.91, 13.3, and 4.24 ng/ml for LSTM, GBM and LR, respectively), MDPE (14.7%, 56.4%, and 19.9%) and MDAPE (26.3%, 59.1%, and 29.3%) (All $p < 0.001$). It was verified whether the tacrolimus concentration was within therapeutic range when the dose was consistent with the suggestion of the model for the target concentration.

Conclusion: We developed and externally validated a high-performance model to predict the tacrolimus concentrations in liver transplantation patients using machine learning techniques. This approach can be helpful for rapidly achieving the therapeutic concentration of tacrolimus in liver transplant patients.

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Acknowledgements None.

001287

A retrospective cohort study of cobra envenomation: clinical characteristics, treatments and outcomes

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Introduction: Snakebite envenoming is a global public health problem. Cobra bite is well-known for severe or fatal neurotoxicity. Three species in the genus *Naja* inhabit Thailand including *Naja kaouthia* (Monocled Cobra), *Naja siamensis* (Indochinese Spitting Cobra) and *Naja sumatrana* (Sumatran Cobra).

Objectives: This study was performed to describe clinical characteristics, treatments and outcomes of cobra envenomation in Thailand.

Methods: We performed a 3-year retrospective cohort study (2018–2020) of patients who were bitten or directly inoculated of cobra venom to eyes, using data from Ramathibodi Poison Center, Thailand.

Results: A total of 737 cases (367 cobra bites patients and 370 patients with direct ocular inoculation with cobra venom) were included. Most were male (68.8%) and the median age was 45.5 years (range: 1–99 years). For patients directly inoculated of venom to the eyes, almost all patients (92.2%) developed ophthalmic injuries as irritation, pain, decreased visual acuity and corneal abrasion. Some developed tachycardia and high blood pressure. All did not develop neurologic symptoms. For patients bitten by cobra, most had local

effects (67.8%) and neurological symptoms (54.8%) after bites including ptosis (90.6%), muscle weakness (23.4%), slurred speech (17%), and dysphagia (11.9%). The median time between bites and onset of neurological symptoms was 1 h (range: 10 min–25.5 h). Besides neurological effects, the patients also developed tachycardia (89 patients), high blood pressure (47 patients), hypokalemia (31 patients), hyponatremia (14 patients) and nonspecific arrhythmia (1 patient). Two hundred forty-two patients received Thai neuro antivenom manufactured by The Queen Saovabha Memorial Institute. Some (45.1%) received tracheal intubation with assisted ventilation for a median of 1 days (range: 1–2 days). Twenty-seven patients developed allergic reaction including anaphylaxis after receiving antivenom. Complications reported were cellulitis (62.8%), local skin necrosis (19.1%) and necrotizing fasciitis (18%). The median length of hospital stay was 4 days. Six deaths were reported, most died from wound infection. Based on The Poisoning Severity Score (PSS) grades severity, most (58.2%) were in PSS grade 3. We compared the clinical characteristics and laboratory findings between patients who had PSS grade 1–2 and PSS grade 3–4 (severe-fatal). No significant differences were found in age, sex, onset of neurological effects after bites, time to hospital visit after bites, initial white blood cells count and time to antivenom treatment after bite.

Conclusion: Our finding emphasized that direct ocular inoculation with venom did not cause neurologic effects. Extra-neurological effects were noted. The mortality was low, however there were deaths from cobra bite. Patient with cobra bite should be observed for at least 24 h after bites. Besides antivenom administration, adequate supportive care including management of complications (especially wound infection), might help decrease fatalities.

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Acknowledgements No grant acknowledgment.

001299

A 20-year perspective of liver trauma

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Introduction: Traumatic injuries are among the top causes of mortality and disability, especially in young people. In Spain in 2020 16.078 people died from external causes (3,2% from total of deaths) according to data from national registry (INE -*Instituto Nacional Estadística*-). It is the leading cause of death in people between 15–39 years (40,4%). In the last 20 years there is a downward trend in traffic accidents as the main cause of death in favor of accidental falls, especially in elder population. After traumatic brain, thoracic and extremity injuries, abdomen is the fourth most frequently affected region. Liver trauma accounts for a high morbi-mortality among abdominal injuries. Its treatment has changed throughout the last decades shifting from operative to non-operative management (NOM).

Objectives: The object of this study is to define liver trauma demographic and management changes through the last 20 years in our hospital and its impact on mortality.

Methods: This is a retrospective registry-based cohort study of liver trauma patients who required admission in our surgical and trauma ICU in a Level I Trauma Center between 2001 and 2020. Data is extracted from the hospital database. Two groups were defined according to the decade in which the trauma occurred. Data from patient's demographics, co-morbidities, mechanism of injury, prehospital and in-hospital management, grade of liver injury, associated injuries and outcome was registered and analyzed. The data also included recorded parameters like systolic blood pressure, Glasgow Coma Score (GCS) and presence of haemodynamic shock defined as systolic blood pressure < 90 mmHg and heart rate > 120 bpm. The severity of the liver injury was graded based on the Organ Injury Scale by American Association of Surgery for Trauma (AAST-OIS) grading injuries from I to V. Statistical analysis: all continuous variables were represented as median with interquartile range (25–75). Mann–Whitney test was used to compare groups. Categorical data is shown as proportions and analyzed by Chi2 test or Fisher's exact test when appropriate.

Results: 231 liver trauma patients were included. 129 suffered the accident in the first decade (1stD) of the century and 102 in the second (2ndD). Average age in 1stD was 28 years old (23–40) and 36 in the 2ndD (29–46) ($p < 0,05$). Arterial hypertension and ischemic myocardiopathy were more frequent in 2ndD [9,8% vs 3,1% ($p < 0,05$) and 2,9% vs 0% ($p < 0,05$), respectively]. In both periods the most common mechanism was blunt trauma (79,7%). In the 2ndD there were less road traffic accidents, but the proportion of pedestrian road accidents and high-energy falls was higher [17,6% vs. 8,5% ($p < 0,05$) and 21,6% vs. 11,6% ($p < 0,05$), respectively]. Thoracic trauma was the most common associated injury (77,4%) in both periods. Patients from 2ndD had higher ISS [27 (17–34) vs. 22 (16–29) $p < 0,05$) and NISS scores [29 (22–35) vs. 27 (17–34) $p < 0,05$]. 30% of all patients needed massive transfusion protocol (MTP) activation. Liver injuries were more severe in the 2ndD; 50% of patients had grade III-IV AAST-OIS injuries whereas in 1stD only 25% ($p < 0,05$). Similar number of full-body CT scans were done in both decades but more abdominal echography was performed in 2ndD (36,3% vs 29% $p < 0,05$). Non operative management (NOM) of the injuries was more common in the 1stD (43% vs 30,4%, $p < 0,05$). The median ICU length of stay of both periods was 5 days (3–14) and the overall mortality was 9,2% without differences between decades.

Conclusion: The injury mechanism of liver trauma has changed in the last twenty years. There is a trend towards more blunt trauma secondary to pedestrian accidents and high-energy falls than road traffic accident. This change is associated with greater severity and a substantially surge in the number of high-grade liver injuries. There is also a significant increase in both age and frequency of cardiovascular comorbidities. Fast full-body CT scan and abdominal echography, multidisciplinary management, protocols and interventional radiology makes non-operative management feasible thus allowing mortality to remain the same between both decades despite the global increase in severity.

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001320

Prediction of Early Severe Hemorrhage in Severely Injured Patients: a Pilot Feasibility Study of a Clinical Decision Support Tool developed by Supervised Machine Learning

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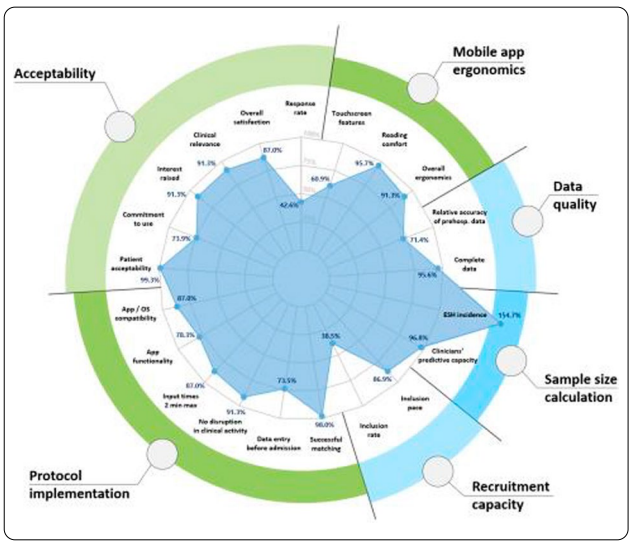
Intensive Care Medicine Experimental 2022, **10(2)**: 001320

Introduction: Hemorrhagic shock is the leading cause of early preventable death in severe trauma and remains a diagnostic challenge. Any approach promoting early detection of patients at risk may be welcome. The recent development of efficient supervised machine learning algorithms makes it possible to design clinical decision support tools that can predict post-traumatic early severe hemorrhage (ESH).
Methods: In **a** prospective observational multicenter pilot study**,** we performed a multidimensional assessment of the feasibility of an external validation protocol of the predictive model of ESH developed by the ShockMatrix working group within the TrauMatrix project. ESH was defined as: packed red blood cell (RBC) transfusion in the trauma room, or transfusion $\geq$ 4 RBC, or any hemostatic interventional procedure (surgery or radiology), or death from hemorrhagic shock, each event occurring in the first 6 h after trauma. When receiving a prealert call from the dispatch center, the participating clinicians used a mobile data collection application to fill in **t**he ten predictive variables required by the model and their binary clinical prediction for ESH. Secondary objectives were to estimate the model's and the clinicians' predictive performances. The performance metric chosen was the F4-score, combining sensitivity (Se) and positive predictive value (PPV) while penalizing "false negative" errors. Clinical data of interest were collected through the Traumabase® trauma registry. Individual feedback data was collected from participating physicians through a dedicated online questionnaire. An ethics committee approved this study.
Results: Regarding feasibility, out of 361 eligible patients screened from 5 centers between June and August 2021, 139 were included (38.5%). Among 54 participating physicians, 23 answered the questionnaire (42.6%). 87.0% of respondents (n = 20) indicated good or excellent overall satisfaction with the study, and 91.3% (n = 21) mentioned a strong or extreme interest. 87.0% of data entries made via the mobile application (n = 20) were completed in less than 2 min, with no major obstacle in implementing the protocol. The ergonomics of the application received 91.3% (n = 21) of positive or very positive opinions. The clinical data identified ESH in 22 patients (15.8%). The clinicians' predictive performance was: F4-score 0.61, Se 64%, Sp 79%, PPV 37%, NPV 92%. The predictive performance of the evaluated model was: F4-score 0.49, Se 50%, Sp 85%, PPV 39%, NPV 90%. Significant differences in some key variables compared to the development sample, such as the proportion of penetrating trauma (21.6% vs. 11.2%, p = 0.001), could partly explain the observed differences (F4-score 0.71, Se 74%, Sp 83%, PPV 36%, NPV 96% for the model in development phase).



Conclusion: This pilot study validated the feasibility of the ShockMatrix protocol and allowed for pre-launch optimization.

001324

The outcome of extracorporeal membrane oxygenation (ECMO) in the major trauma patient with hemorrhagic shock in a level 1 trauma center

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Intensive Care Medicine Experimental 2022, **10(2)**: 001324

Introduction: Major trauma with severe chest injuries or with massive hemorrhagic shock can cause a severe ARDS or acute cardio-pulmonary failure. ECMO can be used as salvage therapy for these major trauma patients and several recent studies among trauma patients report survival rates of 65–79%. But using ECMO to provide advanced life support in adult trauma patients remains a controversial issue now.
Objectives: Aim of this study is to evaluate the outcome of ECMO to provide advanced life support in major trauma patient with hemorrhagic shock and emergency surgery in a level 1 trauma center.
Methods: This retrospective study enrolled 13 adult trauma patients receiving ECMO due to acute cardio-pulmonary failure or severe trauma related ARDS in a level I trauma center between January 2017 and December 2020. Variables collected for analysis were demographics, characteristics of trauma, injury severity score (ISS), amount of transfusion, serum biomarkers, damage-control interventions, indications of ECMO, and associated complications. The outcomes were hospital mortality.
Results: The median age and ISS were 53 (18–66) years and 38 (16 ~ 75). All patients had polytrauma and 8 patients had severe chest trauma (AIS $\geq$ 4) and 1 patient had no chest trauma. Median ISS was 38 (16 ~ 75), initial systolic blood pressure and total transfusion within initial 24 h were 75 (40–80) mmHg and 59 (37–179) units. 11 patient received ECMO during first emergency surgery on admission day and the median time of receiving ECMO from admission was 2.5 h (2-48 h). Prior to ECMO median PaO_2 was 36.5(25–43) mmHg, median $PaCO_2$ was 75 (34–101) mmHg and P/F ratio was 40(25–70). Veno-arterial (V-A) and veno-venous (V-V) ECMO type were used for 7 patients and 6 patients, respectively. Of the 13 patients, 4 patients (33.3%) survived and 9 patients (66.7%) died (6 patients died on admission day and 2 patient died within 48 h).
Conclusion: Although using ECMO to provide advanced life support in adult major trauma patients remains a controversial issue, ECMO can be a salvage therapy for selected major trauma patients who are in severe hemorrhagic shock or severe cardiopulmonary injuries and dysfunctions.

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001326

Hypothermia After Cardiac Arrest in Large Animals Trial (HACA-LA)

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Intensive Care Medicine Experimental 2022, **10(2)**: 001326

Introduction: Lowering body temperature to 32-34ºC post-cardiac arrest is neuroprotective in animal experiments, particularly in rodents. Few high-quality studies have been performed in larger animals with more human-like gyrencephalic brains. The role of induced hypothermia has been questionned after the publication of two large ranomized trials, the TTM- and TTM2-trials, showing no benefit of lower temperatures.
Objectives: To investigate whether immediate cooling to 33C post-cardiac arrest confers a benefit compared to normothermia in large animals. To investigate whether a delay of cooling to 33C by 2 h post-cardiac arrest confers a benefit compared to normothermia in large animals.
Methods: Animals are fasted overnight and anesthetized, mechanically ventilated and kept at baseline parameters including strict normothermia (38 ± 0.2 °C) prior to the intervention. A pulmonary artery catheter is added and an iv cooling catheter (Zoll) is applied via the femoral vein. VF is induced via a pacing wire to the right ventricle. Animals are subjected to 10 min no flow (NF), followed by 4 min low flow (LF) with LUCAS CPR. Adrenalin is delivered every 2 min followed by repeated countershocks. At stable ROSC (10 min), animals are included in the study and randomised to either immediate cooling (0 h), delayed cooling (2 h) or normothermia for a total of 30 h including rewarming. Animals without ROSC are put on ECMO and entered into another study. Animals are kept alive for 7 days with daily neurocognitive testing (NCT) and assessment of neurological function (NDS) in a blinded fashion. Serial blood samples are collected for biomarkers of brain injury (NfL, GFAP). Animals are sacrificed day 7 and brains are harvested for later blinded neuropathological investigation. Modified Histology Damage Score (mHDS) is the primary outcome measure. A power analysis has suggested 10 animals in each intervention arm (total number = 30) to be able to show a significant difference between the delayed cooling arm and the normothermia arm with a statistical power of 80% and a significance level of 2.5%.
Results: Preliminary data per April 30 show that 12 animals have been randomized and survived to seven days. Further results will be presented at the conference in October.
Conclusion: Recent large trials indicate that lowering body temperature after cardiac arrest does not confer a benefit. Well designed animal experiments in relevant large animal models are necessary in order to close the research gaps. Results will be presented at the conference in October.

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Acknowledgements Swedish Heart & Lungfoundation, Hans-Gabriel & Alice Trolle-Wachtmeisters Foundation for Medical Research.

Translational Biology 1

000182

Intestinal and respiratory microbiome in SARS-COV-2 critically ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000182

Introduction: Critically ill patients are known to develop alterations of their microbiome. Little is known of theses alterations in patients infected with SARS-COV-2.
Objectives: To analyze the intestinal and respiratory microbiome of critically ill patients, as well as to compare patients with severe Covid-19 pneumonia, with critically ill patients without Covid-19 and a control group, and to observe different behaviors in order to establish specific preventive or therapeutic measures.

Methods: Longitudinal and analytical study of stool and tracheal samples of patients admitted to the ICU (October 2020 to March 2021) with a diagnosis of severe ARDS secondary to SARS-COV-2 pneumonia. Samples were collected at three different times, the first sample in the first 24 h of admission, the second after 2 weeks of admission and the third at 4 weeks of admission. The samples were compared with the ones of non-COVID patients admitted to the ICU during the same period. Samples were processed in the Institut d'Investigació Biomèdica de Girona biobank (IDIBGI) where they were handled under the COVID protocol and stored at -40ºC. Stools from healthy participants were analyzed as a Reference control group. Bacterial DNA extraction was performed on rectal and tracheal smears using the Godon method. DNA amplification by PCR. Massive sequencing of the 16S rRNA gene using Illumina (Miseq). Quantification of the microbiota by means of (qPCR). Alpha and beta diversity analysis were performed and differential abundance between groups was assessed. Biostatistical analysis was done using QIIME2 software.
Results: Alpha diversity is analyzed in all three groups and in three times, and a significant decrease is observed in diversity or richness of each group. At a taxonomic level there has been a loss over time of the species of the *phylum* Firmicutes and Actinobacteria (local hosts) and on the contrary an increase and predominance of Proteobacteria and Pseudomonas (opportunistic) very remarkable in the tracheal samples of patients with COVID-19.
Conclusion: Patients admitted to the ICU with severe pneumonia due to Covid-19 develop an alteration of the intestinal and respiratory microbiome over the days since ICU admission. These alterations are different from those of the group of critical patients without Covid and, of course, from those of the control group. A significant loss of diversity is observed, highlighting the predominance of opportunistic pathogenic microorganisms such as Pseudomonas sp. most notable in tracheal aspirate.

000306

Aerosol drug delivery performance of nebulisers in a spontaneously breathing adult model

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Intensive Care Medicine Experimental 2022, **10(2)**: 000306

Introduction: Patients in the intensive care unit can experience respiratory distress following extubation from mechanical ventilation. Often, non-invasive forms of respiratory support are utilised to facilitate the progression to spontaneous breathing and reduce the risk of re-intubation1. Aerosol drug delivery can be used simultaneously with these non-invasive supports to alleviate these symptoms assisting in a successful outcome post-extubation. Device selection is a key factor ensuring optimal aerosol drug delivery.
Objectives: The aim of this study was to determine the aerosol performance, in terms of drug dose delivered, of a vibrating mesh nebuliser (VMN) in comparison to two jet nebulisers (JN) in a spontaneously breathing adult model.
Methods: A 3 mL dose of 0.83 mg/mL Salbutamol was nebulized using a VMN (Aerogen Solo, Aerogen, IRE) in combination with an aerosol chamber at 0LPM (Aerogen Ultra, Aerogen, IRE) and JNs (AirLife Misty-Fast, Vyaire, US and NebuTech, Salter Labs, US) operated with a driving gas flow rate of 8LPM. Each nebuliser was attached via a mouthpiece and capture filter (RespirGard II 303, Vyaire, US) to a breathing simulator (ASL 5000, Ingmar, US) set to simulate a healthy adult (Vt 500 mL, BPM 15 and I:E 1:1) breath pattern. Drug dose, captured on the filter, was expressed as a percentage of the nominal dose and determined using UV spectroscopy at 276 nm. Testing was completed in triplicate. A t-test between nebuliser types and one way ANOVA across all nebulisers determined significance at $P \leq 0.05$.
Results: Results are displayed as mean ± SD in the table below.

Nebuliser Type	Aerogen Solo/Ultra (VMN)	Airlife MistyFast (JN)	Salter Labs NebuTech (JN)
Drug dose delivered (%)	41.12 ± 2.01	19.68 ± 1.26	15.91 ± 0.82
P-value	< 0.001		

Conclusion: Across all nebuliser types, there was a significant impact on aerosol delivery to an adult model ($p < 0.0001$). The highest drug delivered was achieved using the Aerogen Solo and Ultra which was statistically significant higher in comparison to the Airlife MistyFast and Salter Labs NebuTech ($p < 0.001$). The Airlife MistyFast delivered a significantly higher dose than the Salter Labs NebuTech ($p = 0.0122$). This study highlights the clinical importance of nebuliser choice on aerosol drug delivery for a simulated spontaneously breathing adult patient.

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000364

The role of endothelial glycocalyx in capillary permeability—experimental pilot study on rat model of endothelial glycocalyx damage

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Intensive Care Medicine Experimental 2022, **10(2)**: 000364

Introduction: Endothelial glycocalyx (EG) is a thin layer of carbohydrate nature on the endoluminal surface of vascular wall endothelial cells which play a crucial role in the integrity and function of the microcirculation. Clinical conditions in which there is sudden EG damage and microcirculatory dysfunction are ischemia–reperfusion (e.g. after CPR), sepsis, or polytrauma. Damage to the EG and capillary barrier per se leads to interstitial edema, followed by diffusion failure with impaired oxygen supply to the tissues. Albumin is considered in many studies to be a promising molecule with a protective effect on EG and capillary membrane integrity.
Objectives: We tested the effect of albumin on EG protection on an experimental model of EG enzymatic damage in rats.
Methods: To assess the degree of capillary permeability damage, we used a spectrophotometric method to analyze the leakage of Evans blue-labeled albumin into the tissues of individual organs: heart, lungs, brain, kidneys, liver, small intestine, spleen, skin, and skeletal muscle. Rats in three groups of 10, 9, and 8 animals were administered the following substances in deep sedation into the jugular vein: Evans blue or Evans blue + hyaluronidase or Evans blue + hyaluronidase + 20% human albumin. After two hours the animals were sacrificed under general anesthesia and then selected organs and tissues were harvested. Evans blue was extracted from the tissues with formamine for 24 h, and the obtained Evans blue eluate was evaluated in a spectrophotometer at a wavelength of 620 nm.
Results: In liver and lung tissues there was a statistically significant trend of increasing tissue concentration after hyaluronidase administration and decreasing to baseline or below baseline after hyaluronidase and albumin administration. These changes were statistically insignificant in the kidney, brain, spleen, intestine, and skeletal muscle tissues.
Conclusion: Our results support the concept of the use of albumin in the protection of capillary membrane integrity and related pathogenetic processes in conditions associated with acute EG damage.

Acknowledgements Supported by the institutional research grant of the University Hospital Hradec Králové: MZ ČZ—RVO UHHK, 00179906, 2022—Influence of endothelial glycocalyx damage on capillary permeability.

000419

Relative telomere length in COVID-19 patients admitted to the Intensive Care Unit

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Intensive Care Medicine Experimental 2022, **10(2)**: 000419

Introduction: Increasing age has been associated with severity and higher mortality of COVID-19 due to the cellular senescence triggered during aging, in which telomere attrition plays an important role. Telomeres constitute the end of linear chromosomes and their shortening is linked to higher risk of get infections. We assessed the association between relative telomere length (RTL) and COVID-19 mortality, considering the effect of additional co-variables.
Methods: A prospective study of 82 patients admitted for COVID-19 to the ICU was carried out. Blood samples were taken in the first day after ICU admission. RTL was quantified by monochromatic multiplex real-time quantitative PCR (MMqPCR) in whole blood. A general lineal model regression were conducted to study RTL association with mortality, adjusting for the most relevant patients characteristics.
Results: Ten patients died during ICU admission. RTL was 0.79 in the alive group and 0.77 in the dead group 90 days after admission ($p = 0{,}4121$). No differences were found between patients who required invasive mechanical ventilation (IMV) and those who did not. No correlations were found for RTL and ICU length of stay (LOS) ($R2 = 0.014$), hospital LOS ($R2 = 0.017$), or gender. When the best model was assessed, the variables that remained were ICU LOS, length of IMV and age.
Table 1 Baseline characteristics

Patients, No	Alive 72 (88)	Dead 10 (12)	p-value
Age (years)	61.5 [53–69]	72 [65.7–75.25]	**0.004**
Gender (female)	16 (22.5)	3 (30)	0.9
BMI (Kg/m2)	30.23[26.56–34.6]	29.43[26.35–32.49]	0.920
IMV, No	54 (75)	9 (90)	0.46
Hypertension	26 (36.11)	9 (90)	**0.004**
Corticosteroids, No	68 (94.4)	10 (100)	1
Hidroxychloroquine	2 (2.78)]	3 (33)	**0.007**
Tocilizumab, No	3 (4.2)	2 (20)	0.19
Hospital LOS (days)	27 [19–38.75]	29 [24.25–35.5]	0.665
ICU LOS (days)	10.5[6.75–20.25]	29 [17–31.75]	**0.017**
Length of IMV (days)	12 [5.5–19]	29 [23–32]	**0.003**

Continuous variables are expressed as median (interquartile range) and categorical variables as absolute number (percentage). p-values for continuous variables were calculated by Mann–Whitney U test and for categoricai variables by chi-square tests. BMI: body mass index.

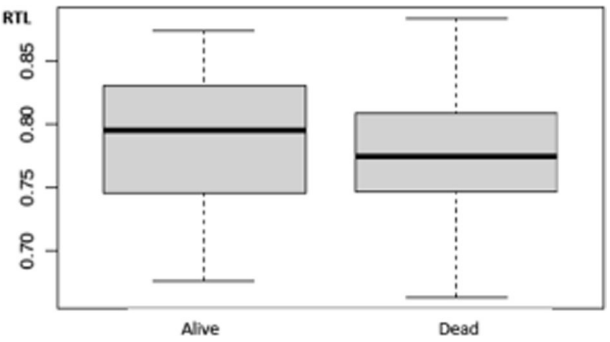

Fig. 1 RTL and survival at 90 days

Conclusion: In this study, RTL was not associated with the survival of patients with COVID-19, nor with other variables. Despite exclusively including critically ill patients, the low mortality of this series could have influenced these results.

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Acknowledgements This study was supported by grants from Fundación Universidad Alfonso X el Sabio [1.013.005], Instituto de Salud Carlos III (ISCIII; grant number COV20/1144 [MPY224/20], and Centro de Investigación Biomédica en Red (CIBER) en Enfermedades Infecciosas (CB21/13/00044).

000441

Inflammation and membrane integrity of epithelial cells and macrophages infected by Pseudomonas aeruginosa and Streptococcus pneumoniae

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Intensive Care Medicine Experimental 2022, **10(2)**: 000441

Introduction: Pulmonary infection is produced by different microbiological agents. In vitro infectious models are needed to elucidate the mechanisms through which microorganism act in pulmonary cells and to evaluate the response to a therapeutic agent.
Objectives: To assess the inflammatory response and tight junctions of alveolar epithelial cells (HAECs) or their coculture with macrophages (THP-1) infected with *Pseudomonas aeruginosa* or *Streptococcus pneumoniae*.
Methods: HAECs alone or combined with THP1 (5:1) were separately infected with *P. aeruginosa* (MOI 1:50) or *S. pneumoniae* (MOI 1:20) for 1 h at 37 °C and 5% CO_2. Then the cultures were washed with PBS and antibiotic and after 24 h the RNA was obtained for subsequent qRT-PCR proinflammatory (IL-8, IL1-β) and cell junction (ZO-1) analysis.
Results: HAECs and HAECs:THP-1 coculture infected by *P. aeruginosa* increase mRNA expression of proinflammatory markers (Fig). Infection with *S. pneumoniae* elevates IL1-β expression in the infected HAECs culture, and raises IL-8 expression in the coculture. *P. aeruginosa* in the coculture enhances ZO-1 expression compared to infected HAECs alone, indicating changes in HAECs membrane integrity in presence of THP-1 cells.

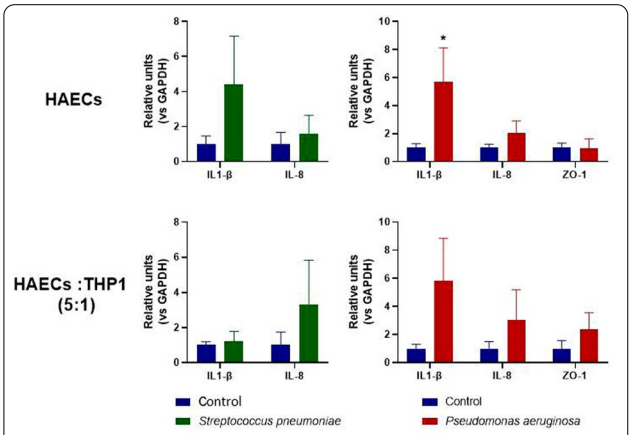

Fig 1. Gene expression of pro-inflammatory (IL1-β, IL-8) and cell junction (ZO-1) mediators assessed by qRT-PCR. Data are expressed as average ± SEM relative to GAPDH expression. *p≤0.05 vs control group.

Conclusion: Culture of HAECs and HAECs:THP-1 coculture infected with *P. aeruginosa* show increased inflammation, and the presence of THP-1 in culture with HAECs influences tight junctions. S. pneumoniae infection in the coculture shows a different expression pattern, increasing neutrophil recruitment compared to the proinflammatory marker IL1-β. Further studies on the development and evolution of infectious models are needed.
Acknowledgements This project was supported by Sociedad Española de Neumología y Cirugía Torácica (SEPAR), Institut d'Investigació i Innovació Parc Taulí (I3PT) and Centro de Investigaión Biomédica en Red de Enfermedades Respiratorias (CIBERes).

000522

Circulating dipeptidyl-peptidase 3 modulates hemodynamics and the renin–angiotensin–aldosterone system in mice

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Intensive Care Medicine Experimental 2022, **10(2)**: 000522

Introduction: Dipeptidyl peptidase 3 (DPP3) is a zinc-dependent metallopeptidase cleaving the N-terminal extremity of various bioactive peptides including angiotensins. Angiotensin II is a vasoactive peptide also known to have an inotropic effect. Although the plasmatic concentration of DPP3 is low in healthy human and animals, an increase in plasmatic DPP3 concentration and activity has been observed in various pathological situations characterized by circulatory failure such as septic or cardiogenic shock with prognostic implications(1–3). In such situation DPP3 could play a pathological role, putatively via an excess of angiotensins cleavage(4).
Objectives: To investigate: 1. Hemodynamics changes induced by DPP3 or anti-DPP3 antibody (Procizumab) injection in healthy mice; 2. Concomitant changes in circulating concentration of renin–angiotensin–aldosterone system (RAAS) mediators.
Methods: Healthy, 10-week-old C57BL/6 J male mice were subjected to intravenous bolus injection of purified human DPP3 (0.55 mg/kg),

Procizumab (10 mg/kg) or phosphate-buffered saline (PBS) as a control. Cardiovascular function was monitored using echocardiography, invasive blood pressure by catheterism of the femoral artery and renal blood flow with an invasive time-of-flight flowmeter. Circulating angiotensin peptides, aldosterone, and renin activity were measured by liquid chromatography-mass spectrometry/mass spectroscopy from venous blood sampled on ice in vials containing enzyme inhibitors completely blocking angiotensin peptides metabolism.

Results: DPP3 injection induced a decrease in left ventricular systolic function as measured by the left ventricle shortening fraction with a maximal depression of -12 ± 8% ($p = 0.01$) compared to baseline and an increase in mean renal blood flow (+45 ± 18%, $p = 0.02$). Conversely, Procizumab did not change left ventricular systolic function but induced a decreased renal blood flow (-20 ± 11%, $p = 0.04$). Invasive blood pressure remained stable after DPP3, Procizumab or PBS injection. Hemodynamic changes induced by DPP3 administration were associated with a significant decrease in circulating angiotensin II (-66%, $p < 0.01$), angiotensin III (-82%, $p < 0.001$) and angiotensin IV (-68%, $p < 0.001$) and a significant increase in angiotensin I (+108%, $p = 0.02$) compared to PBS injected mice. Conversely, Procizumab injection resulted in increased circulating angiotensin II (+113%, $p < 0.01$), angiotensin III (+75%, $p = 0.02$), angiotensin 1–5 (+167%, $p = 0.02$) and angiotensin 1–7 (+60%, $p = 0.01$) as well as increased aldosterone concentration (+49%, $p = 0.04$), when compared to PBS injected mice.

Conclusion: DPP3 injection induced cardiac dysfunction and renal blood flow increase in healthy mice. Additionally, DPP3 injection is associated with a decrease in angiotensin peptides level including angiotensin II while cDPP3 inhibition by Procizumab was associated with opposite changes. Future work on the potential relation between observed hemodynamic changes and DPP3-induced modulation of the RAAS is needed.

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Acknowledgements This work was supported in part by a grant from 4TEEN4 Pharmaceuticals Gmbh.

000586

Experimental determination of Atot and pKa of whole blood of healthy volunteers, patients with sepsis and post-operative patients: an in vitro study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000586

Introduction: During acute respiratory acid–base perturbations, pH changes are limited by the non-carbonic buffers, mainly consisting of proteins and phosphates in plasma, plus hemoglobin in whole blood. According to Stewart's physicochemical approach, the total weak acid concentration (Atot) is one of the three independent variables determining pH [1]. The amount of dissociated Atot (A-) depends on their acidic dissociation constant (Ka), also known in its logarithmic form: $pKa = -\log_{10} Ka$. Experimental estimates for Atot and Ka were previously obtained for human plasma of healthy volunteers (17.2 ± 3.5 mmol/L and $0.80 \pm 0.60 \times 10\text{^}(-7)$, $pKa = 7.10$, respectively) [2]. Of note, while in clinical practice acid–base measurements are performed on whole blood, no data regarding Atot and Ka of blood are currently available.

Objectives: To compute pKa and Atot for whole blood of healthy subjects and two different populations of ICU patients, *i.e.* patients with sepsis and post-operative patients.

Methods: Blood was collected from 30 volunteers, 30 patients with sepsis [3] and 27 post-operative patients (ICU "Vecla", Ospedale Maggiore Policlinico, Milan and 2 ICUs of FNKV University Hospital, Prague). Hemoglobin, albumin, total proteins and phosphates concentrations were measured. Blood was equilibrated with different gas mixtures to obtain 20 experimental points with PCO_2 ranging between 20 and 120 mmHg. For each subject, the variation of Strong Ion Difference (SID) over PCO_2 was modeled, and the normal value of SID at PCO_2 of 40 mmHg (SID_{40}) was computed. Measured pH and PCO_2, SID_{40} and the simplified strong ion electroneutrality equation were used to calculate Atot and Ka through the Marquardt nonlinear regression procedure:

$0.0307 \cdot PCO_2 \cdot 10\text{^}(pH—6.120) = [SID_{40}]—Atot \cdot Ka / (Ka + 10\text{^}(-pH))$

T-test and Mann–Whitney rank sum test were used for analysis.

Results: Age [54 ± 15 *vs.* 61 ± 16 *vs.* 57 ± 18 yr, $p = 0.3$] and gender [14 (47%) *vs.* 9 (33%) *vs.* 12 (40%) of females, $p = 0.6$] did not differ among volunteers, post-operative and septic patients. Both populations of ICU patients had lower hemoglobin, albumin and total proteins concentrations as compared to healthy volunteers (Table 1), while phosphates were similar. Septic patients had lower values of Atot as compared to post-operative patients, which had lower values as compared to healthy controls. Also, pKa showed a decreasing trend going from controls to post-operative and septic patients.

	Controls (N = 30)	Post-operative patients (N = 27)	Septic patients (N = 30)	p
Hemoglobin (g/dL)	14.4 ± 1.0	10.9 ± 1.8	9.6 ± 1.3	< 0.001
Albumin (g/dL)	4.8 ± 0.3	3.2 ± 0.4	2.5 ± 0.4	< 0.001
Total proteins (g/dL)	7.2 (6.7–7.6)	4.8 (4.6–5.1)	4.8 (4.1–5.1)	< 0.001
Atot (mmol/L)	94 (72–132)	53 (43–62)	39 (37–46)	< 0.001
pKa	7.91 (7.84–8.19)	7.74 (7.52–7.82)	7.35 (7.11–7.46)	< 0.001

Table 1 Coomparison between nonvolatile buffers concentration (hemoglobin, albumin and total proteins) and the estimated Atot and pKa values among groups

Conclusion: Healthy volunteers, septic patients and post-operative patients had different values of both Atot and pKa of whole blood. Of note, both estimates performed through whole blood equilibration were remarkably different as compared to the ones previously obtained on plasma. Interestingly, the values of pKa we computed were higher than 7.40, suggesting a higher non-carbonic buffer power of blood against acute respiratory alkalosis rather than acidosis.

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000691

Lipotoxicity is associated with worse outcomes in ICU patients

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Introduction: Lipotoxicity refers to the local or systemic deleterious effects caused by increased levels of fatty acids (FAs), particularly unsaturated fatty acids (UFA) (1). Lipotoxicity has been well described in pancreatitis causing worse outcomes; and recent growing literature has also provided evidence of the potential association of lipotoxicity and worse outcomes in COVID-19 patients (2). While most UFAs exist conjugated to albumin, a small proportion of these are unbound, are biologically active (3), and have been shown to induce cell injury through mitochondrial toxicity (1). The association of lipotoxicity and outcomes in ICU patients has not been well described.
Objectives: To determine the FA profile and their biological activity in sera of ICU survivors as compared to ICU non-survivors.
Methods: Prospective observational cohort study was conducted in a 30-bed multidisciplinary ICU during 2019 and 2020. Consecutive critically ill patients $\geq$ 18 years admitted to the ICU during the study period were screened for inclusion in the study. Exclusion criteria: DNR/DNI and comfort care patients, ICU readmissions, and patients who had not agreed to the use of their medical records for research. Blood samples were obtained in the first 12 h after ICU admission. Serum FAs were analyzed by gas chromatography mass spectrometry and cytokines profile was measured using Luminex. All data are summarized as median [interquartile range (IQR)] or percentages. A p value $\leqslant$ 0.05 was considered statistically significant.
Results: A total of 77 patients (54 males, 70%), were included in the study, 69 of whom survived to hospital discharge. The cohort included 34 (44%) post cardiac surgery patients, 28 (36%) septic shock patients, and 15 patients (20%) with various diagnoses including stroke and hemorrhagic shock. No age difference was found between survivors and non-survivors: 70 years (56–76) versus 66 (54–84), p = 0.91; the severity of disease based on APACHE IV score was higher in non-survivors: 101 (76–107) versus 56 (41–71), p = 0.0007. Total UFAs were significantly higher in non-survivors: 602 uM (321–610) versus 333 (245–408). Unbound FAs were significantly higher in non-survivors: 6.3 uM (5.7–12.4) versus 3.5 (2.9–4.9), p = 0.0005. Serum levels of UFAs Oleic acid (OA) and Linoleic acid (LA) were significantly higher in non-survivors: OA 398 uM (221–422) versus 218 (167–275), p = 0.01; and LA 129 uM (77–158) versus 83 (58–109), p = 0.04. Pro-inflammatory cytokines were significantly higher in non-survivors as compared to survivors including IL-6 pg/mL (490 [158–900] versus 128 [33–388],p = 0.02); IL-8 pg/mL (127 [57–225] versus 27 [17–48],p = 0.0003); and TNFα pg/mL (39 [32–78] versus 16 [6–44], p = 0.02). No differences were seen between the two groups in BMI, lipase, or amylase levels. Septic shock patients presented higher unbound FAs as compared to non-septic patients: 5.2 uM (3.4–9.9) versus 3.4 (2.5–4.7), p = 0.001.
Conclusion: Our study showed that total UFAs, unbound FAs and the UFAs OA and LA Linoleic were significantly increased in the sera of ICU patients that did not survive to hospital discharge as compared to ICU survivors. Non-survivors also presented higher levels of most pro-inflammatory cytokines as compared to survivors. Unbound FAs were also significantly higher in septic versus non-septic patients. The observed association of lipotoxicity with increased mortality in ICU patients merits further investigation as a possible mechanistic process behind worse outcomes observed in critically ill patients.

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Acknowledgements R01DK092460, R01DK119646 from the NIDDK and PR 191,945 from the DOD (VPS), Intramural support from the Mayo Foundation. Intramural funding from the MEGA award (RCC) also contributed to the project.

000936

Adjudin protect cellular damage after status epilepticus

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Introduction: Adjudin, a potential non-hormonal male contraceptive and inhibit cancer growth. Adjudin also has been reported to play a neuroprotective role in an ischemic stroke injury model. However, its effect on status epilepticus (SE) has not been assessed.
Objectives: We investigated whether administration of adjudin can exert beneficial effects in a mouse model of pilocarpine-induced SE.
Methods: For SE induction, mice were given scopolamine methyl nitrate (1 mg/kg, i.p.) 30 min before injection of pilocarpine (325 mg/kg, i.p.). After 2 h of SE, diazepam (10 mg/kg, i.p.) was injected to terminate the seizure activity. Adjudin (50 mg/kg, i.p.) was administrated 1 h after diazepam treatment and continued daily for 3 days after SE. To evaluate the effects of adjudin after SE, the hippocampus was analyzed using immunohistochemistry and western blot.
Results: We found that adjudin treatment protected SE-induced apoptotic neuronal damage in the hippocampus compared with those of vehicle-treated animals. Moreover, adjudin treatment attenuated expression of both ionized calcium binding adapter molecule 1-positive microglia/macrophage and glial fibrillary acidic protein-positive reactive astrocytes in the hippocampus after SE.
Conclusion: The present study demonstrates neuro-protective effects of Adjudin to the hippocampus after SE. These findings suggest that adjudin may be helpful in preventing SE-induced neuronal damage.

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001192

ICU-acquired diaphragm weakness: the role of the myonucleus

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Introduction: ICU-acquired diaphragm weakness affects more than 50% of mechanically ventilated ICU patients and may be caused by ventilator over or under assistance and inflammation, resulting in atrophy and weakness of diaphragm muscle fibers (1). Muscle

fibers are multinucleated cells that may adapt to mechanical load by increasing or decreasing their nuclear content (2). A decrease in myonuclear content has been observed in various animal models of muscle atrophy, including a mechanically ventilated rat model of diaphragm atrophy and weakness (3). Decreased myonuclear content may lead to delayed recovery of muscle size and strength due to diminished transcriptional capacity. Currently, it is unknown whether a decrease of myonuclear content occurs in critically ill patients receiving mechanical ventilation.
Methods: Diaphragm biopsies of mechanically ventilated patients admitted to the ICU with established myofiber atrophy were compared to biopsies of patients who received thoracic surgery for a small, primary, pulmonary nodule (Controls). Immunofluorescent staining of myosin heavy chain and lamin a/c were used together with confocal microscopy to determine myonuclear number, cellular volumes, fiber type and the cytoplasmic volume that is controlled by a single nucleus, the myonuclear domain. Nuclear number was determined per 209 um fiber length and normalized for sarcomere length.
Results: 14 biopsies of ICU patients and 8 control biopsies were analyzed. No significant differences in age or BMI were present between groups. The ICU-group consisted of more males. As expected, volume was significantly lower in both fast and slow-twitch fibers in the ICU group compared to the control group ($p < 0.0001$). Nuclear number was significantly lower in the ICU group with 20[10] vs. 28 [12], $p = 0.0140$ in the slow twitch fibers and 19 [8] vs. 29 [17], $p = 0.0013$ (median[IQR]) in the fast-twitch fibers. Myonuclear domain size was significantly smaller in the ICU group with a size of 2.84[1.90] $\times$ 10^4] μm^3 vs. 4.29[2.08] $\times$ 10^4 μm^3, $p = 0.0088$ in the slow-twitch fibers and a size of 2.71[0.84]] $\times$ 10^4 μm^3 vs. 4.40[1.40]] $\times$ 10^4 μm^3, $p = 0.0011$ (median[IQR]) in the fast-twitch fibers.
Conclusion: Our findings support the hypothesis that myonuclear content is lower in muscle fibers of mechanically ventilated ICU patients with atrophy of the diaphragm. Myonuclear loss was not proportional to the amount of atrophy, resulting in a diminished myonuclear domain size. These findings suggest that, due to lower myonuclear content, transcriptional activity and protein synthesis may be disturbed in diaphragm muscle fibers of mechanically ventilated ICU patients with atrophy. Whether the loss of nuclei drives atrophy or if atrophy results in surplus nuclei that are removed remains to be established.

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Acknowledgements This work was supported by ZonMW Grant 09120011910004 and from institutional and/or departmental sources (i.e.,Amsterdam Cardiovascular Sciences Research Institute).

Nurses & Allied Healthcare Professionals 1

000051

Effects of mechanical insufflation-exsufflation with different pressure settings on respiratory mucus clearance during invasive mechanical ventilation

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Introduction: Mechanical Insufflation-Exsufflation (MI-E) has been proposed as a potential strategy to generate high expiratory flows and simulate cough in the critically ill. However, efficacy and safety of MI-E during invasive mechanical ventilation (MV) are still to be fully elucidated.
Objectives: This study in intubated and mechanically ventilated pigs aimed to evaluate the effects of 8 combinations of insufflation-exsufflation pressures during MI-E on mucus clearance, respiratory flows and pulmonary mechanics.
Methods: 6 healthy Landrace-Large White female pigs were orotracheally intubated, anesthetized and on MV for up to 72 h. 8 combinations of insufflation-exsufflation pressures (+40/− 40, +40/− 50, +40 /− 60, +40/− 70, +50/− 40, +50/− 50, +50/− 60, +50/− 70 cmH_2O) were applied in a randomized order. MI-E device was set to automatic mode, medium inspiratory flow, and inspiratory-expiratory time of 3 and 2 s respectively, with a 1 s pause between cycles. We performed four series of five insufflation-exsufflation cycles for each combination of pressures. Velocity and direction of movement of artificial mucus containing radio-opaque markers was assessed through sequential lateral fluoroscopic images of the trachea. We also evaluated respiratory flows and respiratory mechanics, during, and after each combination of pressures.
Results: In three of the animals the experiments were conducted twice, and once for the remaining three. In comparison to baseline mucus movement (2.85 ± 2.06 mm/min), all insufflation-exsufflation pressure combinations significantly increased mucus velocity ($p = 0.01$). Particularly, +40/−70 cmH_2O was the most effective combination, increasing mucus movement velocity by up to 4.8-fold ($p < 0.05$) (Fig. 1). Multivariate regression analysis confirmed a mild association between mean inspiratory flow (MIF) and mucus clearance (Fig. 2), with a reduction of mucus clearance rate by 0.23 ± 0.08 mm/min per each unit (L/min) increase in MIF (r2 0.12, adj r2 0.10; $p = 0.01$). Expiratory transpulmonary pressure was on average 22.3 ± 9.9 cmH_2O and did not change significantly between pressure combinations ($p = 0.97$), whereas inspiratory transpulmonary pressure was 32.0 ± 5.4 cmH_2O and significantly changed across tested MI-E settings ($p < 0.001$). After MI-E, chest wall elastance and lung elastance were reduced by 0.76 ± 2.41 cmH_2O/L ($p = 0.92$) and 1.33 ± 4.24 cmH_2O/L ($p = 0.13$), respectively, with no significant differences between MI-E settings. MI-E marginally increased airflow resistance post intervention by 0.66 ± 1.84 $cmH_2O/L/sec$ ($p = 0.82$), and tissue resistance by 0.34 ± 2.73 $cmH_2O/L/sec$ ($p = 0.68$), with no significant differences between the combinations of pressures (Table 1).
Conclusion: MI-E appears to be an efficient strategy to improve mucus clearance during invasive MV, particularly when set at +40/− 70 cmH_2O. No safety concerns were identified although a transient significant increase of transpulmonary pressure was observed.

000116

Effect of high flow nasal cannula on mechanical ventilator duration in critically ill children

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Introduction: High flow nasal cannula (HFNC) gained popularity as a non-invasive respiratory support modality among pediatric and adult ICUs due to its simplicity and higher tolerability. The widespread use of HFNC was supported with clinical efficacies in diverse clinical settings including acute hypoxic respiratory failure, chronic obstructive pulmonary disease in adult population, and acute bronchiolitis, asthma and obstructive apnea in pediatric population. The efficacy of HFNC on mechanical ventilation (MV) has been reported in various scales in adult population to help reduce extubation failure rate and increase ventilator-free days among acute respiratory failure patients in ICUs. However, the need for evidences supporting the use of HFNC among ICU patients in clinical situations other than acute respiratory failure and pragmatic evidences for overall ICU patients remains, especially in pediatric patients.
Objectives: This study aims to evaluate the real-world effect of HFNC on duration of MV among critically ill pediatric patients on a nationwide database.
Methods: This was a population-based retrospective cohort study based on the Health Insurance Review and Assessment (HIRA) from the Korean Ministry of Health. 97% of Koreans are covered by The Korean National Health Insurance (KNHI) and the remaining 3% of Koreans who cannot afford national insurance are covered by the Medical Aid Program (MAP). Since HIRA service reviews reimbursement claims from KNHI and MAP, virtually all inpatient and outpatient visits, procedures, and prescriptions are available with the database from HIRA. To evaluate duration of MV before and after introducing HFNC, teriary hospitals are selected if they have issued at least 1 prenscription for respiratory therapy including oxygen therapy, MV between 2012 and 2019 (638,371 admissions from 49 tertiary hospitals). For selected hospitals, pediatric population including or under age of 17 are included. Nonates (N = 460,209) and neonatal ICU admissions (N = 67,188) were excluded due to unavailability of individual identification.
Pre-and post-HFNC application periods are selected for evaluation of effect of HFNC on duration of MV in each hospital. While the first day of HFNC application of each hospital was set as an index date, Pre-HFNC period, transition period and post HFNC period were defined as previous 12 months from index date and 6 months and 12 months after index date, respectevely.
Results: Between January 2012 and July 2019, the use of HFNC gradually increased after its introduction in 2015. In the 49 tertiary hospitals, 4,705, 2,301, and 4,864 patients received respiratory support wthin 12-month before HFNC introduction, transition period, and 12-month after HFNC introduction, respectevely. In post-HFNC period, patients were more likely to be younger (5.4 years old vs 5.2 years old, P = 0.02), and diagnosed congenital anomaly (36.5% vs. 38.4%, P = 0.001). More patients in post-HFNC received MV support (64.8 vs 67.1, P = 0.02) and required vasopressor (63.4 vs. 68.2%, P < 0.01) than in pre-HFNC period. In adjusted model, there was significant reduction in MV duration of 0.99 days in post-HFNC period (95% CI -1.86, -0.12, P value = 0.03). The adjusted model also revealed statistically significant reduction in duration of MV among prolonged MV subgroups (more than 28 days) and surgery subgroups by 6.71 and 1.47 days, respectively. Changes in MV duration in other subgroups including chest surgery, congenital anomaly, respiratory disease, circulatory disease, and infectious disease subgroup were not statistically significant in both crude and adjusted model.
Conclusion: The application of HFNC in pediatric ICU can reduce the MV duration, especially in patients requiring prolonged MV or surgery.

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000146

The impact of a dedicated critical illness rehabilitation team on mobility levels in survivors of critical illness on step down to the ward

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Intensive Care Medicine Experimental 2022, **10(2)**: 000146

Introduction: Early and structured rehabilitation is recommended to improve outcomes for patients admitted to the intensive care unit (ICU) [1]. Despite this increased focus on rehabilitation, only limited data is available to evaluate whether this level of rehabilitation is maintained on ward step down. A study by Hopkins et al. (2012) demonstrated activity levels to decrease in 56% of patients on the first full ward day in comparison to highest levels achieved in the ICU [2], with suboptimal rehabilitation identified as a common factor for those patients who die on the ward following ICU discharge [3]. Within our trust we have created a dedicated critical illness rehabilitation team (CIRT) to support ongoing rehabilitation and patient transition from ICU to the ward.
Objectives: To evaluate whether the presence of a dedicated critical illness rehabilitation team helps to maintain or improve mobility level on the first full ward day after step down from ICU.
Methods: Patients admitted to ICU for ≥ 4 days between 4th October 2021 and 11th February 2022 and surviving to ICU discharge were eligible for inclusion in the analysis. Inclusion criteria were patients who achieved a Manchester Mobility Score of ≤ 5 at ICU discharge but who had been independently mobile prior to ICU admission. Patients were excluded if they had contraindications to mobilise (e.g. major trauma or neurological injury). The critical illness rehabilitation team supported rehabilitation in critical care prior to ward step down, and then continued for up to 2 additional weeks on the ward. Primary outcome was change in activity level, defined as change in Manchester Mobility Score on day 1 on the ward vs the highest level achieved before ICU discharge.
Results: During the trial period 78 patients met the inclusion criteria and were seen by the critical illness rehabilitation team. Just over half of the patients were mechanically ventilated in ICU and the average length of stay was 13.2 days (see Table 1). Mobility levels were maintained in 33 (42%) or increased in 35 (45%) of patients, with only 10 (13%) showing a reduction (see Fig. 1). Median Manchester mobility scores were significantly higher on day 1 on the ward in comparison to ICU discharge levels (5 vs 4, p = 0.01828). Patients received an average of 5 additional rehabilitation sessions from the CIRT on the ward.
Table 1

Age	55 ± 13.9
Gender (male)	48 (62%)
ICU lnegth of stay (days)	13.2 ± 12.6
Ventilated	44 (56%)
ventilation days (n = 44)	12.5 ± 11.1
Median Manchester Mobility Score—ICU discharge	4 (2–5)
Median Manchester Mobility Score—Ward day 1	5 (2.5–6)
Ward length of stay (days)	15.9 ± 16.2

Means (sd) unless stated.

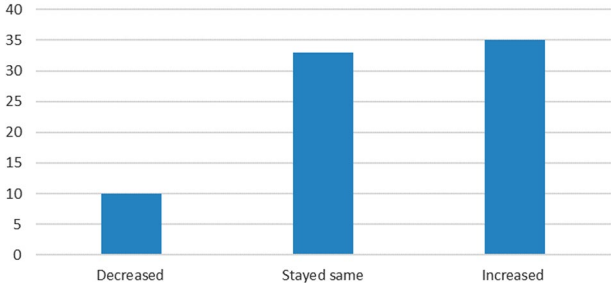

Figure 1

Conclusion: The presence of a dedicated critical illness rehabilitation team was effective in maintaining or improving mobility levels on the first day of ward transfer. This could provide a useful framework to support ward step down and ongoing rehabilitation in survivors of critical illness.

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Acknowledgements n/a.

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What limits early mobilisation of critically ill patients: An observational study

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Intensive Care Medicine Experimental 2022, **10(2)**: 000166

Introduction: Intensive care acquired weakness is a common risk factor of extended intensive care unit (ICU) stays and has been found to be more prevalent when sedation and neuromuscular blocking agents are used, as well as when a patient experiences multiple organ failure and long periods of immobility (1). Early mobilisation has been found to be safe and feasible in acute phases of illness, resulting in a higher level of mobility at point of discharge from ICU in turn, reducing hospital length of stay (2). Despite this, a previous point prevalence survey showed rehabilitation levels in ICU in the United Kingdom were low, particularly in patients receiving mechanical ventilation and organ support (3).
Objectives: 1. To determine mobilisation rates within ICU in a large UK based acute hospital trust. 2. To identify limiting factors to mobilisation in ICU and any potentially modifiable factors.
Methods: We conducted a survey of physiotherapy treatment for two separate five day periods (20/12/2021-24/12/2021; 10/01/2022-14/01/2022) in a UK based 30 bedded ICU. Rehabilitation data was collected for all patients, excluding those with specific contraindications to mobilise (e.g. spinal injuries). Data was collected daily using a predesigned tool establishing mode of ventilation, sedation use, inotropic support, Continuous Veno-Venous Hemofiltration (CVVH) requirement and mobilisation levels. When mobilisation (defined as sitting on the edge of the bed, transferring to a chair, standing or walking) was not completed, the primary reason for this was collected from the therapy notes. Statistical analysis was carried out using Fisher's exact tests.
Results: A total of 164 physiotherapy treatments were administered over the study period, of which 39 (24%) included mobilisation. Levels of mobilisation were significantly lower in patients receiving mechanical ventilation (10% vs 41%, $p < 0.00001$) and those receiving inotropic or vasopressor support (6% vs 33%). Whilst patients receiving continuous renal support mobilised less frequently, this was not statistically significant (12% vs 26%, $p = 0.1356$). Whilst no patients who were receiving sedation mobilised, once sedation had been stopped conscious level and the ability to follow commands was not a barrier for mobilisation (38% vs 37%, $p = 1.00$). For patients who were mechanically ventilated and not receiving sedation, mobilisation rates increased to 26%. The largest barriers to mobilisation were sedation ± paralysis (42%) and cardiac or respiratory instability (23%). A number of potentially modifiable factors were identified, with up to 32% of limitations being potentially modifiable. The largest of these were awaiting neurosurgeon documentation of mobility status (10%) and reason not stated (6%) where no apparent limitation could be identified.

Table 1 Documented barriers to mobilisation

Limitations to Mobilisation	Percentage (n = 125)
Sedated (± Paralysis)	42% (52)
Unstable (CVS/Respiratory)	23% (29)
Awaiting Neuro Documentation	10% (12) *
Not Stated	6% (8) *
Agitated	4% (5) *
Declined	6% (7) *
ETT	2% (3) *
Other (inc. ICP, INR, a/w cardiology r/v)	3% (4)
CVVH	4% (5) *

Data are reported as % (N).
*Potentially modifiable limitations.
Conclusion: This observational study demonstrated that despite the proven benefits of early mobilisation, a number of barriers to delivery still exist. The ability to mobilise were significantly affected by the presence of sedation, invasive ventilation and inotropes / vasopressors. Promisingly, approximately a third of limitations to mobilise were potentially modifiable. Improved education, better management of agitated patients and a more patient centred approach to rehabilitation planning may help to improve overall mobilisation rates.

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Acknowledgements n/a.

000179

Feasibility@ 48: A cross sectional multi-centre study of Intensive Care Unit (ICU) mobility practices across the United Kingdom

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Intensive Care Medicine Experimental 2022, **10(2)**: 000179

Introduction: Mobilisation within 48–72 h of admission to the Intensive Care Unit (ICU) is recommended to mitigate the risk of functional decline. However, point prevalence data suggest that mobility levels within the intensive care setting are low 10%-36%)(1–3). While barriers to rehabilitation have been explored extensively(3–7), there is limited research assessing the relationship between physical activity and physiological status, or indeed whether out-of-bed mobilisation(8) is routinely achieved within 48 h of admission.
Objectives: To determine:

- The level of physical activity achieved for all patients on a single day in adult ICUs across the UK, including the proportion of those achieving out-of-bed mobilisation defined by an ICU mobility score (IMS) of ≥ 3.
- The physiological profile of ICU patients who achieve out-of-bed mobilisation (IMS of ≥ 3).

Methods: Design: Cross-sectional multi-centre observational study of UK adult ICUs on a single day.
Population: Adult ICU patients (level 2/3) on a single day. No exclusion criteria.
Data Analysis: Descriptive statistics were used to describe patients and sites, and the proportion of patients who scored IMS of ≥ 3. We plan to use regression analysis to explore the physiological status of those who achieved IMS of ≥ 3, versus those who did not.
Results: Data were collected for 960 patients (36 NHS organisations across 84 level 2/3 areas). 40.9% (393) achieved an IMS of ≥ 3, i.e. sat over the edge of the bed, stood, or stepped. 5% (48) an IMS of 2, i.e. a passive transfer to a chair, 8.8% (84) did bed exercises only, and 45.3% (435) did not participate in active mobility. Over half, 52.3% (502), had achieved an IMS ≥ 3 at some point during their stay. 284 patients had an oral endotracheal tube. Of these, 3.2% (9/284) achieved an IMS of ≥ 3, none of whom were receiving vasoactive agents, one was receiving continuous renal replacement therapy (CRRT), and five had a Richmond Agitation and Sedation Score (RASS) of < 0 or > 1. Of those patients with a tracheostomy, 39.7% (77/194) achieved an IMS of ≥ 3, none of whom were receiving vasoactive agents, three on RRT, one on ECMO, and seven had a RASS < 0 or > 1. 63.7% (307/482) of those with their own airway achieved an IMS of ≥ 3. 35 of these had ≥ 1 vasoactive agent, 13 RRT, and 23 a RASS of < 0 or > 1. Of the 761 patients with completed dates of admission, who had been in ICU for > 2 days, 53% (400) had achieved out-of-bed mobilisation some point in their ICU stay.
Conclusion: This is the first multi-centre study describing the 'usual care' of ICU mobility practice across the UK. Over 40% of patients achieved out-of-bed mobilisation, greater than reported elsewhere. Analysis of the relationship between physiological status and physical activity is ongoing. This will elucidate why fewer than 15% were unable commence out-of-bed mobilisation within 48 h of admission, and potentially why this may not be a feasible target in practice.

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Acknowledgements Unfunded.

000255

Level of hope and associated factors during first year after intensive care treatment

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Intensive Care Medicine Experimental 2022, **10(2)**: 000255

Introduction: Hope during and after critical illness is important due to the uncertainty and loss of control in the patients' life situation (1). Hope has previously been considered for its potential therapeutic value and as a coping resource for better recovery after treatment in the intensive care unit (ICU) (2, 3).
Objectives: To describe levels of hope in patients during their first year after ICU treatment, and to explore possible associations between selected demographic, clinical and psychosocial factors and hope.
Methods: Data were retrieved from a sub study of a randomized controlled trial with 523 discharged ICU patients from five ICUs at Oslo University Hospital (OUH) included from March 2014 to December 2016 (4). Patients completed self-reported questionnaires at the hospital ward median 4 days (range 0—48 days) after ICU discharge, and at three, six and 12 months later. Hope was measured using Herth Hope Index (5) – Norwegian version (HHI-N) (range 12–48), post-traumatic stress symptoms with Post Traumatic Stress Scale -10 Intensive Care Screen (PTSS10-I) (range 10–70) (6) and social support with the revised Social Provision Scale (SPS) (range 16–64) (7). Univariate and multivariate linear regression analyses for variables expected to be associated with level of hope 12 months after ICU treatment were first performed. Variables significantly associated with hope were further included in a linear mixed model analysis for repeated measurements with hope at three, six and 12 months as the dependent variable.
Results: Mean age was 55 years (SD 17.0), 47% were women, mean length of ICU stay was seven days (SD 9.5), 54% had received mechanical ventilation, and mean SAPS II score was 25 (SD 12.2). Not having a prior psychiatric problem (B 1.93, 95% CI [0.90, 2.98]) and lower levels of post-traumatic stress symptoms (B − 0.08, 95% CI [− 0.11, − 0.04]) immediately after ICU discharge were both independently associated with higher levels of hope at three, six and 12 months after ICU treatment. Higher score of social support (B 0.37, 95% CI [0.31, 0.43]) three months after ICU discharge was independently associated with higher

levels of hope. Our data did not reveal any significant changes in levels of hope assessed at three, six and 12 months, the estimated mean values for hope were 37.9 (three months), 37.9 (six months) and 37.7 (12 months), respectively.
Conclusion: Prior psychiatric problems, higher levels of post-traumatic stress symptoms and social support after ICU discharge have all a significant impact on levels of hope and are important variables to pay attention to during and after ICU treatment.

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Acknowledgements
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000319

Impact of enhanced Occupational Therapy on provision of specialist seating within a multispecialty intensive care unit—A quality improvement project

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Introduction: Evidence suggests Occupational Therapy (OT) involvement in rehabilitation can reduce both physical and non-physical morbidity and hospital length of stay (LOS) (1, 2). One of the core roles of OTs on an intensive care unit (ICU) is the provision of specialist seating which enables the most dependant patients to begin early mobilisation. Despite this, funding for OTs within critical care is limited, often below GPICS recommendations (3). This can result in delayed mobilisation of patients with complex seating requirements. This quality improvement project (QIP) evaluates the impact of increased OT staffing on delays to mobilisation in patients requiring a tilt in space (TIS) wheelchair.
Objectives: To evaluate the impact of enhanced occupational therapy on delays to mobilisation in patients requiring TIS wheelchairs, in a large tertiary UK ICU.
Methods: Pre-QIP, OT were staffed at 1:75 ICU patients, covering cardiac, trauma, neuro and general specialities. An 18 month senior secondment post was created in January 2020, improving staffing ratios to 1:35. All patients admitted to ICU and issued with a TIS wheelchair during the study period were included in analysis. Data was collected retrospectively from electronic patient noting. Primary outcome was delays to mobilisation, defined as time taken from when a therapist identified a patient as requiring a TIS wheelchair to the patient sitting out. Secondary outcomes included ventilation days and ICU and hospital LOS.
Results: 129 patients were issued with a TIS wheelchair and included in analysis. Cohort demographics pre and post QIP were comparable (Table 1). Patients during the QIP had significantly shorter delays to mobilisation (2.5 vs 6 days, $p < 0.05$), shorter ICU LOS (22.65 vs 28 p. 0.041) and one day less on mechanical ventilation (16 vs 15 days). No benefit to hospital LOS was observed.

Table 1 Outcomes

	Pre QIP (n = 80) Jan 2018 – Jan 2020	Post QIP (n = 49) Jan 202	P Value
Mean Age (SD)	51.5 (17.84)	51.1 (17.21)	0.857
Sex n (%)	Male 52 (65%) Female 28 (35%)	Male 34 (69%) Female 15 (31%)	0.701
APACHE 2 (SD)	15.24 (5.92)	15.41 (6.91)	0.984
Patient directorate •General medicine/ surgery •Trauma and Orthopaedics •Neurology	32 (40%) 13 (16%) 35 (44%)	20 (41%) 5 (10%) 24 (49%)	
Delay to mobilisation	6 (4–8)	2.5 (2–4)	< 0.00001
Ventilator Days	16 (11–24)	15 (9–20)	0.395
ICU LOS (days)	28 (22.32 – 38.1)	22.65 (16.6 – 31.8)	0.041
Hospital LOS (days)	40 (29–65.5)	63 (43–104)	0.021

** all figures displayed as median and IQR unless otherwise stated and p values calculated using the Mann Whitney U test.
Conclusion: Enhanced OT staffing on ICU was associated with reductions in delays to mobilisation and ICU LOS for patients requiring TIS wheelchairs. No impact on hospital LOS was observed. This maybe due to the detrimental impact of COVID 19 on patient pathways. Further research is required to confirm these finding and to support ongoing funding for OT within ICU.

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Acknowledgements N/A.

Nurses & Allied Healthcare Professionals 3

000379

The implementation of nUrsiNg DEliRium Preventive INterventions in the Intensive Care Unit (UNDERPIN-ICU): a qualitative evaluation

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Intensive Care Medicine Experimental 2022, **10(2)**: 000379

Introduction: Delirium is common in ICU patients and is associated with worse outcomes. Recently, a multicomponent non-pharmacological nursing intervention program (UNDERPIN-ICU), was implemented

in ten Dutch ICUs. The program was aimed at delirium reduction by optimizing four modifiable risk factors: visual and hearing impairment, cognitive impairment, immobility, and sleep deprivation. Despite its scientific fundament and extensive implementation, this randomized controlled trial showed no effect on delirium outcomes.
Objectives: We explored experiences of healthcare professionals towards factors that hindered or stimulated the application of the UNDERPIN-ICU delirium program in daily practice.
Methods: Semi-structured focus group interviews were performed in the participating centers between April and June of 2019. Interviews were audio recorded and transcribed verbatim. Direct content and thematic analyses were applied. Interviews were coded and thematized for factors that hindered or stimulated program application. Five themes were used from the implementation literature: Factors related to the interventions; Factors related to the Individual health professional; Patient related factors; Factors related to the implementation process; Factors related to the capacity for organizational change.
Results: In total, 24 ICU nurses, 2 ICU physicians and 5 local project leaders participated. The program application was hindered by healthcare professionals' doubts regarding the program's efficiency and feasibility, difficulties tailoring the extensive number of program components to patients' individual needs, limited healthcare professionals' knowledge, limitations in staffing and resources, a focus on physical care and other priorities. The application was stimulated by a structured implementation, support from the research team, incorporation of components in daily routines, study reminders, regular feedback on performance and involvement of other health professionals. A limited number of simple and standardized interventions which provide direct visible results also stimulated intervention application.
Conclusion: Factors that hindered program application may explain why the UNDERPIN-ICU program did not have positive effects on delirium outcomes. Factors that stimulated application should be strengthened in future non-pharmacological nursing interventions to prevent or reduce delirium in the ICU.
Acknowledgements This study was funded by ZonMw, the Netherlands, Organization for Health Research and Development (dossier number: 80–84,300-98–71,006) and the 'RIHS Junior researcher round 2013' of the Radboud Institute for Health Sciences, Radboud university medical center.

000436

Effect of suction circuit flushing with Chlorhexidine on the occurrence of Ventilator Associated Pneumonia among mechanically ventilated patients: A quasi experimental study

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Introduction: Standard practice of flushing saline following endotracheal suctioning can create a medium for bacterial colonization and proliferation inside the suctioning circuit including the suction catheter, suction tube, and collecting jar. These organisms can possibly migrate to patient's lung during suctioning procedure causing ventilator associated pneumonia (VAP). Therefore, there is a need to flush the endotracheal suctioning circuit with an appropriate disinfectant to prevent bacterial colonization, and subsequently reducing VAP occurrence.
Objectives: To investigate the effect of suction circuit flushing with chlorhexidine on the occurrence of VAP among mechanically ventilated patients.
Methods: A quasi-experimental study with a randomized controlled trial design was adopted. Study participants (n = 136) were randomly assigned to either the intervention or control group. The intervention group received suction system flushing with 40 ml chlorhexidine gluconate 0.2%; the control group received normal saline for flushing the system. The primary outcome measure was VAP incidence at day 3 and day 6 of ICU admission corresponding to early onset and late onset VAP, respectively. The secondary outcome was the cost of flushing solution (the price of one Liter of chlorhexidine and saline is 9.80 and 40.00 EGP, respectively). Recruitment was between May and November 2020. Ethical approval was obtained from the Research Ethical Committee and the trial was registered at ClinicalTrials.gov (NCT05206721).
Results: No statistically significant differences were noted of the study participants between the intervention (n = 68) and standard care (n = 68) groups regarding age, gender, reason for ICU admission, past medical history, and mode and duration of mechanical ventilation. The incidence of VAP among patients in the intervention group was significantly lower than in the control group; 15 (22.1%) vs 29 (42.6%), $p = 0.010$. The intervention was more effective in decreasing the incidence of late-onset VAP (26.2% vs 49%, $p = 0.026$) instead of early-onset VAP (13.2% vs 25%, $p = 0.081$). Chlorhexidine reduced the cost of suction system flushing by 75% compared to normal saline (median: 78.4 vs 300 EGP, $p < 0.001$).
Conclusion: Suction circuit flushing with chlorhexidine can significantly reduce the occurrence of VAP among mechanically ventilated patients and reduce the cost of flushing solutions. The results of our study recommends incorporating suction circuit flushing with chlorhexidine into the daily care of mechanically ventilated patients, along with other VAP bundle elements in order to achieve the maximum VAP reduction in ICU.

000448

How patients with COVID-19 died in ICU and the stress level on their relatives

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Introduction: COVID-19 had a high mortality rate, particularly at the beginning of the pandemic in intensive care unit (ICU) (1). Hospital visits were suspended and video calls were proposed to connect patients with their relatives (2), especially during of end of life (3).
Objectives: The primary objective of this study was to describe the treatments delivered to patients affected by COVID-19 dying in ICU. The secondary aim was to explore whether video calls and visits affected the stress level of patients' relatives.
Methods: This is a cross-sectional study performed in the COVID-19 ICUs of the Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, hub center of Milan (Italy) during the first year of pandemic. We collected data on patients who died; stress level was assessed on their relatives using the Impact of Event Scale-Revised (IES-R).
Results: We included 70 patients and 56 relatives. All the patients died with ventilation, hydration, nutrition, analgesia, and sedation ongoing. Cardiopulmonary resuscitation procedures were performed in 5/70 patients (7.1%). Among the relatives interviewed, only 6/56 (10.7%) visited their loved ones and 12/56 (50%) made a video call. End of life video calls was considered useful by 53/56 relatives (94.6%) but all of them (56/56, 100%) would have wanted to visit the patient. High stress levels were found in 38/56 relatives (67.9%), regardless of whether they accessed to intensive care unit or made the video calls. The sons and the daughters were less likely to show a positive IES-R (OR 0.22, 95%CI 0.05 to 0.89).

Conclusion: In the first year of COVID-19 pandemic considered, patients died without their relatives bedside and with ongoing life-sustaining treatments. End of life video calls are appreciated by relatives but not enough to alleviate death-related stress.

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Acknowledgements None.

000476

Enhancing Physiotherapy staffing levels for Rehabilitation: A Quality Improvement Project

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Introduction: Patients requiring mechanical ventilation (MV) on Intensive Care (ICU) experience significant physical and psychosocial morbidity (1). Evidence has demonstrated that early and structured rehabilitation on ICU improves patient outcomes and reduces ICU and hospital length of stay (LOS) (2). To facilitate early rehabilitation, NICE CG83 guidelines recommend a physiotherapist to patient ratio of 1:4. However, many UK ICUs fall below these recommendations.
Objectives: To evaluate the impact of enhanced physiotherapy staffing levels, in conjunction with MDT training and education, on patient outcomes in a large mixed UK medical/surgical ICU.
Methods: All patients admitted and MV $\geq$ 4 days between 1st June and 31st December 2020 (post-QIP) were included in analysis. Patients with significant neurological injury were excluded. Outcomes were compared to historic data from 1st June and 31st August 2018. Physiotherapy staffing ratios were increased from 1:9.5 patients to 1:6 for the quality improvement project (QIP), to enable the consistent delivery of patient specific, structured rehabilitation. Support and guidance was provided by an ICU consultant Physiotherapist to the therapy team and MDT on the feasibility of the project, data collection and analysis. Primary outcome was functional status at ICU discharge, assessed with the Manchester Mobility Score (MMS). Secondary outcomes included time to mobilise, ventilation days, LOS and mortality.
Results: Post-QIP, significantly more patients mobilised within ICU (92% vs 42% P < 0.0001), with mobilisation commencing earlier whilst patients remained on MV compared to post-liberation from MV pre-QIP. This was associated with higher levels of mobility at ICU discharge (MMS 4 vs 1 P = 0.00012), with patients on average able to stand compared to remaining bedbound. A reduction in time to mobilise, ventilation days, ICU and hospital LOS was observed, although not statistically significant. The higher ICU mortality was attributed to the COVID-19 pandemic.

	Pre QIP 1st June–31st August 2018	**Post QIP 1st June–31st December**	**p-value**
N	49	83	
Mean Age (SD) ~	59 (17)	60.5 (14.49)	0.15
Mean APACHE 2 (SD) ~	17.45 (6.12)	15.69 (5.28)	0.819
Ventilator days #	8 (5–1)	7 (4–13)	0.789
ICU LOS*#	12 (8–18)	10 (7–17)	0.313
Hospital LOS**#	25 (18.5–40.5)	22 (13.25–44.5)	0.368
Patients mobilised in ICU*∞	**14/33 (42%)**	**45/49 (92%)**	**< 0.0001**
Time to mobilise*#	11 (4–16)	6 (4–9.5)	0.28
MMS ICU discharge*#	**1 (1–3)**	**4 (3–5)**	**0.00012**
Mortality ICU ∞	16 (33%)	34 (41%)	0.36
Mortality ward∞	3 (9%)	2 (2%)	0.387

Note outcome variables marked with * only include data for patients who survived to ICU discharge and ** for hospital discharge. Date was displayed as median (IQR) unless otherwise stated

#p –value from a Mann Whitney Test ~p –value from t-test ∞p – value from fisher exact

Conclusion: Enhanced physiotherapy staffing accompanied by MDT education resulted in increased rehabilitation activity within ICU and improved functional status at ICU discharge. This reduced patient dependency represents a reduction in ongoing nursing needs on the ward. Although not statistically significant, the reduction in LOS and financial expenditure is clinically important to improving patient flow, and justifies investment in physiotherapy.

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000483

The impact of physiotherapy led education on time to mobilise in high-risk surgical patients admitted to an Enhanced Peri-Operative Care Unit (EPOC).

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Intensive Care Medicine Experimental 2022, **10(2)**: 000483

Introduction: The Sars-Cov-19 pandemic has seen increased pressure on perioperative health systems resulting in protracted waiting times [1]. An EPOC unit was established at our tertiary-level hospital to help restore high-risk elective surgical capacity. For patients admitted to EPOC, achievement of early postoperative mobilisation is an important clinical milestone [2] and now also part of an NHS CQUIN key quality care performance indicator (ref CCG8 [3]).
Objectives: To evaluate the impact of a physiotherapy led teaching bundle on time to mobilise in patients admitted to an EPOC unit following elective cancer surgery at a UK tertiary hospital.
Methods: All patients admitted to the EPOC unit between October to December 2021 following elective UGI and abdominal surgery were included in analysis. Current practice is to screen post-operative patients using the Southampton post-operative screening tool (SPPOST) [4], with high-risk patients having their post-operative mobilisation led by physiotherapists, and low risk by nursing staff. In its infancy, the EPOC unit was staffed primarily by a multi-disciplinary team (MDT) unfamiliar to ERAS and early mobilisation. As part of the education intervention a senior physiotherapist delivered face-to-face

teaching to nursing staff on the feasibility, safety and benefits of early mobilisation and the MDT's role to achieve this. Environmental and logistical barriers to early mobilisation were also reviewed and addressed i.e., appropriate seating, bedrest protocols post line removal. Outcomes were compared to historical data collected from the same EPOC unit between March and April 2021. Primary outcome was time to sit out as assessed on the Manchester Mobility Scale (MMS 5). Secondary outcomes included time to mobilise 30 m (MMS 7), incidence of hospital acquired pneumonia (HAP) and post-op hospital length of stay (LoS).

Results: Following our education intervention, significantly more patients sat out of bed POD1, in both the physiotherapy and nursing led post-op mobilisation cohorts (Table 1). Patients were also significantly quicker to mobilise 30 m within the physiotherapy led cohort. Although not statistically significant, there was a trend towards a reduction in hospital LoS in both cohorts. Incidence of HAP slightly increased post teaching intervention, 6% to 8% although this was not statistically significant (p = 0.6319), however this may reflect the heterogeneity in patient cohort pre and post education intervention.

Table 1 MMS Post-op day 1 pre and post physiotherapy led teaching bundle

		High Risk (Physio Led)		P value	Low Risk (Nurse Led)		P value
		Pre-QIP	Post-QIP		Pre-QIP	Post-QIP	
N		60	94		33	61	
MMS Post-op day 1 (%)	MMS < 5	49 (82%)	36 (38%)		28 (85%)	20 (33%)	
	5	10 (16%)	49 (52%)		5 (15%)	34 (56%)	
	6	1 (2%)	4 (4%)		0 (0%)	0 (0%)	
	7	0 (0%)	6 (6%)		0 (0%)	7 (11%)	
% achieved ≥ MMS 5 POD 1 (n)		18% (11)	62% (59)	**<0.0001**	15% (5)	67% (41)	**<0.0001**
Days to achieve MMS 5 (IQR) *		2 (2–3)	1 (1–2)	**<0.00001**	2 (1–2)	1 (1–2)	**0.0012**
Days to achieve MMS 7 (IQR) *		5 (3.75–6)	3 (2–5)	**<0.00094**	3 (2–6)	3 (2–4)	0.16452
Post-op Hospital LoS Days (IQR) *		9 (6–10)	8 (5.75–12)	0.89656	6 (3–8)	5 (4–7)	0.8493

* Median values

Conclusion. Provision of a physiotherapy led teaching bundle significantly reduced the time to mobilise in post-op surgical patients and has moved us closer to our PQIP target of > 85% of patients sitting out POD1 [5]. We plan to further evaluate the reasons why patients did not achieve early mobilisation to further improve our delivery of care.

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Acknowledgements Nil.

000512

Validation of the ROX index to predict high flow nasal cannula therapy treatment failure in infants with bronchiolitis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000512

Introduction: High flow nasal cannula (HFNC) therapy is commonly used to provide an intermediate level of respiratory support for infants with bronchiolitis.(1) Pediatric morbidity may be increased when non-invasive ventilation inadvertently and inappropriately delays endotracheal intubation for invasive mechanical ventilation.(2) In adult and pediatric patients with diverse respiratory diseases, the ROX index (ratio of SpO_2/FiO_2 to respiratory rate) has demonstrated success in predicting HFNC treatment failure.(3,4).

Objectives: To evaluate the utility of the ROX index in predicting HFNC treatment failure in infants with bronchiolitis.

Methods: Retrospective cohort analysis of previously well infants (< 1 year) hospitalized for bronchiolitis and initiated on HFNC as the primary modality of respiratory support.

Results: Of 64 infants (median age 70 days) included in the study, 5 (7.8%) required intubation within 6 h of HFNC initiation (median time to intubation 225 min). No between-group differences were observed with respect to sex, age, weight, RSV status, presumed bacterial pneumonia, or hospital unit of HFNC initiation. Infants who experienced treatment failure were initiated on HFNC earlier in the course of their illness compared to other infants (3 days vs 4 days, $p < 0.02$). The ROX index did not demonstrate discriminatory ability at time of HFNC initiation (AUROC 0.6, $p = 0.5$) or 1 h after initiation (AUROC 0.6, $p = 0.6$).

Conclusion: The ROX index at HFNC initiation and 1 h did not predict early treatment failure in infants with bronchiolitis. Future study with a larger cohort is warranted.

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Acknowledgements This study was funded by an IWK Mentored Project Grant.

000571

A new high-fidelity Crisis Resource Management and Human Factors Simulation for critical care nurses

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Intensive Care Medicine Experimental 2022, **10(2)**: 000571

Introduction: Critical care nurses are central to the effective management of the deteriorating patient. Principles of crisis resource management (CRM) provide a framework for teaching non-technical skills important for effective teamwork. Simulation has been shown to be an effective method for teaching and training nurses, with higher fidelity simulation effective in cognitive and psychomotor domains of learning as well as improving team performance (1). There is a paucity of literature on human factors and CRM focused simulation for critical care nurses.
Objectives: We aimed to introduce principles of CRM to critical care nurses, to improve their awareness of human factors and non-technical skills and improve their recognition and management of common critical care emergencies.
Methods: Between December 2021 to present, in collaboration with practice development nurses we designed and delivered a high-fidelity simulation course focusing on CRM and human factors for nurses working in critical care. Pre-course learning of three lectures were delivered to candidates. The course consisted of a lecture on CRM and 3 individual simulation scenarios and debriefs. The scenarios focused on managing a difficult intubation, obstructed tracheostomy and a deteriorating patient in the prone position. Candidates completed a survey before and after the course with Likert scale data was collected at both points. Questions assessed confidence in managing the emergencies above as well as familiarisation with relevant guidelines and general course satisfaction. Qualitative data on learning points and "take-homes" from the sessions were also collected.
Results: 32 candidates attended the course with a post-course survey response rate of 87.5%. More than 90% of candidates agreed or strongly agreed that the course was realistic enough to promote learning, met their personal learning objectives and created learning opportunities resulting in reflection on their own practice. All agreed or strongly agreed that they understood the terms "human factors" and "non-technical skills". Post-course mean scores relating to self-reported familiarity with DAS guidelines and NTSP guidelines both improved significantly compared to precourse. Scores relating to confidence in assisting with difficult airway management, assisting with management of a tracheostomy emergency and in managing an acutely unwell patient in the prone position also improved ($p < 0.0001$ for all).
Thematic analysis of qualitative data highlighted the importance of leadership, communication, and early escalation for help as the three most important learning points from the course. Themes regarding changes to future practice were improved confidence to speak up and improved familiarity with relevant management guidelines.
Conclusion: A new CRM simulation course designed for critical care nurses was well received and resulted in improved self-confidence with managing selected emergency situations and increased familiarity with relevant guidelines.

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Nurses & Allied Healthcare Professionals 4

000577

Feasibility study looking into the implementation of using the CPAx Outcome Measure within a Liver Critical Care setting at a London Hospital

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Intensive Care Medicine Experimental 2022, **10(2)**: 000577

Introduction: NICE guideline CG83 requires the use of regular outcome measures (OMs) in rehabilitation of critical care (CC) patients. An abstract benchmarking outcome measures used within adult CC reported The Chelsea Critical Care Physical Assessment Tool (CPAx) was the most widely used. A literature review showed the lack of evidence into the feasibility of implementing CPAx in adult CC.
Objectives: To assess the feasibility of using CPAx within adult CC. To guide standarisidation of outcome meausres across a London CC centre.
Methods: A pilot study was conducted by a Physiotherapy (PT) team on a Liver CC at a London Hospital over 1 month. Inclusion criteria; all patients admitted during study period. The following resources were gathered; a dynamometer, laminated grip strength, score sheets and radar charts. Training was provided to the PTs completing the study. Documentation was completed on the computer system with an acronym which could be copied and pasted for convenience to generate scores. Adaptations were made to the PT priortisation sheet to prompt the frequency of recording CPAx, which was agreed to; clerk, initial rehab, weekly from clerk and within 72 h of discharge. The data was then collected through informal focus group interviews at half way and end of study.
Results: The half way focus group common themes included; poor compliance to grip strength component, time consuming documentation, poor compliance with use of radar charts, unclear guidance of when to complete CPAx for each patient. Strategies implemented; grip strength result scoring guide attached to dynamometer, long term plan for computer system update create pre-populated scoring tabs, standard placement of radar chart in all bed spaces of patients engaging in rehab, updated daily planning sheets to ensure clearer prompts along with completing weekly only after patients commenced rehab. The end of study focus group common themes included: improved compliance to grip strength component, changes to prompts at half way considered helpful, limited compliance at weekends with intermittent staffing, overall positive experience from all parties.
Conclusion: CPAx was found to be a feasible OM on CC to aid PT teams to achieve standards of NICE CG83 and aid in standardising OMs used across London NHS Trusts. Adequate equipment provision and training is required for all users to ensure compliance and quality of results. To standardise the use of CPAx across this CC centre updates to current computer systems will be required.

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000599

Impact of the implementation of an early mobilization protocol on critically ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000599

Introduction: Muscular weakness associated with patients of the Intensive Care Unit (ICU) is characterized by a reduction in muscle mass and loss of force that appears during or after a stay in the UCI, with no other apparent cause other than serious disease and treatment. In order to prevent this, early diagnosis and treatment may be decisive. There are many studies supporting the safety, feasibility and potential benefits of early mobilization (EM), but they have not yet been standardised in different geopolitical scenarios and the results are not homogenous.
Objectives: To describe the impact of the implementation of an EM protocol on patients admitted in an Intensive Care Unit.
Methods: Prospective, observational and cohort study in a polyvalent ICU. All patients admitted three months prior and after the implementation of an early mobilization protocol (Gen-Mar 2018 and 2020, PRE

and POST cohorts) were included. Demographic data, comorbidities, treatments, rehabilitation-related data, complications, ICU length of stay (LOS) and ICU mortality were collected. They were considered significant $p \leq 0.05$. IRB:2019/8868/I.
Results: A total of 115 patients were included, 55% (n = 63) in the cohort PRE and 45% (n = 52) in the cohort POST. There were no differences in general characteristics between both groups. In the cohort POST it was more frequent to receive rehabilitation when the EM was indicated (90% vs 46%, $p \leq 0.05$) with a trend to decrease the need for invasive mechanical ventilation (IMV, 66% vs 53%, $p = 0.162$), the presence of ulcers (30% vs 20%, $p = 0.203$) and mortality (27% vs 23%, $p = 0.436$). Among patients who received rehabilitation, those included in the cohort POST presented significantly higher mobility levels (postural changes, bed sitting, sitting in chair, and standing). Patients who received rehabilitation in the cohort POST required fewer IMV (57% vs 88%, $p \leq 0.05$), presented fewer ulcers (23% vs 50%, $p \leq 0.05$) and shorter ICU length of stay (LOS, 9 (4–13) vs 13 (8–19), $p = 0.05$) without differences in age, comorbidities or severity scores at admission compared to patients in the cohort PRE.
Conclusion: Implementation of an early mobilization protocol in an ICU increases the mobility of critical patients and is accompanied by a decrease in the need for mechanical ventilation.

000720

Vascular access unit within an ICU: First steps experience

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Intensive Care Medicine Experimental 2022, **10(2)**: 000720

Introduction: Most hospitalized patients have the need, at some point, of intravascular access as part of point of care. Depending on whether the venous access is extremely difficult or the medication administered is too aggressive, there's a necessity of canalization of central venous catheter (CVC) or peripherally inserted central catheter (PICC).
Objectives:—Describe the increase of PICC as an alternative to the classic CVC.

- Analyze the described complications associated with this central lines.
- Highlight the importance of the implantation teams composed by ICU personnel and lead by an ICU nurse.

Methods: This is an observational retrospective study in which we reviewed each peripherally inserted central catheter (PICC) and central venous catheter (CVC) inserted in the years 2020–2021 and 3 months of 2022 by the Vascular Access unit within the ICU from a Regional Hospital. We documented the basic demographic characteristics of the patients, the reason why it was inserted, the time of duration of said catheter and if there were any complications. Cuantitative variables are represented as median ± median (intercuartile range), cualitative ones as percentage. Statistical analysis with SPSS V22.
Results: A total of 720 catheters were placed during 2.3 years, 16.9% (120) CVC, 80.6% (580) PICC and 2.1% (15) port-a-cath. The most common reason for its implant being: chemotherapy 65.3% (470), no peripheral venous access 19.4% (140), need of parenteral nutrition 10.6% (76) and long-standing antibiotic treatment 2.9% (21). Of the inserted CVC, the median number of days until withdrawal was 10 (5–15) while in the PICC group it was 66 (14–157.2). Regarding the CVC, the main reason for its canalization is the need of chemotherapy, as well as the PICC. Nevertheless, we observe a downward trend in the request of CVC as a venous access from 2020 to 2021, decreasing from 20.7% (67) to 14.2% (37); meanwhile we see a small increase in the requests for PICC in 2021 (251 vs 260). The 19.6% (114) of PICC were removed due to complications compared to the 26.2% (32) of CVC; the main complications presented were:

Main complications

	CVC	PICC
Line Associated Bloodstream Infections	25% (8)	35% (40)
Fever	14.2% (5)	9.6% (11)
Accidentally pulled out	25% (8)	14% (16)
Erythema on insertion site	31%(10)	10.5% (12)
Thrombosis	3.1% (1)	12.3% (14)

It's worth noting that out of the 580 requests for PICC canalization, we have found that 15.9% (92) were removed within 15 days, 66.3% (61) of them were removed because of completion of treatment or patient's demise.

Conclusion:
- In our series have observed a downwards tendency to request less CVC as central venous access.
- We have detected an alarming number of line associated bloodstream infections on PICCs, probably related to the inexperienced management of these catheters.
- Regarding the complications, we believe that is crucial to expand the training program to the nurses working on the hospitalization wards through the venous access implantation team.

000736

Benchmarking ERAS oesophagectomy ICU mobilisation targets; A service evaluation

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Intensive Care Medicine Experimental 2022, **10(2)**: 000736

Introduction: Enhanced Recovery After Surgery (ERAS) can reduce hospital and Intensive Care Unit (ICU) length of stay while minimising the risk of post-operative pulmonary complications (PPC)1. The risk of developing PPC's post upper gastrointestinal surgery (UGI) is higher than other surgical specialities with oesophagectomies having a fivefold increased risk2. Current guidelines advocate early mobilisation to reduce this risk but no standardised post-operative mobility targets exist3. A local service evaluation found that a high percentage of patients do not achieve the locally set mobility targets on day one post-op with one of the primary reasons being hypotension. Benchmarking mobility targets will allow comparison of the local ERAS targets in relation to those set in other UGI centres and identify if the failure to achieve these is a local or national issue.
Objectives: To benchmark day one and two post-operative oesophagectomy ERAS mobility targets across similar sized UGI centres to the local trust. To determine how targets were established and identify potential reasons for failure to meet them.
Methods: Purposive sampling was used to invite UGI centres in England with an established ERAS pathway to participate via telephone or email. An online survey evaluating mobilisation service provision and targets was created and sent to all participating centres. All centres were given a three week period to complete the survey focusing on patients admitted between 1st May 2021 to 31st October 2021.
Results: Ten centres agreed to take part with a completion rate of 70%. All questions had a 100% completion rate with varying depth of information gathered. Two centres reported not having standardised mobility targets. The other five centres reported mainly progressive ambulatory targets but there was no consensus between any centres with varying intensities aimed for from sitting out of

bed to walking 50–100 m. There was wide variation in how mobility targets were determined, ranging from expert opinion to the consensus of the group with no clear evidence base reported by any centre. Various reasons for missing mobility targets were detailed with the most common reasons being hypotension (65.5%) and pain (50%).
Conclusion: There was no consensus in ICU mobility targets across centres despite mobilisation being advocated in oesophagectomy ERAS guidelines. In the absence of evidence, mobility targets were informed by expert opinion. Future research should focus on investigating the optimum level of mobilisation on days one and two post operatively for oeseophagectomy ERAS pathway patients.

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Acknowledgements
1. Annika Jarman was supported by the NIHR Oxford Biomedical Research Centre. The views expressed are those of the authors and not necessarily those of the NIHR, NHS or the UK Department of Health and Social Care
2. Owen Gustafson, Clinical Doctoral Research Fellow, NIHR301569, is funded by Health Education England (HEE)/ National Institute for Health Research (NIHR).

000764

Exploring the Lived Experiences of Nurses to Understand What Constitutes Early Recognition of Sepsis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000764

Introduction: Sepsis remains a leading cause of death worldwide [1], significantly because life-saving interventions require to be delivered within a short period of time [2]. Evidence-based guidelines offer useful information for the prompt recognition of sepsis. Guidelines provide a common ground for clinical decision-making, irrespective of one's expertise [2]. However, the recognition of complex patients who do not fit a specific disease definition and might benefit from treatment remains unclear [2, 3]. This lack of understanding may hinder educational efforts to improve recognition of sepsis and derive potential benefits from advances in sepsis treatment.
Objectives: The aim of the study was to examine the lived experiences of a group of nurses to understand what constitutes early recognition of sepsis in a wide spectrum of clinical situations.
Methods: Semi-structured interviews were conducted with 26 nurses with various levels of experience in caring for patients with sepsis from different hospital settings, including intensive care, medical, surgical, research, oncology, neurosurgery, sepsis and practice development departments. The interviews were phenomenographically analysed [4]. Findings were categorised according to the Cynefin framework [5].
Results: The study identified several reasoning pathways that made use of various sorts of knowledge, depending on the level of clinical complexity. Nurses adopted reasoning based on protocol-based care when dealing with a clear disease pattern. However, the same generalised approach was abandoned when exposed to complex patients who do not fit a specific disease definition. Nurses embraced personalised management of these patients, adapting 'recommended' care based on each patient's individual needs. In protocol-based care, nurses made use of knowledge that is commonly known. Whereas in complex contexts, the knowledge was not fully known and had to be learned by monitoring the patient individual response to intervention and evaluating whether a preset target had been reached. Based on that knowledge, nurses decided whether to keep or change the intervention according to the patient individual needs.
Conclusion: Our findings suggest that sepsis is clearly a multidimensional construct where 'one size does not fit all'. Therefore, determining the correct forms of knowledge to define 'best practice' may be of limited value. Guidelines can serve as a principal Reference document when exposed to a clear disease pattern that fits a specific sepsis definition. Yet, individualised management needs to be adopted as the basic principle of complex patient care. This approach demands personnel and bedside expertise; however, unless we learn to adopt the approach that is appropriate to the level of complexity, significant improvements in sepsis recognition might not be seen.

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Acknowledgements 6. PhD studentship funded by Northumbria Research Development Fund (RDF).

000807

Pressure ulcers onset in patients with ARDS undergoing ECMO: 5 years preliminary analysis

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Intensive Care Medicine Experimental 2022, **10(2)**: 000807

Introduction: The application of prone positioning (PP) during veno-venous extracorporeal membrane oxygenation (ECMO) has shown to be a safe technique. [1] Several clinical studies confirmed the safety and efficacy of PP in mechanically ventilated patients; however, a higher frequency of pressure ulcers has been reported. [2].
Objectives: To determine the prevalence of pressure ulcers in patients with ARDS undergoing ECMO treated or not with prone positioning.
Methods: Observational retrospective analysis of all patients admitted to our intensive care unit (ICU) of a tertiary level hospital from January 2015 to December 2019. Only patients with ARDS treated with ECMO were included. The Braden scale was used to assess the patients' risk of developing pressure ulcer at ICU admission, whereas the pressure ulcers were staged according to the NPUAP staging system (National Pressure Ulcer Advisory Panel). Age, sex, BMI, ICU length of stay, SAPS and SOFA scores and data about prone positioning therapy were recorded.

Results: A total of 116 patients undergoing ECMO were identified in the medical records and 56 (48.3%) were treated with PP. The overall pressure ulcer prevalence was 58.6% (68/116). Despite some differences between groups, once we adjusted for age, BMI, SAPS, Braden score, days on ECMO and ICU, the chance of pressure ulcer was not statistically associated with prone positioning (Odds Ratio 1.17, 95% Confidence Interval: 0.44—3.13). The other characteristics of patients are summarized in Table 1.

Characteristics	Supine (n = 60)	Prone (n = 56)	P-value
Age (median, IQR)	50.3 [36.9, 58.9]	52.6 [43.4, 60.3]	0.309
Sex (female)	24 (40.0)	21 (37.5)	0.932
BMI (median, IQR)	24.2 [20.9, 27.8]	26.3 [23.1, 29.6]	0.065
SAPS II score (median, IQR)	39.5 [31.0, 57.5]	41.5 [31.2, 58.5]	0.652
Braden Score (median, IQR)	9.0 [8.0, 10.2]	9.0 [8.0, 9.0]	0.109
Pressure ulcers (n, %)	29 (48.3)	39 (69.6)	0.032
Lenght of ICU stay (days)	13.0 [8.0, 19.0]	32.5 [18.8, 48.2]	< 0.001
Length of MV (days)	8.0 [3.0, 15.0]	25.0 [14.8, 44.0]	< 0.001
Length of ECMO (days)	5.0 [3.0, 8.0]	13.0 [10.0, 20.8]	< 0.001
Alive (n, %)	44 (73.3)	39 (69.6)	0.815

Conclusion: Prevalence of pressure ulcers in patients undergoing ECMO remains high. However, the occurrence of pressure ulcers does not seem associated with prone positioning maneuver.

000849

From anxiety to growth—a multi-center investigation of relationship between nurse' COVID 19 stress symptoms and post-traumatic growth levels during COVID 19

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Intensive Care Medicine Experimental 2022, **10(2)**: 000849

Introduction: Since COVID 19 outbreak, multiple papers have been published exploring nurses' stress and anxiety symptoms. Recent literature demonstrates that individuals can grow in a positive fashion after stressful events, achieving post-traumatic growth. Exploring the relationship between stress and growth may assist nurses to find positive perspective and significance in their professional.
Objectives:—to compare levels of anxiety, physical, mental stress symptoms among hospital nurses and examine the relationship between symptoms and posttraumatic growth.
Methods: multicenter, prospective, cohort study, convenience sampling. Method- data collection occurred during first quarter of 2021. Questionnaires included; socio-demographic, COVID 19 stress score, Post-traumatic growth inventory.
Results: A sample of 536 nurses (86.7% females), average age of 45.15 years. Most were married (79.3%), and (78%) had academic education. Most Medical Center A nurses treating COVID 19 patients, (72.4%), and the rest Medical Center B- not treating COVID 19 patients. (27.6%). Total average anxiety level was 3.84, average physical symptoms 1.15 (sd 1.75) and average mental symptoms 1.63 (sd 1.97). The average Post traumatic growth score was 2.83 (sd1.65). Post-traumatic growth had a positive correlation with physical symptoms ($r = 0.17$, $p < 0.01$), but it not found to be correlated with the mental symptoms. There is a positive correlation between anxiety levels and post-traumatic growth ($r = 0.14$, $p < 0.01$).
Conclusion: For nurses to be able to grow after traumatic situations in health organizations, it is important to reinforce the sources of strength that allow nurses to grow. This study addressed the challenge of finding positive outcomes from working in high stress COVID 19 environment. The findings show there may be professional growth as a result of caring for COVID 19 patients. It is essential that nurses and leaders are aware of the relationship between COVID 19 work stress, anxiety and physical symptoms, positive aspects and opportunities. Knowledge about post-traumatic professional growth may assist nurse leaders and educators in preparing frontline nurses providing care to COVID 19 patients.

000897

Physiotherapy within the abcdef bundle in an intensive care unit

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Intensive Care Medicine Experimental 2022, **10(2)**: 000897

Introduction: For the last 20 years, the critically ill patient care has shifted its focus from survival of the patients to recovery and long-term consequences. The ICU acquired weakness has been a major problem since the beginning of Intensive Care Medicine and that is the reason why physiotherapy play an increasing role in critically ill patient care.
Objectives: To reflect the current situation of physiotherapy and rehabilitation in a third level Intensive Care Unit.
Methods: Descriptive observational study, carried out during the month of July 2021 with data collection once a week. All patients admitted to the 35-bed Intensive Care Unit of a third level hospital in Madrid were included, collecting data from the medical and nursing comments and the nursing care chart about postural changes, mobilizations and both motor and respiratory physiotherapy.
Results: A total of 103 questionnaires corresponding to 58 patients were collected. Regarding postural changes, despite the fact that they were performed in 100% of the patients, only 51% received 6 or more changes per day. Twenty-three patients (22.3% of the total) were transferred from bed to chair. It is even morerevealing that 41 of 62 patients in recovery phase were not transferred to chair (67.2%). Concerning physiotherapy, 26% of the patients received therapy (25/103 patients), 1 patient received passive physiotherapy, 2 motor physiotherapy, 3 respiratory therapy and 18 patients mixed physiotherapy (motor and respiratory); only 37.6% of the patients whose clinical situation allowed it received physiotherapy and only 47.9% of the patients in whom active physiotherapy was indicated, received it. In 53% of cases it was considered that the physiotherapy received was not appropriate.
Conclusion: The introduction of physiotherapy in Intensive Care Units has been shown in multiple studies to be beneficial in the recovery of critically ill patients. With this study we have tried to raise awareness on our current situation regarding physiotherapy in the context of the ABCDEF strategy and highlight possible aspects for improvement.

000911

Bedside physiological measurements and behavioral tools for measuring pain and discomfort in deeply sedated mechanically ventilated patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 000911

Introduction: Hospitalization in the Intensive Care Unit (ICU) often results in pain and discomfort. Self-report is considered the gold standard for assessing pain and discomfort, yet this method is often not possible for non-communicative deeply sedated mechanically ventilated patients. Previously, observational behavioral tools or physiological measurements were used, but lacked sufficient sensitivity and specificity.
Objectives: To explore the utility of measuring pain and discomfort using both bedside physiological parameters and observational behavioral tools during routine nursing care in deeply sedated mechanically ventilated patients.
Methods: This study was part of an observational prospective descriptive cohort study using a repeated measures design. The assessment

included baseline and responses to routine nursing interventions (endotracheal suction, repositioning, dressing changes, and oral care) of mechanically ventilated ICU patients. Measures included the Behavioral Pain Scale (BPS), Visual Analog Scale of Discomfort (D-VAS), Heart Rate (HR), and Blood Pressure (BP).
Results: A total of 84 interventions were assessed in 18 deeply sedated patients. All measurements demonstrated a significant increase between baseline and during interventions. A Mann–Whitney U test revealed that there were greater increases in BPS (Median = 3.5) and D-VAS (Median = 3.1) with suctioning than with repositioning BPS (Median = 0) (n = 28, p = 0.003) and D-VAS (Median = 1) (n = 42, p = 0.003), but not with HR or BP. There was an increase of at least 10% in HR and SBP during endotracheal suctioning. Almost half (42%) of the endotracheal suctioning and 21% of repositioning events showed parallel increases in both BPS and HR and/or SBP while 28% of endotracheal suctioning and 47% of repositioning events had increases in only physiologic or observational measures.
Conclusion: Physiologic parameters alone are not sensitive enough to discern pain and discomfort and should be used in combination with the BPS when performing routine care interventions. Improved methods are needed to assess the presence and intensity of pain and non-pain discomfort to discern whether the patient is in pain or is uncomfortable.

000933

Pulmonary and systemic burden of oxygen in invasively ventilated children with severe bronchiolitis

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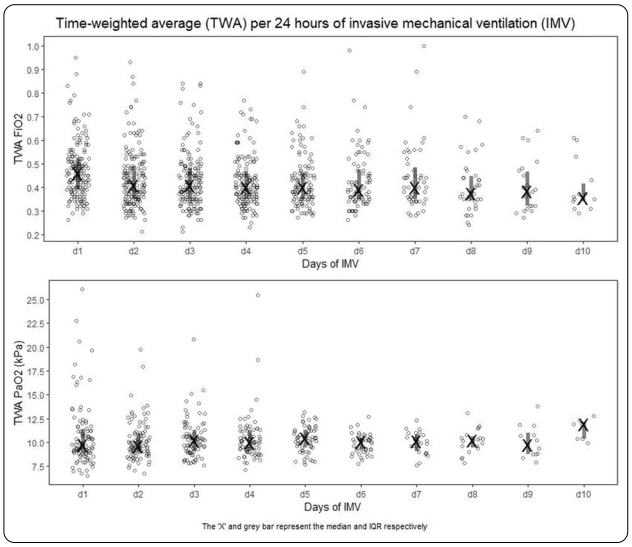
Intensive Care Medicine Experimental 2022, **10(2)**: 000933

Introduction: Severe viral-induced bronchiolitis constitutes one of the most important injurious hits to the pulmonary system in early life.(1) Infants admitted for severe bronchiolitis to the pediatric intensive care unit (PICU) are treated with supplemental oxygen. However, the toxic effects of prolonged high dose oxygen have been well established, and studies in critically ill children report an association between hyperoxia and adverse outcomes.(2;3) Up to date, the overall pulmonary and systemic oxygen burden in children with severe bronchiolitis remains unclear. As a result, titration of oxygen is still largely based upon expert opinion. Further insight in the exposure of oxygen in this potentially vulnerable population could help to substantiate future study protocols on oxygen titration.
Objectives: Our primary aim was to assess the overall pulmonary (local) and arterial (systemic) burden of oxygen over the duration of invasive mechanical ventilation (IMV) in children with severe bronchiolitis admitted to the PICU. Our secondary objective was to estimate avoidable exposure to high dose oxygen in these children.
Methods: We performed a retrospective, single-center observational cohort study in children aged < 2 years, who were admitted to the PICU because of bronchiolitis and received IMV. Ventilatory data, including fraction of inspired oxygen (FiO_2), peripheral oxygen saturation (SpO_2) and partial pressure of arterial oxygen (PaO_2), were extracted every hour during IMV up to the 10th day of ventilation. Time-weighted averages (TWA) were calculated using a trapezoid area-under-the-curve model for these variables. Statistical analysis was performed using R (version 4.0.3).
Results: A total of 22,667 h (944.5 days) of IMV were recorded in 161 patients between Oct 2008 and April 2020. Median duration of IMV was 5.6 days [IQR 4.5–7.3]. The pulmonary burden of oxygen was highest on the first day of IMV: median $TWAFiO_2$ 0.46 [IQR 0.39–0.52], during which the arterial burden of oxygen was low (median $TWAPaO_2$ 9.7 kPa [IQR 8.8–11.4]) (Fig. 1). Moreover, severe arterial hyperoxia over total IMV was rare with only 0.8% of values ≥ 33.3 kPa. Patients spent most of their time on FiO_2 of 0.30–0.39 (median 31.1% of total IMV [IQR 14.4–50.4]) and 0.4–0.49 (median 24.9% [IQR 15.4–38.1]) and with SpO_2 > 98% (median 23.1% of total IMV [IQR 13.1–36.1]). Yet, overzealous use of oxygen was still common when SpO_2 was > 96% with 22.9% of FiO_2 values set at ≥ 0.50. Additionally, in a large proportion of these cases FiO_2 was left unchanged at high levels.
Conclusion: In this cohort of children receiving IMV for severe bronchiolitis, the overall pulmonary exposure to oxygen was moderate, while the systemic burden was low. Yet, we estimate that exposure to supplemental oxygen was often avoidable in a substantial part of the patients. Further insight in oxygen titration and acute- and chronic effects of pulmonary oxygen exposure in critically ill children with severe bronchiolitis is warranted.



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Acknowledgements Thijs A. Lilien received an AMC PhD Scholarship (Amsterdam UMC).

Nurses & Allied Healthcare Professionals 5

000967

Virtual education yey or nay- feedback on virtual education for physiotherapy staff new to working in critical care environment

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Intensive Care Medicine Experimental 2022, **10(2)**: 000967

Introduction: Physiotherapy staff newly rotating into a critical care environment have many learning needs and undergo intensive training to achieve competency. Current newly qualified staff are digital natives, hence comfortable with technology and its use (Tabatabai, 2020). In addition, due to the pandemic response there was a need to rapidly induct, upskill and respond to staff training needs whilst maintaining social distance. In an attempt to address these factors, the senior physiotherapy team developed virtual education sessions as part of an induction package for new staff. In person education sessions ran concurrently with the virtual educations sessions. Five 30-min virtual education sessions were developed, education topics included

mechanical ventilation, critical care assessment, arterial blood gas analysis and treatment techniques.
Objectives: To provide feedback on virtual education sessions as part of an induction package for new physiotherapy staff in a critical care environment.
Methods: Over the course of 12 months, feedback was obtained from all staff rotating through the critical care environment. At the end of the trial period, feedback was also gathered from senior staff. All feedback was sought via electronic survey.

Results: 13 rotational and 5 non rotational senior staff were surveyed on their opinions of the virtual education sessions. 50% (n = 9/18) felt the virtual education sessions were less effective than in person education session. The reasons given were difficulty in finding time to access sessions (n = 9), pReference for in person sessions (n = 3) and no opportunity to ask questions (n = 1). Rotational staff stated a key benefit was being able to access sessions on demand (n = 2). Senior staff reported benefits such as self-directed learning (n = 3), less time consuming for senior staff (n = 2) and virtual resources available for multiple reviews (n = 2).
Conclusion: Adapting to working in a critical care environment is demanding. It appears that completing virtual education sessions was more challenging than attending in person education for physiotherapy staff new to the critical care environment. As a result of staff feedback, all critical care induction education sessions for physiotherapy staff have reverted back to in person education. The virtual education sessions remain available for staff to access as required.

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000982

Early rehabilitation interventions in critically ill adults with COVID-19 pneumonia: Experience from a tertiary care centre

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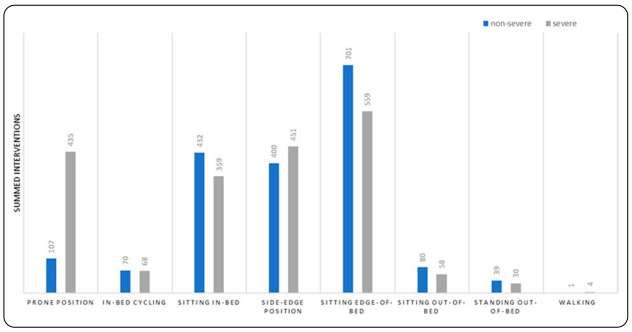
Intensive Care Medicine Experimental 2022, **10(2)**: 000982

Introduction: Prolonged mechanical ventilation, neuromuscular blockers, steroids and prone positioning make critically ill patients with COVID-19 particularly susceptible to develop intensive care unit (ICU) acquired weakness [1]. Previous studies have shown that early rehabilitation on ICU is safe [2] and significantly reduces neuromuscular complications [3]. However, it is unclear if early mobilisation could be sustained during the COVID-19 pandemic.
Objectives: The primary objective was to investigate the "time-to-first edge-of-bed" (T-EOB) mobilisation. Secondary objectives were the analysis of implemented interventions and factors associated with delayed mobilisation.
Methods: We included all critically ill patients with COVID-19 and an ICU stay $\geq$ 72 h between March 2020 and May 2021. Patients were divided into 'non-severe' or 'severe' COVID-19 pneumonia according to their lowest PaO_2/FiO_2 ratio within the first 24 h [4]. Kaplan–Meier and logistic regression were used to investigate T-EOB mobilisation and a-priori specified factors' association with a delayed mobilisation.
Results: 168 patients were analysed, whereof 77 (46%) had 'non-severe' and 91 (54%) 'severe' COVID-19 pneumonia. Mean age was 63 $\pm$ 12 years and median SOFA 11 [IQR 9—14]. Actual, median T-EOB mobilization was 3.9 days [95% CI 2.3 to 5.5] with significant differences between subgroups ('non-severe' 2.5 days [1.8 to 3.5] vs. 'severe' 7.2 days [5.7 to 8.8], p = 0.014). ECMO use and high SOFA scores were independent factors related with a delayed mobilisation (adjusted effect 13.7 [95% CI 10.1 to 17.4] and 0.3 days [0.1 to 0.6]). Median time-to-first physiotherapy session was 1 day [95% CI 0.9 to 1.2], without subgroup-differences (p = 0.637). Overall, 1260 edge-of-bed and 212 out-of-bed mobilisations were performed (Fig. 1).
Fig. 1 Summed proning, rehabilitation interventions and mobilizations according to severity-group



Conclusion: Our study shows that early mobilisation was feasible during a pandemic. Contributing factors may have been interprofessional management, physiotherapy service extension, daily screening and an ongoing culture of early mobilization. The association between delayed mobilization in patients with 'severe' COVID-19 pneumonia should be further explored to develop safe and effective treatments for this severely ill patient population.

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000994

Writing a Diary for "You"

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Intensive Care Medicine Experimental 2022, **10(2)**: 000994

Introduction: Diaries written by nurses for critically ill patients have been implemented in some intensive care units as an intervention to construct patients' "lost time" and fill in their gaps in memory. Studies have shown that diaries have an impact on patients' psychological recovery after intensive care. However, little is known about how nurses view and carry out the process of writing a diary on behalf of a patient.
Objectives: To investigate the choices nurses make in content and language, the rationale by which they make them, and how these narrative aspects shape the story of critical care that is constructed in the diary.
Methods: The study was conducted within a qualitative approach informed by narrative methodology. Nine nurses from three intensive care units at a university hospital in Denmark participated. Each of the participants handed in five anonymized diary notes written for different patients they had cared for. Additionally, the nurses were

individually interviewed about their narrative choices when writing the diary. The study combined textual analysis of the diary notes and a thematic analysis of the interview data.
Results: Three prominent strategies that characterize nurses' choices of content and language were identified: 1) Making the situation of intensive care more manageable, 2) Showing acts of perceiving the patient, and 3) Constituting relations through actions and interactions. The study showed that on one hand these strategies engage the patient and depict nurses' care, empathy and support, yet on the other, reveal the nurses' power to interpret, passivize and downplay the patient's experiences.
Conclusion: It was demonstrated that although the narrative, written for a *you*, is ostensibly about the patient, the nurse's interpretations, evaluations, perceptions, and actions figure prominently throughout the diary. Narrating for a *you* relegates the patients to a secondary position in their own diary. Having the power of control over the narrative, nurses' linguistic choices may either narrow down or expand possibilities for the patient's own understanding when reading the diary after intensive care.
Acknowledgements None.

001095

Fluid Overload and Kidney Injury Score (FOKIS) Evaluation During The First 7 Days of Pediatric Intensive Care Unit Stay

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Intensive Care Medicine Experimental 2022, **10(2)**: 001095

Introduction: Acute kidney injury (AKI) affects 30% of critically ill children. Lack of standardization of AKI definition limited the ability to diagnose AKI accurately. Fluid overload kidney injury score (FOKIS) is an automatically calculated system that combines AKI severity according to pRIFLE, fluid overload severity, and nephrotoxic medication exposure into one numerically measurable metric.
Objectives: To evaluate the relationship between FOKIS and critically ill children's morbidity and mortality.
Methods: We used a database generated from the electronic health records of patients, admitted Pediatric Intensive Care Unit (18-bed tertiary care unit) between August 2020 and October 2021. Demographical data, calculated values of FOKIS during the first 7 days of PICU admission; PRISM 3 (Pediatric Risk of Mortality 3), pSOFA (Pediatric Sequential Organ Failure Assessment), PELOD-2 (Pediatric Logistic Organ Dysfunction-2) in the first 24 h of admission were recorded. Patients who died or were discharged in the first 72 h were excluded.
Results: 200 children (88 girls, 112 boys, median 39.5 months; IQR 1–213 months) were included FOKIS of the patients varies between 0 and 8. 62% had respiratory support (n = 124), and 9.5% (n = 19) received renal replacement therapy (RRT) (3 had chronic kidney disease). The median length of PICU stay (LOS) was 9 days (IQR, 3–340 days) and mortality was 8.3%. Mortality was associated with FOKIS at 1-7th days values, PRISM 3, pSOFA, PELOD-2, LOS, and the number of days on mechanical ventilation ($p < 0.0$). All FOKIS were positively correlated with PRISM 3, pSOFA, and PELOD-2, the highest correlation was found with FOKIS 1., 3., 4., and 6. day ($p < 0.01$). While all FOKIS values were positively correlated with LOS (FOKIS at 2., 4., 6. day, $p < 0.05$, and, FOKIS at 1., 3., 5., 7.day $p < 0.01$), the number of days on mechanical ventilation was only positively correlated with FOKIS at 1., 6. ($p < 0.05$)and 7. day ($p < 0.01$). There was a positive correlation between respiratory support and FOKIS on Day 6 ($p < 0.05$), RRT with FOCIS on Day 2., 5., and 6. day ($p < 0.05$), and blood culture positivity with FOKIS at 3., 4. ($p < 0.05$), and 7.day ($p < 0.01$). There are no correlation between hypertension and FOKIS.
Conclusion: Fluid overload kidney injury score which was calculated during the first 7 days of PICU admission FOKIS is independently associated with risk of mortality scores, respiratory support, renal replacement therapy, and mortality.

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001196

Comparison of New Injury Severity Score, Injury Severity Score, Revised Trauma Score, Trauma and Injury Severity Score and Paediatric trauma Score for Mortality Prediction in Paediatric Trauma Patients

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Intensive Care Medicine Experimental 2022, **10(2)**: 001196

Introduction: This study tests the accuracy of the New Injury Severity Score (NISS), Injury Severity Score(ISS), Revised Trauma Score (RTS), Trauma and Injury Severity Score (TRISS) andPaediatric Trauma Score (PTS) in prediction of mortality in paediatric trauma patients.
Methods: The study population consisted of retrospectively identified, consecutive ER traumaadmissions (n = 390) from one Level I trauma centre in south of Tunisia. Probabilities ofdeath were calculated by using logistic regression analysis and model discrimination wasbased on the area under the receiver operating characteristic curve (AUC). The outcome wasgauged through the comparison of receiver operating characteristic curves using DeLong'smethod.
Results: In 2-by-2 decision matrices with a decision criterion of 0.5, the sensitivities, and specificitieswere 66.7%, and 73.2%, respectively, for the ISS; 47.2% and 96.9%, respectively, for theNISS; 69.4% and 70.3%, respectively, for the PTS; 97.2% and 64%, respectively, for theRTS and 83.3% and 85%, respectively, for the TRISS method. In the receiver operatingcharacteristic curve analysis, NISS vs PTS (0,744 vs 0,902; z statistic = 3,018; p = 0.0025)and NISS vs TRISS (0,744 vs 0,868; z statistic = 2,194; p = 0.0282).
Conclusion: TRISS and PTS were the strongest predictor of mortality in petdiatric trauma patients whencompared to the NISS, ISS and RTS.

001149

The evolution of activities of daily living in critically ill COVID-19 patients in a 1-year follow-up

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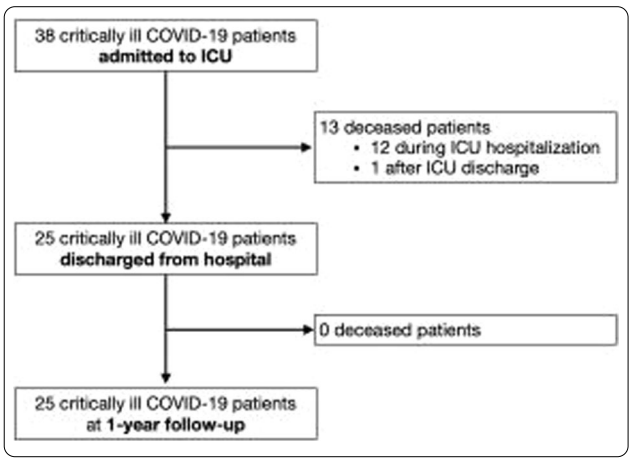
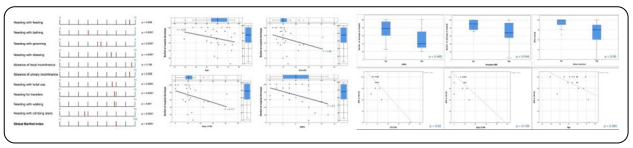
Intensive Care Medicine Experimental 2022, **10(2)**: 001149

Introduction: The most common long-term symptoms after COVID-19 disease in the ICU are fatigue, dyspnea, and impaired cardiopulmonary function. In this context, adequate assessment of long-term morbidity allows for better management of patients after hospital discharge, especially through analysis of activities of daily living.
Objectives: The aim of the study was to describe the long-term consequences in critical COVID-19 patients 1 year after discharge from the ICU by identifying long-term sequelae in patients' activities of daily living through a temporal analysis of the Barthel index and Karnofsky status at 1 year after hospital discharge.

Methods: This was a retrospective analysis of consecutive patients from March to May 2020 admitted to the ICU with COVID-19 ARDS. Follow-up was performed 1 year after hospital discharge; activities of daily living were assessed by both the Barthel index and Karnofsky status.
The primary outcome was to assess differences in activities of daily living at hospital discharge (acute activities of daily living) and 1 year later (chronic activities of daily living). Secondary outcomes reported correlations between activities of daily living and clinical, biological, and therapeutic events performed during the ICU stay.



Results: Thirty-eight consecutive patients were admitted to the ICU; 13 (34%) patients died during the first 28 days; no patients died after discharge from the hospital. A t-test analysis between acute and chronic activities of daily living using the Barthel index showed significant improvement ($t = -5.211$, $p < 0.0001$); similarly, each individual Barthel index task such as the need to bathe, clean, dress, use the bathroom, transfer, walk, and climb stairs ($p < 0.0001$ for each task). The mean KPS at hospital discharge was 86.47 (SD 20.9), at 1 year it was 99.6 (SD 2.0, $p = 0.02$) with complete improvement. No correlation was identified between BI and demographic, biological, and intra-Intensive Care Unite events.



Conclusion: In critically ill COVID-19 patients, at 1-year follow-up, patients presented complete functional recovery of self-care activities of daily living, suggesting that surviving patients presented all characteristics to overcome the massive disease- related catabolic state.

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001249

Improving patient safety and experience regarding the use of vascular access devices within the Intensive Care Unit at the Royal Victoria Infirmary—Newcastle Upon Tyne UK.

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Intensive Care Medicine Experimental 2022, **10(2)**: 001249

Introduction: This project was undertaken to examine the current level of knowledge and understanding of 2 different types of vascular access devices commonly used within the Intensive Care Unit at the Royal Victoria Infirmary (RVI) in Newcastle upon Tyne. Each year at the RVI there are approximately 800 patients admitted to the intensive care unit who have a vascular access device inserted.1 These devices may be present on admission to intensive care, or they may be inserted during their stay. This project reviewed the uses of both midlines and PICC lines. As these devices may be left in situ for longer periods of time than traditional cannulas, the need for cannula insertions should be reduced.2 We reviewed the reasons why cannulas continued to be inserted despite this. The reduction in the number of vascular access devices inserted per patient confers a reduction in the number of skin entry points and provides a more positive experience for many patients, especially those who have a prolonged length of stay on the intensive care unit.3
Objectives: The aims and objectives of this quality improvement project included:

- To evaluate the understanding of the medical and nursing staff about the uses of each vascular access device
- To highlight any recurring issues with the devices usage
- To develop and implement further education and training on how to use these devices effectively including managing blockages

By improving the knowledge of the team who are most commonly using these devices we hoped to encourage the use of the longer-term lines and therefore reduce the number of new cannula insertions.
Methods: Major phases of project:

1. Planning and writing of initial questionnaire – a questionnaire was disseminated to a mix of consultants, junior doctors, advanced critical care practitioners and nursing staff regarding current level of knowledge
2. Design of presentation to be delivered during initial audit meeting with first set of results – results from the initial questionnaire were presented in the intensive care audit meeting to highlight issues to be addressed
3. Conception and design of poster to implement around intensive care unit and design of bedside teaching sessions – posters created and disseminated around the unit. Ad-hoc bedside teaching sessions were undertaken 1:1 with medical and nursing staff when workload permitted
4. Monitoring phase – collection of post education data using questionnaire—repeat questionnaire disseminated to review for improvement in knowledge, results collated

Results: Initial questionnaire total responses: 41. Repeat questionnaire total responses: 28. Distribution of participants varied from medical students up to consultant level, with the majority of responses from nursing staff. Improvement in knowledge around indications for midlines and PICC lines was demonstrated, alongside an improvement

in knowledge around confidence in managing blocked lines, and improvement in knowledge around securacath insertion and usage. Knowledge regarding CT compatability of midlines improved from 22% of staff to 61% of staff. Awareness of how to manage a blocked line using urokinase improved from 40% of staff to 78%. Greater awareness of methods for follow up also showed improvement. Requests for further training decreased following the intervention.
Conclusion: The results of this project demonstrate a significant improvement in the knowledge of the team who are most commonly using midlines and PICC lines within the intensive care unit. All staff were engaged with the teaching process and the feedback they provided showed the benefits of having a poster as a quick Reference guide. An improvement in their knowledge will lead to an improved patient experience and ultimately patient safety.

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001291

Exploring the recovery journey of COVID-19 critical care survivors during the first year after hospital discharge

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Intensive Care Medicine Experimental 2022, **10(2)**: 001291

Introduction: The first wave of COVID-19 pandemic (March–May 2020) has resulted in an increased number of critical care survivors whose longitudinal progression after hospital discharge has not yet been explored. This study aimed to identify the key aspects of survivors' recovery and their caregivers' experiences during the first year after hospital discharge.
Objectives: Exploration of the longitudinal progression of patients admitted to critical care following COVID-19 over 1 year after hospital discharge. Understanding of the significant aspects of the survivors recovery and the key elements of their caregivers' experiences of the recovery.
Methods: A longitudinal descriptive qualitative study using semi-structured interviews; data analysis using thematic analysis. Six COVID-19 critical care survivors from the first wave of the pandemic (March–May 2020) and five relatives were recruited across 2 acute hospitals in South-East England. Six survivors and five relatives were interviewed 3 months after hospital discharge. The same six survivors and one relative were interviewed again at one year. Interviews were transcribed, anonymised and a thematic analysis was conducted.
Results: Three themes were developed: (1) "The cycle of shame and stigma" explores the feelings of guilt and shame experienced by the survivors which increased over the year as the pandemic progressed; (2) "Facing the uncertainties of recovery—together and alone" shows the troubles faced by relatives during discharge amidst a pandemic, and the frustrations of both the survivors and relatives when confronted with a life-limiting illness; (3) "Coping with lingering symptoms—the new norm" analyses the mechanisms survivors developed to come to terms with the remnants of their illness and their feelings towards the changes in their lives.
Conclusion: The findings show the feelings of shame and guilt experienced by COVID-19 critical care survivors, and a reluctance to share their stories with strangers due to public stigma associated with the disease. Relatives faced considerable difficulties during and after their kin's admission and described the coping strategies they implemented. The longitudinal nature of the study highlighted the persisting symptoms of long COVID-19, their impact on survivors and coping methods amidst the ongoing pandemic. Further research into the experiences of those affected in the first and subsequent waves of the COVID-19 pandemic, is desirable to help guide the formulation of the optimally supported recovery pathways.

About this supplement
These abstracts have been published as part of Intensive Care Medicine Experimental Volume 10 Supplement 2, 2022. The full contents of the supplement are available online at https://icm-experimental.springeropen.com/articles/supplements/volume-10-supplement-2.

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