ICMx 2022, **10**(Suppl 2):39
https://doi.org/10.1186/s40635-022-00468-1

Intensive Care Medicine
Experimental

MEETING ABSTRACTS

Open Access

ESICM LIVES 2022: part 1

Paris, France. 22-26 October 2022

Published: 19 October 2022

Abstract Award Winning Session

000816

Performance improvement of healthcare processes in Argentine Public Health Sector ICUs during COVID-19 using Quality Improvement Collaborative

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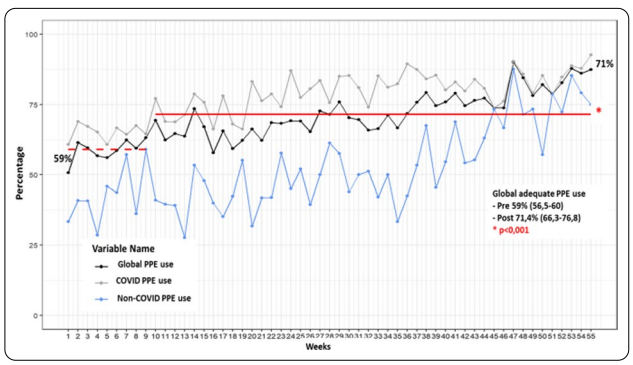
Intensive Care Medicine Experimental 2022, **10(2)**:000816

Introduction: The demand on healthcare services during the SARS-CoV2 pandemic was particularly excessive for less developed countries. Intensive care units (ICUs) have taken the heaviest toll in terms of resource allocations, staff burnout and burden of disease. A quality improvement collaborative (QIC) was implemented during the COVID-19 pandemic in 14 ICUs in the public sector in Argentina to improve healthcare delivery and outcomes, and provide emotional support tools to personnel.
Objectives: To achieve adequate personal protective equipment (PPE) use in 90% of patient encounters and 90% compliance with objectives of patient flow. To provide emotional support tools to 90% of professionals.
Methods: Interrupted time series study in 14 ICUs in Argentina, July2020-January2021(8 and 46 weeks of measurements in Pre-Intervention and Intervention periods). During the Intervention period a special team (intensivists/nurses/physical therapists) promoted in each ICU a collaborative process to share ideas/innovations/experiences. The intervention included learning sessions, periods of action and Improvement Cycles (Plan-Do-Study-Act) by mean of web-based activities and coaching and feedback by improvement experts. Outcome variables were correct use of PPE, adherence to 9 patient quality indicators (QI) using of a daily goals sheet (DGS), and use of a web tool for detection and mitigation of emotional distress in the personnel. Medians of weeks proportions of adequate PPE use, and accomplishment of the 9 QI were compared between both periods using Wilcoxon ranksum test. A p value < 0.05 was considered significant for all comparisons.
Results: There were 1002 observations of PPE use and 903 measurements of the QI in the Pre-I, and 6364/ 6549 during Intervention period, respectively. Figure 1 shows the significant improvement in the adequate PPE use throughout weeks (59% (56.5–60) vs 71.4% (66.3–76.8), p < 0.001). The accomplishment of the 9 QI all together was present in a median of 54% [CI95%50–61] in Pre-I and 66.4% [CI95%64–73] in Intervention period (p < 0.001). There were 1358 emotional measurements. The use of the emotional support tool was low in all weeks (mean use of 5 ± 3% fortnightly).



Conclusion: In the context of pandemic, the QIC was effective to improve healthcare delivery and adequate PPE use (much better with COVID patients). The limited scope of the emotional support

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tool could indicate lack of emotional openness or severe emotional distress.

Acknowledgements: Global Pfizer® Grant.

000879

Immunosuppressive phenotypes and theragnostic targets in sepsis—a prospective cohort study

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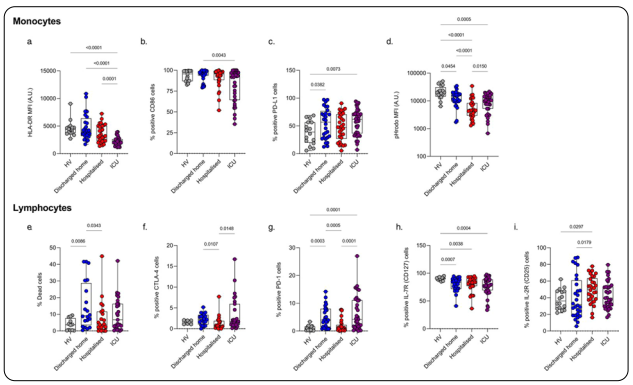
Intensive Care Medicine Experimental 2022, **10(2)**:000879

Introduction: Sepsis survivors are at increased risk of subsequent infection due to persistent immunosuppression [1]. Well characterised features include suppressed monocyte HLA-DR expression and lymphopenia [2, 3]. Early clinical studies using GM-CSF or interferon—gamma to reverse restore monocyte HLA-DR have not demonstrated clinical benefit. This may be due to simultaneous failure of monocyte antigen presentation, and lymphocyte senescence. Modulating a single immune target may thus be insufficient to improve monocyte-lymphocyte crosstalk [4].
Objectives: Characterise immune phenotypes of patients with increasing severity of infection or sepsis with a focus on monocyte-lymphocyte crosstalk.
Methods: We included patients presenting to the Emergency Department (ED) and those admitted to the ICU with suspected infection or sepsis respectively. Patients presenting to the ED were either discharged home or hospitalised. Healthy volunteers served as controls (HV). Immune phenotypes were assessed using flow cytometry panels to assess monocyte antigen presentation (HLA-DR, CD86, CD80) and phagocytosis (opsonised pHRodo bioparticles), and lymphocyte cell signalling and senescence (CTLA-4, PD-1, IL-7RA and IL-2RA) [5].
Results: 93 patients were recruited; 28 were discharged home from ED, 30 were hospitalised, and 35 admitted to ICU. Additionally, 16 volunteers were recruited. Increasing illness severity was associated with reduced classical monocyte surface HLA-DR (a.), CD86 (b.), and phagocytosis (d), whereas PD-L1 expression was increased (c.). CD4 + lymphocytes showed increased cell death (e.), associated with increased expression of CTLA-4 (f.), PD-1 (g.), and reduced IL-7RA (h.), and increased IL-2RA (i.). (Figure 1). Similar findings were identified in CD8 + and CD19 + lymphocytes (data not shown).



Conclusion: Increasing severity of infection and sepsis is associated with

1. Decreased monocyte HLA-DR and CD86
2. Monocyte PD-L1 and CD4 + lymphocyte PD-1 are increased, associated with increased lymphocyte death
3. Reduced lymphocyte proliferation markers

Potential future theragnostic approaches will need to identify those patients at risk of post-sepsis immunosuppression and may require multiple pathways to be altered to reverse the detrimental effects on monocyte-lymphocyte crosstalk.

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Acknowledgements

1. Intensive Care Society New Investigator Award (2021)
2. Precision AMR Seed Funding Grant
3. ESICM Next Start Up (2018)

000972

Intracranial pressure monitoring practice, treatment and effect on outcome in aneurysmal subarachnoid hemorrhage: a subanalysis of the International prospective observational StudY on iNtrAcranial PreSsurE in intensive care—SYNAPSE-ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000972

Introduction: There is still much debate on the use of intracranial pressure (ICP) monitoring and its management in aneurysmal subarachnoid hemorrhage (aSAH) patients.
Objectives: The present study aimed to explore the practice of ICP monitoring, its variability across countries and the association with 6 months outcomes.
Methods: A pre-planned subanalysis of the "International prospective observational StudY on iNtrAcranial PreSsurE in intensive care (SYNAPSE-ICU)", a multicentre, international, prospective, observational cohort study, specifically focused on patients with a diagnosis of aSAH. Patients' demographics and clinical data at hospital admission, ICP monitoring and values (i.e. daily ICP and maximum daily value on days 1, 3 and 7) were recorded. Intracranial hypertension (HICP) was defined as ICP $\geq$ 20 mmHg. Variability in the practice to insert ICP monitoring across countries was evaluated through a logistic regression model adjusted for case-mix and considering countries as a random effect. The association between ICP probe insertion with 6 months mortality and poor neurological outcome measured by the Glasgow Outcome Scale Extended (GOSE $\leq$ 4), was assessed using a propensity score approach.
Results: A total of 423 aSAH patients from 92 centers across 32 countries were included in this analysis. The median age was 57 years (I–III quartiles, Q1–Q3 = 48–66) and 277 (65.5%) were females. ICP monitoring was used in 295 (69.7%) cases. Significant between-countries variability in ICP insertion was observed, with an incidence ranging between 4.7 and 79.9% (Median Odd Ratio = 3.04). The median duration of ICP monitoring was 12 days (Q1–Q3 = 8–18) with an overall daily median ICP value of 14 mmHg (Q1–Q3 = 10–19) and a median maximum value of 21 mmHg (Q1–Q3 = 16–30). More than half of the patients (54.7%) experienced at least one episode of HICP (151 episodes). Patients monitored with ICP received more aggressive therapy

intensity level (TIL) treatments compared to non-monitored (TIL score 10.33 (standard deviation, SD = 3.61) vs 6.3 (SD = 4.19), p < 0.001). In more severe patients (i.e., one or more pathological pupils), ICP monitoring was significantly associated with better 6 months outcomes (unfavorable GOSE: OR = 0.14, 95%CI = 0.02–0.53, p = 0.0113; mortality HR = 0.25, 95%CI = 0.13–0.49, p < 0.0001); however, no significant effect was observed in patients with both reactive pupils.

Conclusion: In our cohort, high variability in ICP insertion practice between countries was observed. A more aggressive treatment approach was applied in ICP monitored patients. ICP monitoring in severe aSAH patients was associated with a reduction in unfavorable outcomes and mortality at 6 months.

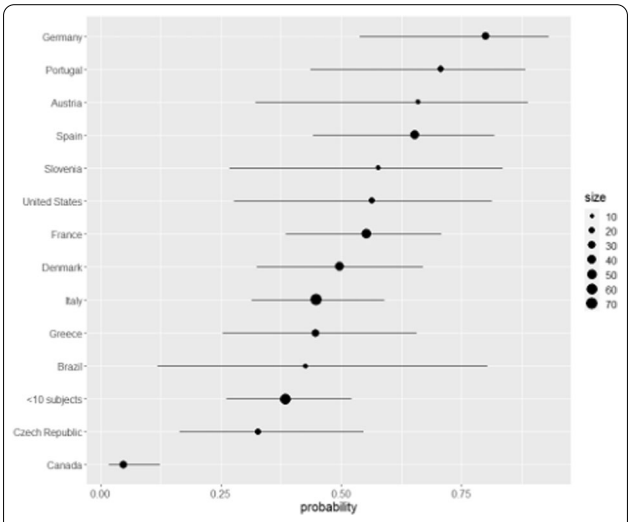

Figure 1. Caterpillar plot of the probability of ICP monitor use among countries.

Predicted probability of ICP monitoring (dots) with their 95% CIs (lines) are given on the horizontal axis, and countries are reported on the vertical axis. The size of dots showed the number of patients enrolled in each country.

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000974

Ceftazidime therapeutic drug monitoring in ICU: impact of obesity and glomerular filtration rate

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Intensive Care Medicine Experimental 2022, **10(2)**:000974

Introduction: Ceftazidime (CAZ) is a broad-spectrum cephalosporin commonly used as empirical therapy for intensive care unit (ICU) patients with sepsis [1, 2]. Critically ill and obese patients have severely altered and variable antibiotic pharmacokinetics due to several pathophysiological modifications [3], resulting in lower antimicrobial concentrations and consequently, poor outcome [4–8]. Experts recommend to routinely perform Therapeutic Drug Monitoring (TDM) to optimize dosing of beta-lactam antibiotics in ICU [9].

Objectives: The primary objective was to describe the target threshold attainment for CAZ concentration with standard of care dosing regimen. The second endpoint was to describe the impact of obesity and renal function on CAZ plasma concentrations and dosing regimens in ICU patients.

Methods: This retrospective observational cohort study was approved by the institutional review board [IRBN992021/CHUSTE]. All consecutive adult patients from 6 French medical and surgical ICUs, treated with CAZ using continuous infusion and under TDM evaluation between 11/01/2019 and 10/31/2021 were included. Patients had at least one CAZ plasma concentration collected at steady-state, considered to be at least 6 h after its introduction using continuous infusion. The obesity was defined as body mass index $\geq$ 30 kg/m^2. The glomerular filtration rate (GFR) was estimated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). Indicative threshold of interest for CAZ followed usual recommended levels for plasma concentrations: between 35 and 80 mg/l.

Results: A total of 111 patients (85 males, 45 obese), aged 66.0 $\pm$ 11.4 years, weighted 90 (77–96) kg, were included in this study. Mean time for sample collection was 70 (19–92) hours after CAZ introduction. Mean GFR was 84.3 mL/min/1.73 m^2 (53–106). Mean SOFA (Sequential Organ Failure Assessment) score [10] at the CAZ introduction was 7.3 (5–10). CAZ plasma concentrations were lower than recommended threshold for 58 out of the 111 patients (52.3%) at the first collection, with a median dosing regimen of 6 g/d. Moreover, obese patients had lower CAZ plasma concentrations compared to non-obese patients (37.8 vs 56.3 mg/L; *p = 0.0042**) *(Fig. 1)* despite similar dosing regimens (5.83 g/d vs 5.52 g/d, *p = 0.2529*). Figures 2 and 3 display CAZ concentration-to-dose ratio (C0D) according to GFR. Graphically, CAZ C0D seemed different for obese and non-obese patients except for GFR above 100 mL/min/1.73 m^2. Considering weight-based CAZ dosing seemed to attenuate such obesity-related discrepancies, regardless of GFR.

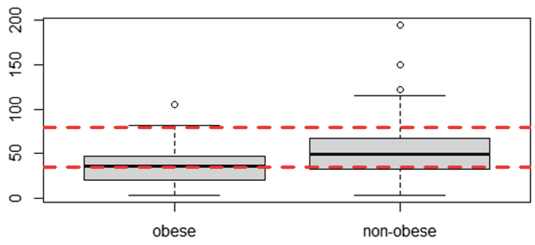

Figure 1: Box plot representing the difference of mean CAZ concentrations between obese and non-obese patients. Target CAZ concentration was drawn using red dashed lines between 35 and 80 mg/L.

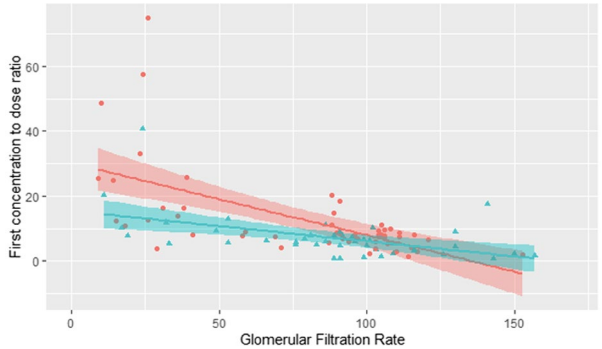

Figure 2: Comparison between obese (blue point) and non-obese (red points) patients of first CAZ concentration to dose (g/d) ratio according to GFR. Linear regression was drawn using blue and red lines and subsequent confidence intervals for obese and non-obese patients, respectively.

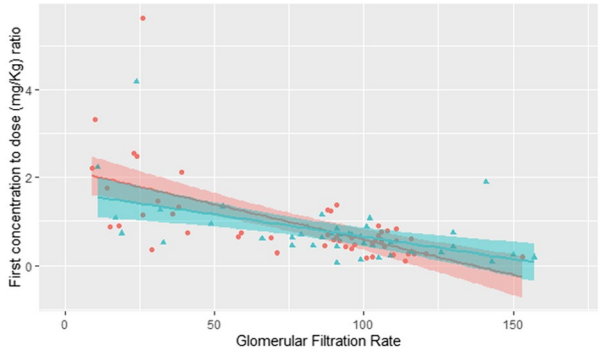

Figure 3: Comparison between obese (blue point) and non-obese (red points) patients of first CAZ concentration to weight-normalized-dose (mg/kg) ratio according to GFR. Linear regression was drawn using blue and red lines and subsequent confidence intervals for obese and non-obese patients, respectively.

Conclusion: TDM for ICU patients is mandatory to achieve target range for CAZ concentrations, especially for obese patients. Based on these primary results, weight-based dosing strategy seems to be more suitable than standard one. Randomized controlled studies should be performed to determine CAZ optimal dosing regimen for this expanding population.

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001069

Argumentation in end-of-life conversations with families in Dutch Intensive Care Units

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Intensive Care Medicine Experimental 2022, **10(2)**:001069

Introduction: In NICUs, PICUs and ICUs, decisions about continuation or discontinuation of life-sustaining treatment (LST) are made nearly every day [1]. Professional guidelines recommend an open exchange of standpoints and underlying arguments between doctors and families to come to appropriate decisions. Yet, it is unknown how doctors and families argue in real-life conversations.
Objectives: To identify which arguments doctors and families of critically ill patients use in support of their standpoints to continue or discontinue LST, how they structure those arguments, and how their argumentative practices unfold during the conversation.
Methods: Qualitative inductive analysis of audio-recorded conversations between doctors and families.
Results: Families of 36 critically ill patients and 71 doctors from the NICU, PICU, and ICU of a large university-based hospital participated. We collected and analyzed 101 conversations. Doctors and families presented 12 overarching arguments to either continue or discontinue LST. Their arguments largely overlapped. The arguments presented by doctors were in line with the arguments presented in professional guidelines for end-of-life decision making [2–9]. Additionally, we identified one new argument which doctors in our study often put forward, namely that the remaining uncertainties were a reason to continue LST. Doctors and families rarely substantiated their main arguments with sub-arguments. By effect, their argumentation remained abstract and rather vague. In most conversations, doctors as well as families put forward one standpoint and stuck to this standpoint during the conversation. Overall, doctors more often plead to discontinue LST than to continue LST. In the NICU, parents mainly advocated continuation of LST in response to doctors' standpoint that LST should be discontinued. Parents in the PICU either argued in line with doctors' previously presented standpoint to discontinue LST or in the opposite direction. When they agreed with the doctors' standpoint, they often deepened this standpoint by providing additional arguments. Families in the ICU mainly argued in line with the doctors' standpoint to discontinue LST. They less often provided additional arguments.
Conclusion: Our study offers a detailed insight in the argumentation practices of doctors and families. Overall, we observed that both doctors and families clung to their own line of argumentation. They did not substantiate their arguments and no real exchange occurred. Our knowledge will help doctors to have a sharper eye for the arguments put forward by all participants—doctors and families—and to offer room for true deliberation. This will add to the most appropriate decision for individual patients. Yet, while argumentation is an important part of end-of-life decision-making, the tone of voice must not be lost out of sight in these delicate conversations [10].

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Acknowledgements: ZonMw [project number 844001316].

Acute Kidney Injury 1

000127

Hemoadsorption as adjuvant therapy in acute hypoxemic respiratory failure (ARDS)

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Intensive Care Medicine Experimental 2022, **10(2)**:000127

Introduction: Acute respiratory distress syndrome (ARDS) is usually a secondary result of a dysregulated inflammatory host response, leading to capillary congestion, atelectasis, hyaline-membrane formation, and interstitial lung edema [1]. It is a hyperinflammatory condition, hence immunomodulation by extracorporeal cytokine removal conceptually could enhance lung recovery during the early course of the disease [2].
Objectives: The aim of our study was to investigate the effects of hemoadsorption (HA) therapy on clinical outcomes in patients with ARDS.
Methods: We performed a systematic literature search on Pubmed, Embase, CENTRAL, Scopus, and Web of Science (PROSPERO registration: CRD42022292176). The target population was ARDS patients, receiving hemoadsorption therapy. The primary outcome was the change in the PaO2/FiO2 (PF) ratio before and after hemoadsorption therapy. Secondary outcomes of interest included the before and after values of laboratory findings (CRP, lactate, IL-6), and noradrenaline (NA) dose. We consider a p-value of < 0.05 to be statistically significant.
Results: After conducting a systematic search, we identified 12 case reports, 8 case series, 3 retrospective cohort studies) eligible, with

a total number of 178 ARDS patients who received hemoadsorption therapy. Pooling data on different outcomes was only possible from 11 case reports and 2 case series (5 patients). These patients received Cytosorb (n = 14), Jafron HA-380 (n = 1), or oXiris (n = 1) for the HA treatment. The pooled individual patient data revealed significant improvement in the P/F ratio (n = 9, before: 116.26 ± 38.8 after: 169.5 ± 56.4 mmHg, mean difference ± SD: + 53.25 ± 62,39 mmHg p = 0.034); reduction of NA dose (n = 6 before: 0.395 ± 0.12 after: 0.040 ± 0.047 µg/kg/min, mean difference ± SD: -0.355 ± 0.131 µg/kg/min p = 0.001) and CRP (n = 11, before: 222.95 ± 170.34 after: 103.32 ± 109.14 mg/L, mean difference ± SD: -119.63 ± 100.94 mg/L, p = 0.003) following HA therapy. No device-related adverse events were reported.
Conclusion: Although our results indicate a signal towards improvement after hemoadsorption therapy, the available data is insufficient to draw firm conclusions. Further research is needed to identify the role of adjuvant HA therapy in ARDS.

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000136

Augmented renal clearance in severely burned patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000136

Introduction: Augmented renal clearance (ARC) is a phenomenon recently described in intensive care patients. It can modify the pharmacological properties (PK/PD) of various drugs, in particular antibiotics. This may be responsible for therapeutic failure involving the prognosis in patients with sepsis.
Objectives: Our study aims to determine the prevalence of ARC and to assess the impact on mortality in severely burned patients.
Methods: A retrospective, descriptive study, conducted in intensive burn care department in Tunis over a period of four years (2018–2021). Were included adult patients with acute burn surface area (ABSA) ≥ 20% and an ICU stay > 3 days. ARC was retained only in patients with a mean creatinine clearance ≥ 130 ml/min/1.73 m^2 for a period ≥ 3 days.
Results: During the study period, 1656 patients were admitted. ACR was retained in 183 patients, which corresponds to a prevalence of 11%. The majority were men (75%; n = 136) with low comorbidity (Charlson score < 2). The mean age was 36 ± 15 years, the mean ABSA was 38 ± 16%, and the mean ABSI score was 6 [2–15]. The use of mechanical ventilation was in 65% of cases. The average length of stay was 10 days [7–19]. In the ARC group, 131 patients (72%) presented sepsis during their stay, of which 55% (64/75) progressed to a septic shock with a mortality attributable to sepsis equal to 54% (72/131).
Conclusion: The prevalence of ARC is high in severely burned patients. It is accompanied by a high mortality in septic burn patients, related probably to modifications of the PK/PD of antibiotics. So antibiotics monitoring is necessary to guide dose optimization in this population.

000223

A continuous kidney extracellular matrix modification occurs within the first six months in sepsis survivors

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Intensive Care Medicine Experimental 2022, **10(2)**:000223

Introduction: Preserved extracellular matrix (ECM) components and their spatial interrelation with the kidney functional units are crucial to its well-functioning physiology, especially in critical illnesses. [1]. Hypoxia, driven by microcirculatory dysfunction in inflammatory diseases, is a stimulus associated with enhanced collagen synthesis. Microcirculatory disturbances in sepsis cause oxygen supply alterations and mitochondrial malfunction that impair cellular recovery and may contribute to collagen dysfunction. [2]. Persistent inflammation, catabolism, and immunodeficiency have been characterized as post-sepsis syndrome. [3]. Considering that the effects of long-term sepsis survivors are still little known, the understanding of the consequences of the disease in kidney structures may bring new knowledge for the intensive care patients' pathophysiology.
Objectives: This study aimed to carry out a kinetic evaluation of the presence of collagen I and III in the kidneys of septic and sepsis-surviving animals.
Methods: Wistar female rats were submitted to an experimental sepsis model (2 mL *E.coli* 108 CFU/ mL, iv) and after 6 h, 30, 60, and 180 days, samples of the kidneys of 3 animals per period were collected for histological assay, besides samples of the kidneys of three naive animals. The kidney tissue samples were stained with HE and Picrosirius Red and examined under polarized light.
Results: The results showed the predominance of Type III collagen on the glomeruli and renal tubules walls 30 days after sepsis induction. At 90 days, the prevalence of Type I was observed, which increased even more by the sixth month, especially in the inter-capillary spaces of the glomeruli, in Bowman's capsule, and in the walls of the convoluted tubules close to the glomeruli. Statistically significant deposition of type I collagen was observed in the thickened glomeruli capillary walls, as well as in adjacent venules and in the ECM between the tubules.
Conclusion: These findings suggest the advancement of multifocal renal fibrosis within the first six months after sepsis and the presence of a process of atherosclerosis could be implicated in increased renal vascular resistance and progression to chronic renal disease. These findings could imply that the renal structures are unable to function properly in the post-sepsis period, which could be linked to the ease of renal failure in the post-sepsis period and thus contribute to the increased morbidity of sepsis survivors.

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Acknowledgements: Grant 2017/21052–0, São Paulo Research Foundation (FAPESP).

000408

Characterization of amino acid loss in critically ill patients on renal replacement therapy

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Intensive Care Medicine Experimental 2022, **10(2)**:000408

Introduction: For patients undergoing renal replacement therapy (RRT), unintended loss of amino acids may occur. Amino acid loss is a negative process that may be associated with lower muscle mass, hypercatabolism, and generally worse clinical outcome.
Objectives: The aim of this study was to evaluate the amount and the determinants of amino acid loss in critical care patients during RRT.
Methods: This was a prospective study of patients who were admitted to a tertiary referral university hospital ICU. Inclusion criteria were as follows: start of RRT, being mechanically ventilated and compatible with either SEPSIS-3 or SIRS criteria. Every day for 7 days after inclusion in the study amino acid concentrations were measured once a day in three sampling points in the RRT circuit: A (coming from the patient to the RRT machine), V (coming from the RRT machine to the patient after the therapy) and N (waste from the RRT machine). The concentration of the effluent (N) amino acids was used to calculate the mmol of the net lost amino acids per day, further converting this amount to the mass of amino acids. Incoming amino acid concentration, CRRT dose and type were included in multivariate regression analysis to evaluate their effect on lost amino acid amount.
Results: 35 patients were included in the study, of which 54.3% were women. The average age of the patients was 67.23 ± 12.04 years; average CRRT dose 25.79 ± 7.29 ml/kg/h, CRRT type (CVVHD 62.9%, CVVH 8.6%, CVVHDF 28.6%). The mean first day amino acid concentration was 1.96 ± 0.98 mmol/l. There was a statistically significant difference in A and V concentrations (1.96 ± 0.98 vs. 1.61 ± 0.99 $p < 0.001$), which accounts for 17.6% extraction. The effluent concentration of amino acids (N) was calculated by the volume of effluent generated per 24 h to provide the net mmol/l amino acids lost. The average loss of amino acids in the first day was 9.21 ± 5.32 g, the highest loss was recorded during days 5–7 (on average 15.86 g). Multivariate regression analysis of effluent amino acid concentration revealed incoming amino acid concentration as the only independent factor of amino acid loss. (Table 1).

Table 1. Multivariate regression analysis

Variable	*B* coefficient	CI 95%	*p*
Incoming amino acid concentration	2.97	1.37–4.58	0.001
CRRT dose (ml/kg/h)	n.i	n.i	0.130
CRRT type (CVVHD, CVVH, CVVHDF)	n.i	n.i	0.242

n.i. not indicated, CRRT: continuous renal replacement therapy, CVVHD: continuous veno-venous hemodialysis, CVVH: continuous veno-venous hemofiltration, CVVHD: continuous veno-venous hemodiafiltration.

Conclusion: The study demonstrated that a substantial amino acid loss is seen in patients on RRT. The loss of amino acids is increasing when the critical state is prolonged, leading to a meaningful net negative balance of amino acids per 1st week in ICU. Furthermore, the study demonstrated the systemic concentration of amino acids as a determinant of the amino acid loss during renal replacement therapy.
Acknowledgements : Research Council of Lithuania. Biosensor Platform for Fast, Cheap and Accurate Quantification of Amino Acids in Patients Undergoing Renal Replacement Therapy (DIALSENS) (No. 01.2.2-LMT-K-718-01-0019).

000496

Anticoagulation management in renal replacement therapy in COVID-19 critically ill patients: heparin vs citrate. Which one is better?

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Intensive Care Medicine Experimental 2022, **10(2)**:000496

Introduction: At the beginning of COVID-19 pandemic many patients were admitted to intensive care unit with bilateral pneumonia with severe ADRS. Some of them develop acute kidney injury that needed continuous renal replacement treatment that may require anticoagulation to prevent clotting of the extracorporeal circuits. Different strategies have been considered but, as COVID-19 patients have a prothrombotic contidion, we do not exactly know how current strategies apply to these patients.
Objectives: To assess whether the use of citrate in continuous renal replacement therapy (CRRT) in COVID-19 patients on treatment with systemic enoxaparin at intermediate doses lengthens the duration of filtration kits compared to those using heparin sodium as a regional anticoagulant.
Methods: It was performed a retrospective analysis of all patients admitted to the ICU and resuscitation unit of the Hospital Universitario la Paz in Madrid with a diagnosis of bilateral COVID-19 pneumonia and requiring CRRT from March 1, 2020 to October 30, 2020. Demographic data, number of kits per patient, anticoagulation strategy and duration of each system were recorded and compared using Student's t-test, considering statistical significance with $p < 0.05$.
Results: During the analysis time period a number of 41 patients requiring CRRT were collected. 39 (95.1%) were men. The mean age of the sample was 63.15 ± 10.7. A total of 279 filtration kits were used, 177 (63.4%) of which were anticoagulated with heparin, 64 (22.9%) with citrate, 19 (6.8%) with epoprostenol and 19 (6.8%) without anticoagulation. All patients received enoxaparin at intermediate doses. A total of 3 patients (7.3%) received ECMO therapy. The mean length of stay in the critical care unit was 35.4 ± 25 days and mortality rate was 82.9%. Within the subgroup of heparin kits, the mean duration was 29.9 ± 25 h and that of citrate 26.5 ± 25.2 h. According to statistical criteria and applicability conditions, a mean comparison analysis was performed with Student's t-test, obtaining $t = 0.916$ and p-value = 0.361 with CI 95% (-3.8–10.6).
Conclusion: The analysis of the data shows that there were no differences in the duration of the hemofilter systems depending on the anticoagulant chosen in critically ill COVID-19 patients admitted at our center on the dates indicated, Two relevant facts should be taken into account that may have led to these results, which differ from the data obtained in another patient profile: 1—All the patients were receiving subcutaneous enoxaparin at intermediate doses as part of the treatment for COVID. 2—The excessive workload of the healthcare personnel,being citrate strategy a more complex technique, despite the fact that in our Center regional therapy with citrate has been the first choice since 2014.

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Acknowledgements: To all our COVID-19 patients and all the health team that has fought day by day against the pandemic.

000519

Graduated compression stocking application in the lower extremities during hemodialysis for prevention of intradialytic hypotension in critically ill patients: a single-center randomized crossover trial

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Intensive Care Medicine Experimental 2022, **10(2)**:000519

Introduction: Intradialytic hypotension (IDH) is a frequent complication of hemodialysis, particularly in critically ill patients. IDH limits adequate fluid removal, results in early termination of hemodialysis, and is associated with worse outcomes.
Objectives: To assess the efficacy of the application of graduated compression stocking (GCSs) in lower extremities during hemodialysis in preventing IDH in critically ill patients.
Methods: We conducted a single-center randomized crossover trial in patients requiring intermittent hemodialysis or sustained low-efficiency dialysis in intensive care units from March 2021 to February 2022. We randomly assigned eligible patients to start dialysis with or without GCS application, and alternated them to receive the other intervention in the subsequent dialysis. The primary outcome was the incidence of IDH, defined as the nadir systolic blood pressure < 90 mm Hg, a decrease in either systolic blood pressure ≥ 20 mm Hg, or mean arterial pressure ≥ 10 mm Hg from the baseline.
Results: Forty-two patients were enrolled in this study. Pre-dialysis hemodynamic parameters and dialysis prescription were comparable between dialysis session with and without GCS application. There was no significant difference in the incidence of IDH between dialysis session with and without GCS application (35.7% in GCS vs. 57.1% in no GCS group; $p = 0.09$). The mean ratio of delivered to prescribed ultrafiltration was higher in dialysis session with GCS application (1.1 ± 3.4 in GGS vs. 0.9 ± 0.3 in no GCG group; $p = 0.04$).
Conclusion: The use of GCSs during dialysis in critically ill patients did not reduce the risk of IDH but it could improve the likelihood of achieving target fluid removal.

000527

Risk factors for post-contrast acute kidney injury in patients sequentially administered iodine- and gadolinium-based contrast media on the same visit to the emergency department: a retrospective study

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Intensive Care Medicine Experimental 2022, **10(2)**:000527

Introduction: Objectives: This study aimed to compare the incidence of post-contrast acute kidney injury (PC-AKI) between single iodine-based contrast media (ICM) and sequential administration of ICM and gadolinium-based contrast media (GBCA) on the same visit to emergency department (ED); and investigate its risk factors.
Methods: This retrospective study analyzed the data from 2016 to 2021. Patients who had eGFR of < 30 mL/min/1.73 m^2 measured in ED were excluded in this study. The primary outcome was the development of PC-AKI (increase in creatinine of ≥ 25% or 0.5 mg/dL over the baseline; or reduction in eGFR of ≥ 25%), and assessed using a propensity score matching (PSM) analysis between the ICM alone and ICM + GBCA groups. Additionally, its risk factors were assessed from multivariable logistic regression.
Results: Of the 29,635 patients administrated ICM, 6318 were included. Among them, 139 patients were ICM + GBCA group. The ICM + GBCA group showed significantly higher rate of development of PC-AKI as compared with the ICM alone group in the total cohort (adjusted odds ratio [OR], 3.09;95% confidence interval [CI], 2.09–4.58]) and PSM cohort (adjusted OR, 2.38 [95% CI, 1.25–4.55]). On multivariate analysis in the ICM + GBCA group, osmolality (adjusted aOR, 1.05 [95% CI, 1.01–1.10]) and eGFR (adjusted OR, 0.931; 95% CI, 0.883–0.983) were associated with PC-AKI.
Conclusion: The sequential administrations of ICM and GBCA on the same visit to ED may be a risk factor for PC-AKI as compared with single administration of ICM alone. Osmolality and eGFR may be independently associated with PC-AKI after sequential administrations.

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000676

Use of proenkephalin in early diagnosis of acute kidney injury in covid critically ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000676

Introduction: Acute Kidney Injury (AKI) is a common complication in critically ill patients. The pooled incidence of AKI among COVID-19 patients was 19.45% and of AKI COVID-19 patients requiring Renal Replacement Therapy (RRT) was 39.04% (16.38– 64.57%). Implementation of novel reliable biomarkers that permit a reliable AKI risk stratification for covid patients would allow developing early management strategies with potential positive impact on patient outcome.
Objectives: In this preliminary study we examined if proenkephalin (PenKid) could be used as an early marker that can reliably predict incident AKI in critically ill covid patients. The primary endpoint investigation was development of AKI and need of RRT at day 7. The secondary endpoint was assessment of AKI severity.
Methods: Inclusion criteria included: age over 18 years, confirmed covid19 infection, admission into the ICU. Exclusion criteria were: age less than 18 years, pregnancy, chronic renal disease, and participation in any interventional study in the previous 45 days. So far 28 patients are included in the study 0.64,28% (18) of the patients were male and 35,28% (10) were female Median age was 67 years (range 54–76). Blood was drawn upon admission and at the 7th and 14th day and levels of PenKid were measured. Serum creatinine levels were measured on a daily basis and creatinine clearance in 24 urine collection samples were monitored every 72 h. Measurements of PenKid were performed using chemiluminescence immunoassay (Sphingotec GmbH, Hennigsdorf, Germany NexusDx.
Results: 18 patients were alive with no need of RRT at some point during the first 7 days Median PenKid concentrations were < 50 pmol/L. 7 patients were alive with persistent AKI without having received RRT. 2 of the patients were alive and were receiving RRT by the 7th day and one patient has died on the 4thday. Median PenKid concentrations in patients with AKI were ≈ 98 pmol/L. Patients who had higher concentrations of PenKid on admission showed a stepwise increase with developing severity of AKI. Results indicate a higher probability of developing AKI and subsequent need of RRT with higher levels of PenKid ($p < 0.001$). Increases in PenKid concentrations preceded serum creatinine concentrations increases as well as decreases in creatinine clearance.
Conclusion: The results of this preliminary study indicate that PenKid can be used as a biomarker for early detection of acute kidney injury and is a promising biomarker for tracing the severity of developing renal failure. The results are in accordance with data published by other researchers although data from critically ill covid patients are lacking.

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000683

Acute kidney injury in burned patients admitted to the intensive care unit: incidence and outcome

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Intensive Care Medicine Experimental 2022, **10(2)**:000683

Introduction: Acute kidney injury (AKI) is defined as an acute decline in glomerular filtration rate (1). Its occurrence aggravate the prognosis of patients hospitalized in the intensive care unit.
Objectives: The aim of this study was to determine the incidence and characteristics of burned patients admitted to the intensive care unit who have developed AKI.
Methods: This is a retrospective, monocentric study conducted over a period of 21 months (July 2020-March2022) in the burn intensive care unit of the trauma and burns center in Tunisia. All patients who developed AKI during hospitalization were included. AKI was defined according to the KDIGO classification (1).
Results: During the study period, 764 patients were hospitalized. Of these, 43 developed AKI with an incidence of 18%. There were 33 male and 10 female patients with a sex ratio of 3.1. The mean age was 49 years [19; 90]. Twelve patients (28%) had hypertension and 9 patients (21%) had diabetes. The burns were caused by a domestic accident in 22 cases (51%), by a suicide attempt in 16 cases (37%) and by a work accident in 5 cases (12%).
The burns were thermal in 91% of cases. The average total burned skin area was 49% with a minimum of 7% and a maximum of 100%. The average UBS score was 83. The average SOFA score was 8. AKI was established on average on the first day of hospitalization. It was stage 1 in 33% of cases, stage 2 in 44% of cases and stage 3 in 23% of cases. AKI was complicated by anuria in 68% of cases, hyperkaliemia in 23% of cases, metabolic acidosis in 84% of cases and acute pulmonary edema in 5 cases (12%). The renal replacement therapy (RRT) was indicated for 14 patients. Only 10 patients were able to benefit from RRT, for the rest it was impossible to do it because significant hypothermia or profound thrombocytopenia. The mortality rate was 86%.
Conclusion: Our study shows that AKI in burn patients is a frequent complication (18%). It further aggravate the prognosis and it is associate with a high mortality.

000726

Mortality rate benchmarks from real-world studies and clinical trials of patients with sepsis-associated acute kidney injury: a systematic literature review

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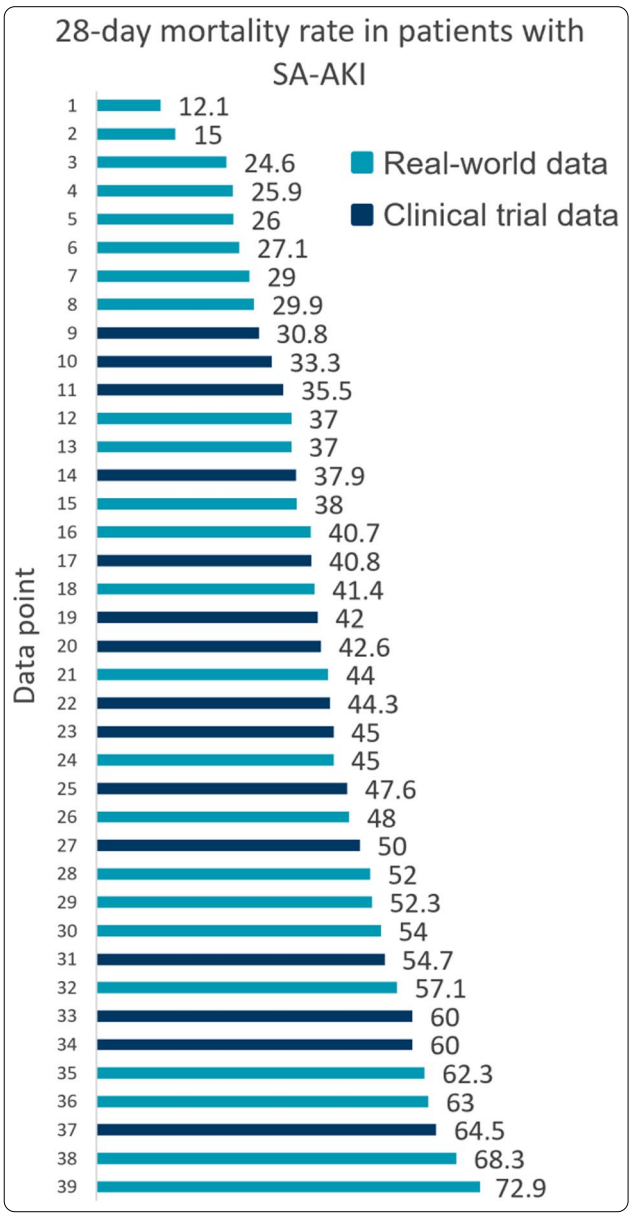
Introduction: Drug development in the field of sepsis-associated acute kidney injury (SA-AKI) is challenging, with manufacturers requiring adequate benchmarks with which to design interventional trials to demonstrate the potential benefit for investigational therapies. Gold standard measures such as mortality require appropriate benchmarks to adequately determine expected effect size, sample size requirements for adequate statistical powering, and potential confounders with which to pre-plan stratification and/or patient selection criteria.
Objectives: In order to explain the various benchmarks, characterise the burden of this disease and to aid in future trial design, we conducted a systematic literature review of mortality evidence from controlled clinical trials and real-world studies in SA-AKI.
Methods: A systematic review was conducted to identify studies reporting mortality in patients with SA-AKI by searching EMBASE (2006–present) and conferences (ISPOR, ESICM, ISICEM, AKI & CRRT

and World Congress of Nephrology [2017–2020]) using various search terms for 'mortality', 'acute kidney injury' and 'sepsis'. Data were extracted for single- or multi-centre North American, Western European and global studies.



Results: In total, 11 controlled clinical trials and 101 real-world studies were identified. These studies provided 313 data points for mortality rates. Published datasets represented 714,758 total SA-AKI patients (including cohorts where ≥ 80% patients had SA-AKI). The most common measure of mortality in clinical trials was 28-day mortality (5/11 trials, 45%) and 90-day mortality (4/11, 36%). The most common measure in real-world studies was in-hospital mortality (53/101 studies, 53%) and in-ICU mortality (27/101, 27%). Mortality rates ranged from 10.4–64.5% in clinical trials and from 0–87.8% in real-world studies. Rates of mortality varied across in-ICU (0–87.8%), in-hospital (0–87.5%), 28-day (12.1–72.9%), 30-day (5.0–57.9%) and 90-day (22.5–71.6%). Mortality at 28 days was reported in 17 real-world studies and 5 clinical trials. Mean 28-day mortality was 41.8% (weighted average 35.2%) in real-world studies and 45.9% (weighted average 44.5%) in clinical trials (Figure). Distinct characteristics were associated with higher mean in-hospital mortality rates, including Stage 3 AKI (as defined by AKIN or KDIGO), renal failure or RRT (55.1%), comorbid enrolled populations (55.1%) and presence of septic shock (53.8%). The average in-hospital mortality in patients with none of these characteristics was 27.6%, in patients with 1 of these characteristics was 49.2%, with 2 characteristics was 54.3% and with all 3 characteristics was 65.3%.

Conclusion: The choice of benchmark and enrolled patient populations in studies can dramatically change the mortality rate used in design of clinical trials. Smart drug development requires a thorough understanding of these benchmarks and the informed design of clinical trials in SA-AKI.

Acute Kidney Injury 2 + Nurses & Allied Healthcare Professionals 2

001290

Decreased renal cortical perfusion, independent of changes in renal blood flow and sublingual microcirculatory impairment, is associated with the severity of acute kidney injury in patients with septic shock

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Intensive Care Medicine Experimental 2022, **10(2)**:001290

Introduction: Acute kidney injury (AKI) associated with septic shock is an important condition with a high mortality. Reduced renal perfusion has been implicated in the development of septic AKI. However, the relative contributions of macro and microcirculatory blood flow and the extent to which impaired perfusion is an intrinsic renal phenomenon or part of a wider systemic shock state remains unclear.
Methods: Longitudinal assessments were made of renal cortical perfusion at Day 0, 1, 2 & 4 after ICU admission in 50 patients with septic shock and 10 healthy volunteers using contrast enhanced ultrasound (CEUS). Contemporaneous measurements were made using transthoracic echocardiography of cardiac output. Renal artery blood flow was calculated using the velocity time integral and vessel diameter. Assessment of the sublingual microcirculation was made using hand held video microscopy. Patients were classified based on the degree of AKI: severe = KDIGO 3 v non severe = KDIGO 0–2.
Results: 37/50 patients had severe AKI; these patients had higher SOFA scores (15.3 v 9.3, $p < 0.001$), noradrenaline dose (0.34 v 0.21 mcg/kg/min, $p < 0.01$) and lactate (3.9 v 2.7 mmol/l, p 0.03). At study enrolment patients with severe AKI had prolonged CEUS mean transit time (mTT) (10.2 v 5.5 s, $p < 0.05$), and reduced wash in rate (WiR) (409 v 1203 au, $p < 0.05$) and perfusion index (PI) (485 v 1758 au, $p < 0.05$); these differences persisted throughout the entire study period. Conversely, there were no differences, based on AKI severity, in either cardiac index, renal blood flow or renal resistive index across the entire study period. Sublingual microcirculatory variables were not significantly different between groups at study enrolment: Microcirculatory Flow Index (MFI) 2.55 (2.17–2.82) v 2.74 (2.54–2.81), p 0.43 or at any subsequent time point. Although lactate was higher in the severe AKI group at study enrolment these differences did not persist and there were no differences in either ScvO2 or ScvCO2-SaCO2 between groups. Linear regression analysis showed no correlation between mTT and cardiac index (R-0.18) or MFI (R-0.16).
Conclusion: Renal cortical hypoperfusion is a persistent feature in critically ill septic patients who develop AKI and does not appear to be caused by reductions in macrovascular renal blood flow or cardiac output. Cortical hypoperfusion appears not be associated with changes in the sublingual microcirculation, raising the possibility of a specific renal pathogenesis that may be amenable to therapeutic intervention.

001385

Use of bioimpedance vector analysis (BIVA) for evaluation of fluid status in critically ill patients undergoing renal replacement therapy

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Intensive Care Medicine Experimental 2022, **10(2)**:001385

Introduction: Accurate assessment of fluid status is necessary to manage fluid overload. Bioimpedance vector analysis (BIVA) is a convenient non-invasive tool for estimation of fluid status, but there are scant published data regarding the use of BIVA in critically ill patients undergoing renal replacement therapy (RRT).
Objectives: To compare tools of fluid assessment between percentage of fluid accumulation (%FA), a calculated measure, and BIVA-derived values and to determine which parameter is the best for predicting 28-d mortality.
Methods: This study is a prospective observational study in patients admitted to medical ICUs and underwent RRT. We recorded clinical values and performed fluid assessment by calculating %FA and by BIVA measurements on day 1, 3 and 7 after initiating RRT. BIVA-derived values included percentage of fat free mass hydration (%FFMH), and phase angle (PhA). The association between BIVA-derived values, %FA, and 28-d mortality were identified. Additionally, the significant parameters were analyzed using the ROC curve for searching the best cutoff value to predict the mortality.
Results: Sixty-five patients were enrolled, with a mean age of 66 ± 16 year, and a mean APACHE II score of 22 ± 7. The median %FA were 10.28%, 10.90%, and 8.65%, the median %FFMH were 81.35, 81.44, and 79.34, and the median PhA were 4.27, 3.86, and 4.17 on day 1, 3, and 7, respectively. According to 28-d mortality, no differences of %FA and BIVA values, which measured on day 1 and day 7 between non-survivors and survivors. The median %FFHM on day 3 was higher in non-survivors than in survivors [83.44% (81.46, 83.97) vs 80.30% (75.58, 82.78), $p = 0.007$] and the median PhA on day 3 was lower in non-survivors than in survivors [3.22 o (2.65, 4.24) vs 4.02 o (3.41, 5.26), $p = 0.030$]. Whereas the median %FA on day 3 of non-survivors was not statistically different from that of survivors. Percentage of FFMH of more than 80.9% on day 3 could predict 28-d mortality with the OR of 7.50 (95% CI 1.86–30.16, $p = 0.002$) and PhA of less than 3.4o on day 3 could predict 28-d mortality with the OR of 6.00 (95% CI 1.78–20.19, $p = 0.002$).
Conclusion: BIVA-derived values, %FFMH and PhA on the third day after RRT initiation were associated with the 28-d mortality. %FFMH of more than 80.9% or PhA of less than 3.4o could be used as the cutoff value for guidance of fluid management in ICU patients undergoing RRT.

001412

How does acute kidney injury affect metabolic compensation of respiratory acidosis in patients with acute exacerbation of COPD in the intensive care unit? A retrospective study

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Intensive Care Medicine Experimental 2022, **10(2)**:001412

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of death worldwide (1). Acute exacerbation (AECOPD) can lead to severe respiratory acidosis which is associated with poor outcome and often requires treatment in an intensive care unit (ICU) (2–4). Renal retention of bicarbonate is one of the main mechanisms compensating acidosis (3). Acute kidney injury (AKI) is a common complication in ICU-patients and can affect the metabolic compensation mechanisms of acid–base-disorders (5–7).
Objectives: The aim of this analysis was to objectify the influence of AKI on metabolic compensation of respiratory acidosis in AECOPD and to look for predictors of poor outcome.
Methods: The clinical data of all patients who were admitted with AECOPD to two medical intensive care units of Charité—Universitätsmedizin Berlin from January 2009 to June 2021 was retrospectively analysed. Considering KDIGO criteria the study population was divided into a group presenting an AKI (AKI) and a group with stable kidney function (NOAKI). Cox proportional hazard regression model was used to inspect survival adjusting for sex, age, time on ventilator and the SOFA score. Daily measurements of pH, arterial carbon dioxide partial pressure (paCO2) and concentration of bicarbonate (HCO3-) were analysed within a correlation analysis with respect to the degree of kidney injury.
Results: A total of 498 patients were included in this analysis. 278 patients (55.8%) suffered from an AKI. From those patients 139 (50%) presented an AKI stage 3. Age and sex were evenly distributed in the two groups. The prevalence of diabetes mellitus, chronic heart failure or chronic kidney disease was higher in patients with AKI. Patients with AKI had a higher initial SOFA score (6 vs. 3), were intubated more often (53.6 vs. 13.6%) and ventilated longer (92 vs. 14 h). They were also treated longer in the ICU (8 vs. 3 days). The ICU mortality in the group with AKI was higher (16.2 vs. 4.5%). The concentration of bicarbonate (25.8 vs. 27.5 mmol/l on day 1) in relation to the carbon dioxide partial pressure (68.5 vs. 61.8 mmHg on day 1) was significantly lower in the AKI-group during their whole stay in the ICU (HCO3-/paCO2 0.38 vs. 0.45 on day 1; $p = 0{,}001$). The pH values in this group were also lower during their whole ICU treatment (7.23 vs. 7.28 on day 1; $p = 0.001$). The concentrations of HCO3- in relation to the paCO2 of patients with AKI stage 3 were lower than those of patients with AKI stages 1 and 2. The values of patients with AKI stages 1 and 2 were nearly similar to patients without AKI. The lowest HCO3- and pH and highest paCO2 were found in the patients in need of acute dialysis.
Conclusion: Acute kidney injury affects metabolic compensation of respiratory acidosis in patients with acute exacerbation of COPD in ICU.

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8. The results will also be part of the dissertation "Effects of renal function on metabolic compensation of respiratory acidosis in patients with acute exacerbation of COPD in the intensive care unit", written by Goettfried Katharina, but still not published at Charité—Universitätsmedizin Berlin.

Acknowledgements: This study was conducted without external financial support.

001426

Clinical impact of a program to improve renal replacement therapy in critically ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001426

Introduction: Renal replacement programs in critically ill patients, due to their clinical, prognostic and logistical implications, should be subject to continuous analysis in search of potential improvements. After analyzing the results of 2018, an improvement program was launched that included training for doctors and nurses, new protocols that were collected in a clinical guide and meetings with the nursing group specialized in renal replacement therapies. The main novelty of the protocols was the implementation of a dynamic dosage system in acute patients based on a kinetic model of urea. In this study we present the clinical impact of the application of these changes.
Objectives: To analyze the evolution of two cohorts of patients treated with renal replacement therapy (RRT) after implementing an improvement plan, and to determine if there are differences in mortality, dialysis dependency and length of stay both in the Intensive Care Unit (ICU) as in the hospital.
Methods: Design: Retrospective and observational study in critical patients.Setting: Multipurpose ICU of the General University Hospital of Castellón. Patients: Inclusion of patients with renal failure who received intermittent RRT (HDI) or continuous RRT (CRRT) in the ICU. Intervention: Updating of protocols, individualized selection of the different RRTs, training actions, dynamic dosing according to a urea kinetic model and protocolization of the weaning of the RRTs. Main variables: Epidemiological, severity (SAPS 3), duration of RRT, mortality and dialysis dependency at ICU and hospital discharge. Study period: Duration of 7 years divided into 2 periods: before (2015–2018) and after (2019–2021) implementing the improvement plan. Statistical analysis: Quantitative variables are expressed as median and interquartile range (25% and 75%). To quantify the relationship between variables, the Mann–Whitney U test was used.Categorical variables are expressed as counts and percentages and were compared using a chi-square (χ^2) or Fischer test and calculation of the Odds Ratio to quantify the relationship between variables.A significance level of 5% bilateral was considered.
Results: In total, 340 patients were analyzed (190 in the before group and 150 in the after group). The median age was 67 years (interquartile range -IQR- 57.25–74.00) and 68.8% were men, with no significant differences between the groups for both variables (67 years [58–75] vs 66 [57–73], p = 0.09 and 66.8% vs 71.3%; p = 0.38). The medical pathology was more frequent (70.9% overall; 69.5 vs 72.7; p = 0.52) and the main cause of admission was septic origin (35% overall; 36.3 vs 33.3; p = 0.57). The median duration of global RRT was 3 days (IQR 2–7), with no significant differences between the two groups (p = 0.958). Dependence on dialysis at ICU discharge was higher in the first group (33.3% vs 11.9%; p = 0.004). Overall mortality in the ICU and in the hospital were 46.9% and 50.9%, respectively, with significant differences between both periods in the hospital mortality (56.8% to 43.3% p = 0.013; in the ICU 51.1 to 41.3%, p = 0.075). Between the survivors, the hospital stay was shorter in the second group (35 vs 22 days; p 0.00). Factors related to mortality were a SAPS 3 score greater than 64 points (odds ratio [OR] 3.13, 95% confidence interval [95% CI] 2.01–4.89) and belonging to the initial cohort (OR 1.72; CI95% 1.12–2.65). In the recent period, we found a decrease in the use of IHD in the ICU (median 2 days [IQR 1–6] vs 1 [IQR 1–4] p = 0.001).
Conclusion: Our study indicates that the implementation of an improvement and follow-up plan for critically ill patients treated with RRT improves outcomes.In our unit, the use of IHD was associated with a higher risk of dialysis dependency at ICU and hospital discharge.In acute patients, reduction of ICU IHD treatments was associated with a significant reduction in dialysis dependency at ICU and hospital discharge.Overall, program improvements are associated with shorter hospital stays and lower hospital mortality.Periodic follow-up and evaluation of RRT is recommended to improve results in the ICU.

001444

Acute kidney injury during COVID 19 in ICU patients: incidence, risk factors and outcome. Is COVID-19 a higher risk?

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Intensive Care Medicine Experimental 2022, **10(2)**:001444

Introduction: Compared to patients with viral pneumonitis from other virus, SARS-CoV-2 is not associated with a significant higher risk of AKI in critically ill patients. However, it became apparent that many COVID-19 patients also displayed kidney abnormalities, primarily acute kidney injury (AKI). The incidence of AKI still poor documented in Tunisia.
Objectives: The aim was to determine the incidence, the severity degree of AKI, the risk factors and prognosis during hypoxemic pneumonia related to COVID-19.
Methods: We conducted a monocentric retrospective study in an intensive care unit including critically ill patients with confirmed SARS-COV2 infection between January 2021 and December 2021. Demographics characteristics, comorbidities, clinical, paraclinical, therapeutics and outcomes were collected. The primary endpoint was mortality. Two groups were identified: Group 1 = AKI + and Group 2 = AKI-. The differences in data of the patients were evaluated.
Results: 338 patients were enrolled, median age was 57 ± 13 years (IQR, 25–85), sex ratio = 1.15, Medians of SAPS II and APACHE II scores were, respectively, 26 ± 8 and 8 ± 3. Hypertension (37%) and diabetes (33%) were the most frequent underlying diseases. Two hundred five patients (70%) have a pulmonary injury more than 50% on CT scan. The mean PaO2/FiO2 ratio was 123. All patients received a curative anticoagulation and 66.9% were received antibiotic on the first day of ICU admission. the use of amines was 62.8%. The incidence of thrombi-embolic events was 22.1%. And 57% required invasive mechanical ventilation. Mortality was 45%. The average length of stay was 10 ± 8 days. During hospitalization, 50 patients (21%) developed secondary AKI (10 kept their renal failure from admission) the average of development a acute kidney injury was 8 ± 5 days. The mean renal clearance was 25.6 ± 12.9. Hospital acquired AKI were classified on stage 1 of KDIGO classification in 29 cases (58%), stage 2 in 16 patients (32%) and stage 3 in 5 patients (10%). Identified risk factors of developing AKI were: history of cardiovascular (p = 0.009), history of thromboembolic events (p = 0.021), the high level of oxygen needed (p = 0.002), need for invasive mechanical ventilation (p < 0,001), and shock (p < 0.001). Duration of ventilation and ICU stay were similar in AKI group and non-AKI group (6 [3–8] vs 3 [2–8], p = 0.2 and 7 [5–10] vs 8 [4–15], p = 0.59). Mortality was significantly higher in AKI patients (85% vs 39.4%, p < 0.001) and AKI increased the death risk by 6 (p = 0.009).
Conclusion: The incidence of AKI among patients with critical illness of COVID-19 was important. Several factors were shown to contribute to its occurrence and vasopressors use was an independent factor. This complication was highly associated with mortality.

001336

Proning related pressure injury prevention project

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Intensive Care Medicine Experimental 2022, **10(2)**:001336

Introduction: COVID 19 pneumonitis has increased the frequency of use of prone positioning for sedated and ventilated patient in the Critical Care setting (1), as a manoeuvre to attempt to optimise gas exchange and improve mortality (2). This has been extrapolated from evidence for its use in patients with Adult Respiratory Distress

Syndrome (3). Prior to the COVID 19 pandemic, the prone position was only infrequently used on our Critical Care Unit. Prone positioning poses many challenges for staff and patients (4). One significant and frequent risk to the patient is the development of pressure related skin necrosis (5). This became apparent during the pandemic with an increase in pressure ulcer related incident reporting on our critical care.
Objectives: Implement a new pressure relief protocol to reduce the number of proning related pressure ulcers in patients with COVID 19 pneumonitis.
Methods: Data analysis looked at adult patients with COVID 19 Pneumonitis in Critical Care who were nursed in the prone position. Information obtained from incident reporting systems demonstrated a surge in proning related pressure ulcers, highlighting a need for change in practice to improve patient safety. NHS improvement (6) empowered us to implement several new preventative measures, comprising of a standardised prone positioning chart, a skincare checklist, customised memory foam pillows, use of the hoist for repositioning and innovative education.
Results: Data collection demonstrates 174 patients were proned during the period of March 2020 until January 2022 on our Critical Care Unit. Between March 2020 until December 2020, 78 patients were proned, of which 31 patients (39%) developed proning related pressure ulcers. Following comprehensive small group training, interventions were implemented over 2 months (November and December 2020). From 1st January 2021 until 31st January 2022, 96 patients proned. Of these, only 29 patients (30%) developed proning pressure ulcers. This highlights a 9% reduction in pressure ulcers after intervention demonstrating a marked decrease in proning related pressure sores post implementation of interventions and education, despite an increase in the total number of patients proned.
Conclusion: Prior to COVID 19, prone position was rarely used on our Critical Care Unit; practice was adapted to meet the demand. The results highlight a significant decrease in proning related pressure ulcers after the launch of the preventative measure protocol and thus a reduction in harm to patients.

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Acknowledgements: Nothing to declare.

001367

Early rehabilitation during ICU management to enable recovery from COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**:001367

Introduction: Patients with severe coronavirus disease (COVID-19) whose admitted to the intensive care unit (ICU) are at risk of developing ICU-acquired weakness and disuse syndrome. Although their medical management may include prolonged deep sedation for pulmonary protection and ventilator use, early rehabilitation is a critical therapeutic tool to reduce complications of immobilization, such as myopathy, neuropathy, and ventilator dependency.
Objectives: To evaluate the effectiveness of early rehabilitation on improving respiratory and other functional independences in severe COVID-19 patients.
Methods: We had 23 patients diagnosed with Acute Respiratory Distress Syndrome (ARDS) due to COVID-19 divided in 2 groups. The first group, with 15 patients, received early rehabilitation program in the ICU during their first 5 days after admitted, while the second group, with 8 patients, started their late rehabilitation program after being admitted for more than 5 days. All of the patients needed High Flow Nasal Cannula (HFNC) or ventilator to keep their arterial blood oxygen saturation levels (SpO2) over 90%. The rehabilitation program included proning position for 8 h per day, semi-proning position every 2 h, respiratory exercises twice a day which included: diaphragmatic deep breathing, chest stretching, effective coughing; and muscle exercises twice a day which included: mobilization, range of motion exercises, and joint relaxation.
Results: In the first group, 46.7% (n = 7) were able to be transferred to the ward in their first week after admission, and 46.7% (n = 7) in their second week. 1 patient from the first group did not survive. All patients from the first group that were transferred to the ward had SpO2 above 96% with non-rebreathing mask, which indicated improvement of their respiratory function. Patients' muscle strength also recovered to the range of 4–5 on the Manual Muscle Testing Scale and were able to independently walk to the toilet without experiencing respiratory distress. All patients from the second group did not survive their second week after admission. Therefore, this proved that early rehabilitation improved patients' recovery better than late rehabilitation (p 0.000; RR 15.00).
Conclusion: Early rehabilitation therapy improves respiratory and physical function in patients with severe COVID-19. Although further validation using larger scale of research is required, our results suggest that patients with severe COVID-19 whose admitted to the ICU should undergo early exercises and mobilization programs to improve their recovery.

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Acknowledgements: No grant funded.

001393

Is there a role for continuous flow peritoneal dialysis in children after congenital cardiac surgery? A retrospective comparison of the effectiveness of post-operative peritoneal dialysis modalities in a single quaternary centre over 15 years

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Intensive Care Medicine Experimental 2022, **10(2)**:001393

Introduction: Acute Kidney Injury (AKI) is estimated to occur in 30–50% (1) of children following surgery for congenital heart disease and is associated with increased morbidity and mortality (2). Fluid overload is an important risk factor for AKI following surgery (2). Peritoneal dialysis (PD) is the most commonly utilised modality of renal replacement therapy to manage AKI and fluid overload, particularly in smaller patients (3). A variation of this method is continuous flow peritoneal dialysis (CFPD) which involves continuous input of dialysate through one catheter and drainage via a second catheter, with no dwell time. Theoretically, CFPD provides greater ultrafiltration and solute clearance however research on CFPD is sparse.
Objectives: To determine and compare the effectiveness of conventional PD and CFPD in the management of fluid overload and AKI in paediatric post-operative cardiac patients.
Methods: A retrospective study of patients who were treated with conventional PD, CFPD, or both following cardiac surgery between the years 2006–2021 in the paediatric intensive care unit (PICU) at the Royal Hospital for Children, Glasgow. Data was extracted from PICU Clinical Information System and analysed using Microsoft Excel. The interquartile ranges with median change from the start and end of treatment were calculated for the percentage fluid overload.
Results: 133 patients underwent 137 runs of dialysis, comprising 97 runs of conventional PD, 20 runs of CFPD, and 20 runs of combined therapy. Percentage fluid overload was calculated at both the time of commencing and discontinuing peritoneal dialysis. A reduction in percentage fluid overload was noted with conventional PD and CFPD, ranging from 9.2 to 57.5% (median 30.3%) and 80.6 to 177.7% (median 108.8%) respectively. Ten patients treated with conventional PD progressed to CFPD within 24 h of conventional PD ending. For these patients, the reduction in percentage fluid overload ranged between − 2.0 to 34.8% (median 4.9%) on conventional PD, and between 10.4 to 192.8% (median 80.4%) on CFPD. 7.5% of patients were escalated to haemo(dia)filtration: one from conventional PD, three from CFPD, and six from the group that started on conventional PD and progressed to CFPD.
Conclusion: All modalities of peritoneal dialysis were able to demonstrate a reduction in percentage fluid overload in the post-operative congenital cardiac patient. A greater median reduction in percentage fluid overload was observed in patients treated with CFPD alone, compared with conventional PD alone. A similar result can be seen in those treated sequentially with conventional PD followed by CFPD. These results suggest that CFPD may be more effective than conventional PD at fluid removal in paediatric patients after cardiac surgery. Future consideration should be given to the use of CFPD as a potential primary modality of renal replacement therapy in this patient group.

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001416

Robotic assisted early mobilization in ventilated ICU patients with COVID-19: an interventional randomized, controlled feasibility study (ROBEM II Study)

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Intensive Care Medicine Experimental 2022, **10(2)**:001416

Introduction: Functional impairments are main challenges in survivors of critical care. There is substantial evidence that these impairments can be attenuated by early mobilization [Waldauf 2020, Klem 2021]. Although the current German guideline recommends early mobilization twice daily for 20 min each within 72 h after ICU admission [Bein 2015], barriers, especially lack of staff, limit the clinical translation substantially [Hermes 2020]. This problem was aggravated during the COVID-19 pandemic. Robotic technology may be able to overcome this and other barriers and facilitate early mobilization of critically ill patients.
Objectives: The aim of this pilot study was to test feasibility of robotic-assisted mobilization in critically ill COVID-19 patients in a surge ICU.
Methods: Twenty invasive mechanically ventilated critically ill patients with COVID-19 in a surge ICU of the Department of Anesthesiology and Operative Intensive Care Medicine (CVK, CCM) at Charité—Universitätsmedizin Berlin were included. Patients were randomized 1:1 into intervention and control. The intervention group received five days of early mobilization twice daily for at least 20 min using the VEMO® system (Reactive Robotics GmbH, Munich, Germany) which allows to mobilize the patient within his own bed. Control group received standard of care. The primary outcome parameters were the mobilization level measured by the ICU Mobility Scale (IMS) and the Surgical Optimal Mobilization Scale (SOMS) at Day 5. Ultrasound measurements of the right rectus femoris and vastus intermedius were performed at the day of study inclusion, at day five and at the day of discharge from the ICU. In addition, a telephone follow-up was conducted after six months assessing quality of life and disability.
Results: Patient characteristics are described in Figure 1. Robotic intervention was provided twice daily in 39 days out of total of 45 ventilated patient days (87%) compared to 0 days out of 41 ventilated patient days (0%). There was no significant difference in primary outcome (Figure 2). Analysing the secondary parameters, intervention group got significant more frequent ($p = 0.001$) and longer ($p = 0.011$) early mobilization, with other secondary parameters except ICU and hospital length of stay indicating a positive effect of robotic mobilization (Figure 2).

Variable	Intervention group* (n = 10)	Control group* (n = 10)
Age (years)	55.5 [47 - 67]	61 [56.75 - 68]
Gender male - n (%)	7 (70)	8 (80)
BMI	26.5 [25 – 35.5]	29.3 [27.3 - 33.4]
Charlson Comorbidity Index	3 [1.75 - 3.5]	4 [2.75 - 6]
SOFA	6. [3.75 - 9.75]	11[6.75 - 11.5]
APACHE II	17.5 [6.5 - 23.5]	20.5 [10 – 31.25]
Days in ICU until study inclusion	3 [1 – 5.5]	3 [2 – 6.5]
ICU admission from n (%)		
Home	1 (10)	3 (30)
Normal ward	3 (30)	2 (20)
Other ICU	6 (60)	5 (50)

Figure 1: Patient clinical and demographic characteristics.
Values expressed as median [IQR] or n (%)
* There were no significant differences between the groups ($p > 0.05$).
BMI = Body Mass Index; SOFA =Sepsis-related organ failure assessment score; APACHE II = Acute Physiology and Chronic Health Evaluation II; ICU = intensive care medicine.

Variable	Intervention group (n = 10)	Control group (n = 10)	p-value
Primary endpoints			
Maximum IMS at study day 5	0 [0-0]	0 [0-0.5]	0.58
Maximum SOMS at study day 5	1 [0-1]	1 [0-1.25]	0.74
Secondary endpoints			
Time to first mobilization after study inclusion (min)	113 [82.75 - 278.75]	344 [171 – 674.75]	
Number of mobilizations in the study period (n)	8.5 [7.75 - 10]	4.5 [3.5 - 5]	
Mobilization time in the study period (min)	232.5 [188 - 265]	147.5 [130 - 165]	
Days mechanically ventilated (days)	29 [13 - 58]	32 [11 - 71]	
ICU LOS	42.5 [18 - 64]	33 [15 - 97]	
Hospital LOS	45 [25.25 - 82.75]	40 [24.25 - 116.75]	
ICU discharge to			
Other ICU	3 (30)	0 (0)	
Normal ward	5 (50)	5 (50)	
Rehabilitation facility	1 (10)	2 (20)	
Home	0 (0)	0 (0)	
Dead	1 (10)	3 (30)	
Hospital discharge to			
Other hospital	3 (30)	2 (20)	
Rehabilitation facility	3 (30)	4 (40)	
Home	2 (20)	1 (10)	
Dead	2 (20)	3 (30)	
Ultrasound of rectus femoris muscle (under compression)			
Delta Day 5 – Day 1 (mm)	-1.1 [-3.9 - 4.1]	-2.3 [-3.4 - -0.8]	
Delta ICU discharge – Day 1 (mm)	-1.5 [-3.8 - -0.2]	-3.6 [-3.8 - -3.5]	

Figure 2: Outcomes of the ROBEM II pilot study.
IMS = Intensive Care Unit Mobilization Score; SOMS = Surgical Intensive Care Unit Optimal Mobilisation Score; ICU = Intensive Care Unit; Median [IQR]; Mean ± standard deviation.

Conclusion: A short robotic-assisted intervention in mechanically ventilated patients was feasible and lead to guideline recommended mobilization but did not result in increased mobilization level. Patients, however, were more frequent and longer mobilized and there was indication of additional benefit for the patients in the secondary endpoints of this pilot study. These have to be confirmed in an adequately powered intervention study.

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Acknowledgements: This investigator initiated study was partly funded by Reactive Robotics GmbH, Munich, Germany.

001420

"In good hands": patients' experiences of being infected by COVID-19 and cared for in a Danish Intensive Care Unit

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Intensive Care Medicine Experimental 2022, **10(2)**:001420

Introduction: The coronavirus disease 2019 (COVID-19) has led to high demand for intensive care actions all over the world. Patient treatment and outcomes as well as the impact of the pandemic on health care providers in the intensive care have been subject to research. However, less focus has been on COVID-19 patients' perspectives on living through critical illness in intensive care. Moreover, since the Pandemic was handled differently according to national policy, society lockdown and guidelines to prevent contamination, we wanted to explore the patients' experiences in a Danish context of intensive care.
Objectives: To explore patients' experiences of being infected by COVID-19 and cared for in a Danish intensive care unit.
Methods: Individual semi-structured interviews with patients, who had been severely ill due to COVID-19, four to eight weeks after they were discharged from the intensive care unit. The interview guide was organized by topics inspired by Van Manens' existentials; Lived body, place, time, relations and technology (1). The interviews were transcribed and analysed by qualitative, thematic analysis (2).
Results: Between May 2020 and April 2021 were 11 patients included in the study. Eight male and three female, age between 48 and 83 years (median 67 years), length of stay in the intensive care unit between three and 35 days (median 11 days). The overarching theme " In good hands" emerged in the analysis and was further unfolded in four sub-themes: (a) An unexpected entry, (b) Altered relations, (c) Fragmented reality and (d) Relentless isolation.
Conclusion: Overall, the patients felt cared for and safe during their time in the intensive care unit. This was despite the fact, that they were severely ill due to infection by a deadly virus, isolated and did not have the opportunity for visits by close relatives during the admission. Although the intensive care unit was on high alert and had enhanced the capacity for intake of patients during the pandemic, the nurses allocated to the unit had all previous experiences in intensive care or were specialized nurse anesthetists. This way, contextual factors as organization and well educated nurses to care for patients with respiratory challenges, could have contributed to patients infected by COVID-19 sensed they were "in good hands" in the intensive care unit.

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Acknowledgements: None.

Acute Kidney Injury 3

000876

The effect of extra-corporeal cytokines removal by hemoadsorption column (CytoSorbTM) on the systemic hemodynamic, renal oxygenation, renal function and renal tissue damage in a rat model of sepsis-induced acute kidney injury

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Intensive Care Medicine Experimental 2022, **10(2)**:000876

Introduction: Sepsis is defined as a life-threatening infection associated with an unregulated systemic inflammation causing acute kidney injury (AKI) (1). A novel synthetic hemoadsorption column (CytoSorbTM) in addition to the extra corporeal circuit has been successfully used for pro-inflammatory cytokines removal in patients with continuous veno-venous hemofiltration (CVVH) (2–5).
Objectives: The purpose of this study is to explore the effects of extracorporeal circulation combined with hemoadsorption filter on systemic hemodynamics, renal oxygenation and function in a well-controlled fully instrumented model of septic AKI.
Methods: 32 fully instrumented, mechanically ventilated and anesthetized rats were divided into 2 control and 2 LPS (10 mg/kg LPS) groups (Fig. 1). All animals received extra corporeal circulation (flow rate: 1 ml/min and priming volume (% 4 Albumin solution): 6–7 ml) with or without hemoadsorber filter. The systemic and renal hemodynamics (MAP, HR, CVP and RBF), renal cortical oxygenation, renal function, renal tissue damage and inflammation were assessed.

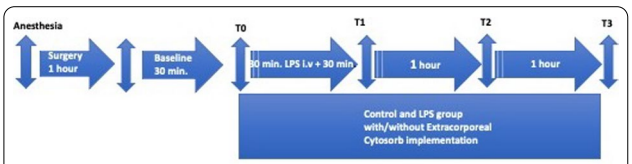

Figure 1: Experimental design.

Results: We found that extra corporeal circulation is itself associated with the impairment of MAP and RBF in regardless of presences of hemoadsorber ($p < 0.05$). This resulted in a low renal cortical oxygenation and tissue oxygen saturation, and damage in the kidney ($p < 0.05$). Use of hemoadsorber in combination with an extra corporeal circuit could partially prevent the depletion of renal oxygen availability and saturation in septic group. Furthermore, histological assessments revealed that hemoadsorber filter in the circuit prevented tubular damage ($p < 0.05$) and reduced plasma IL-6 levels ($p < 0.05$).
Conclusion: In conclusion, extra corporeal circulation itself may cause the systemic and renal impairment due to its effect on the inflammation, coagulation and hemodilution. However, use of the hemoadsorber filter can restore the oxygen availability, renal tubular damage and inflammation in sepsis.

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Acknowledgements: This study is supported by Cytosorbents Corporation, New Jersey, USA.

001034

Dexamethasone use decreases severe COVID-19-induced acute kidney injury incidence: a prospective multicenter study

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Intensive Care Medicine Experimental 2022, **10(2)**:001034

Introduction: Since the first wave of COVID-19, the management of patients with severe SARS-CoV-2 infection in intensive care unit (ICU) has changed with the use of dexamethasone (DXM). Acute kidney injury (AKI) in ICU patients with severe COVID-19 was frequent (> 50%). Specific inflammatory process was previously suggested in AKI pathogenesis and could be improved by DXM.
Objectives: The aim of this study was to investigate in a prospective multicentric study, the impact of DXM in severe COVID-19-induced AKI.
Methods: We carried out a prospective multicentric study in two French ICU from March 1st, 2020 to August 21st, 2021. All patients admitted for a severe COVID-19 in ICU were included. DXM was exclusively used from the second wave. AKI was defined according to the KDIGO classification. Acute kidney disease (AKD) was the persistence of the KDIGO criteria for AKI for ≥ 7 days. Multivariate analysis was proceeded using logistic regression. Independent variables were previously described to be associated with AKI or DXM efficiency. Absence of collinearity was checked.
Results: 1014 patients were included. 284/1014 patients (28%) were hospitalized in ICU number 1 and 730/1014 (72%) patients in ICU number 2. DXM was administered in 635/1014 (63%). Mean age was 62.9 ± 12.2 years, 520/1014 (51%) patients had hypertension, 75/1014 (7%) suffered from previous chronic kidney disease (CKD) and 385/1014 (38%) required invasive mechanical ventilation (MV) in the first 24 h. Mean SAPSII was 38.9 ± 15.8 and non-renal SOFA was 4.2 ± 2.4. ICU mortality was 264/1014 (26%). AKI was present in 735/1014 (73%) patients: 284/735 (39%), 195/735 (27%) and 256/735 (35%) had respectively AKI KDIGO 1, 2 and 3 and 88/735 (12%) patients required renal replacement therapy. AKD was observed in 383/735 (52%) of AKI patients. Among the 635 patients who received DXM, 143/635 (23%) developed AKI before or the same day of DXM exposure and were excluded from the analysis. In univariate analysis, DXM exposure decreased AKI incidence: 262/492 (53%) patients vs. 317/379 (84%) patients; OR = 0.23 [0.16–0.31]. In multivariate analysis, DXM (OR = 0.26 [0.17–0.40]) and tocilizumab (OR = 0.16 [0.03–0.74]) use were independently associated with AKI.
Conclusion: In our study, DXM and tocilizumab exposure were independently associated with a decrease of AKI incidence in severe COVID-19 patients. These results support the hypothesis that COVID-19-induced AKI is partially secondary to an inflammatory process that could be improved by DXM use.

001054

Sodium and chloride sieving coefficient during continuous venovenous hemofiltration (CVVH) in the critically ill patients

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Introduction: Continuous venovenous hemofiltration (CVVH) is applied in 8–12% of patients with acute kidney injury (AKI) admitted to the intensive care unit (ICU)[1]. Solute removal through the filter is described by the sieving coefficient (SC). The sieving coefficients of sodium (SCNa+) and chloride (SCCl-) are considered to be 1[2]. Actual experimental data are however scarce.
Objectives: Aim of the present study was to measure the sodium and chloride SC both in vitro and in critically ill patients.
Methods: ICU patients with a clinical indication for CVVH (PrismaMax, Baxter) were enrolled. Blood flow was set at 150 ml/min, regional anticoagulation was achieved with diluted citrate (Prismocitrate 18/0; Gambro) administered at a rate of 1500 ml/h. Phoxilium (Baxter Healthcare Spa) was employed as replacement solution (1500 ml/h), administered in post-dilution. In-vitro experiments were performed with the same setup, using 2L of normal saline as reservoir volume. Electrolytes and hematocrit (Ht) were assessed (RAPIDPoint 500 Blood Gas System, Siemens Healthcare Diagnostics) in-vitro and in-vivo after 5 min from the CVVH beginning. Samples were collected (1) pre-filter, after citrate infusion, (2) post-filter, before Phoxilium infusion, and (3) in the ultrafiltrate. Osmolality was measured by the freezing-point technique in in-vivo samples. The SCs [3] and the difference in sodium and chloride concentration between sites 1 and 2 ([Na+]2–1 and [Cl-]2–1) were calculated.
Results: Six patients were enrolled, and 11 in-vitro experiments were performed. Mean values of in-vivo experiments are reported in Table 1. SCNa+ was 0.96 ± 0.01 in-vivo and 1.00 ± 0.01 in-vitro ($p < 0.001$). The SCCl− was 1.06 ± 0.01 in-vivo and 0.99 ± 0.02 in-vitro ($p < 0.001$). Of note, the changes in electrolytes concentration were not followed by osmolality variations along the filter. No relationship was found between the [Na+]2–1 or [Cl−]2–1 and the Ht ($p = 0.54$ and $p = 0.38$, respectively).
Table 1. In vivo Na+, Cl−, Ht and osmolality variations across the filter of CRRT

	Pre-filter (1)	Post-filter (2)	Ultrafiltrate (3)	*p**
[Na+] mmol/L	136 ± 7	139 ± 6	132 ± 6	pa = 0.01 pb < 0.001
[Cl−] mmol/L	99 ± 3	97 ± 3	104 ± 4	pa = 0.01 pb < 0.001
Ht %	26 ± 6	33 ± 5		pa = 0.02
Osmolality mOsmol/kg	309 ± 16	308 ± 15	308 ± 17	pa = 0.62 pb = 0.75

*pa, between (1) and (2). pb, between (1) and (3).

Conclusion: Sodium and chloride concentrations change across the filter and differ between filter and ultrafiltrate. The in-vitro SCs were in line with available data. However, the in-vivo SCNa + was slightly but significantly lower than 1, while the in-vivo SCCl− was slightly higher than 1. Further studies need to assess the underlying mechanisms and the possible clinical implications.

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Acknowledgements: No funding to disclose.

001055

Protective effect of synthetic angiotensin II (Giapreza) on the systemic hemodynamic, renal function, renal oxygenation and damage in a rat model of sepsis-induce acute kidney injury

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Intensive Care Medicine Experimental 2022, **10(2)**:001055

Introduction: SSeptic shock is associated with systemic hypotension, inflammation and organ hypoperfusion despite adequate fluid resuscitation (1). Consequently, vasopressors are needed to maintain adequate blood pressure for organ perfusion and oxygenation. Norepinephrine is the first-line agent recommended during resuscitation of septic shock for correcting hypotension due to loss of vascular tone. However, acute kidney injury (AKI) is still common complication of sepsis and is significantly associated with mortality.
Objectives: The aim of this study is to test the effects of a newly introduced synthetic Angiotensin II (Ang II) (Giapreza) (2) treatment in comparison to norepinephrine (NE) on the systemic hemodynamics, inflammation, renal oxygenation and function in a rat model of sepsis induced AKI.
Methods: 48 fully instrumented and anesthetized rats were divided into 1 control and 5 sepsis groups. Sepsis induced by iv injection of 20 mg/kg LPS and mean arterial pressure (MAP) below 50 mmHg is accepted to start resuscitation. The resuscitation was achieved by 30 ml kg^{-1} h^{-1} Ringer acetate (RA), 0.5 mg kg^{-1} min^{-1} NE and 200 ng kg^{-1} min^{-1} Ang II, or in combination with 0.2 mg kg^{-1} min^{-1} NE and 100 ng kg^{-1} min^{-1} Ang II (Fig. 1). The systemic and renal hemodynamics, renal cortical oxygenation, renal function, renal tissue damage and inflammation were assessed.

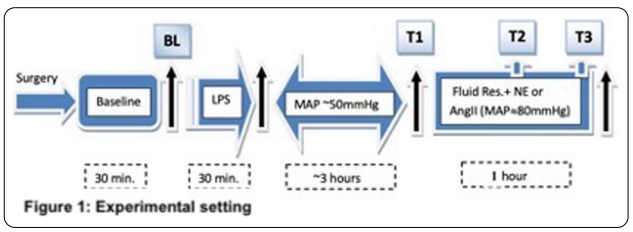

Figure 1: Experimental setting

Results: In this study, we found out that MAP was restored in LPS groups received Ang II, NE and Ang II + NE ($p < 0.05$). In kidney, none of the resuscitation strategy were able to restore RBF and cortical PO2. However, urine output was improved after Ang II resuscitation in comparison to the LPS and LPS + RA groups ($p < 0.05$). Plasma hemoxygenase 1 (HO-1) and IL-6 levels were considerable improved in groups received Ang II alone and together with the NE ($p < 0.05$). Parallel to this, renal injury markers, NGAL, is markedly decreased in LPS group received both NE and Ang II ($p < 0.05$). Use of Ang II also reduced the renal tubular damage in compare to other groups ($p < 0.05$).
Conclusion: In conclusion, our study showed that synthetic angiotensin II improves MAP comparable to norepinephrine. Despite none of vasopressors have effect on the renal hemodynamics and oxygenation, AngII leads to increase urine output in comparison to norepinephrine. Ang II used in additional to norepinephrine, shows more anti-inflammatory effect to reduce IL-6 and HO-1 levels. Also additional of Ang II to norepinephrine, showed a significant protective effect on sepsis-induced renal tissue injury.

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Acknowledgements: This study is supported by La Jolla Pharmaceutical Company, San Diego, USA.

001075

Incidence and factors associated with acute kidney injury in COVID-19 ARDS patients undergoing prone positioning: the PRONE-AKI study

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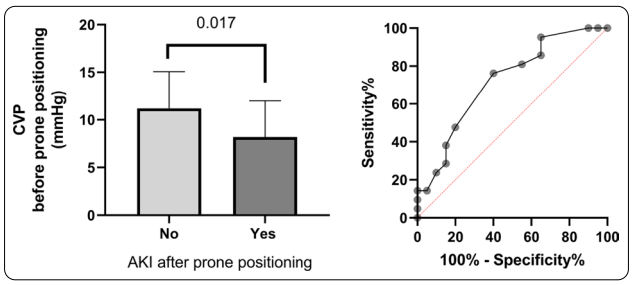
Intensive Care Medicine Experimental 2022, **10(2)**:001075

Introduction: Prone positioning (PP) can improve gas exchange in COVID-19 ARDS patients requiring invasive mechanical ventilation (IMV) [1]. However, how PP affects abdominal organs function remains unclear [2]. Acute kidney injury (AKI) in critically-ill COVID-19 patients can affect 20–40% of patients [3], but it is still unknown if PP can be temporally associated to its onset. Moreover, no data exist on the possibility to predict PP-associated AKI from bedside clinical variables.
Objectives: To investigate the incidence of PP-associated AKI in patients affected by moderate-severe COVID-19 ARDS undergoing IMV and to test if it could be predicted by any clinical variable before PP.
Methods: We retrospectively analyzed COVID-19 ARDS patients undergoing IMV and admitted to the ICU of the Sant'Anna Hospital (Ferrara, Italy) between March 2020 and March 2021 who underwent at least one PP cycle. For each patient we collected demographic data (BMI, age) baseline clinical data (SAPS-II, PaO2/FiO2 at ICU admission) hemodynamics (SAP, central venous pressure (CVP), HR), 24-h fluid balance, respiratory mechanics, circulating biomarkers (Hb, Hct, creatinine, and lactates) and use of diuretic drugs before, during, and after the PP cycle. Patients were divided into two groups based on the onset of PP-associated AKI, defined as AKI diagnosed using the KDIGO criteria [4] from PP start to 48 h after resupination. Independent samples t-test was used to test difference between groups while binomial logistical regression was performed to estimate correlation between variables and PP-associated AKI. ROC curves were built to test the predictivity of any significant variable. A p value < 0.05 was considered statistically significant.

Results: We analyzed data from 41 patients. No patient had kidney diseases before ICU. Twenty/41 patients (48%) developed AKI according to the KDIGO criteria, and the diagnosis was made at 27.8 (± 19.6) hours after starting PP. No statistically significant differences were found among the two groups in age, BMI, SAPS-II, PaO2/FiO2 ratio at admission, nor in serum lactates, Hgb, fluid balance and diuresis at admission and 24 h before pronation. Nevertheless, CVP was different between the groups (AKI patients: 8.2 ± 3.7; non-AKI patients: 11.2 ± 3.9) and the difference was statistically significant (p = 0.017). A logistic regression was performed to evaluate the impact of pre-pronation serum lactates, CVP, total fluid balance and Hct on AKI development. The model was statistically significant (p < 0.05) and correctly classified 73.2% of cases with CVP having the best contribution in the model (p = 0.04). The ROC analysis for CVP revealed a good classifying capability, with an AUC of 0.72 (p = 0.012) (Fig. 1, right panel).



Conclusion: AKI can be temporally associated to PP in COVID-19 ARDS patients undergoing IMV and may be related to hypovolemia. The CVP before PP can potentially predict PP-related AKI with a good accuracy.

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Acknowledgements: This study did not receive any financial support.

001162

The Risk Factors of Major Adverse Kidney Events at 6-months among COVID-19 Patients with ARDS

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Introduction: Acute kidney injury (AKI) is one of the most common complications among hospitalised COVID-19 patients who develop acute respiratory distress syndrome (1, 2). Major adverse kidney events (MAKEs), a composite of renal replacement therapy (RRT), or decline in eGFR of < 75% of baseline, or all-cause mortality, is a validated long term measure of the impact of AKI on patient-related outcomes (3). To date, this has not been investigated in patients with COVID-19 related ARDS or non-COVID ARDS. This study aimed to identify the MAKEs at 180 days after intensive care unit (ICU) admission in non-COVID and COVID-ARDS.
Methods: This retrospective observational study was conducted at the Queen Elizabeth Hospital Birmingham (QEHB). COVID-ARDS patients admitted to ICU between 11 March 2020 and 17 January 2021 and ICU patients diagnosed with ARDS between 1 January 2017 and 1 November 2019 were included (non-COVID group). All data were routinely collected on the hospital's electronic patient records. The primary outcome was the incidence of MAKE at 180-days (MAKE-180) after ICU admission. Secondary outcomes included the risk factors for MAKE-180 and renal recovery at hospital discharge (defined as eGFR of ≥ 60 ml/min/1.73 m^2) (4). Chi-squared test, unpaired t-test, or Wilcoxon rank-sum test was used for multiple comparisons among groups. Univariate and multivariate analysis with logistic regression was performed to determine independent risk factors for MAKE-180.
Results: 519 ARDS patients were included in this study, 262 COVID-19 patients and 257 non-COVID patients. Both groups demonstrated a male predominance (70.2% vs 60.3%) however, the non-COVID group were older (61.0 (IQR, 49.0–71.0) vs 57.0 years (IQR, 48.0–63.8), P < 0.001). The incidence of AKI was higher in the non-COVID group (180 (70.0%) vs 136 (51.9%); P < 0.001). The incidence of MAKE-180 outcomes was significantly greater in the non-COVID group (170 (66.1%) vs 112 (42.7%); P < 0.001). In terms of the individual MAKE-180 outcome, there were overlaps between the classifiers. In non-COVID group, RRT = 123, decline in eGFR = 87, deaths = 104 compared to COVID group, RRT = 89, decline in eGFR = 84, deaths = 65. Only one patient in each group still required an RRT at 180 days. There were no differences in the rate of complete renal recovery between the two groups (36.8% vs 26.7%, P = 0.526). The strongest independent risk factors for MAKE-180 in both groups were CKD and high bilirubin. Other independent risk factors for MAKE-180 were age (OR = 1.04, CI:1.01–1.07, P = 0.007) in COVID group and obesity (OR = 2.20, CI:1.17–4.27, P = 0.017) and low albumin (OR = 0.93, CI:0.89–0.97, P = 0.001) in non-COVID group.
Conclusion: MAKE-180 is common in both groups but higher in those with non-covid ARDS. This is an important long-term patient-centred outcome, and interventions should be targeted at reducing it, especially in critically ill patients. Recognition of factors associated with MAKE-180 might help guide future practice and management strategies in critical care.

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Acknowledgements: N/A.

001180

Augmented renal clearance in COVID-19 and non-COVID adult critically ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001180

Introduction: Augmented Renal Clearance (ARC) is a phenomenon defined by a Glomerular Filtration Rate (GFR) over 130 ml/min/1.73 m^2 in men and 120 ml/min/1.73 m^2 in women with an prevalence of around 30% [1]. In the first wave of Covid there was widespread concern regarding AKI associated with Covid. But, what about COVID-19 critically ill patients?
Objectives: The main objective of the study was to compare ARC prevalence in COVID-19 critically ill patients with a non-COVID group of critically ill patients. Another objective was to assess the concordance of the GFR measured in 24-h urine collection and the estimated formula Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).
Methods: This was an observational study in a single center in the ICU of a university hospital. GFR was measured (mGFR) from 24-h urine collection. At the same time the CKD-EPI estimation formula was calculated. Inclusion Criteria: Patients over 18 years old admitted to the ICU due to COVID-19 during the first wave (from March to April, in 2020). And a previous cohort of non-COVID patients recorded during the same months' period but a year earlier (from March to April, in 2019). Exclusion Criteria: Anuric patients; patients with vesical lavages; patients without urinary bladder catheterization; and patients under continuous or intermittent Renal Replacement Therapy (RRT). Statistical Analysis: Qualitative variables are expressed as n (%) and quantitative variables as median (min–max). The qualitative variables are compared by Student's t test orby the Mann–Whitney U test according to their normal distribution or not, respectively. A type 1 error below 0.05 ($p < 0.05$) was considered statistically significant. For the concordance analysis, the Passing-Bablok regression and Bland-Alman plot were employed.
Results: The study included 82 patients, 35 COVID-19 patients and 47 non-COVID ones. The comparative analysis between the COVID-19 group and the non-COVID group only showed differences in gender and mechanical ventilation (MV). We found 91.4% male in the COVID-19 group vs. 72.34% in the non-COVID group, $P = 0.041$, and 100% MV in the COVID-19 group vs. 82.61% in the non-COVID group, $P = 0.026$. We found no differences in the remaining variables comparing the COVID-19 and the non-COVID group: Not in age [59 (38–71) vs. 57 (18–83) years old, $P = 0.750$]; mGFR [111.80 (0.81–204.33) vs. 85.86 (3.45–284.59) mL/min/1.73 m^2, $P = 0.646$], CKD-EPI [99 (10–143) vs. 94 (11–167) mL/min/1.73 m^2, $P = 0.792$]; Urine creatinine [54 (17–156) vs. 50 (16–150) mg/dL, $P = 0.192$]; Serum creatinine [0.78 (0.32–5.52) vs. 0.87 (0.26–4.92) mg/dL, $P = 0.775$]; CKD [5 (14.29%) vs. 4 (8.51%), $P = 0.638$], AKI [20 (58.82%) vs. 25 (53.19%), $P = 0.782$], nor in ICU mortality [6 (17.14%) vs. 11 (23.4%), $P = 0.677$]. ARC was also similar in the two groups ($P = 0.195$). ARC was found in 39.13% in the COVID-19 group and in 25.53% in the non-COVID (P ns). GFR < 90 mL/min/1,73m2 was also similar in both groups, 36.96% in COVID-19 patients and 55.32% in the non-COVID group (P ns). Estimated CKD-EPI was similar in both groups [94 (11–167) vs. 99 (10–143), P 0.792]. There was no concordance between the estimation of GFR by the CKD-EPI formula and GFR calculated from the 24-h urine.
Conclusion: This study highlights that ARC is a very frequent phenomenon in COVID-19 patients, with an incidence of 39%. When comparing with other critically ill patients admitted during the same months' period in 2019, the prevalence of ARC was similar. As there is no concordance between measured and estimated GFR, ARC diagnosis is challenge. This in turn is of concern because COVID-19 is associated with other infections and thrombosis, whose treatments usually have a renal clearance route and their effectiveness may be compromised in these Covid patients with ARC.

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Acknowledgements: NA.

001214

Net buffer load during regional citrate anticoagulated continuous renal replacement therapy

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Introduction: Regional citrate anticoagulation (RCA) has proved to be superior to systemic anticoagulation during continuous renal replacement therapy (CRRT). Citrate can however lead to systemic hypocalcemia, metabolic alkalosis, and in some cases to direct citrate toxicity. The net bicarbonate load from citrate is under debate, and the current model of citrate metabolized to bicarbonate as the main contributor to alkalinization is too simplified. Bicarbonate from CRRT fluids may also play a significant role. The aim of this study was to evaluate the normalized Net Buffer Load (nNBL) and its relation to development of metabolic alkalosis.
Methods: The parameter nNBL, which will be introduced in the CRRT PrisMax software Version 3 (Baxter, Deerfield, USA), was defined as the sum of the amount of the following: 1. buffer balance from the CRRT (the difference between input from replacement and dialysate fluids and removal of effluent) and 2. the bicarbonate generation from the systemic citrate load. nNBL was estimated by a complex set of calculation steps. The acid–base status of 60 patients receiving CRRT for at least 3 consecutive days was evaluated and the median nNBL was calculated for the whole population at each time interval.
Results: It is assumed that steady state is reached when there prevails equilibrium between nNBL and proton generation rate. Review of published data has shown that the normal range for nNBL at steady state is 0.1–0.2 mmol/h/kg. nNBL values > 0.3 mmol/h/kg imply a risk of developing metabolic alkalosis, whereas negative values imply a risk of developing metabolic acidosis. Normally, nNBL will decrease over time, because patients with acute kidney injury typically present with low bicarbonate levels, and low losses to the effluent. While bicarbonate corrects the losses to the increases in effluent, and thus the computed nNBL decreases, as shown in Figure 1. Of 60 patients analyzed only 2 patients showed metabolic alkalosis related to high nNBL values.

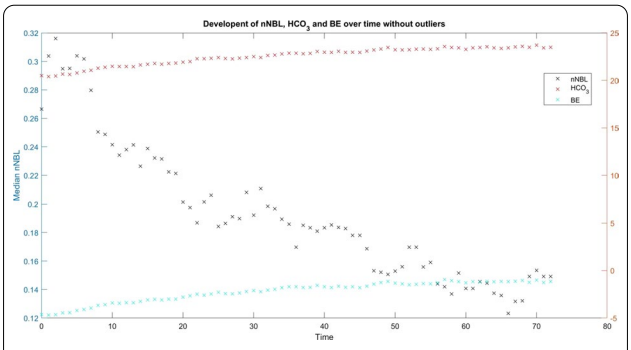

Figure 1. Evolution of nNBL (mmol/h/kg), patient bicarbonate (mmol/l) and base excess (BE, mmol/l) over the course of CRRT. The values are medians of the population at each time interval for all 60 patients with the exclusion of a few statistically identified outliers.

Conclusion: nNBL estimates the systemic bicarbonate balance in the patient, provided by the CRRT treatment, considering both citrate load and bicarbonate losses to effluent. In our computation of nNBL, it can be calculated either from a constant bicarbonate value of 25 mmol/l or from a measured patient systemic bicarbonate value. We found that nNBL stabilizes over time at 0.15 mmol/h/kg, BE at -1 mmol/l and

bicarbonate at 24 mmol/l. Steady state is reached after 48 h of uninterrupted CRRT. nNBL is to be considered a safety parameter which can be used during CRRT to provide information of the risk of development of metabolic alkalosis, or metabolic acidosis, including the risk of citrate overload/toxicity.

001254

Urinary CCL14 biomarker to predict renal replacement therapy initiation in critically ill patients with severe acute kidney injury?

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Intensive Care Medicine Experimental 2022, **10(2)**:001254

Introduction: Recent trials confirmed that an early renal replacement therapy (RRT) initiation does not confer any survival benefice compared with a delayed one during severe acute kidney injury (AKI) when no severe complications are present. Tools to enable personalized management are still needed and evidence for biomarkers guided RRT initiation are lacking [1]. In a cohort of critically ill patients with AKI, an elevation in urinary CCL14 could predict the persistence/progression of AKI [2].
Objectives: We aimed to assess the utility of urinary CCL14 for the prediction of RRT initiation in a conservative approach in Intensive Care Unit (ICU).
Methods: In an ancillary study of AKIKI2 (Comparison of two delayed strategies for renal replacement therapy initiation for severe acute kidney injury), we included ICU patients with severe AKI (stage 3 KDIGO) and available urinary sample at the first day of severe AKI. We did not include patients with chronic kidney disease. CCL14 was measured by enzyme-linked immunosorbent assay (ELISA) in urinary samples at D0. The primary endpoint was the occurrence of a criteria for RRT (according to a conservative approach of RRT initiation) within the 72 h after severe AKI. Those criteria were: life threatening complication of AKI, or oliguria/anuria (urine output < 0·3 mL/kg per h or < 500 mL/day) for more than 72 h, or serum urea concentration of 40 mmol/L or more.
Results: A total of 230 patients were enrolled. Ninety patients (39.1%) met the primary endpoint. Urinary CCL14 was not associated with serum creatinine concentration at D0 (Pearson correlation $r^2 = 0.024$). Median urinary CCL14 was 15.03 (IQR 24.88) mg/ml in patients reaching the primary endpoint and 5.8 (IQR 12.18) mg/ml in patients who did not ($p < 0.001$). In multivariate analysis, urinary CCL14 (OR = 1.02, [1.01;1.04], $p = 0.0021$) was associated with higher rate of occurrence of a criteria of RRT initiation. The area under the ROC curve was 0.701 (95% CI: [0.633;0.770]) for urinary CCL14 to predict the occurrence of a criteria of RRT initiation within 72 h after severe AKI.
Conclusion: Although interesting, urinary CCL14 alone might not be precise enough to discriminate patients with RRT initiation criteria in a conservative approach. However, it might be useful when used in combination with other clinical or biological variables.

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001286

Contrast-enhanced renal ultrasound predicts the severity of sepsis-associated acute kidney injury and is superior to conventional biomarkers

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Introduction: The diagnosis and assessment of AKI is imperfect using currently clinical methods. Novel renal biomarkers provide further insight into the diagnosis and severity of AKI, but so far have not been used to tailor therapy decisions. We hypothesize that contrast enhanced ultrasound (CEUS) has similar diagnostic accuracy for AKI and provides complementary information to biomarkers, with the potential to provide personalized assessment of AKI.
Methods: Longitudinal observational study of 50 patients commenced within 24 h of admission and all patients had septic shock. CEUS, insulin-like growth factor binding protein 7 * tissue metalloproteinase 2 (IGFBP7*TIMP2), urinary neutrophil gelatinase associated lipocalin * urinary albumin (NGAL*Alb), proenkephalin-A (PENK), C–C motif chemokine ligand 14 (CCL14) were measured on admission, day 2 and day 4. Biomarkers and CEUS were compared using receiver operator curve analysis. In addition to the performance analysis of renal CEUS, we attempted to define the phenotype of patients with reduced renal perfusion by comparing those with impaired and those with maintained cortical perfusion and healthy controls. Biomarkers, systemic variables and markers of inflammation were compared between groups.
Results: CEUS has similar power to predict AKI as established renal biomarkers, area under receiver operator curves CEUS 0.83, IGFBP7*TIMP2 0.87, NGAL*Alb 0.78, creatinine 0.70, CCL14 0.69, PENK 0.67. On admission, patients with poor renal perfusion had lower urine output (10(0–30)ml/hr vs 40(27–55)ml/hr $p < 0.05$), higher creatinine (153 (103–183) µmol/L vs 113 (91–132)µmol/L, $p < 0.05$) and higher TIMP2*IGFBP7 (617 (242–1899)µg/L2 vs 146 (63–633)µg/L2) than patients with preserved perfusion. These differences existed to day 2 and an additional association with inflammation was demonstrable by day 4, with increased levels of TNFR (13.3 (9.3–19.8)ng/L vs 8.41 (6.4–15.4)ng/L, $p < 0.05$) and IL8 (63.6(32.6–116)ng/L vs 27.3(13.4–55.1) ng/L, $p < 0.05$). Patients with cortical hypoperfusion on admission were less likely to survive (survival probability 0.25 vs 0.73, $< p < 0.001$), had an increased likelihood of requiring RRT (probability 0.9 vs 0.55, $p < 0.05$) and if established on RRT are more likely to be on it for longer than those with maintained renal perfusion.
Conclusion: CEUS proved superior to some established biomarkers to predict severe sepsis associated AKI. In patients with biomarker positive AKI from septic shock, patients with poor renal perfusion have worse outcomes than those who maintain renal perfusion. Hence, CEUS provides complimentary information to biomarkers and could form a component of a comprehensive renal assessment.

Acknowledgements: This study was sponsored by the ESICM and GE Healthcare.

Anaesthesia & Peri-operative Medicine 1

000032

Safety and feasibility of continuous ketamine infusion for analgosedation in medical or cardiac ICU patients

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Introduction: Some mechanically ventilated patients require deep sedation during acute respiratory distress syndrome management, and these patients frequently receive opioids, benzodiazepine, and propofol. A recent meta-analysis has reported an increasing trend of ketamine use in mechanically ventilated patients, indicating that ketamine may play a role as a sedative-sparing agent. However, with small sample sizes, most previous continuous ketamine studies were conducted in patients with traumatic, post-operative, or cerebral ischemia.
Objectives: This study was conducted to assess the effect of continuous ketamine in patients who were admitted to medical or cardiac ICUs and received mechanical ventilators.
Methods: We conducted a retrospective cohort study between March 2012 and June 2020 at Samsung Medical Center. Adult patients who received mechanical ventilation support over 24 h and continuous ketamine infusion at least 8 h were included.
Results: Of all 12,534 medical or cardiac ICU patients, 564 were eligible for analysis. Ketamine was used 33.3 (19.0–67.5) hours and median continuous infusion dose was 0.11 (0.06–0.23) mcg/kg/hr. Of all patients, 469 (83.2%) received continuous ketamine infusion concomitant with analgosedation. Blood pressure and vasopressor inotropic scores were not changed before and after continuous ketamine infusion. Heart rate was decreased significantly from 106.9 (91.4–120.9) in 8 h prior- and to 99.8 (83.9–114.4) in 24 h post-ketamine initiation. In addition, the respiratory rate was decreased from 21.7 (18.6–25.4) in 8 h prior- and to 20.1 (17.0–23.0) in 24 h post-ketamine initiation. Overall opioid usage was significantly reduced; 3.0 (0.0–6.0) mcg/kg/hr as fentanyl equivalent dose in 8 h prior- and to 1.0 (0.0–4.1) mcg/kg/hr as fentanyl equivalent dose in 24 h post-ketamine initiation. However, the use of sedatives and antipsychotic medication was not decreased.
Conclusion: Ketamine may be a safe and feasible analgesic for medical or cardiac ICU patients as an opioid-sparing agent without adverse hemodynamic effects.

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000054

Effectiveness of anakinra therapy in COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**: 000054

Introduction: In the COVID-19 disease, which causes a serious pandemic all over the world; As the pandemic progresses, the pathophysiology of the disease becomes clearer and new treatment regimens are on the agenda.It has been reported that COVID-19 disease is associated with both immunodeficiency and hyperinflammation, and hyperinflammation manifests itself with cytokine storm.Although Tocilizumab treatment was used in 2020 when the disease first appeared, its use has gradually decreased due to the opinions that the current treatment prolongs the immunosuppression period and increases the risk of secondary infection. Due to the side effects of tocilizumab treatment, Anakinra treatment, which has a short duration of action and acting on IL-1, has come to the fore. Anakinra, as an IL-1 receptor antagonist, studies are continuing that it may be useful in macrophage activation syndrome that occurs in COVID-19 disease. In a study conducted in 21 patients receiving anakinra treatment; Although there was a significant decrease in fever, white blood cell count, ferritin, procalcitonin, creatinine and bilirubin values compared to the group that did not receive treatment, no difference was observed in terms of mechanical ventilation time and length of stay in the intensive care unit. In another study conducted in Italy, patients; They were divided into 3 groups: high-dose Anakinra (5 mg/kg twice daily, 29 patients), low-dose Anakinra (100 mg once daily, 7 patients) and patients receiving standard therapy (16 patients).When the group receiving high-dose Anakinra and the group receiving standard treatment were compared, it was found that the respiratory functions of the patients receiving Anakinra treatment were improved and the 21-day life expectancy was significantly higher. Studies on the effectiveness of anakinra treatment on COVID-19 disease are continuing. In this study, we aimed to investigate the significance of clinical and laboratory findings between patients who received Anakinra treatment and those who did not receive Anakinra treatment, but who received high-dose MPZ.
Methods: The characteristics of the patients receiving Anakinra treatment in the MH3 COVID Intensive Care Unit of Ankara City Hospital were retrospectively reviewed. The patients' age, gender, mechanical ventilation duration, length of stay in the intensive care unit, CRP, procalcitonin, LDH, IL-6, lymphocyte, D-dimer, ferritin values and the corticosteroid doses they received in addition to Anakinra treatment were also evaluated. In addition, the data of the patient group who did not receive Anakinra but received high-dose ($\geq$ 250 mg) methylprednisolone (MPZ) treatment were compared with the existing patient data and evaluated in terms of treatment effectiveness.
Results: When the patients who received Anakinra + high-dose MPZ were compared with the patients who received only high-dose MPZ, the mortality rate was significantly higher ($P = 0.038$), mechanical ventilation and hospitalization days in the intensive care unit were significantly longer in patients receiving Anakinra ($p = 0.001$, $p = 0.004$) was seen. However, there was no significant difference in secondary reproduction rates between the two groups ($P = 0.484$). While the mean hospitalization days of the group receiving Anakinra + high-dose MPZ and the group receiving Anakinra + low-dose (< 250 mg) MPZ were found to be significantly longer in the group receiving Anakinra + high-dose steroids ($p = 0.018$), there was no significant difference in terms of mechanical ventilation time and mortality rates. ($p = 0.193$, $p = 1.0$).

Conclusion: In our study, the patients who received Anakinra treatment had a longer hospitalization day and mechanical ventilation period, and the higher mortality rate was attributed to this patient group being the patient group with a more severe course. It was observed that the administration of anakinra treatment after low-dose and high-dose MPZ treatment did not cause a significant difference in mortality rates. However, due to the small number of patients and the heterogeneity of the patient group, more comprehensive and randomized studies are needed.

000062

Renal function monitoring from pre-operative day 1 until post-operative day 30 after cardiac surgical procedures

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Introduction: Cardiac surgery-associated AKI (CSA-AKI) is a quite common complication which may occur in various time points after a procedure. Furthermore, there is also a potential risk of progression to chronic kidney disease.
Methods: During a ten month period, a total of 384 patients underwent cardiac surgery procedures in our Cardiothoracic department. The following renal function related factors were prospectively collected: preoperative GFR (MDRD formula) incidence of AKI (KDIGO criteria) and GFR 30 days after the procedure. Furthermore we collected the following parameters: age, gender, Euro score II, preoperative NYHA stage, cardiopulmonary bypass time(CPB), diabetes mellitus, ejection fraction, smoking, peripheral artery disease, dyslipidemia hypertension, postop Low Cardiac Output Syndrome(LCOS), postop Atrial Fibrilation(AF) and postoperative rhabdomyolysis (CPK > 2000).
Results: A total of 41 pts were burdened with AKI(10,7%). The AKI group compared with the rest of the cohort, was older (70±8.4 vs 65.6±9.2, $p<0.05$), with lower preop GFR(76±17 vs 81.6±22, $p<0.05$). The AKI group also showed a higher incidence of NYHA stage > 1 ($p<0.05$), higher incidence of emergency operation(7,3% vs 1%, $p<0.05$), longer CPB time(122±57vs 95.2±31.8, $p<0.05$), higher incidence of postoperative LCOS (17.1% vs 2.9% $p<0.05$), postoperative AF(39%vs 24% $p<0.05$) and rhabdomyolysis (37.5% vs 4.7%, $p<0,05$). In terms of statistical analysis for our results, Mann–Whitney U test and χ2 test were used. On the 30th Postoperative day 178 (46,3%) patients had a decline in their GFR compared with preop values. GFR decline correlated with lower preop GFR(74.3±21 vs 86.6±22, $p<0.05$), peripheral vascular disease (20.8 vs 13.1% $p<0.05$), postoperative AKI during early hospital days (13.6% vs 7.3% $p<0.05$) and postoperative atrial fibrillation (31% vs 19.1% $p<0.05$). Mann–Whitney U test, student's t test and χ2 test were used in this analysis. Finally, with regards to the 41 patients who were burdened with perioperative AKI we compared their GFR values to one month post op. Decline was seen in 12 patients (compared with preop values). The only factor with a statistically significant negative relationship with recovery was arterial hypertension(100% vs 69%). Mann–Whitney U test and χ2 test were used in this analysis.
Conclusion: CSA AKI is significantly correlated with age, preop GFR, NYHA stage, urgent operations, longer CPB time, postop LCOS, post op AF and rhabdomyolysis. GFR decline one month after operation was related with lower preop GFR, peripheral vascular disease, AKI and AF. All hypertensive patients with early AKI had lower GFR 1 month after operation.

000064

Postoperative lactate kinetics in diabetic patients treated with metformin compared with other antiglycemic agents

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Introduction: The aim of this retrospective study is to compare preoperative metformin use with other antiglycemic agents in diabetic patients with regards to the impact on lactate concentrations and clearance during the first postoperative day after elective cardiac surgery.
Methods: Demographic and perioperative characteristics were recorded for the entire cohort. In all patients, arterial blood samples were taken postoperatively on 4 time points: arrival in the ICU, H6, H12 and H24 after ICU arrival. Lactate clearance was calculated using the following formula:

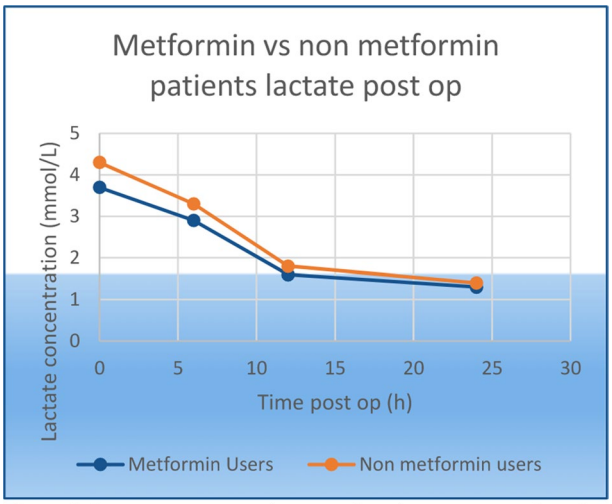

Figure 1. Lactate concentrations metformin vs. non metformin

Results: There was no statistically significant difference between groups in terms of age, gender, Euroscore II, preoperative GFR, NYHA stage, preop ejection fraction, Cardiopulmonary Bypass Time or Adrenaline dosage (in μγ/kg/min). Among 109 were patients with diabetes mellitus, 74 were treated with metformin. The rest of the diabetic patients (35 patients) were treated either with different oral agents or with insulin. No difference was found between metformin users and non-users neither on lactate concentrations ($p=0.61$) nor on lactate clearance ($p=0.86$).
Table 1 Lactate concentration comparison of metformin users vs other antiglycemic medication

Lactate concentration (mmol/Lt)	Metformin users ($n=74$)	Non-metformin users ($n=35$)	*p*-value	Group effect	Time effect	Time*group effect
On arrival	3.7±0.2	4.3±0.3	0.2061	0.2045	<0.0001	0.6112
6 h	2.9±0.2	3.3±0.3	0.3789			
12 h	1.6±0.1	1.8±0.2	0.2517			
24 h	1.3±0.1	1.4±0.1	0.3523			

Table 2. Lactate clearance comparison of metformin users vs other antiglycemic medication

Lactate clearance	Metformin users ($n=74$)	Non-metformin users ($n=293$)	*p*-value	Group effect	Time effect	Time*group effect
6 h	0.2±0.0	0.2±0.1	0.9093	0.5991	<0.0001	0.8621
12 h	0.5±0.0	0.5±0.1	0.5850			
24 h	0.6±0.0	0.6±0.0	0.2954			

Conclusion: Lactate concentrations decreased significantly over time in all patients indicating a good clearance. Lactate clearance increased over time in both groups No differences on lactate clearance were found between the two groups of the subgroup analysis.

000075

Predictive role of changes in postoperative presepsin level and early postoperative sepsis in intensive care unit patients after abdominal surgery

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Intensive Care Medicine Experimental 2022, **10(2)**: 000075

Introduction: It is difficult to identify the early sepsis after surgery due to postoperative inflammatory reactions. Presepsin, a glycoprotein expressed on the surface of innate immune cells, is produced during bacterial phagocytosis and its level increases in the bloodstream of sepsis patients. This study aims to measure the differences between the diagnostic ability of presepsin and other biomarkers to identify postoperative sepsis and septic shock in acute period after major abdominal surgery.
Methods: From March to August 2020, patients who underwent surgery due to intra-abdominal infection were enrolled. Level of presepsin and procalcitonin, and white blood cell counts were prospectively measured every morning for 3 days from the intensive care unit admission after surgery (from T0 to T3). Diagnostic values of inflammatory markers were compared to predict early development of sepsis or septic shock within 7 days after surgery. The cutoff value of significant risk factor associated with postoperative sepsis or septic shock were also evaluated.
Results: Among 298 patients, postoperative sepsis and septic shock occurred in 91 and 38 patients, respectively. For prediction of early postoperative sepsis or septic shock, presepsin and procalcitonin had a comparable diagnostic ability. In multivariate analysis, presepsin level over 406.5 pg/ml at T0 [odds ratio (OR): 4.055, $p=0.047$], presepsin level over 1216 pg/ml at T2 (OR: 40.030, $p=0.005$) and procalcitonin level over 1.685 ng/ml at T2 (OR: 5.229, $p=0.008$) were significant factors for predicting the occurrence of early postoperative septic shock.
Conclusion: Diagnostic accuracy of presepsin for sepsis or septic shock was feasible in acute postoperative period. It would be useful to monitor the newly developed sepsis from the normal inflammatory response, especially in patients who underwent surgical operation for the elimination of intra-abdominal infection.

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000107

Acute gastrointestinal dysfunction in critically ill patients with COVID-19

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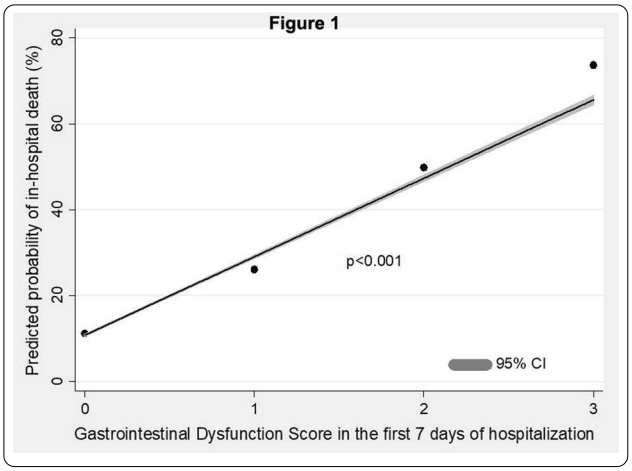
Introduction: Gastrointestinal (GI) dysfunction in critically ill patients is associated with increased short term morbidity and mortality. Previous studies have relied on the combination of signs and symptoms to develop scores that may reflect the deterioration of GI function. The Gastrointestinal Dysfunction (GID) score has been recently evaluated in this context, and demonstrated prognostic value both alone or in combination with the Sequential Organ Failure Assessment score [1].
Objectives: This study aimed to analyse the prognostic value of the GID score in hospitalized patients with severe Coronavirus Disease-2019 (COVID-19).
Methods: Medical records from **c**onsecutive patients with confirmed COVID-19 admitted to an intensive care unit (ICU) in Rio de Janeiro, Brazil between March and July 2020 were retrospectively analysed. Only patients hospitalized for more than 24 h were included. Clinical variables and components of the GID score were collected during the first 7 days of hospitalization. Patients were classified according to a 5 scale (0-IV) progressive GI injury grading system, which was correlated with in-hospital complications and death.
Results: Among 230 patients who were screened, 215 remained in the ICU for more than 24 h, and were included in the analysis. Median age was 68 years (54–82) and 57.7% were males. Previous comorbidities included hypertension (52.6%), diabetes (27.9%) and coronary artery disease (11.6%). Mechanical ventilation (MV) was required in 21.4% of patients and total in-hospital mortality was 15.8%. Total GID scores were: 0 (79.1%), I (15.3%), II (4.7%), III (0.9%) and IV (0%). Any GI dysfunction was present in 20.9% of patients and decreased bowel motility was the most common finding (20.5%). Those with GID scores > 0 had longer lengths of stay [20 days (11–33), vs. 7 days (4–16), $p<0.001$] and C-reactive protein (CRP) levels on admission [12.8 mg/mL (6.4–18.4), vs. 5.7 mg/mL (3.2–13.4), $p<0.001$]. In the univariate analysis, the GID score was significantly associated with mortality (OR 2.8; 95% CI 1.7–4.8, $p<0.001$) and MV (OR 2.8; 95% CI 1.7–4.6, $p<0.001$). Figure 1 represents the predicted probability of in-hospital death according to GID scores. After adjusting for age, previous coronary artery disease, CRP levels, systolic blood pressure and oxygen saturation on admission, GID scores remained significantly associated with mortality (OR 2.0; 95% CI 1.1–4.0, $p=0.04$).



Conclusion: In the current series of hospitalized patients with severe COVID-19, the GI system was frequently affected. Although symptoms

were mostly mild, any manifestation of GI dysfunction was predictive of adverse outcomes. Future studies should validate these findings by further implementing the GID score among patients with COVID-19.

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Acknowledgements: There are no grants to acknowledge.

000134

Early prediction of delirium in critically ill patients at admission to intensive care units

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Intensive Care Medicine Experimental 2022, **10(2)**:000134

Introduction: Delirium is associated with increased complications and mortality in critically ill patients (1). Early prediction of delirium is crucial for planning prevention, screening, and treatment strategy. Most prediction models of delirium in intensive care units (ICUs) are designed to predict the mortality at 24 h after ICU admission (2).
Objectives: This study aimed to develop several machine learning (ML) models to predict early ICU delirium at ICU admission.
Methods: Data of 4,061 patients admitted between August 2020 and April 2021 were recruited for model training, and data of 559 patients admitted between May 2021 and June 2021 were recruited for model testing. Data were processed using the missing value imputation of RapidMiner, and features collected at ICU admission were selected for predicting ICU delirium developed within 2 days after ICU admission. Machine learning model were trained with the following algorithms: logistic regression (LR), gradient boosted trees (GBT), and deep learning (DL). Feature importance of ML model were analysed. The areas under the receiver operating characteristic curve (AUROC), accuracy, recall, precision, and F1 score were used to compare performance among the three models.
Results: In the testing dataset, mean age of the patients was 66 (15) years, 41.5% of patients received surgery, 45.1% of patients were intubated in the first day, and the observed incidence of ICU delirium within 48 h was 36.1%. 12 features were selected for machine learning model training, and the AUROC) were 0.884 (0.854–0.913) in LR model, 0.894 (0.866–0.922) in GBT model, and 0.881 (0.851–0.910) in the DL model. The accuracy, recall, and precision at cutoff value of 0.5 were shown in Table 1.

Figure 1 Model performance

	LR	GBT	DL
AUROC	0.884	0.894	0.881
Accuracy	0.8068	0.8229	0.8157
Recall	0.5743	0.6139	0.5990
Precision	0.8406	0.8552	0.8462
F1 score	0.6824	0.7147	0.7014

Conclusion: ML models could predict early delirium right after ICU admission. Further studies are warranted to deployment the model and investigate the impact on clinical practices.

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Acknowledgements: NTUH 109-A150.

000158

Clinical characteristics of chronic obstructive pulmonary disease patients admitted to intensive care unit

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Introduction: Chronic obstructive pulmonary disease (COPD) is known to be one of the most common diseases with significant morbidity and mortality. In this study, we evaluated clinical characteristics of COPD patients who were admitted to intensive care unit (ICU).
Methods: The study was based on a multicenter cohort of COPD patients who were recruited from 54 medical centers in South Korea. Baseline characteristics including general characteristics, symptom scores, pulmonary function test results and radiologic findings were compared whether presence of ICU admission history. One year follow-up exacerbation risk were compared using negative binomial regression model. Also, 3-year lung function decline rates were compared with linear mixed model.
Results: Of the 2147 patients, 11 (0.5%) patients were admitted to ICU in previous year to the enrollment. There were no significant difference in age, sex, smoking history and BMI according to ICU admission history. Patients who had history of ICU admission showed poor health-related quality of life, regarding total St. George Respiratory Questionnaire (SGRQ) score (31.5 ± 18.8 vs 45.4 ± 26.8, $p = 0.02$), however there were no significant difference in mMRC, CAT score and 6-min walk distance test. Patients who admitted to ICU suffered more from depression regarding BDI score (6.8 ± 8.2 vs 14.4 ± 9.3, $p < 0.01$). There were no significant difference in future exacerbation risk in 1 year. Moreover, there were no significant difference in lung function test results. Three year follow-up data showed no significant difference of lung function trajectories, however there were prominent decrease of FEV1 in first year of ICU admission.
Conclusion: Patients who were admitted to ICU showed poor health-related quality of life and depression compared to those who were not. There were no significant difference in exacerbation risk nor lung function decline trajectories, however there were prominent decrease in first year after ICU admission.

Acknowledgements: This research was supported by funds (2016ER670100, 2016ER670101, 2016ER670102 and 2018ER670100, 2018ER670101, 2018ER670102) from Research of Korea Centers for Disease Control and Prevention.

000175

Efficacy of programmed intermittent bolus infusion with serratus anterior plane block catheter for analgesia in the intensive care unit after minimally invasive cardiac surgery: a randomized, double-blind, controlled trial

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Introduction: Minimally invasive cardiac surgery (MICS) involves a small lateral thoracotomy, which is expected to result in less complications and faster recovery compared with median sternotomy. However, difficulties with postoperative pain control after MICS can

counteract this benefit, and opioid-based analgesia can cause side effects such as respiratory depression, nausea, and vomiting. Serratus anterior plane block (SAPB), which requires high-volume infusion of local anesthetics into the optimal compartment under the serratus muscle, allows effective analgesia after thoracic surgery. Thus, programmed intermittent bolus infusion (PIBI) with an SAPB catheter may improve postoperative pain management after MICS. This study aimed to evaluate the effects of PIBI with an SAPB catheter for postoperative fentanyl consumption following MICS.

Methods: This study was a prospective, randomized, double-blind trial. Twenty patients, aged 19–80 years, ECOG 0-II, and scheduled for elective MICS were randomly allocated to 2 groups (SAPB or Control). Before the surgery, all patients underwent SAPB followed by insertion of a catheter and received a bolus of 3 mg/kg 0.375% ropivacaine through the catheter. In the SAPB group, participants received a bolus of 20 mL 0.25% ropivacaine every 6 h after surgery, while a bolus of 20 mL saline was administered in the control group. All participants received intravenous fentanyl via patient-controlled analgesia. The primary outcome was the cumulative fentanyl consumption up to postoperative day (POD) 5. The secondary outcomes were: the Numerical Rating Scale (NRS) at rest and on movement at the time of extubation and 1, 2, 6, 12, 24, 48, 72, and 96 h after extubation; the length of intensive care unit and hospital stay; evaluation of rehabilitation (grip strength, length around the thorax, and upper limb range of motion at preoperative and postoperative days 1–5); side effects (postoperative nausea and vomiting (PONV) and adverse events due to ropivacaine); and time to the first postoperative fentanyl dose.

Results: Seventeen patients were left in the final analysis. The cumulative fentanyl consumption at 5 days did not significantly differ between the two groups (the SAPB group, median [interquartile range (IQR)], 511.6 μg [457.3–752.9] versus the control group, 654.1 μg [439.1–982.0]; P = 0.963). The incidence of PONV were significantly lower in the SAPB group compared with the control group (11.1% versus 62.5%; P = 0.049). The median NRS score on movement during the study period was lower in the SAPB group, but the result was not statistically significant (P = 0.057).

Conclusion: Programmed intermittent bolus infusion with an SAPB catheter did not reduce postoperative fentanyl consumption compared with the control group after MICS. However, this method was associated with a significantly lower incidence of PONV.

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001450

Prolongation of QT interval following cytoreductive surgery with hyperthermic intraperitoneal chemotherapy: a retrospective analysis

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Intensive Care Medicine Experimental 2022, **10(2)**: 001450

Introduction: Abnormal cardiac repolarisation indicated by QTc prolongation in intensive care unit (ICU) can have serious consequence including ventricular tachycardia and sudden death. QTc prolongation is common in surgical ICU after non-cardiac surgeries (3); but hyperthermic intraperitoneal chemotherapy (HIPEC) (1,2) can have more deleterious effect due to chemotherapeutic drugs & direct effect of hyperthermia. Dys-electrolytaemia in post-operative period along with altered fluid homeostasis can complicate it further.

Objectives: Aim of this retrospective analysis is to evaluate the incidence of QTc prolongation related to HIPEC surgery and the perioperative risk factors associated with it.

Methods: Institutional review board waiver has been applied for this retrospective data analysis. Perioperative data were collected from hospital electronic medical record (EMR) of 52 patients undergone HIPEC over last 1 year and had been analysed. Perioperative managements were conducted as per institutional protocol. Temperature, acid–base balance and electrolytes including magnesium were monitored and actively maintained within normal limit throughout the perioperative period. The primary outcome was to assess increase in QTc-interval. Emphasis was placed on absolute QTc prolongation and the ΔQTc (difference from the baseline preoperative value). Secondary objective is to evaluate the perioperative risk factors associated with it. Standard descriptive summaries were used for continuous variables (N) i.e. mean, median, standard deviation, minimum and maximum and categorical variables (number and percent). All statistical tests of comparison were based on 5% level of significance. The ΔQTc was determined by a two-sided paired Student t test.

Results: Total 52 patients' data were retrieved, median age was 55 years; 39 were female and 13 were male, mean BMI 24.77 (SD 5.02). In our patient population, 25 (48%) had Carcinoma (Ca) ovary, 8 had (15.4%) Ca stomach, 6 had (11.6%) Ca appendix and 13 (25%) patients had colorectal Ca. Out of 52, 30 patients (57.6%) received chemotherapy preoperatively with various regimens depending on the primary diagnosis.

ECG was obtained for all patients within 30 min of arrival in the surgical ICU. Out of 52, 51 patients (98%) experienced QTc interval prolongation {ΔQTc 58.6 ± 29.98 ms. (mean ± SD)}, 95% CI 58.49 ± 8.23, P < 0.0001. Approximately 30.7% (16 of 52) had a baseline preoperative QTc greater than 440 ms, but no patient had a QTc greater than 500 ms. The ΔQTc was > 30 ms in 46 patients (88%), > 60 ms in 21 (40%) and > 100 ms in 3 (5.7%) patients. One patient developed ventricular bigeminy with ectopics with a ΔQTc: 71 ms (1.9% incidence rate).

Conclusion: We found that significant postoperative QT prolongation is associated with HIPEC surgery, The symptom manifestation was minimal—may be due to aggressive electrolyte optimisation, specially magnesium. The factors responsible for this high incidence rate is under evaluation.

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Anaesthesia & Peri-operative Medicine 2

000198

Clinical analysis of factors associated with 30-day mortality in critically ill patients who underwent emergency gastrointestinal perforation surgery

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Intensive Care Medicine Experimental 2022, **10(2)**: 000198

Introduction: Gastrointestinal perforation is a surgical emergency that requires immediate operation and intensive care is often indicated. The clinical characteristics and predictors of postoperative morbidity and mortality in critically ill-patients who underwent emergency operation are still not well established. Therefore, the aim of this study is to identify risk factors for postoperative morbidity and mortality after emergency operation for gastrointestinal perforation.

Methods: We retrospectively analyzed 412 patients who underwent emergency operation after hospitalization through the emergency room for gastrointestinal perforation at a single institution in Korea from January 2003 to September 2021. All patients were admitted to intensive care unit (ICU) after surgery and received intensive care. Factors related with postoperative mortality at one month and necessary to obtain APACHE II score were investigated. Restricted cubic splines were modeled for the analysis of mortality according to the time taken from admission to surgery.
Results: Overall mortality at 30 days was 0.09% (36 patients). Univariate analysis indicated that patient-related factors associated with mortality were age, APACHE II score and initial serum lactate level; duration of surgery and total hospital stay were also indicators associated with mortality. Multivariable analysis showed that the higher the APACHE II score, the higher the mortality rate at the significance level $p < 0.01$. Adjusted splines modeled an area of inflection around 12 h when the probability of mortality began to increase.
Conclusion: Various factors were associated with postoperative clinical outcomes of patients with gastrointestinal perforation. The APACHE II score is a useful indicator for predicting patients' prognosis even after surgical intervention. A wait time of 12 h may demonstrate a threshold defining greater risk of mortality.

000229

Clinical practice survey: assessment and ventilatory management of sickle cell patients in intensive care

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Introduction: Sickle cell disease is a haemoglobinopathy characterised by a β-globin abnormality producing haemoglobin S. This genetic disease is common in France. Hyperalgesic vaso-occlusive crisis (VOC) and acute chest syndrome (ACS) are the main complications leading to intensive care units (ICU) admissions. Despite being a frequent cause of ICU admissions, their management might be heterogeneous due to a lack of ICU-specific guidelines. We aimed to gather the medical practices of ICUs nationwide.
Methods: We carried out an online survey that was sent to medical teams of all ICUs of French hospitals identified as expert centers in the Orphanet database (https://www.orpha.net). Physicians from the same unit sent consensual answers to capture the usual care in their ICU. Each center provided only one answer. The survey included sections related to: demography; usual pain management, and three clinical situations (hyperalgesic VOC, VOC with chest pain, and ACS with chest pain, dyspnea and fever).
Results: Of 55 centers contacted, 32 (58%) answered the survey, including 20 (62,5%) university-hospitals, 11 (34.4%) non-university hospitals and 1 (3.1%) private hospital. The median [IQR] number of ICU beds was 22 [18–28]. We grouped centers according to the annual number of admissions and 17 (53%) centers admitted less than 10 patients with sickle cell disease per year. Regarding pain management, 69% of the centers used nitrogen monoxide-oxygen mixture, and 59% of the centers never used nonsteroidal anti-inflammatory drugs in sickle cell patients. Ketamine was widely prescribed (88%) if Morphine failed to ease the VOC pain. Regarding oxygenation and physiotherapy, conventional oxygen therapy was used regardless of the oxygen saturation in 56% and 59% of the centers for VOC and for VOC associated with chest pain or ACS respectively. Physiotherapy and incentive spirometry was systematically ordered in 69% of the centers during a VOC, 81% in case of VOC with chest pain and 63% during ACS. Regarding ACS prevention and antibiotics, the PRESEV score (a validated ACS-predictive score) was used in only 2 centers (6,3%). During ACS, most physicians (94%) used empiric antibiotherapy. Regarding ventilatory support, most physicians considered non-invasive ventilation main benefit during ACS was the effect on alveolar recruitment and hypercapnia (91%), but 72% of them reported that patients' tolerance was the main limitation for non-invasive ventilation use. Most physicians (88%) considered High-flow nasal oxygen was simple to use and well-tolerated by patients (84%), however, 78% of the responders declared that its efficacy during ACS still needs to be confirmed by large studies.

	Total (N=32)	< 10 admissions per year (N=17)	> 10 admissions per year (N=15)
Nitrogen monoxide oxygen mixture (MEOPA) use	22 (69%)	13 (77%)	9 (60%)
NSAID use	13 (41%)	5 (29%)	8 (53%)
Systematic conventional oxygen therapy (during VOC and chest pain)	19 (59%)	10 (59%)	9 (60%)
Physiotherapy and incentive spirometry (during VOC)	22 (69%)	12 (71%)	10 (67%)
NIV main benefit : alveolar recruitment and effect on hypercapnia	29 (91%)	15 (88%)	14 (93%)
HFNO main limitation : no proof of efficacy during ACS	25 (78%)	14 (82%)	11 (73%)

Table 1: main management and respiratory devices effects according to the number of patients with sickle cell disease admitted per year. NSAID = non-steroidal anti-inflammatory drugs; VOC = vaso-occlusive crisis; NIV = non-invasive ventilation; HFNO = high-flow nasal oxygen; ACS = acute chest syndrome.

Conclusion: Pain and respiratory management of patients with sickle cell disease acute complications is heterogeneous amongst expert centers. Incentive spirometry to treat or prevent ACS needs to be generalised. Further studies evaluating the benefits of HFNO are needed.

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000239

International analgesia and sedation weaning and withdrawal practices in critically ill adults: the AduLt iatrogEnic withdRawal sTudy in the ICU (ALERT-ICU)

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Intensive Care Medicine Experimental 2022, **10(2)**:000239

Introduction: Iatrogenic withdrawal syndrome (IWS) from opioids and sedatives in critically ill patients has a reported prevalence of 32% to 68% (Curley et al., 2015; Cammarano et al., 1998). It is associated with prolonged mechanical ventilation and ICU stay (Amigoni et al., 2017; Cammarano et al., 1998); however, little is known about practices utilized to monitor, assess, prevent or treat IWS.

Objectives: Describe analgesia and sedation weaning and withdrawal practices in critically ill adults.
Methods: We conducted an international, prospective, observational, one-day point prevalence study. Professional networks, listservs, a study website, and social media were used for study site recruitment. The study was determined to be exempt by the Wilkes University Institutional Review Board. Study sites obtained local research ethics approval, and selected a data collection date between June 1and September 30, 2021 for each of their participating ICUs. Patients aged 18 years and older in the ICU on the data collection date were included, and those receiving parenteral analgesics or sedatives during the previous 24 h had demographic, medication, and outcomes data collected for that time period using Research Electronic Data Capture (REDCap). The primary outcome was the proportion of patients weaned from continuous parenteral analgesics and sedatives using an institution-defined standardized approach. Secondary outcomes included proportion of patients assessed for IWS using a standardized approach, proportion receiving continuous analgesics and sedatives, and weaning and IWS practices. Descriptive and comparative statistical analyses were performed using IBM SPSS Statistics version 28.0.0 (Armonk, New York). Parametric and non-parametric tests were used according to level of measurement, data distribution and assumptions. An alpha less than 5% demonstrated statistical significance.
Results: Data were collected at 87 hospitals in 229 ICUs from 11 countries on 2402 patients. More than half the hospitals (56%) were located in the United States and United Kingdom, 61% were academic medical centers, and 68% of participating ICUs were using a closed practice model and had a mean of 19 (SD ± 9) beds. Most patients (55%) were from the United States and continuous parenteral analgesics or sedatives were administered in the previous 24 h in 1506 (63%) patients. The mean age of patients who received continuous parenteral analgesics or sedatives was 56 (SD ± 16) years, 38% were female, 41% were admitted primarily for respiratory disease, and 30% were COVID-19 PCR positive. On the day of data collection, the median duration of ICU stay for these patients was 6 (IQR; 12) days, 31% had active ARDS, and 74% were on mechanical ventilation. Among these patients 521 (34%) were admitted to 90 (39%) ICUs with a weaning protocol, and 97 (6%) patients to 23 (10%) ICUs with a withdrawal protocol. By the day of data collection, a weaning protocol for analgesia-sedation was utilized in 176 (12%) and withdrawal protocol in 9 (0.6%) patients in these ICUs. In ICUs with a weaning protocol 20 (22%) initiate the protocol < 24 h after starting continuous analgesics or sedatives, 12 (13%) 24 to < 72 h, and 11 (12%) ≥ 72 h, but the majority (52%) do not specify. A validated tool is used to determine the degree of weaning in 48 (53%) ICUs, absolute dose reduction in 22 (24%), and percent reduction in 23 (26%). Significantly more ICUs with a withdrawal protocol initiate weaning 72 to < 96 h after analgesia-sedation initiation (40% vs 0%; $p < 0.001$), and use an absolute (30% vs. 7%; $p = 0.003$) and percent (39% vs. 7%; $p < 0.001$) dose reduction for weaning compared to ICUs without a withdrawal protocol.
Conclusion: Although two-thirds of patients received continuous parenteral analgesics or sedatives, a small proportion were weaned and assessed for withdrawal from these agents using a standardized approach. A little over one-third of patients were admitted to an ICU with a weaning protocol, and about 1 in 20 to an ICU with a withdrawal protocol.

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Acknowledgements: Supported by funding from a Wilkes University Provost Research and Scholarship Grant.

000241

Analgesia, sedation and neuromuscular blocking agents to optimize mechanical ventilation in Coronavirus Disease 2019

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Intensive Care Medicine Experimental 2022, **10(2)**:000241

Introduction: Acute respiratory distress syndrome (ARDS) was present in the most severe patients with COVID-19. Deep sedation, or even neuromuscular blocking agents (NMBAs) were required to optimize mechanical ventilation (MV). An analgosedation (AS) protocol implemented in our ICU since 2016 was tested.
Objectives: To analize AS and neuromuscular blockade strategies in COVID-19 patients on MV.
To identify independent predictors of hospital mortality.
Methods: Cohort study in a 28-bed medical-surgical ICU in Argentina. Consecutive patients on MV > 2 days were included from July 2020 to June 2021. AS protocol consisted in nomogram templates for each AS drug and NMBAs, as a tool to properly prescription (maximum doses, adequate ranges/dilution, promotion of not using benzodiazepines). We recorded: patient characteristics and outcomes, prescribed doses, and days of treatment of midazolam (MDZ), propofol, (PROPO) dexmedetomidine (DEXME), fentanyl (FNT), remifentanil(R-FNT), and NMBAs. Variables were compared between survivals and non-survivals. A logistic regression model was built to identify independent predictors of hospital mortality; variables with $p < 0.20$ were tested in the model. A p value < 0.05 was considered significant for all comparisons.
Results: In the period, 163 patients were included: 94.5% received FNT, 90.2% MDZ, 39.9% DEX, 34.4% PROP and 60.7% NMBAs (mainly atracurium). Patient's characteristics and doses/days of drugs for AS and NMBAs are shown in Table 1.
Table 1 Patient characteristics and doses/days of AS and NMBAs drugs.

Variables	All (*N*:163)	Survivals(65)	Non-survivals(98)	Drug		All (*N*:163)	Survivals(65)	Non-survivals(98)
Age	54 ± 14	50 ± 13	57 ± 14*	FNT	mcg/kg/h	4[3–5]	4[3–5]	4[3–5]
Sex (m)	109 (67)	48 (75)	60 (61)		days	12 [7–20]	16 [8–27]	10.5 [6–17]*
BMI	31 ± 6	32 ± 4	31 ± 7	MDZ	mg/kg/h	0.17[0.14–0.2]	0.16[0.14–0.2]	0.16[0.13–0.2]
APACHE II	18 ± 7	14 ± 6	20 ± 7*		days	9[5–17]	11[6–17]	9[5–15]
SOFA24	7[5–9]	5[4–7]	7[6–9]*	DEXME	mcg/kg/h	0.7[0.5–0.8]	0.7[0.5–0.8]	0.6[0.4–0.7]
Dialysis	73/157 (47)	18/61 (30)	55/96 (57)*		days	7[4–12]	7[5–12]	7[3–13]
MV days	22[11–38]	36[17–59]	15[9–26]*	PROPO	mcg/kg/h	1.9[1.6–2.3]	1.9[1.6–2]	1.8[1.6–2.4]
ICU days	23[11–41]	41[25–61]	15[9–25]*		days	3[1–5]	4[2–8]	2.5[1–4]*
Hosp days	30[14–52]	52[34–73]	18[12–31]*	R–FNT	mcg/kg/h	13[10–15]	13[12–15]	11[10–15]
PRONO	100/161 (62)	39/64(61)	61/97(63)		days	5[2–11]	7[4–12]	3[2–10]
NMBAs	102/163 (63)	38/65(58)	64/98(65)	ATRA	mcg/kg/h	11[8–14]	11[8–14]	11[8–14]
NMBA days	8[4–12]	8[4–11]	7[4–12]		days	7[3–11]	7[4–11]	6[3–10]

* p value < 0.05. Data are presented as median ± SD, median [p25–75] or N (%).

Hospital mortality was 60.1%. In the multiple logistic regression model Age > 55 (OR 2.27, 95%CI [1.10–4.67]) SOFA (OR 1.28, 95%CI [1.10–1.49]) and days of FNT(OR 0.96, 95%CI [0.93–0.99]) were independent predictors of hospital mortality.
Conclusion: Despite the severity of the population, no differences were observed in the prescription of AS and NMBAs between survivals and non-survivals, reflecting the consistency and reliability of our AS program. Hospital mortality was high, being SOFA and age > 55 independent predictors. The inverse relationship between FNT days and mortality shows that survivors were appropriately managed, prioritizing analgesia.

000264

A systematic review of the generation of Directed Acyclic Graphs (DAGs) in perioperative observational studies: a critique against best practice as defined by the 'Evidence Synthesis for Constructing Directed Acyclic Graphs' (ESC-DAG) framework

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Introduction: The Directed Acyclic Graph (DAG) is a graph that denotes causal and confounding pathways in an observational study. The use of DAGs allows transparent communication of a putative causal model between researchers and can prevent over-adjustment biases when conducting multivariable modelling. This permits a greater degree of confidence in identified effects between selected exposures and outcomes. In this era of 'big data' and increasing number of observational studies, the role of the DAG is becoming more important. DAGs can be a particularly useful tool when undertaking observational studies in anaesthetics and intensive care, given the copious amounts of different variables available to analyse in these settings. The DAG is also being used more frequently in other areas of health literature [1]. Despite this increased importance and utility of the DAG, their use and effectiveness in the perioperative observational literature has not been assessed. To understand whether the DAG is being used effectively in the perioperative literature, it is vital to ascertain how they are being built. A best practice framework for constructing DAGs had been recently published. The 'Evidence synthesis for constructing DAGs' (ESC-DAG) [2] protocol provides authors with a methodological approach to DAG construction. It consists of four main stages to build robust DAGs. These are outlined in *Figure 1*.

Figure 1. An outline of the stages of the ESC-DAG protocol, including an example construction of a perioperative DAG.

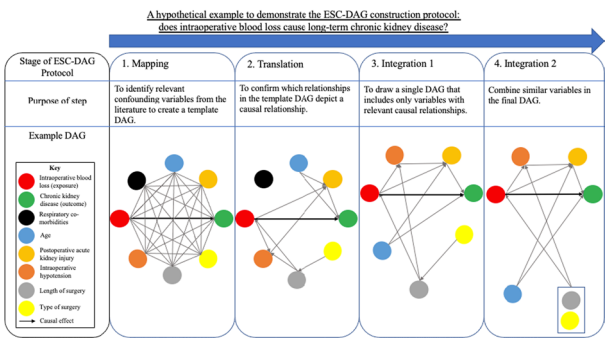

Figure 1. An outline of the stages of the ESC-DAG protocol, including an example construction of a perioperative DAG.

Objectives: To assess whether DAGs in the observational perioperative literature are constructed in accordance with the ESC-DAG protocol.

Methods: MEDLINE, Cochrane Library and Embase were searched using terms to identify perioperative observational studies that constructed a DAG. 515 abstracts were screened by 2 authors. 12 studies were included in the final synthesis. 2 reviewers assessed the final studies against the steps proposed in the ESC-DAG protocol. A study was scored as having fulfilled a stage if over 50% of the steps within that stage of DAG construction were completed. Cohen's kappa statistic [3] was calculated to be 0.8. Disagreements were discussed amongst all the reviewers to reach a unanimous decision. The study was registered on PROSPERO (CRD42021279183).
Results: 12 studies were included that met inclusion/exclusion criteria. *Figure 2* demonstrates the number of studies fulfilling each stage of the ESC-DAG protocol. No study undertook 'Mapping'.

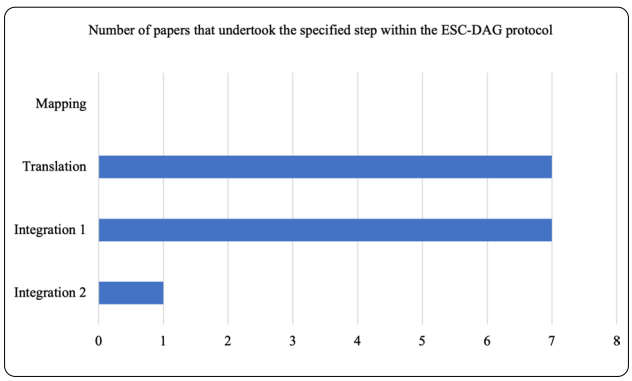

Figure 2. Bar chart demonstrating the number of final papers fulfilling stages laid out in the ESC-DAG protocol.
Conclusion: Relatively few studies using DAGs to guide perioperative observational research were identified. The ESC-DAG protocol was not used consistently between studies. Greater adherence to this protocol in the perioperative literature will ensure DAG construction is consistent and transparent.

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Acknowledgements: Dr Daniel Stubbs is funded by the Wellcome Trust (220542/Z/20/Z).

000275

Incidence of Catheter Associated Asymptomatic Thrombosis in intensive care unit patients: a prospective cohort study

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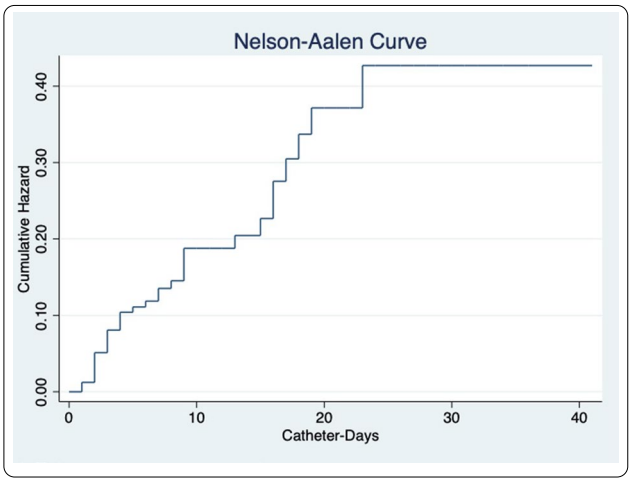
Intensive Care Medicine Experimental 2022, **10(2)**:000275

Introduction: Central venous catheter (CVC) insertion and use is common practice in Intensive Care Unit (ICU) and, according to guidelines, is a safe procedure. However, complications may occur, such as catheter related thrombosis (CRT). CRT severity ranges from asymptomatic

to pulmonary embolism. Risk factors for CRT have been described, such as site and number of cannulation attempts, number of lumens, and catheter-vein diameter ratio. In addition, oncologic and thrombophilic patients have increased risk of developing CRT. In literature, CRT complicates 1–5% of CVC insertions, but incidence rates vary widely. Indeed, most of the studies considered only oncologic or pediatric populations and focused on symptomatic thrombosis.
Objectives: Primary aim of this study was to assess the proportion of patients and the incidence rate of asymptomatic CRT in an adult non-oncologic ICU population. Secondary aims were different types of CRT.
Methods: Monocentric prospective observational cohort study started on September 14, 2019. All ICU patients who needed a CVC were considered for enrollment. Exclusion criteria were: 1) age < 18 years; 2) history of neoplasia or thrombophilia. Patients were included at first CVC insertion. Patient's characteristics, catheter's features, dates of insertion and removal, site of puncture, and veins' diameters, were collected at enrollment and for every new cannulation. Duplex ultrasound screening was performed using Rapid Central Vein Assessment (RaCeVA) protocol before the first CVC positioning and then daily to diagnose CRT. Follow-up ended when one of these events occurred: 1) CRT of at least one catheter; 2) removal of all CVCs; 3) ICU discharge; 4) patient death; 5) > 28 days after last catheter insertion. Nelson-Aalen estimator was used to figure out cumulative hazard rate of developing CRTs. Current analysis is limited to the primary outcome on patients enrolled up to March 31, 2022.
Results: We enrolled 147 patients and followed them for 1335 patients-days (pd) in total. Ninety-six (65%) were males and median [IQR] age was 61 [53–71] years. At enrollment, SOFA Score and Charlson's Comorbidity Index were 4 [3–6] and 2 [1–4], respectively. Non-surgical diseases were the most important causes of ICU admission (118/147, 80%) and septic shock was the most represented diagnosis (25/147, 17%). Median number of inserted catheters per patient was 2 [1–2]. Two-hundred-seventy-seven catheters were placed and then followed for a total of 2123 catheters/day (cd). Centrally Inserted Central Catheters (174, 63%) were the most used, followed by Swan-Ganz catheters (47, 17%), non-tunneled Hemodialysis Catheters (32, 12%), and Femorally Inserted Central Catheters (24, 8%), with a median of 3 [3–4] lumens per catheter. The most frequent site of cannulation was internal jugular vein (223, 80%). Catheter-vein diameter ratio was 0.22 [0.17–0.26]. Twenty-one (8%) CVC insertions needed more than one cannulation attempt. Thirty-nine (27%, 95%CI 20–34) patients suffered from CRT. Patient's crude incidence rate was 29.2 (21.3–40.0) CRT*1000/pd. Considering all catheters, the proportion of CRT was 39/277 (14%, 95%CI 10–19). Crude incidence rate (95% CI) was 18.3 (13.4–25.1) CRT*1000/cd. Nelson-Aalen cumulative hazard estimation of developing CRT is shown in Figure 1. Thirty-five CRTs (90%) were partial thrombosis, while only 4/39 (10%) were complete thrombosis. Notably, no CRT was symptomatic.



Conclusion: In our population, the proportion of patients who developed a CRT was 27%. Incidence rate of CRT was 18.3 CRTs*1000/cd. All CRTs were asymptomatic. To our knowledge, this is the first prospective observational cohort of an adult non-oncologic ICU population assessing the incidence rate of CRTs.

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Acknowledgements: The nature of the study is nonprofit medical research.

000299

Improved Survival with Extracorporeal Membrane Oxygenation Bridging to Lung Transplantation: a 10-Year Experience of a Single High-Volume Center

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Intensive Care Medicine Experimental 2022, **10(2)**:000299

Introduction: Lung transplantation (LTx) is the last resort for end-stage lung diseases, but donor scarcity limits timely lung transplantation. Extracorporeal membrane oxygenation (ECMO) as a bridge to transplantation (BTT) has prolonged survival and delayed deconditioning until the donor lungs become available. Our center has increasingly used ECMO bridging to LTx since 2011.
Objectives: We aimed to review our high-volume experience of BTT over the past 10 years and determine factors associated with better patient outcome.
Methods: Electronic medical records of patients undergoing LTx from 2008 to 2021 at our institution were retrospectively analyzed. The data was divided into the earlier period ("Period 1") and the later period ("Period 2"), and the basic characteristics and patient outcomes of the two groups were compared. Kaplan–Meier estimation was used to evaluate differences in mortality of BTT and non-BTT patients within each group.
Results: Out of 169 adult patients receiving LTx or heart-LTx, 99 (59%) patients were on ECMO. The number of BTT patients increased over time, and 27 out of 36 (75%) LTx patients were on BTT in 2021 alone. Overall, the mortality rate decreased with increments of cumulative BTT cases. Mortality within 28 days of LTx was significantly lower in Period 2 compared to that of Period 1 ($p < 0.01$). Probable contributing factors include use of right ventricular assist device with an oxygenator (Oxy-RVAD), adoption of veno-arterial (V-A) ECMO as the intraoperative circulatory support, and implementation of rehabilitation program during the more recent period (Period 2).

Conclusion: Employment of preoperative Oxy-RVAD, intraoperative V-A ECMO, and perioperative rehabilitation program were associated with improved survival in patients bridged to LTx on BTT. Accumulation of expertise and competence through deliberate practices over time can promote patient survival with BTT.

000320

Red blood cell transfusion in veno-arterial extracorporeal membrane oxygenation: a mixed-methods cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000320

Introduction: Transfusion thresholds and occurrence rates of red blood cells (RBC) transfusion in patients receiving veno-arterial extracorporeal membrane oxygenation (VA ECMO) have been evaluated only in single-center observational studies, thereby showing large heterogeneity.
Objectives: To assess transfusion practices by describing a) the number of RBC transfusion during ECMO, b) the differences in hemoglobin (Hb) course during ECMO between different applied Hb thresholds and c) patient outcomes.
Methods: A survey and retrospective observational study were conducted in 16 ICUs worldwide. The survey aimed to make an inventory of local transfusion thresholds and practices. RBC transfusion thresholds were grouped as 'restrictive' (Hb $\leq$ 7.5 g/dL), 'liberal' (Hb $\geq$ 9 g/dL) or 'intermediate' regimen (7.5–9 g/dL). Data was collected retrospectively from Jan-2018 to Jul-2019. Exclusion criteria were: other modes than VA ECMO, or treatment duration < 24 h. Data collection consisted of demographics, ECMO-characteristics, patient outcomes and daily questionnaires (laboratory values and transfusion). After checking for normality, the threshold-groups were compared using either a Kruskal Wallis or one-way ANOVA and post-hoc using Dunn's or Tukey's test for multiple comparisons.
Results: Out of 420 included patients receiving VA ECMO, 375 patients (89%) received one or more RBC transfusions. During a median ECMO duration of 5 days (interquartile range [IQR] 3–5 days), a total of 8 RBC units (IQR 3–17) were transfused, resulting in 1.6 RBC units (IQR 0.7–3) per day while on ECMO. A restrictive threshold was applied to 117 patients (4 centers), intermediate to 150 patients (6 centers) and liberal to 153 patients (6 centers). Daily nadir Hb was significantly higher in patients with a liberal transfusion threshold, independently of RBC transfusion and hemorrhage (all $p < 0.001$). Also, in case of a RBC transfusion in patients with a liberal threshold, nadir Hb was higher than the threshold (median difference in Hb + 0.4 g/dL [IQR -0.7 to 1.1]), also in the absence of bleeding. The opposite accounted for patients with a restrictive threshold (median difference in Hb -0.5 g/dL [IQR −1.5 to 0.1], $p < 0.001$). No differences were found in patient outcomes including 28- and 60-day survival, hemorrhagic complications and acute kidney injury (AKI) between the threshold groups.
Conclusion: Transfusion of RBC was very common in patients receiving VA ECMO, and the quantities were large. During ECMO, the Hb course was in line with the applied thresholds, independently of hemorrhage, therefore implying protocol adherence. No differences in patient outcomes were found between liberal and restrictive thresholds.

Anaesthesia & Peri-operative Medicine 3

000323

Effect of incremental PEEP titration on postoperative pulmonary complications in patients undergoing emergency laparotomy: a randomized controlled trial

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Intensive Care Medicine Experimental 2022, **10(2)**:000323

Introduction: Pulmonary complications following surgery adversely affect clinical outcomes and lead to increased hospital costs, longer hospital stays, and higher mortality [1–3]. Postoperative pulmonary complications (POPC) are among the more serious complications following emergency abdominal surgery with an estimated incidence of 20–30%. Previous data indicated that personalized positive end expiratory pressure (PEEP) titrated by the lowest driving pressure might reduce postoperative atelectasis and postoperative pulmonary complications [4].
Objectives: The primary objective of this study was to identify whether individualized PEEP titration reduces the incidence of POPC up to 7 days after surgery when compared to a fixed PEEP of 5 cm H2O. The secondary objectives were to compare intraoperative oxygenation status, hypotension & bradycardia, requirement of rescue therapy, length of postoperative hospital stay & ICU stay, oxygen free days at day-28 and in-hospital mortality.
Methods: n = 168 adult patients (aged between 18 and 75 years), undergoing emergency laparotomy (of an expected duration of more than 2 h) under general anaesthesia were recruited in this study. Patients were randomized according to a computer-generated random number table in two groups. In group T patients, PEEP was titrated incrementally till lowest driving pressure was achieved and in group F patients, PEEP of 5 cm H2O was used throughout the surgery. All analyses were performed on Jamovi (The Jamovi Project, v 2.3), which is a R (R version 4.1) based statistical programme. Binary outcomes were reported as relative risk (RR) with 95% confidence interval (CI) and continuous outcomes were reported as mean or median difference with 95% CI.
Results: Mean (standard deviation) of the recruited patients was 41.7(16.1)y and 48.8% (82 of 168 patients) were female. Incidence of POPC at postoperative day 7 were similar in both the study groups [RR (95% CI) 0.81 (0.58, 1.13); p = 0.25]. Incidence of intraoperative hypotension [p = 0.75], oxygen free days at day 28 [p = 0.27], length of postoperative hospital stay [median difference (95% CI) -1 day (-3, 1); p = 0.57], length of postoperative ICU stay [p = 0.28] and in-hospital mortality [RR (95% CI) 0.84 (0.58, 1.21); p = 0.38] were similar in two groups.
Conclusion: We have found that titrated PEEP by lowest driving pressure was not associated with a reduced incidence of POPC in patients undergoing emergency laparotomy when compared to a fixed PEEP of 5 cm H2O. However, the incidence of hypotension and bradycardia was also not increased with titrated PEEP. Titrated PEEP was used in a

number of previous clinical studies in the various elective surgical scenarios and postoperative atelectasis was reduced with titrated PEEP [4, 5]. Despite physiological benefits, the association between titrated PEEP and POPC is less well defined and needs further evaluation.

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Acknowledgements: No Grants were received for this study.

000337

Cardiac Surgery Outcomes of COVID-19 Recovered Patients in a Cardiology Referral Center in the Philippines: A Single Center Experience

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Intensive Care Medicine Experimental 2022, **10(2)**:000337

Introduction: Current data suggest elevated mortality and poor surgical outcomes in patients with peri-operative COVID-19 infection. Limited studies have looked into the outcomes of cardiac surgery in patients who have recovered.
Objectives: This study investigates the in-hospital outcomes of adult patients who had COVID-19 prior to their cardiovascular surgery at the primary cardiac referral center in the Philippines.
Methods: This retrospective cohort study included 40 adult patients with previous COVID-19 diagnosis who underwent cardiac surgery at our institution from April 2020 to December 2021. Baseline characteristics, pre-operative assessments, operative details and in-hospital outcomes were collected through chart and electronic medical records review. Data were compared to 50 propensity-matched randomly selected non-COVID-19 patients who underwent cardiac surgery and generally identical post-operative management during the same study period.
Results: There were no significant difference in most of the baseline characteristics between groups except for the functional status (p-value 0.006), cardiopulmonary bypass time (p-value 0.027) and vaccination status (p-value 0.006). The mean age was 55 years, predominantly male; and hypertension is the most common co-morbidity. The median Euroscore is 1.15% (IQR, 0.76–2.19). Longer cardiopulmonary bypass times were observed in COVID-19 patients, median 165 min (IQR, 137–228) vs 134 min (IQR, 118–193) for non-COVID patients. COVID-19 recovered patients have a 10% in-hospital mortality rate, mostly due to Hospital Acquired Pneumonia. In both groups, however, there was no significant difference in their primary and secondary post-surgical outcomes.
Conclusion: This research is the first study done locally that specifically addressed cardiovascular surgery outcomes in COVID-19 recovered patients. The outcome of cardiac surgical patients who had COVID-19 pre-operatively is comparable to their non-COVID cohort.

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000363

Let's wake up and breathe! A quality improvement project to improve sedation practice and increase frequency of nurse-led spontaneous awakening trials on our ICU

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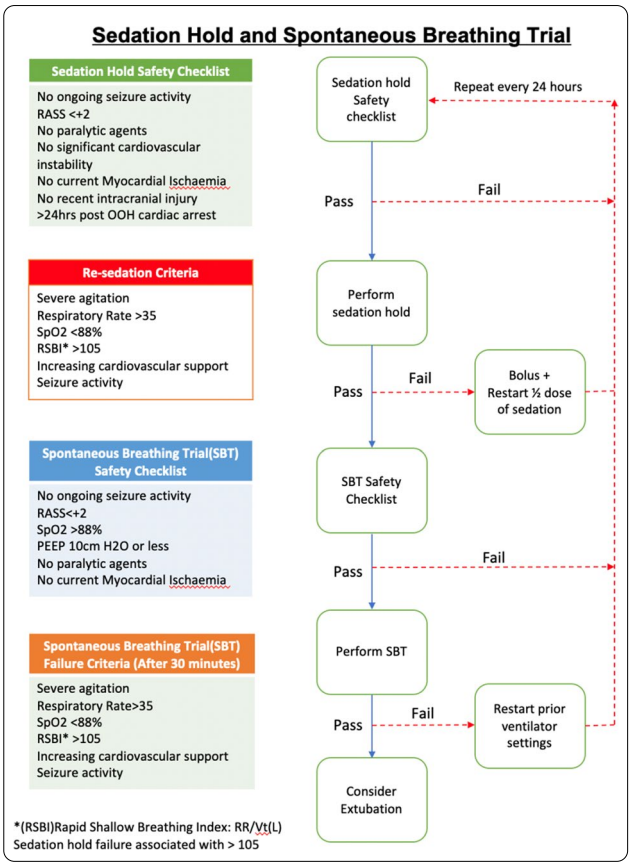
Intensive Care Medicine Experimental 2022, **10(2)**:000363

Introduction: While intravenous sedation is ubiquitous on the intensive care unit, there is an awareness of its deleterious effects. Daily sedation holds (otherwise known as spontaneous awakening trials, SATs) have been recommended where clinically appropriate. The intended aims are to reduce cumulative sedation dose and allow assessment of a patient's neurological status and readiness for extubation. There is evidence that this results in a reduced duration of mechanical ventilation, reduced ICU stay and reduced mortality. One of the consequences of the COVID-19 pandemic has been a reduced focus on sedation practice, with increased dosage of sedative agents reported for such patients. With this in mind, we sought to evaluate and improve sedation practice on our ICU.
Objectives: To evaluate our practice of sedation, frequency of SATs for eligible patients and survey our nursing staff to seek out barriers to their use. Using initial audit and survey data, we aimed to implement change by raising awareness of the benefits of lighter sedation and daily SATs. By creating a standardized approach to SATs, we aimed to empower the nursing staff to carry them out independently.
Methods: The project took place between August 2021 and January 2022 and followed the PDSA cycle methodology. 34 patient files were examined retrospectively from 23/08/2021 to 05/09/2021. Data was recorded for: Depth of sedation (RASS), documented plan for SAT, contraindications to SAT, method of performing SAT, indications to restart sedation and method of restarting sedation. A survey for nursing staff (n = 28) was undertaken to evaluate awareness of the rationale for SATs and confidence in practice of SAT independently. A package of interventions was delivered during a 'sedation week'. This included the launch of a local sedation hold checklist and flowchart (a modified version of the 'Wake up and breathe' protocol) with daily teaching sessions on sedation and the benefits of SAT. A repeat audit following intervention was performed, with retrospective analysis of data from 28 patient files between 03/01/2022 and 26/01/2022.



Results: In the baseline audit, 26/34 had no contraindications to SAT, with 15/26(57%) undergoing SAT. Of the 8/15(53%) restarted on sedation, 4/8 patients were restarted at the same rate of IV sedation, with 3/8 patients restarted on an increased rate and only 1/8 restarted at a reduced rate. The key themes from the survey of nursing staff were: Low confidence to perform a SAT (primarily amongst junior nurses) and low levels of awareness of the intended benefits of lighter sedation and SAT. There was a wide variability in determining suitability for SAT, preferred method of SAT and restarting sedation. The post intervention audit demonstrated a reduction in mean RASS from -3 to -2. 21/28 patients were eligible for a SAT, with a larger proportion (14/21, 67%) undergoing SAT. Of the patients requiring re-sedation, 3/4 received a bolus and restarted on half the original rate of infusion (as per the protocol), with 1/4 restarted at the same rate of infusion. There were no adverse events recorded during the study period.
Conclusion: We have demonstrated an improvement in number of sedation holds performed, resulting in a cumulative reduction in level of sedation of our ventilated patients without any adverse effects. Our survey results highlighted the need for stakeholder involvement, education and empowerment. Our modification of the wake up and breathe protocol was tailored for our unit in conjunction with senior nursing staff. This allowed for sedation holds led by the nursing team, which we feel is a vital component of successful practice change on the ICU. Further PDSA cycles have been organized to identify sedation champions amongst nursing and medical staff, involving nursing educators to improve awareness and modifying the protocol to create sustained change.

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Acknowledgements: No grants were required in this project.

000375

Postoperative clinical outcomes after emergency abdominal surgery in patients with hematologic malignancy admitted to the surgical intensive care unit

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Intensive Care Medicine Experimental 2022, **10(2)**:000375

Introduction: Hematologic malignancy (HM) alters the immune response due to intrinsic changes in their immune system, and the resulting immunosuppressed status affect recovery after surgery. However, there were insufficient studies on clinical outcomes about postoperative critical care in patients with HM after emergency abdominal surgery.
Objectives: The aim of this study was to compare clinical outcomes after emergency abdominal surgery in patients with HM to patients with solid tumor.
Methods: A total of 143 patients admitted to the intensive care unit (ICU) immediately after emergency surgery for the acute abdomen from January 2016 to December 2020: HM group (N = 23), solid tumor (ST) group (N = 120). Among them, we matched 23 patients with HM to 46 controls based on age, sex, severance nutritional screening index (SNSI), American Society of Anesthesiologists (ASA) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, and Sequential Organ Failure Assessment (SOFA) score, and compared postoperative and clinical outcomes.
Results: The HM group had a better nutritional status (87.0% vs. 60.8%, $p = 0.016$) and a higher frequency of previous steroid use (78.3% vs 52.5%, $p = 0.022$). In addition, in the HM group, the frequency of preoperative abdominal pain was less (65.2% vs 85.0%, $p = 0.037$) and the proportion of acute abdomen by perforation was higher (78.3% vs 66.7%, $p = 0.045$). Clinical outcomes showed that the HM group had a longer length of hospital stay (65.2 ± 53.3 vs 24.3 ± 20.0, $p = 0.001$) and a longer postoperative hospital stay (50.5 ± 10.6 vs 21.6 ± 20.0, $p = 0.012$), and higher in hospital mortality (34.8% vs 15.8%, $p = 0.044$). After propensity score matching, the HM group still had a higher rate of previous steroid use (78.3% vs 54.4%, $p = 0.048$), a longer length of hospital stay (65.2 ± 53.3 vs 26.0 ± 20.1, $p = 0.001$), and a longer postoperative hospital stay (50.5 ± 10.6 vs 22.0 ± 15.0, $p = 0.003$). However,

there was no statistically significant difference in in-hospital mortality (34.8% vs 13.0%, p = 0.068).
Conclusion: Critically-ill patients with hematologic malignancy had comparable clinical outcomes after emergency abdominal surgery compared to those with solid tumors. Therefore, surgical interventions can be under active consideration in patients with hematologic malignancy when it is necessary.

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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.

000377

The Association of Albumin and Nutritional Indices with the Occurrence of Delirium in Patients Admitted to the Cardiac Intensive Care Unit

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Intensive Care Medicine Experimental 2022, **10(2)**:000377

Introduction: Malnutrition was related to development of delirium which is associated with clinical outcomes in patients admitted to the intensive care unit. However, limited data are available on the association of nutritional indices with the development of delirium in cardiac intensive care unit (CICU). Thus, the assessment of the nutritional status and nutritional therapy are a crucial for prevention of delirium in patients admitted to ICU. To date, various tools have been developed to identify the risk of malnutrition in critically-ill patients. Among these, the prognostic nutritional index (PNI) was first suggested to be a nutritional index and used as a predictor of surgical risk for patients with gastrointestinal malignancy in the 1980. The Geriatric Nutritional Risk Index (GNRI) is a simple and accurate tool for the estimating the risk of morbidity and mortality in hospitalized elderly patients. The Controlling Nutritional Status (CONUT) is useful tool for early detection of undernutrition in all hospital inpatients. However, limited data are available on the clinical significance of nutritional indices and their association with the development of delirium in CICU.
Objectives: We aimed to investigate whether the nutritional indices can predict the occurrence of delirium and predictive performance of each component constituting nutritional indices in patients admitted to CICU.
Methods: We enrolled 2,783 patients admitted to the CICU of Samsung Medical Center for more than 24 h between September 2012 and December 2018. We assessed the nutritional status at admission using three nutritional indices GNRI, PNI, and CONUT and compared predictive performances for the development of delirium among nutritional indices using Delong's test. Receiver-operating-characteristics (ROC) curve analysis was used to explore discriminant functions (area under the curve, AUC) to predict delirium, and the optimal cut-off value was acquired using the Youden index method. Discriminant functions were compared by 2-tailed paired comparison of ROC analysis. Logistic regression analysis was performed to identify the risk factors for delirium development. In addition, the cubic spline curve shows the distribution of delirium occurrence by value of each component of nutritional indices, and a histogram was added to indicate the relationship between delirium and spline curves. Four continuous variables of albumin, ALC (absolute lymphocyte count), body weight/IBW (ideal body weight), and total cholesterol were analyzed.
Results: Delirium was developed in 678 patients (24.3%) when patients were assessed three times daily until seven days of ICU stay. Nutritional indices had fair predictive performances of the development of delirium in patients with critically-ill cardiovascular disease using areas under the receiver-operating characteristic curve (AUROC: 0.729 for the GNRI, 0.728 for PNI and 0.762 for CONUT). Furthermore, the AUROC of albumin alone (0.77, 95% CI, 0.75–0.79) was significantly greater than those of GNRI ($P < 0.001$) and PNI ($P < 0.001$). In multivariable analysis including each component of nutritional indices, albumin was significant predictor for the occurrence of delirium but not ALC, body weight/IBW, and total cholesterol level as component of nutritional indices. In cubic spline curve, the development of delirium decreased linearly as the albumin levels increased. However, ALC, body weight /IBW and total cholesterol show a U-shaped graph in which the development of delirium initially decreases and then increases as each value continues to increase.
Conclusion: Predictive performances of nutritional indices for the development of delirium were acceptable and albumin alone as a common component of nutritional indices may be a simple and useful indicator for the development of delirium in patients admitted to CICU.

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000434

Prognostic significance of red blood cell transfusion trigger in critically ill patients with sepsis or septic shock: A Prospective Observational Study

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Intensive Care Medicine Experimental 2022, **10(2)**:000434

Introduction: This study was conducted in septic critically ill patients to find out the transfusion trigger and whether this trigger is associated with any difference in 28-day and 90-day mortality. In addition whether the number of RBCs transfused and the age of RBCs at transfusion can predict mortality and other adverse outcome was also assessed.

Methods: In this prospective observational study n = 108 adult critically ill patients with sepsis of 18–70 years of age were included. Baseline demographic and severity of illness parameters were observed. Transfusion trigger, number of RBCs transfused, and the age of RBCs at transfusion were noted. The primary outcome was 28-day mortality. Secondary outcomes were 90-day mortality, length of ICU stay, length of hospital stay, duration of mechanical ventilation, vasopressor days, and requirement of renal replacement therapy.
Results: Out of 108 patients, 28-day survival was 72.2% (n = 78) and 90-day survival was 61.1% (n = 66). Median (IQR) transfusion trigger was 6.9(6.7–7.1)g/dl. On multivariate logistic regression analysis, APACHE II [adjusted OR(95%CI) 0.86(0.78, 0.96); p = 0.005], admission platelet count [adjusted OR(95%CI) 1.69(1.01, 2.84); p = 0.043] and cumulative fluid balance (CFB) [adjusted OR(95%CI) 0.99(0.99, 0.99); p = 0.005] were predictors of 28-day mortality (model AUROC 0.81). APACHE II [adjusted OR(95%CI) 0.88(0.81,0.97); p = 0.013], transfusion trigger [adjusted OR(95%CI) 3.00(1.07,8.34); p = 0.035] and CFB [adjusted OR(95%CI) 0.99 (0.99,0.99); p = 0.044] were predictors of 90 day mortality (model AUROC 0.82).
Conclusion: In critically ill adult patients with sepsis, hemoglobin transfusion trigger, number of RBC transfused and age of RBC do not affect 28-day mortality or other adverse outcomes.

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Acknowledgements: Nil.

000435

Comparison of two different doses of intrathecal dexmedetomidine as adjuvant to levobupivacaine for spinal anesthesia in patients undergoing infra-umbilical surgery

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Introduction: Spinal anesthesia is the most commonly performed central neuraxial block for surgeries below umbilicus. Multiple adjuncts have been utilized previously to alter the sensory and motor block characteristics for better patient care. Dexmedetomidine, a selective alpha 2 agonist has been used intrathecally for its nociceptive properties. We aim to compare the clinical efficacy of two different doses of dexmedetomidine given intrathecally as an adjunct to isobaric levobupivacaine.
Methods: This prospective, randomized study was carried out amongst 100 adult patients undergoing below umblical surgeries, in the age group of 18–65 years of physical status American Society of Anesthesiologists Classes I and II. Group D1 patients received 3 ml (15 mg) of 0.5% isobaric levobupivacaine + 2.5 µg dexmedetomidine (in 0.5 ml saline) while Group D2 patients received 3 ml (15 mg) of 0.5% isobaric levobupivacaine + 5 µg dexmedetomidine (in 0.5 ml of saline). The volume of the drug administered was kept constant (3.5 ml) in both the groups to avoid any potential bias in the study. Sensory and motor block characteristics, duration of effective analgesia and side effects were analyzed between the groups.
Results: There was no difference in Groups D1 and D2 in time to reach T6 level (8.09 ± 3.09 vs. 8.40 ± 2.18 min, P = 0.561). Two-dermatome block regression in group D2 (153.72 ± 12.46 min) was significantly (P < 0.001) prolonged than group D1 (109.52 ± 12.23 min). Early onset of motor block was found in group D2 (1.00 ± 0.00 min) in comparison to D1 (1.16 ± 0.37 min) and was significant (P = 0.003). The mean Visual analogue score (VAS) at 6 h after block were significantly better and lower in Group D2 as compared to group D1 (2.02 ± 0.84 vs. 3.66 ± 0.75, P < 0.001). Adverse effects were similar in both the groups.
Conclusion: It is concluded that Group D2 has early-onset motor block and prolonged duration of sensory and motor block and longer duration of postoperative analgesia than Group D1.

000444

Comparison of premedication in nebulized form of dexmedetomidine and ketamine in preschool children undergoing abdominal surgery

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Intensive Care Medicine Experimental 2022, **10(2)**:000444

Introduction: The most distressing and stressful period for children undergoing surgery is the preoperative period.1 Parentral separation, peer of surgeon and hospital, and fear of injection increases preoperative anxiety, Various sort of premedication used in paediatric population to sedate the patient, To avoid preoperative anxiety and emergence delirium.
Objectives: The aim of our study was to compare efficacy of dexmedetomidine and ketamine for sedation, emergence delirium, administered by nebulization 30 min prior to induction in preschool children undergoing abdominal surgery.
Methods: Ninety selected patient were randomized to 3 group to be premedicated with nebulized dexmedetomidine 3 micro/kg (group D), ketamine 3 mg/kg (Group K), Normal saline 3 ml (group NS). The primary objective was to compare sedation, parent separation and emergence agitation. Secondary objective were to compare hemodynamic parameter, mask acceptance and complication if any.
Results: The median sedation score in operating room was 2, 2.5 and 4 in group D, K and NS respectively (p < 0.001). Subjects of group D showed higher mask acceptance (p < 0.001), and better parent separation anxiety (p < 0.001). The incidence of emergence agitation was lower in group D compare to group K (p < 0.001).
Conclusion: Preschool children premedicated with nebulized dexmedetomidine had more satisfactory sedation, less postoperative agitation, less parent separation anxiety than patient medicated with ketamine.

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000462

Severity score derived from COVID-19-associated hemostatic abnormalities (CAHA) study in patients with severe COVID-19 disease: the HEMOCOV Study

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Introduction: CAHA is a condition linked with inflammation, endothelitis and coagulation dysregulation related to immunothrombosis. Although this coagulopathy has been described as a significant pathophysiologic mechanism for severe COVID-19, patient stratification based on CAHA analysis is still missing.
Methods: An open-label, prospective observational study, conducted in patients with COVID-19-related acute respiratory failure (ARF) admitted in Intensive Care Unit (ICU) in an Academic Tertiary Care Hospital. Clinical performance evaluation and protocol coagulation studies, including thromboelastometry, were analyzed at ICU admission and thereafter at pre-established 5 day-interval until day 30, ICU discharge or death. Main objective was the identification of a biomarkers score for poor outcome.
Results: 145 patients with COVID-19 related ARF admitted in ICU were eligible for analysis. Median age was 68 years (IQR 55–74). During ICU hospitalization, 66.9% were submitted to invasive mechanical ventilation (IMV) and 18.4% to extracorporeal membrane oxygenation support. Thrombotic (22.1%) or hemorrhagic (15.1%) events were documented, as ICU mortality (35%). Hypercoagulability and specially hypofibrinolysis since ICU admission was observed, being more severe and pronounced in non-survivors when compared with survivors. Multivariable logistic regression model to predict mortality identified seven parameters. In ROC analysis, a severity score consisting in 5 parameters [age (> 68 years), LI30-INTEM (equal 100%), CFT-FIBTEM (< 70 mm)], platelets count (> 253 × 109/L), and hematocrit (< 37.8%)] was associated with poor outcome prediction.
Conclusion: The use of viscoelastic testing for assessing CAHA in patients with severe SARS-CoV-2 infection may be useful for further risk stratification, based on application of a severity score derived from coagulation studies.

Anaesthesia & Peri-operative Medicine 4

000467

Hemocov Study: a prospective study of conventional and point-of-care coagulation parameters in severe COVID-19 patients

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Introduction: COVID-19-associated hemostatic abnormalities (CAHA) includes profound inflammation, endothelitis and coagulation dysregulation related to immunothrombosis. Coagulation studies, mainly regarding conventional coagulation essays (CCE), have been proposed to identify severe patients, and possibly to guide anticoagulation therapy.
Methods: An open-label, prospective observational study, ethical committee approved, was conducted in patients with COVID-19-related acute respiratory failure (ARF) admitted to an Intensive Care Unit (ICU) in an Academic Tertiary Care Hospital. CCE, thromboelastometry and biochemical analysis plus clinical performance evaluation were analyzed at ICU admission, at pre-established 5 day-interval until day 30, ICU discharge or death.
Results: 145 patients with COVID-19 related ARF admitted to ICU were eligible for analysis. Mean age was 68 years (IQR 55–74). During ICU hospitalization, 66.9% were submitted to invasive mechanical ventilation (IMV) and 18.4% to extracorporeal membrane oxygenation support. Thrombotic (22.1%) or hemorrhagic (15.1%) events were documented. 35% of patients died.
Some coagulation and biochemical parameters were significantly different ($p < 0.05$) between ICU admission and discharge. Several factors associated with mortality, with significant p-value, were identified at ICU admission: age, IMV, hematocrit, platelets and lymphocyte count, uremia, glomerular filtration rate, albumin, troponin, FVIII, vWF:RCo and thromboelastometry parameters (hypercoagulability and hypofibrinolysis).
Conclusion: CAHA is characterized by hypercoagulability and hypofibrinolysis. Integration of viscoelastic testing for coagulation analysis may improve identification of patients with particular ominous prognosis.

000474

Isoflurane sedation delivered via a device with reduced dead space in intensive care patients: a prospective substudy of a randomized trial

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Introduction: Devices used to deliver inhaled sedation increase ventilatory dead space, potentially resulting in higher minute ventilation requirements. The Sedaconda ACD-S for the administration of isoflurane has reduced dead space (50 ml) compared to the first larger version ACD-L (100 ml), enabling the ventilation of patients with lower tidal volumes [1,2]. We therefore hypothesized that the use of the ACD-S reduces minute ventilation mostly by reducing tidal volumes compared to the ACD-L in intensive care patients over the first 24 h of sedation.
Objectives: To assess the effects of dead space reduction in a device used for isoflurane sedation of mechanically ventilated intensive care patients.
Methods: This is a substudy of a randomized trial that assessed the non-inferiority of inhaled isoflurane sedation to intravenous propofol sedation in 301 intensive care patients [3] (DRKS-ID: DRKS00020240), approved by the responsible ethics committee (approval no. 11/17, Saarland Medical Association). Data of the first 24 h after study inclusion was analyzed. Primary outcome was minute ventilation. Secondary outcomes were tidal volume, respiratory rate, arterial carbon dioxide tension, and isoflurane consumption. Linear mixed models were used to compare the effects of using no device (propofol sedation), ACD-S (dead space 50 ml) or ACD-L (dead space 100 ml).
Results: In the underlying trial, 151 patients were randomized to propofol and 150 to isoflurane sedation. In the inhaled sedation group, 64 patients received isoflurane via the ACD-S and 86 via the ACD-L. ACD-L significantly increased minute ventilation, tidal volume, respiratory rate and arterial carbon dioxide pressure compared to propofol sedation (Table 1). In contrast, ACD-S did not significantly affect ventilatory parameters compared to propofol sedation (Table 1). However, volatile anesthetic consumption was slightly reduced with the ACD-L compared to the ACD-S: mean difference: -0.13 [(mL/h)/(L/min)] (95%CI: -0.20, -0.07); $p < 0.001$.
Table 1 Comparative effects of using the ACD-L, ACD-S or no device (propofol) on ventilation

Parameter	Comparison	Average difference	95% confidence interval	*p*
Minute ventilation [L/min]	ACD-L vs. ACD-S	1.3	[0.6, 2.0]	< 0.001
	ACD-L vs. propofol	1.3	[0.7, 1.8]	< 0.001
	ACD-S vs. propofol	− 0.07	[− 0.7, 0.6]	0.823
Tidal volume [mL]	ACD-L vs. ACD-S	20	[− 15, 55]	0.255
	ACD-L vs. propofol	44	[16, 72]	0.002
	ACD-S vs. propofol	24	[− 7, 55]	0.126
Respiratory rate [breaths/min]	ACD-L vs. ACD-S	1.7	[0.4, 2.9]	0.011
	ACD-L vs. propofol	1.2	[0.1, 2.2]	0.025
	ACD-S vs. propofol	− 0.5	[− 1.6, 0.6]	0.392
Arterial carbon dioxide partial pressure [mmHg]	ACD-L vs. ACD-S	2.3	[− 0.4, 5.1]	0.098
	ACD-L vs. propofol	3.4	[1.2, 5.6]	0.002
	ACD-S vs. propofol	1.1	[− 1.4, 3.5]	0.380

Conclusion: Administering isoflurane with the new dead space-reduced ACD-S enables lower minute ventilation (mostly due to a reduction in tidal volume compared to the larger ACD-L) and does not significantly affect ventilatory measures compared to propofol sedation. Volatile anesthetic consumption increases slightly with the smaller ACD-S device but the difference appears clinically unimportant as long as the device is used within the recommended range of tidal volumes (300–800 mL).

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Acknowledgements: The statistical analysis was performed by an independent statistician paid by Sedana Medical AB, Danderyd, Sweden.

000477

Increased respiratory drive after prolonged isoflurane use in spontaneously breathing intensive care patients: a retrospective cohort study.

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Intensive Care Medicine Experimental 2022, **10(2)**:000477

Introduction: Isoflurane compared to propofol sedation is associated with increased respiratory drive being beneficial for maintaining spontaneous breathing in intensive care patients [1–3]. Own clinical observations suggest that this effect may extend well beyond the actual period of sedation. We therefore hypothesized that isoflurane versus propofol sedation for at least 48 h is associated with increased respiratory drive in spontaneously breathing intensive care patients within 72 h after sedation stop.
Objectives: To assess the post sedative effects of prolonged isoflurane versus propofol sedation on respiration.
Methods: This study was approved by the responsible ethics committee (approval no. 67/22, Saarland Medical Association). All patients treated throughout 2019 at a single academic intensive care center that were ventilated for at least 96 h and received isoflurane or propofol sedation for at least 48 h were included. Patients were observed 48 h before and 72 h after sedation stop. Only data from periods during which patients breathed spontaneously (including pressure-support ventilation and non-invasive ventilation) were collected from electronic health records. The primary outcome was increased respiratory drive within 72 h after sedation stop, defined as arterial carbon dioxide pressure < 35 mmHg and base excess > -2 mmol/L. Secondary outcomes were measures of acid–base balance and ventilation.
Results: 23 patients sedated with isoflurane and 41 patients sedated with propofol fulfilled inclusion criteria. Age, total ventilation and sedation time, tracheostomy, hemodialysis, and simplified acute physiology score II were not balanced between the sedation groups but had no significant influence on respiratory drive. Patients sedated with isoflurane were more likely to have increased respiratory drive after sedation stop than those sedated with propofol: risk ratio [95%CI]: 2.6 [1.3, 5.2], p = 0.005, whereby increased respiratory drive was equally frequent during sedation: risk ratio [95%CI]: 0.03 [-0.03, 0.09], p = 0.305. After sedation stop, tidal volumes were greater (mean [95%CI]: isoflurane: 609 [556, 668] mL, propofol: 503 [471, 540] mL, p = 0.002) and arterial carbon dioxide partial pressures were lower (median [95%CI]: isoflurane: 37 [35, 42] mmHg, propofol: 41 [39, 45] mmHg, p = 0.007), while respiratory rate did not differ in isoflurane versus propofol-sedated patients (Figure 1).

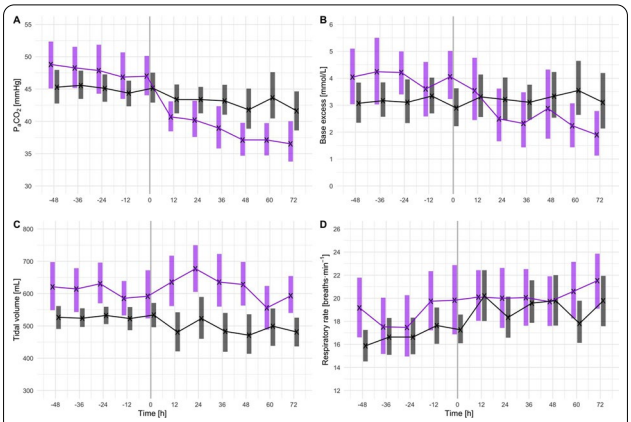

Figure 1: Acid–base balance and ventilation over time.

Sedation was stopped at time point 0. Data are presented in 12-h intervals as means ± 95% confidence intervals. Purple: isoflurane, grey: propofol.

Conclusion: Prolonged isoflurane use in intensive care patients is associated with increased respiratory drive after sedation stop. Stimulating effects of isoflurane on respiratory drive thus extends beyond the actual period of sedation.

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000545

The effect of continuous positive airway pressure in dengue with pulmonary leakage syndrome

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Intensive Care Medicine Experimental 2022, **10(2)**:000545

Introduction: Pulmonary leakage syndrome is a frequent complication of dengue patients with plasma leakage which has not had any specific treatment.
Objectives: We conducted a single-blind randomized controlled trial to determine the effect of continuous positive airway pressure (CPAP) in Dengue patients with evidence of pulmonary leakage syndrome.
Methods: Seventy Dengue patients with pulmonary leakage syndrome are either randomized to CPAP with or without supplementary oxygen (the 'CPAP group') or to symptomatic treatment (the 'control group'). In the CPAP group, CPAP between 8 and CPAP 14 cm H2O is applied in blocks of 4 to 12 h, alternated with 2-h blocks of supplementary oxygen if still needed. In the control group, only supplementary oxygen is given, and only if needed. To determine the effect of CPAP on clinical outcomes, lung ultrasound (LUS) aeration scores have been measured 3 times/day, a total of 9 measurement points over the three days follow-up period. Efficacy of CPAP at 72 h by proportional reduction in b line and pleural effusion accessed by LUS, dyspnea score, need for and duration of supplementary oxygen, rate of chest tube drainage rate, tracheal intubation, and hospital length of stay.
Results: CPAP accelerate reabsorption of water in lungs including interstitial edema as well as pleural effusion. Use of CPAP has been successful in the management of pulmonary leakage syndrome in Dengue patients in terms of decrease modified Borg scale and need for oxygen supplementation. (In analysis process).
Conclusion: CPAP is feasible and shortens time to resolution of pulmonary leakage syndrome in Dengue infection.

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Acknowledgements: The authors would like to express gratitude to the patient and the staff of the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

000547

Camera-based detection of cardiac arrhythmias in clinical setting

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Intensive Care Medicine Experimental 2022, **10(2)**:000547

Introduction: Vital signs can be measured contactless using video-cameras. This enables unobtrusive continuous monitoring also in low acuity settings, which could contribute to earlier detection of deterioration. This camera-based technology has been proven valid in controlled settings with healthy volunteers, but clinical validation is limited (1). For instance, validation during challenging conditions like cardiac arrhythmias is lacking. Atrial fibrillation (AF) is the third most common postoperative complication (2), therefore useful to detect fast and with high accuracy on hospital wards.
Objectives: The first objective of this study is to assess the validity of remote photoplethysmography (rPPG) in the detection of sinus rhythm (SR) and cardiac arrhythmias in comparison with ECG. The second objective is to assess the performance of a rPPG-based arrhythmia detection algorithm.
Methods: In an observational methods comparison study among patients presenting with AF or atrial flutter (AFl), heart rate (HR) before and after cardioversion was assessed with a visible light (RGB) camera and a standard ECG monitoring system (Philips MP70) as a reference. The rPPG algorithm (3,4) estimates heart rate based on subtle changes in skin color, caused by the cardiovascular pulse wave. Outcome measure was HR, classified per rhythm based on the ECG, as compared with the reference, presented as bias and precision (95% limits of agreement). Moreover, a machine learning algorithm was developed based on interbeat interval (IBI) related features to automatically detect cardiac arrhythmias. The diagnostic performance is evaluated with a receiver operating characteristics (ROC) curve and the area under the curve is determined.
Results: Thirty patients were included in the preliminary Bland–Altman analysis. Average recording duration per patient was 37 min. For SR and cardiac arrhythmias bias and 95% limits of agreement were -0.12 bpm (-4.64 to 4.41 bpm) and -0.59 bpm (-10.52 to 9.34 bpm), respectively. Forty patients were included in the preliminary machine-learning model. Cardiac arrhythmias were detected with 92.5% accuracy (sensitivity 92.5%, specificity 92.5%, AUC 0.96).
Conclusion: These preliminary results show how rPPG provides valid measurements of HR during SR and cardiac arrhythmias. Moreover, it shows the feasibility of automatic camera-based cardiac arrhythmia detection. Thus, inexpensive, off-the-shelf cameras have the potential to be a useful monitoring tool in clinical practice.

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Acknowledgements

1. This study is part of the research proposal funded by ZonMw, NWO, the Hartstichting and the Dutch CardioVascular Alliance (DCVA) of the funding call "Heart for a sustainable healthcare. Medical devices for early

recognition, prevention and treatment of cardiovascular diseases contributing to sustainable healthcare".
2. This study was initiated from the Eindhoven MedTech Innovation Center (e/MTIC), a research collaboration of the Technical University Eindhoven, Catharina hospital in Eindhoven and Philips Research (Netherlands). The authors wish to thank Philips Research for their constructive and practical contributions.

000560

Evaluation of nociception in unconscious critically ill patients with a multimodal approach

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Intensive Care Medicine Experimental 2022, **10(2)**:000560

Introduction: The assessment of pain in critically ill patients still remains a challenge for clinicians, in particular among those unable to communicate, mainly because of the paucity of reliable available tools [1].
Objectives: The aim of the study was to compare the pupillary dilation, the skin conductance and the autonomic nervous system function to pain stimulation in critically ill unconscious patients.
Methods: Prospective observational study including adult (> 18 years) patients admitted to the Intensive Care Unit and who were unconscious (Glasgow Coma Scale < 9 with a motor response < 5) and mechanically ventilated. Baseline electroencephalographic (EEG) activity was assessed using the spectral edge frequency (SEF, SedLine, Masimo, USA); a SEF $\leq$ 8 was considered as slow EEG (i.e. excessive sedation or brain injury). A tetanic stimulation was used to assess nociception; automated pupillometry (Algiscan, ID-MED, France) was used to compute the pupillary pain index score (PPI); a PPI > 4 was considered nociception. Concomitantly, the number of peak per second (NSCF) measured using skin conductance (MEDSTORM Innovation AS, Norway; > 0.27 peak/sec indicating nociception) and the instantaneous Analgesia Nociception Index (iANI, MDoloris Medical Systems, France; < 50 indicating nociception) were also collected.
Results: 80 patients were included; at baseline, patients showed a median Behaviour Pain Scale (BPS) of 3 [3–3] and Glasgow Coma Scale (GCS) of 3 [3–5], while SEF was 9 [6–13] Hz and pupil size 2.2 [1.9–2.9] mm. The tetanic stimulation resulted into a median pupillary dilation of 16 [6–25]% and a PPI of 5 [2–7]. A total of 44 (55%) patients showed nociception according to the PPI assessment, while 23 (29%) and 18 (23%) patients showed nociception according to the algesimeter and iANI assessment, respectively. No significant changes in physiologic variables, such as heart and respiratory rate or mean arterial pressure, were observed after the tetanic stimulation. No correlation between PPI, post stimulation iANI and SCA-derived variables was observed.
Conclusion: Detection of nociception is not reproducible across different devices in critically ill unconscious patients.

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000567

Chronological changes in multiple frontal EEG characteristics after general anesthesia in patients with or without postoperative delirium

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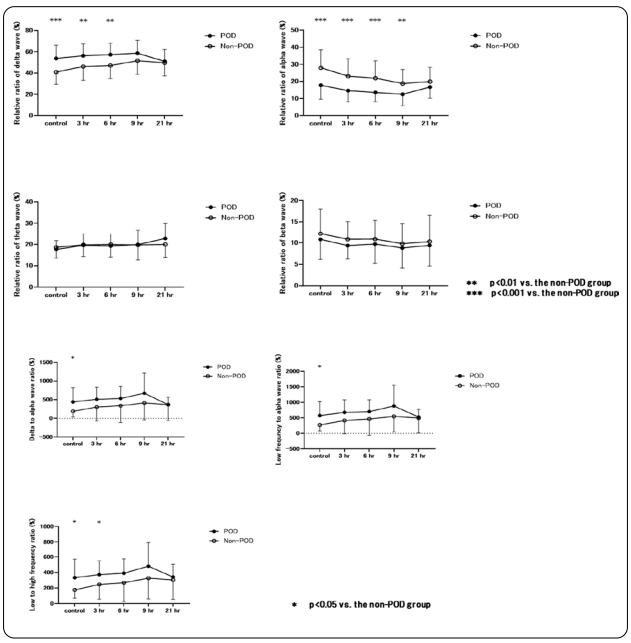
Intensive Care Medicine Experimental 2022, **10(2)**:000567

Introduction: It has been demonstrated that postoperative delirium (POD) patients showed decreased alpha power during the emergence from anesthesia (1) and increased delta power after the operation (2), suggesting possibility of multiple EEG waves indicating the POD. We have investigated the chronological changes in multiple EEG characteristics after general anesthesia in patients with or without POD.
Methods: This study was conducted after the approval of the ethical committees (UMIN 000,033,038). The patients who underwent radical cancer surgeries with reconstruction for esophageal cancer, oral floor cancer, or pharyngeal cancer under total intravenous anesthesia with propofol and remifentanil were included in this study. POD was diagnosed with the Intensive Care Delirium Screening Checklist in ICU. We have analyzed a continuous 3-min window of EEG data at control (within 20 min after anesthetic induction), and 3, 6, 9, and 21 h (sedation in ICU) after anesthetic induction. The depth of general anesthesia was adjusted by applying a bispectral index target between 40 and 60. We have compared the chronological changes in the relative ratio of each frequency band (delta, theta, alpha, and beta), delta-to-alpha ratio, low (delta and theta) frequency-to-alpha ratio, low-to-high (alpha and beta) frequency ratio between the patients with and without POD. Statistical analysis was performed with RM-ANOVA followed by Bonferroni correction. Furthermore, receiver operating characteristic curve analyses were performed to determine the best cut-off value of each EEG characteristics at control time for predicting POD. $P < 0.05$ was considered as significant.
Results: 84 patients were included in this study and 4 patients were excluded from the analysis. Of the remaining 80 patients, 25 developed POD and the other 55 did not. The POD group's relative ratio of delta wave at control was significantly higher than that of the non-POD group (53.8 ± 12.5 vs. 41.0 ± 11.6, $p < 0.001$). On the other hand, the POD group's relative ratio of alpha wave at control was significantly lower than that of the non-POD group (17.8 ± 8.2vs. 28.0 ± 10.6, $p < 0.001$). Relative ratio of theta and beta were no significant differences in each time between two groups. In both groups, the relative ratio of alpha waves in the EEG kept decreased, and the relative ratio of delta waves kept increased during surgery. The areas under the receiver operating characteristic curves of the relative ratio of delta wave, alpha wave, delta-to-alpha, low-to-alpha, and low-to-high frequency power ratio were 0.783 (95% confidence interval, 0.673–0.892), 0.776 (0.669–0.883), 0.783(0.676–0.889), 0.772(0.662–0.881), and 0.757 (0.642–0.872), respectively.



Conclusion: This study suggested that the behaviors of delta and alpha waves during the anesthesia could be useful indicators for predicting POD. In addition, delta-to-alpha, low-to-alpha, and low-to-high

frequency power ratio were also moderately accurate in predicting POD after highly invasive surgery.

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Acknowledgements: Not applicable.

000583

Efficacy of acute normovolemic hemodilution in pediatric and adolescent scoliosis surgery: a retrospective observational study

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Intensive Care Medicine Experimental 2022, **10(2)**:000583

Introduction: Scoliosis surgery is one of the most invasive and complex of the orthopedic surgeries, and the allogeneic blood transfusion (ABT), which can affect patient's postoperative outcomes, is often given to patients undergoing this surgery. Acute normovolemic hemodilution (ANH) can reduce the need for perioperative ABT in cardiac and non–cardiac surgery.
Objectives: The aim of the present study is to investigate whether acute normovolemic hemodilution (ANH) can reduce the rate and amount of perioperative allogeneic blood transfusion (ABT) in pediatric and adolescent scoliosis surgery.
Methods: This single-center, retrospective, observational study was approved by the ethical review board of our institution (2022–142). This study included 125 pediatric and adolescent patients who underwent scoliosis surgery between April 1, 2013 and December 12, 2021. The data were obtained from medical and anesthesia records. We divided the patients into groups according to ANH use: i.e., an ANH group and a control group, and compared their characteristics, perioperative data, and postoperative outcomes. Statistical differences between the ANH and control groups were assessed using Fisher's exact test for categorical variables and Mann–Whitney's U test for continuous variables. Propensity-score-adjusted multivariable logistic regression analysis was performed to determine whether ANH can reduce the need for perioperative ABT after adjusting patient's characteristics. P-value < 0.05 was considered statistically significant in all analyses.
Results: 125 patients were analyzed, with 95 and 30 in the ANH and control group, respectively. Characteristic and perioperative data and postoperative outcomes of patients are shown in Table 1. There were significant differences in age, height, body weight, and diagnosis between the two groups. 28 patients (22.4%) received intraoperative and/or postoperative ABT in the study. The intraoperative and postoperative ABT rate was significantly lower in the ANH group than in the control group (17.9% vs. 36.7%, p = 0.044). The amount of ABT was also significantly lower in the ANH group than in the control group [median (IQR): 0 (0, 0) mL/kg vs. 0 (0, 16.3) mL/kg, p = 0.033]. Although the incidence of surgical site infection was not significantly different between the groups, the incidence of other infectious complications including pneumonia and urinary tract infection were lower in the ANH group than in the control group. Additionally, the length of hospital stay was shorter in the ANH group than in the control group. The result of the propensity-score-adjusted multivariable logistic regression analysis is in Table 2. ANH use was independently associated with lower risk of perioperative ABT (OR: 0.15, 95% CI: 0.03, 0.77; p = 0.021), which suggests that ANH use can reduce the need for perioperative ABT. Additionally, intraoperative blood loss (per 1 mL/kg increase, OR: 1.09, 95% CI: 1.04, 1.13; p < 0.001) and duration of surgery (per 1 h increase, OR: 1.78, 95% CI: 1.18, 2.68; p = 0.006) were also independently associated with perioperative ABT.
Conclusion: This study showed that ANH use can reduce the rate and amount of intraoperative and postoperative ABT in pediatric and adolescent scoliosis surgery without increasing postoperative complications.

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000618

Survival analysis of lung transplant recipients in the United States between 2008–2015

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Introduction: Lung Transplants (LT) have helped improve survival and overall outcomes for many patients with end stage lung diseases. This study aims to determine survival in LT recipients based on age, gender and ethnicity.
Methods: We queried the Organ Procurement and Transplantation Network (OPTN) registry to calculate the 1 year, 3 year and 5-year overall survival (OS) rates using Kaplan–Meier method for LT performed in U.S. between 2008–2015. A comparison was made by subgrouping the LT recipients based on age (<1, 1–18, 18–49, 50–64 and > 65 years), gender (male and female), and race (Whites, Blacks, Hispanic/Latino, Asians, and Others).
Results: For all LTs performed between 2008–2015, OS rates were lowest in recipients aged > 65 years at 1 year [83.9 (95% CI: 82.2–85.3)], 2 year [62.1 (95% CI: 59.9–64.3)] and 5 years [44.8 (95% CI: 42.3–47.3)] as compared to other age groups. The overall survival rates at 1-year, 3-years and 5-years for different ethnicities and gender are tabulated in Table 1. Whites and males have proportionately higher rates of receiving LTs, but the OS rates are lesser as compared to Asians/Hispanics and females. Blacks have the lowest OS rates.
Conclusion: There is evident racial and gender disparity in overall survival of LT recipients in U.S. The likely explanation may be related to genetic factors, nature of underlying pathologies or social support.

000633

Mobilization practice in European ICUs and the impact of a structured sedation, analgesia and delirium training: a secondary analysis of data from the prospective, multicenter EuMAS study

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Intensive Care Medicine Experimental 2022, **10(2)**:000633

Introduction: Mobilization is a guideline-recommended intervention that directly improves patient outcomes [1]. Its implementation in routine practice has been subpar [2]. Commonly stated mobilization barriers include deep sedation, pain and delirium [3].
Objectives: To evaluate the impact of a structured training program on sedation, analgesia and delirium on mobilization practice in European ICUs.
Methods: This is an exploratory, preplanned, secondary analysis of the Enhancing European Management of Analgesia, Sedation, and Delirium (EuMAS) study (ClinicalTrials: NCT03553719), which assessed delirium, pain, and sedation (PAD) management for patients across 12 European centers at 3 cross-sectional time points. Between the first and second time point, centers received a structured, 6-week PAD training. We collected data on participating ICU patients' mobilization practice on a 6-point Likert scale from no mobilization to ambulation. Mobilization practices at the three point-prevalence assessments were compared using Chi-squared tests.
Results: A total of 430 patients (point prevalence 1: 195; 2: 129; 3: 106) across 12 ICUs were included. Baseline characteristics did not reveal significant differences between the time-points. Median length of stay in the ICU up to the day of the assessment was 7 days across all three timepoints and the median SOFA at admission was between 7 and 8 for all three timepoints. The proportion of patients receiving any kind of mobilization increased significantly (Fig. 1; $p = 0.03$) from 76% before to 89% one year after the training program. However, the intensity of mobilization, measured via the Likert scale, decreased significantly (Fig. 2; $p < 0.001$).

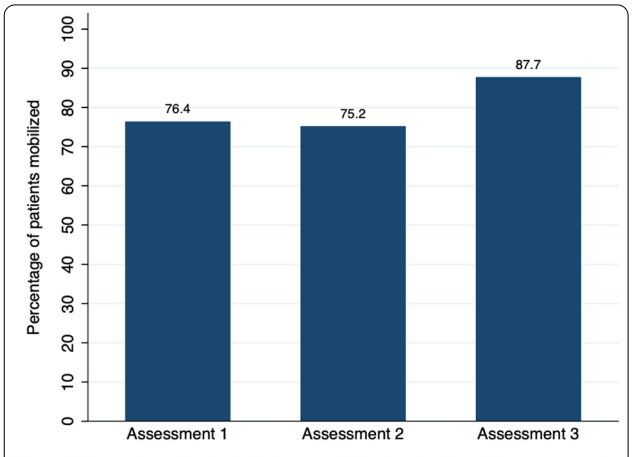

Figure 1. Percentage of patients that were mobilized on the day of the assessment.

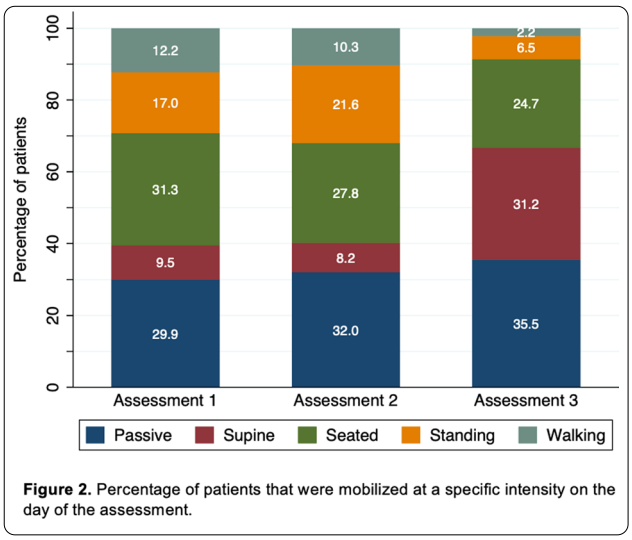

Figure 2. Percentage of patients that were mobilized at a specific intensity on the day of the assessment.

Conclusion: One year after the training program, the propability for mobilization increased significantly, however, the intensity of mobilization significantly decreased. Further analysis are necessary to investigate the detailed impact on delirium management on qualitative and quantitative aspects of mobilization.

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Acknowledgements: Funded by the European Society of Intensive Care Medicine (ESICM) with the Next Start-up Grant.

Anaesthesia & Peri-operative Medicine 5

000651
Analysis of surgical patients in the ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000651

Introduction: Complicated surgical patients have a high prevalence in the ICU with variable mortality.
Objectives: Analyze the differences observed between surgical and medical patients, and also factors related to mortality in surgical patients admitted to the Intensive Care Unit (ICU) in Punta Europa Hospital.
Methods: Prospective analysis of a cohort acomplished in an ICU of 15 beds, between 2019 and 2021. Data registered: demographics, risk factors, Central Venous Cathether (CVC), Invasive Mechanical Ventilation (IMV), Urinary Catheter (UC), severity scale, length of stay, antibiotherapy, microbiological isolation and mortality. Statistical analysis: numerical (mean and standards deviation or median and interquartile range [IQR]) and categorical variables (frequency and percentages). Comparisons: test of the chi2 (percentages) and t-test (mean) or Wilcoxon-Test (median). Multivariate logistics regression. Statistically significance with $p < 0.005$.

Results: 989 patients were included. Surgical patients (n = 127): SAPS II (34 [29] vs 27.5 [22], p = < 0.001), APACHE II 14 [9] vs 12 [10], p = 0.004). Neoplasia (46.5% vs 12.3%, p = < 0.001), malnutrition (11% vs 2.1%, p = < 0.001). Risk factors: previous ATB (64.6% vs 27.1%, p = < 0.001), parenteral nutrition (PN) (27.6% vs 4.3%, p = . < 001), CVC (95.3% vs 57.3%, p = . < 001), IMV (70.1% vs 39.4%, p < 0.001), UC (97.6% vs 70.2%, p = . < 001). Length of stay (hospital, days) 16.5 [21] vs 10 [14], p = < 0.001. Time (days): IMV (1 [1] vs 0 [4], p = 0.001), UC (4 [6] vs 4 [7], p = 0.025). Urgent surgery (n = 82) vs scheduled surgery (n = 45). Neoplasia (35.4% vs. 66.7%, p < 0.001). Origin: Community (29.3% vs. 6.7%), hospital (70.7% vs. 93.3%). Previous ATB (70.7% vs. 53.5%, p = 0.049). IMV days (1 [± 1.5] vs 1 [± 4], p < 0.015). Mortality (29.1%). SAPS II (50 [28] vs. 31.5 [24.5], p < 0.001), APACHE II (17 [7] vs 12 [9], p < 0.001). Comorbidities: ERC (27% vs. 11.1%, p = 0.025); EPOC (24.3% vs. 6.7%, p.005). Risk factors: RRT (16.2% vs 3.3%, p = 0.018). Intra-ICU infection(p = 0.035): secondary bacteremia (18.9% vs. 4.4%), abdominal infection (10.8% vs. 15.9%). Multivariate analysis (mortality): SAPS-II (OR 1.06 [IC 95% 1.03–1.09], p = 0.001). RRT (OR 6.92 [1.33–42.34], p < 0.024).

Conclusion: Surgical patients had a higher severity score and increased use of ATB, PN, IMV, CVC and UC. There were no differences in severity, complications or mortality between patients with urgent and scheduled surgery. The mortality of surgical patients was 29%. Both the need of RRT and the punctuation in SAPS II were mortality predictors.

000690

New and persistent sedative prescription after critical illness among older adults: a population-based cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000690

Introduction: Older adults who survive critical illness often have complex care needs due to cognitive, psychological, and physical impairments. Inadequate medication review related to sedative use and harmful polypharmacy is common. It is unknown which older adult ICU survivors are at greatest risk for receiving a prescription for a new sedative after hospital discharge.

Objectives: To determine frequency of and risk factors associated with short- and long-term sedative prescribing after critical illness in sedative-naïve older adults.

Methods: We performed a population-based cohort study using healthcare databases in Ontario, Canada. We included all adults ≥ 66 years discharged alive from a hospitalization including an ICU stay between April 1, 2003 and Sept 30, 2019 who had not filled a sedative prescription within 6 months prior to the hospitalization (sedative-naïve). We randomly selected one of the hospitalization in those patients meeting inclusion criteria more than once during the study timeframe. Outcomes were the proportion of patients who (1) filled a new sedative prescription (≤ 7 days of discharge) and who had (2) persistent sedative use, defined as a new prescription within 7 days of discharge and ≥ 1 other prescriptions within ≤ 6 months of discharge. We describe baseline demographic, clinical and hospital characteristics and examined their associations with an early prescription for a sedative using multivariable, multilevel logistic regression model adjusting for clustering of patients within hospitals. We quantified variation among hospitals using the median odds ratio (MOR). We assessed the associations between baseline measures and persistent prescription using multivariable proportional hazards model accounting for the competing risks of death and rehospitalization.

Results: 250,428 sedative-naïve older adults met inclusion criteria: mean age 76 years, 61% male, 85% admitted to hospital from the community, 8% frail. During hospitalization, 63% had surgery, 26% received invasive ventilation, and 14% had sepsis or septic shock. A total of 15,277 (6.1%) filled ≥ 1 sedative prescription ≤ 7 days from discharge; 9,499 (62.2%) filled a benzodiazepine, 3,512 (23.0%) filled an antipsychotic, and 3,322 (21.7%) filled a non-benzodiazepine prescription. The proportion of patients filling a new prescription varied substantially by discharge hospital (n = 153 hospitals), ranging from 2% (95% CI 1 to 3) of patients to 44% (95% CI 3 to 57). Of those receiving a new prescription, 8,458 (55%) met our definition for persistent sedative use. After adjustment, factors associated with a new sedative prescription after hospital discharge included: discharge to long-term care facility (aOR 4.00, 95% CI 3.72 to 4.31); receipt of inpatient geriatric (aOR 1.95, 95% CI 1.80 to 2.10) or psychiatry (aOR 2.76, 95% CI 2.62 to 2.91) services, invasive ventilation (aOR 1.59, 95% CI 1.53 to 1.66), and ICU length of stay ≥ 7 days (aOR 1.50, 95% CI 1.42 to 1.58). Discharge from a community hospital (vs. academic) (aOR 1.40, 95% CI 1.16 to 1.70) or from a rural hospital (vs. urban) (aOR 1.67, 95% CI 1.36 to 2.05) were also associated with a new sedative. The residual heterogeneity between hospitals (adjusted MOR 1.43, 95% CI 1.35 to 1.49) had a stronger association with filling of a new sedative prescription than Charlson comorbidity score, drug exposure pre-hospitalization, sepsis, or age. Patients with advanced age were less likely to fill a new sedative, especially those 80–84 years (aOR 0.87, 95% CI 0.83 to 0.93) or ≥ 85 years of age (aOR 0.88, 0.83 to 0.94) as were patients with pre-existing polypharmacy (aOR 0.91, 95% CI 0.88 to 0.95). Factors associated with persistent sedative use were similar to those above with the addition of female sex (sHR 1.07, 95% CI 1.02 to 1.13).

Conclusion: Among older sedative-naïve critically ill patients in Ontario, 1 in 15 were discharged from the hospital with a new prescription for a sedative (primarily benzodiazepines). Of these, more than half continued to fill prescriptions in the 6-months post-discharge. Prescribing of new sedatives on discharge varied widely across hospitals, even after accounting for other factors, suggesting hospital/prescriber-level interventions may be a target for quality improvement.

Acknowledgements: Canadian Institutes of Health Research (Grant no. # 159696).

000693

Association between remimazolam and postoperative delirium in older adults undergoing elective cardiovascular surgery: a prospective cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000693

Introduction: Postoperative delirium is one of the most common complications after cardiovascular surgery in older adults [1]. Benzodiazepines are a reported risk factor for delirium [2]; however, there are no studies investigating remimazolam, a novel anaesthetic agent.

Objectives: To investigate the effect of remimazolam on postoperative delirium.

Methods: After the trial registry (UMIN000041316), we included elective cardiovascular surgery patients aged ≥ 65 years at Hamamatsu University Hospital between August 2020 and February 2022. Patients

who received general anaesthesia with remimazolam were compared with those who received other anaesthetics (control group). The primary outcome was delirium within 5 days after surgery. Secondary outcomes were delirium during intensive care unit stay and hospitalisation, total duration of delirium, subsyndromal delirium and differences in the Mini-Mental State Examination (MMSE) scores from preoperative to postoperative days 2 and 5. To adjust for differences in the groups' baseline covariates, we used stabilised inverse probability treatment weighting (IPTW) as the primary analysis and propensity score matching as the sensitivity analysis. The following variables were used to calculate the propensity score: age, sex, BMI category, ASA class, comorbidities, preoperative oral medication, preoperative MMSE score, living alone, type of surgery, cardiopulmonary bypass and scheduled surgery time. All analyses were performed using Stata/BE 17. Two-sided p-values of < 0.05 were considered significant.

Results: We enrolled 200 patients; 78 in the remimazolam group and 122 in the control group. After stabilised IPTW, both groups' baseline characteristics were almost balanced. For primary outcome, 30.3% of the remimazolam group patients and 26.6% of the control group patients developed delirium within 5 days (risk difference [RD], 3.8%; 95% confidence interval [CI], − 11.5% to 19.1%; $p = 0.63$). The development of delirium in the ICU and during the hospital stay ($p = 0.59$, $p = 0.97$, respectively), and the differences in MMSE scores from the preoperative measurement to the measurements on postoperative days 2 and 5 did not differ between the groups ($p = 0.93$, $p = 0.14$, respectively). In addition, the total duration of delirium and the rate of development of subsyndromal delirium did not differ significantly between the groups ($p = 0.57$, $p = 0.47$, respectively). After one-to-one propensity score matching, delirium developed within 5 days of surgery in 16/61 (26.2%) patients in the remimazolam group and 17/61 (27.9%) patients in the control group, with no significant difference between the groups (RD, − 1.6%; 95% CI, − 17.4 to 14.1; $p = 0.84$). For all other secondary outcomes, sensitivity analysis showed similar results to those for the primary analysis.

Conclusion: Remimazolam was not significantly associated with postoperative delirium compared with other anaesthetic agents, suggesting that it may be a promising future sedative.

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Acknowledgements: None.

000694

Hypernatremia in ICU: which is better for treatment? Enteral free water vs. dextrose 5% in water. A retrospective cohort study from a mixed ICU in Japan

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Intensive Care Medicine Experimental 2022, **10(2)**:000694

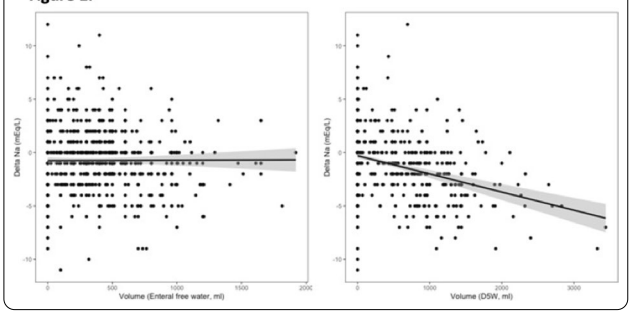
Introduction: Hypernatremia is one of the most common electrolyte disturbances found in the intensive care unit (ICU). [1] While its various detrimental effects strongly support the need for treatment of the condition, [2–4] there are only limited treatment options available to date. Either enteral or intravenous free water administration is the current mainstay of the treatment, [5] but it is not known which is more effective in lowering serum Na.

Objectives: To assess the effectiveness of enteral free water vs. dextrose 5% in water (D5W) in treating ICU-acquired hypernatremia.

Methods: A retrospective cohort study was conducted in a single, mixed medical-surgical ICU in Japan by utilizing an electronic data-storage system. All the adult patients admitted to our ICU from August 2017 to July 2021 were included. After exclusion, patients who stayed in ICU > 24 h and received treatment fluid for hypernatremia e.g. serum Na > = 145 mEq/L were retained. Patients' daily data including treatment fluid and its volume, morning lab, net in–out balance, and total Na intake per patient day were explored. The primary outcome was delta Na (a difference in serum Na during 24 h) and the secondary outcomes were gastrointestinal complications, serum glucose level, ICU/hospital mortality, ICU/hospital length of stay, and the duration of mechanical ventilation. Repeated measurement within each patient was addressed by utilizing a generalized estimated equation (GEE) for multiple linear regression. The analysis was conducted with R version 4.0.2.

Results: In total, 256 (125 with enteral free water, 131 with D5W) out of 6596 patients were analyzed. The baseline characteristics of the 2 groups on ICU admission were similar, except for statistically higher creatinine and serum potassium levels in the D5W group. The total median volume of the treatment fluid per one patient day was 412 ml [Inter Quantile Range (IQR): 296–600 ml] in the enteral free water group and 813 ml [IQR: 471–1232 ml] in the D5W group. The baseline characteristics at treatment initiation were similar except for a significantly lower negative net fluid balance in the D5W group. Serum Na level at treatment initiation was 150 mEq [Inter Quantile Range (IQR): 148–153] in the enteral free water group and 151 mEq [IQR: 149–154] in the D5W group. The simple linear regression lines for the primary outcome were presented in Fig. 1. GEE multiple linear regression analysis showed an estimated mean delta Na per 1L of treatment fluid was − 1.2 mmol/L [95% Confidence Interval (CI): − 1.87 to − 0.52] for enteral free water and − 2.0 mmol/L [95%CI: − 2.39 to − 1.64] mmol/L for D5W, respectively. Diarrhea was significantly more common in the D5W group, with no significant difference in any of the secondary outcomes.

Figure 1.



Conclusion: This is the first study that compared the effectiveness of enteral free water and D5W in treating ICU-acquired hypernatremia. The results suggested D5W is more effective in reducing serum Na.

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Acknowledgements: The authors received no grant support for this study.

000698

Delirium severity and its association with short and long-term outcomes of COVID-19 patients admitted to the ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:000698

Introduction: Delirium is a form of acute organic brain dysfunction, often associated with adverse outcomes in the ICU. Besides the viral infiltration in the central nervous system and his indirect action through the inflammatory response causing brain damage, COVID-19 population are at increasing risk for delirium due to other factors such as hypoxemia, deep sedation, prolonged mechanical ventilation, and isolation. The Confusion Assessment Method for the ICU 7 (CAM-ICU 7) assesses delirium presence and severity. To the best of our knowledge, there are few studies on the impact of delirium in COVID-19 population using the CAM-ICU 7.
Objectives: The aim of this study is to describe the incidence and severity of ICU delirium in patients with COVID-19. Additionally, we analyzed its association with clinically relevant outcomes.
Methods: This is a prospective cohort in two tertiary ICUs in Rio de Janeiro, Brazil between May and August 2020. Patients admitted with confirmed COVID-19 were considered to evaluated during the first 7 days of ICU stay using the RASS, CAM-ICU and CAM-ICU 7. The mean of CAM-ICU 7 was analyzed in three groups of delirium severity: mild (< 3), moderate (between 3–6), and severe (6–7). SAPS, comorbidities (CCI), frailty (m-FI) and SOFA scores, clinical and lab characteristics were also collected. Main outcomes of interest were delirium incidence, ICU and hospital mortality and LOS.
Results: 381 patients were admitted in the period and 277 patients met the eligibility criteria. Delirium was diagnosed in 101 patients (36.5%). Delirium patients had more comorbidities and high severity scores (CCI, m-FI, SOFA and SAPS 3). The overall crude hospital mortality in delirium were 25.74% vs 5.11% in non-delirium patients (CI 95%, p-value < 0.001). One-year mortality of patients with delirium who were discharged from hospital was 5.3% vs 0.6% in non-delirium patients (CI 95%, p-value < 0.001). Delirium severity accordingly with the CAM-ICU 7 means (mild, moderate and severe), were respectively associated with a higher SAPS 3 score [51.96 (48.94–54.98) vs 56.75 (51.35–62.15) vs 57.85 (51.36–64.34), CI 95%, p-value < 0.001]; a higher m-FI score [21.61 (18.31–24.9) vs 33.13 (27.09–39.17) vs 35 (28.99–41.00), CI 95%, p-value < 0.001] a longer length of ICU stay [20.20 (14.89–25.51) vs 23.41 (13.19–33.63) vs 31.46 (10.79–52.13), CI 95%, p-value < 0.001] and a higher in-hospital mortality [17.86% vs 34.38% vs 38.46%, CI 95%, p-value < 0.001].
Conclusion: Delirium incidence was high in COVID-19 ICU patients (36.5%) and associated with increased hospital mortality and one-year mortality rates. Delirium severity accessed by the mean CAM-ICU 7 during the first week in the ICU was also correlated with worse outcomes as length of ICU stay and in-hospital mortality.

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Acknowledgements: We are grateful for all the support and collaboration of the teams of staff and managers of the ICUs of the Copa Dór and Copa Star hospitals during the performance of our work.

000707

Association between intraoperative hypotension and perioperative complications in oesophagectomy

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Intensive Care Medicine Experimental 2022, **10(2)**:000707

Introduction: Oesophagectomy is a highly invasive procedure and can lead to serious complications such as pneumonia, suture failure and multi-organ failure. Studies have shown that intraoperative hypotension (IOH) in non-cardiac surgery is associated with the development of acute kidney injury (AKI) and increased postoperative mortality.
Objectives: As the association between IOH and postoperative AKI in oesophagectomy has not been sufficiently studied, we performed a retrospective study of IOH and perioperative complications of oesophagectomy in our hospital.
Methods: Patients who underwent oesophagectomy between 1 February 2018 and 31 March 2021 at our hospital were included; patients undergoing two-stage surgery, cervical oesophageal cancer surgery, dialysis and eGFR < 60 mL/min/1.73 m2 were excluded. The primary endpoint was the development of AKI up to 48 h postoperatively; AKI was defined by increased postoperative creatinine levels and postoperative urine output based on KDIGO criteria. Secondary endpoints were lactate levels in the immediate postoperative period, postoperative suture failure, pneumonia and the development of wound infection. Intraoperative invasive arterial pressure was recorded at 1-min intervals and IOH was defined as a mean blood pressure of less than 60 mmHg for more than 20 consecutive minutes. Patient characteristics were compared according to the presence or absence of IOH. Continuous variables were subjected to the t-test and categorical variables to the χ-square test or Fisher's direct probability test. All statistical tests were two-tailed and $p < 0.05$ was considered significant.
Results: A total of 137 patients underwent oesophagectomy and 82 patients were enrolled in the study. The mean age was 64.9 ± 9.6 years, 66 (80.5%) were male. There were 47 in the hypotensive group and 35 in the non-hypotensive group. More patients in the non-hypotensive group had preoperative cerebrovascular complications, but no other differences were observed. AKI occurred in 12.2% of patients overall, 10.6% in the hypotensive group and 14.3% in the non-hypotensive group, with no significant differences. The mean lactate levels in the immediate postoperative period were 1.90 in the hypotensive group and 1.58 in the non-hypotensive group, with lactate levels significantly higher in the hypotensive group. There were no significant differences in other complications.
Conclusion: There was no association between IOH and AKI in oesophagectomy, but postoperative lactate levels were higher in the hypotensive group.

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000719

The effect of COVID-19 on the comparability of the traditional and viscoelastic coagulation monitoring

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Introduction: A widely used laboratory method for monitoring anticoagulation by low molecular weight heparin (LMWH) is the anti-Xa assay, which detects the level of heparin (IU/ml), especially the fractions containing less than 18 pentose subunits in the plasma. Regarding viscoelastic measurements, the RVV test can be applied from the ClotPro© system, which contains the derivate of the Russel viper's venom as an activator of factor X. Groene et al. examined the effect of anticoagulants, including LMWH and found a correlation between the standard laboratory tests and viscoelastometric tests in healthy volunteers[1].
Objectives: We examined the relationship between anti-Xa assay and ClotPro© RVV tests in critically ill patients and whether COVID-19 affects this relationship.
Methods: In our retrospective observational study data were collected from patients receiving treatment at the Intensive Care Unit of the Department of Anaesthesiology and Intensive Therapy at Semmelweis University. 39 cases from 31 patients (13 females/18 males; average age: 60,07 yrs ± 12,59 SD; average APACHE-II: 18 ± 9,51 SD) were found when laboratory anti-Xa assays and bedside RVV tests were taken simultaneously. The anti-Xa activity was detected using the Innovance© Heparin Assay in the Department of Laboratory Medicine. We also documented the patient's COVID-19 status (pos./neg.: 16/15). Data were analysed with the program GraphPad Prism 9.3.1. We carried out simple linear regressions to examine the relationship between plasma heparin levels and clotting time (CT) measured during the RVV test. We defined the anticoagulant level of anti-Xa activity above 0,6 IU/ml. To compare maximal clot firmness (MCF) in the case of COVID-19 and non-COVID-19 patients unpaired t-test was applied.
Results: In the case of COVID-19 negative patients, there was a relatively strong correlation between anti-Xa activity measured in the serum and RVV CT with simple linear regression (R^2:0,8029; F: 73,32; $p < 0{,}0001$). Such correlation was not presented in the case of COVID-19 positive patients (R^2: 0,1055; F: 2,005; p: 0,1748). There was also a significant difference between the MCF of COVID-19 positive and negative patients (unpaired t-test: mean neg./pos.: 59,75 vs. 66,26 mm; p: 0,0037), especially in the subgroup of anticoagulated patients (unpaired t-test: mean neg/pos.: 55,25 vs. 66,36 mm; p: 0,0003).
Conclusion: In the case of COVID-19 positive patients, there seems to be no reliable, linear correlation between plasma anti-Xa activity and the clotting time of the viscoelastic test with RVV reagent. The differences observed in the two groups may be due to the hypercoagulable state of COVID-19 patients[2], which is also supported by the significant differences in MCF values. Our findings could explain the clinical observation of the INSPIRATION randomized clinical trial that the administration of a higher dose of prophylactic anticoagulation did not result in a significant difference in the primary outcome[3].

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Acknowledgements: Another randomised study of the investigators is supported with reagents of the ClotPro© system by Diacare Solutions Kft.

000721

Natural language processing diagnosed behavioural disturbance phenotypes in the intensive care unit: characterization, treatment, and outcomes

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Intensive Care Medicine Experimental 2022, **10(2)**:000721

Introduction: Natural language processing (NLP) software can be used to automatically analyse text from caregivers progress notes. In a previous study, we used NLP to detect words or phrases that may be suggestive of disturbed behaviour and possible delirium in the medical, nursing and allied health progress notes of 12,375 critically ill patients. We referred to patients thus identified as having natural language processing diagnosed behavioural disturbance (NLP-Dx-BD). We found that NLP-Dx-BD identified a population of patients who may be expected to be at risk of delirium. In a further study of 2,313 critically ill patients we found that NLP-Dx-BD and the confusion assessment method for intensive care (CAM-ICU) describe partly overlapping populations. However, NLP-Dx-BD identified significantly more patients likely to receive antipsychotic medications than CAM-ICU. NLP-Dx-BD also identified patients with longer length of stay in the ICU and hospital and greater in-hospital mortality. In the current study we hypothesised that NLP-Dx-BD may be effective in identifying phenotypes of disturbed behaviour in critically ill patients.
Objectives: To evaluate the characteristics, treatments, and outcomes of patients with Natural Language Processing (NLP) diagnosed behavioural disturbance (NLP-Dx-BD) phenotypes in the Intensive Care Unit.
Methods: We obtained progress notes, patient demographics, outcomes and antipsychotic medication use from three medical-surgical ICU's. We applied NLP to the progress notes to screen for behavioural disturbance phenotypes.
Results: We studied 2,931 patients. Of these 225 had the NLP-BD-Dx hyperactive phenotype and 544 had the hypoactive phenotype and 667 experienced both phenotypes during their ICU admission. These patients differed at baseline for several key characteristics, with hyperactive phenotype patients being younger ($P < 0.001$) and more likely to be admitted via the Emergency Department ($P < 0.001$). Compared to patients with hypoactive NLP-Dx-BD, hyperactive phenotype patients were more likely to receive antipsychotic medications, and more likely to die in ICU and in hospital ($P < 0.001$). However, patients with a mixed phenotype were much more likely than the hyperactive and hypoactive phenotypes to receive antipsychotic medications and to die ($P < 0.001$).
Conclusion: Patients with hyperactive NLP-Dx-BD differ from hypoactive patients for baseline characteristics, treatment and outcome but both phenotypes are overwhelmed in terms of risk, treatment and poor outcome by the mixed phenotype. This implies that the mixed phenotype should be a target for future trials.

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000744

Comorbidities and in-hospital complications among elderly ICU patients: retrospective observational study

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Introduction: As geriatric population tends to increase, the number of elderly patients admitted to the Intensive Care Unit (ICU) is also increasing over the years. Geriatric patients usually possess lower functional reserve with higher comorbidities. This study aimed to evaluate the association between number of comorbidities with in-hospital complications among elderly patients admitted to the ICU in Indonesia.
Methods: This was a retrospective observational study conducted in single hospital in Indonesia between July and December 2021. ICU admission was decided by attending physician according to the admission criteria. Patient demographic and clinical profiles, including the use of mechanical ventilation, duration of ICU stay, duration of hospital stay, mortality in the ICU, were collected based on electronic medical record. Comorbidities were categorized in these criteria: cardiovascular, respiratory, neurology, renal, liver, and malignancy. In-hospital complications were defined as any secondary complications during hospital stay; categorized in these criteria: acute coronary syndrome, cerebrovascular disease, renal failure and pneumonia. Subjects were divided into two groups: < 3 comorbidities and ³ 3 comorbidities.
Results: A total of 60 elderly patients were admitted to the ICU during study period. Mean age was 75 ± 6.8 years old with 38.33% of patients had more than 3 comorbidities. The presence of sepsis and the use of mechanical ventilation were found higher among patients with ³ 3 comorbidities. Also, total duration of ICU and hospital stays were longer in this group. However, mortality in the ICU was found higher in elderly with < 3 comorbidities (48.6% vs 36%). Overall, the most common in-hospital complications among elderly were pneumonia (46.67%) and renal failure (33.33%). Acute coronary syndrome was found higher in elderly with < 3 comorbidities. In the contrary, renal failure (43.47% vs 27.02%) and pneumonia (65.2% vs 35.13%) were significantly higher among patients with ³ 3 comorbidities.
Conclusion: Elderly patients with more than 3 comorbidities generally had longer ICU and hospital stays. Also, they had higher incidence of obtaining renal failure and pneumonia during their hospitalization.

000747

Postbariatric EArly discharge Controlled by Healthdot (PEACH): preliminary results of a patient preference based non-inferiority study

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Intensive Care Medicine Experimental 2022, **10(2)**:000747

Introduction: Bariatric surgery in an outpatient setting may reduce workload and hospital costs and increase patient satisfaction. While the feasibility and safety of such a care pathway has been demonstrated (1), the implementation of same-day discharge is hampered by concerns about timely detection of complications (2). The use of a portable continuous monitoring device can enable the detection of clinical deterioration (3) and support the transition towards same-day discharge.
Objectives: This study evaluates the non-inferiority of same-day discharge supported by remote monitoring, relative to the current standard recovery route.
Methods: In total, 200 adult patients with approval for primary bariatric surgery were assigned to a postoperative trajectory based on their preference: same-day discharge with one week ongoing remote monitoring of vital parameters, or standard care with discharge on postoperative day one. Continuously measured data (device: Healthdot, Philips) of heart and respiration rate, activity and body posture, were averaged over 5-min intervals and transmitted wirelessly. Data was visualized into a software dashboard located in-hospital which is also designed to implement custom EWS-based protocols (4). Non-inferiority was tested using a thirty-day composite primary outcome consisting of mortality, mild (Clavien-Dindo 2 and 3a) and severe complications (Clavien-Dindo 3b), readmission and prolonged length-of-stay. Secondary outcomes were patients' satisfaction and data-handling dimensions.
Results: From March to July 2021, 157 patients (82% female) were included, of which 103 patients had surgery. The mean age was 40.4 years (SD 11.9) and the mean BMI 42.4 kg/m2 (SD 5.1). Procedures were equally distributed (sleeve 50.9%/bypass 49.1%). Most participants (98%) gave preference to a treatment group, half of them for the outpatient setting with remote monitoring. The mortality of the first 100 patients was 0%. Serious complications occurred in 4% (n = 2) of patients in the remote group versus 0% in the control group. Mild complications occurred once in both groups. Same day discharge was feasible in 70% (n = 35) of the patients. The total number of hospital days including readmission was halved (21 in the remote group versus 56 in the standard group) while maintaining patients' satisfaction (8.0 versus 8.0).
Conclusion: Most patients undergoing bariatric surgery have clear preference for their postoperative care-path. An outpatient recovery pathway was feasible in most cases. Anecdotal evidence showed benefits of telemonitoring beyond first day. This study showed promising results for implementation daycare surgery as a standard alternative.

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Anaesthesia & Peri-operative Medicine 6

000787

Evaluating propofol dosing at University Hospitals Birmingham (UHB) in a critical care setting: prospective audit

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Intensive Care Medicine Experimental 2022, **10(2)**:000787

Introduction: Propofol is a highly protein bound (98%) 2, 6-diisopropylphenol anaesthetic used primarily for its potent sedative properties

[1] and exhibits it's mechanism of action via the α-amino butyric acid agonist (GABA) pathway [1]. Factors including rapid onset/offset, antiemetic and anticonvulsant effects are advantageous properties in the critical ill patient however higher doses (> 4 mg/kg/hour for ≥ 3 days) can bring about the onset of propofol-related infusion syndrome (PRIS) [2]. PRIS is characterised by several symptoms that affect multiple organ systems including urine discolouration [3], renal failure, rhabdomyolysis, hyperlipidaemia, hyperkalaemia, cardiac failure, arrhythmias, metabolic acidosis and hepatomegaly [4]. It has been suggested this condition is due to the inhibition of cytochrome C and accumulation of lactic acid [3], leading to negatively charged free fatty acids into the blood vessels, metabolic acidosis [4] and lipolysis impairment. To reduce the risk of developing PRIS, it is recommended that the maximum propofol dose of 4 mg/kg/hour is not exceeded. At Birmingham Heartlands Hospital, propofol 2% is usually prescribed via a central venous catheter as a standard 1000 mg in 50 mL sodium chloride 0.9% over a rate 0-20 ml/hour.

Objectives: The primary aim of this audit is to evaluate prescription compliance for propofol dosing in mechanically ventilated patients on the intensive care unit to the local Trust guidelines. Secondly; this audit investigated that if a higher maintenance dose of propofol were to be administered, was the justification recorded and were the symptoms of PRIS monitored.

Methods: Using local Trust guidelines for propofol administration, a prospective audit was undertaken on the intensive care unit for adults (≥ 18 years; n = 43, males and females) requiring mechanical ventilation and sedation with propofol. Data items were recorded using a piloted online data capture form which included length of stay, BMI, propofol dosage (mg) and rate (mL/hour), correct prescription requirements, Richmond Agitation and Sedation Score (RAAS) score, justification for exceeding recommended dose and other sedatives in conjunction with propofol. The locally agreed standards include 100% of propofol prescriptions are at the correct dose and have been written correctly as per local protocol and Royal Pharmaceutical Prescribing Competency Framework[5], 100% of propofol prescriptions exceeding the maximum dose are justified and 100% of patients receiving propofol exceeding the maximum dose are monitored for symptoms of PRIS.

Results: Data was collected via an online questionnaire (22.2.22–10.3.22) during weekdays only. Alfentanyl was administered frequently 84% (n = 35), midazolam, clonidine/dexmedetomidine(2%) not so often and 'other' sedatives prescribed were primarily remifentanil 14% (n = 6). Junior doctors –FY1/SHO grade (16.7%), advanced critical care practitioner (ACCP) (14.3%) and SPR grade doctors (11.9%) were involved with the prescribing of propofol at the time of the audit. Prescription particulars (i.e. printed names/signatures) were omitted (57.1%, n = 25) and generally illegible therefore not complying with the Trust's Medicines Code. Documentation of the dose (i.e. mgs/kg) of propofol were not considered in 88.4% of responses (n = 38). Data collection involved information regarding patient's RASS score at the time of the highest propofol rate. RASS score should be kept between -1 and -2 to ensure the patient is sedated and comfortable but not overly sedated. The data indicates that 76.6% of ICU patients audited were over-sedated with a RASS score at -3 or -4. A dose of greater than 4mgs/kg/hr was administered on 3 episodes and the highest dose administered was 5.42 mg/kg/hr in one patient. There were 3 patients administered 4mgs/kg of propofol 2% during the audit. Fortunately, zero patients were identified as having symptoms of PRIS.

Conclusion: Propofol is a potent sedative, however at higher doses can predispose individuals to propofol-related infusion syndrome (PRIS). Prescribing of propofol is a complex process and errors to prescribing are multifactorial. Although some propofol prescriptions were greater than 4 mg/kg/hour, symptoms of PRIS were not observed.

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000791

Hemorrhagic and thrombotic complications under VV-ECMO in patients with SARS-CoV-2 infection: learnings from a single center

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Intensive Care Medicine Experimental 2022, **10(2)**:000791

Introduction: Venovenous extracorporeal membrane oxygenation (VV-ECMO) is a potential life-saving strategy for patients with COVID-19 related refractory respiratory failure (RRF). SARS-CoV-2 infection alters coagulation system, which in association with a pro-inflammatory potential derived from the ECMO circuit, cause increase the risk for bleeding and thrombosis.

Objectives: We characterize severe hemorrhagic and thrombotic events during VV-ECMO.

Methods: Retrospective review of prospectively collected data from a protocol driven ECMO program. Patients with COVID-19 diagnosis and RRF treated with VV-ECMO were included. Patient's characteristics, outcome, VV-ECMO duration, thrombotic and hemorrhagic complications were collected. Circuit exchanges and their causes were registered.

Results: 92 patients were treated with VV-ECMO. Mean age was 50 ± 12.1 years, 71% were male. Most prevalent comorbidities were obesity (45%), hypertension (35%) dyslipidemia (18%) and type 2 diabetes (12%). Average SAPS II was 35 ± 14, admission SOFA score 6 ± 3, and mean SOFA score on day 1 of cannulation 6 ± 3. Patients had average ECMO run of 31 days and 32% were outreached from other hospitals. ICU mortality was 24% and one patient died during hospital stay. All hospital survivors are alive up to present day. All but one patient received anticoagulation with unfractionated heparin (n = 60, 65%) or with bivalirudin (n = 30, 33%). Incidence of heparin-induced thrombocytopenia was 16% and hemolysis was 27%. During ECMO, 51% of patients needed circuit changes, most frequent reason being coagulopathy (n = 34, 48%). Hemorrhagic events occurred in 68 patients (74%) and thrombotic events in 26 patients (28%). Major hemorrhagic complications (brain, airway, gastrointestinal bleeding) were identified in 84% of bleeding patients (62% of total sample). Most frequent were airway (n = 32, 47%), GI (n = 14, 21%), hemothorax (n = 7, 10%) and central nervous system (n = 6, 9%). Minor complications were found in 56 of bleeding patients (61% of total sample) the most frequent being hemorrhage from blood lines (catheters, arterial lines, cannulas) in 47% (n = 32), oral cavity 35% (n = 24) and hematuria 24% (n = 16). There was more than one bleeding event in 65% patients (n = 44, 48% of total sample). The most frequent thrombotic complication was pulmonary embolism in 69% (n = 18, 20% total) followed by venous thrombosis in 31% (n = 8, 9% total) and arterial ischemia 19% (n = 5, 5% total). Although mortality did not have statistical significance, it was higher in patients with hemorrhagic (major 31% and minor 29% vs 17%) and thrombotic events (25% vs 23%).

Conclusion: Bleeding and thrombosis remains a major challenge in the management of patients under ECMO support. These complications increase costs, morbidity and possibly mortality. Future research

is needed to identify biomarkers that can predict hemorrhagic and thrombotic risk, optimizing treatment.

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000847

Blood preserving arterial line system: Hematic Auto Management & Extraction for arterial-Line (HAMEL)

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Intensive Care Medicine Experimental 2022, **10(2)**:000847

Introduction: Intensive care unit (ICU) has possibility of frequent human error from medical staffs which can cause devastating problem to patients. Invasive arterial line (A-line) insertion is common procedure on intensive care unit patients, but sometimes it can cause unexpected blood loss with some mistakes, and unnecessary blood loss while sampling for blood. Majority of intensive care unit patients show high prevalence of anemia due to lots of reasons and frequently needs transfusion, but blood transfusion itself has its own complications so it's important to prevent unnecessary blood loss. To reduce the blood loss for flushing out arterial line dead space, we are presenting a new blood preserving arterial line system; Hematic Auto Management & Extraction for arterial-Line (HAMEL). We designed swine study for evaluating 1) How much blood should be withdrawn prior to blood sampling for accurate blood test results, and 2) Does the test results of the blood sample obtained by the device is same as blood sample acquired by traditional hand sampling method.
Methods: We used total 5 pigs for study. For proper arterial line insertion and management, pigs were maintained under general anesthesia with endotracheal intubation and ventilator. We used i-STAT1® (Abbott Inc.) for blood gas analysis (CG4 + cartridge) and chemistry analysis (CHEM8 + cartridge) tests. Experiment No.1 was for evaluating adequate amount of blood which need to be withdrawn prior to blood sampling for exact blood test results. We planned to figure out degree of sample's dilution by testing hemoglobin and hematocrit. Serial experimental group sampling was done via arterial line for 10 times with prior withdrawn amount of 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5 ml. Second experiment was for testing whether traditional sampling method and HAMEL system shows statistically identical result of blood test. For each pig, left arterial line was for control group, and right side was experimental group. Both sampling was done simultaneously, for 10 serial sampling with 5 min interval.
Results: Hematocrit results from 3 ml removal group placed within 5% differential range compared to control group. Hemoglobin present similar results to hematocrit. We analyzed intraclass correlation coefficient between control group, hand managed blood sampling, and experimental group, sampling by HAMEL, and all test results shows intraclass correlation coefficient above 0.990. Total unnecessary blood loss of the control group was 5 ml per each sampling, which is 50 ml for 10 samplings.
Conclusion: We concluded that at least 3 ml should be removed prior to actual sampling for blood test. Considering variations, 4 ml removal would be recommended option. Utilization of HAMEL system causes no bias to blood test results compare to control group. With reliable intraclass correlation coefficient value, HAMEL system is not inferior to traditional hand sampling method. Additionally, blood sampling with HAMEL system does not lose blood other than blood for actual blood test, which can reduce unnecessary blood loss.

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000850

Exploring analgesia, sedation and paralysis (ASP) utilization in severe COVID-19 pneumonia: a retrospective cohort study

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Introduction: COVID-19 causes a spectrum of illness from self-limiting symptoms to severe respiratory failure necessitating invasive mechanical ventilation (IMV), which can progress to COVID-19 Acute Respiratory Distress Syndrome (CARDS) (1). IMV patients with CARDS are reported to have higher analgesia (opioid), sedative and paralysis (ASP) requirements compared to non-CARDS, and experience increased delirium, ICU and hospital length of stay (2,3). Increased ASP requirements are likely multifactorial and interrelated (3). Contributing factors include pathobiological effects of COVID-19 on the Central Nervous System (4), ASP drugs to manage IMV, refractory hypoxaemia and proning. Additionally, system stress effects of managing a novel pathology in a pandemic, including increased patient numbers, absence of family, and increased patient to nurse ratio may also lead to increased sedation depth. This is to prioritise safety and prevent self-extubation, at the cost of optimal management by reducing ASP over-exposure, as per international guidance (5). Finally, drug shortages meant first line short-acting agents were switched to benzodiazepines, known to increase delirium risk and over sedation (6). There is a paucity of UK data describing ASP usage and staffing ratios during

Covid-19. In order to capture this, we conducted a retrospective, single day, multi-centre point prevalence cohort study describing ASP consumption of patients admitted with COVID-19 pneumonia requiring IMV.
Objectives: To describe ASP consumption on day of peak critical care occupancy during the UK COVID-19 surge 1, surge 2, and historical non-CARDS control, at Guy's and St Thomas', and Lewisham and Greenwich adult critical care units.
Methods: The peak day of adult critical care occupancy during COVID-19 surge 1, surge 2 and a non-CARDS control was used as 24 h point prevalence data collection period. All IMV patients admitted to adult critical care with Covid-19 pneumonia, receiving propofol, benzodiazepines, or alpha-2 agonists by continuous infusion were included.
Results:

	Surge 1–April 2020	Surge 2–January 2021	Non-COVID control– April 2019
Total IMV patients/ with COVID-19 pneumonia	140 / 129	133 / 121	17 / 0
Median age (IQR)	55 (46–61)	58 (49–67)	66 (53–73)
Administered paralysing agents (%)	32/129 (24.8%)	22/121 (18.2%)	0
Administered benzodiazepines (%)	49/129 (38.0%)	36/121 (29.8%)	1/17 (5.9%)
Mean midazolam dose equivalents in mg/h (SDev)	8.5 (5.1)	5.7 (7.0)	19.6 ($n=1$)
Mean propofol dose in mg/h (SDev)	148 (80)	152 (78)	118 (63)
ICU patient:ICU nurse day shift ratio (GSTFT data only)	0.8	0.6	1.4

Conclusion: IMV patients with Covid-19 pneumonia were younger, were five times more likely to receive benzodiazepines and unsurprisingly exposed to higher doses of propofol and opioids. Additionally, 20–25% received paralysing agents, compared to none in the control group. This represents a seismic shift in ASP practice and contradicts international guidance (5). ICU trained nurse to patient ratio decreased by approximately 50% in COVID surge, highlighting increased nursing strain, with potential impact on patient care and nurse burnout. Further work is required to identify factors contributing to increases in ASP exposure, and describe any long term effects such as ICU-acquired weakness and post-intensive care syndrome in this younger cohort of patients.

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000858

Risk models for predicting major complications in hepato-pancreato-biliary surgery and their limitations

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Introduction: Despite surgical and peri-operative advancements, major hepatopancreatobiliary (HPB) surgery remains high-risk abdominal surgery, with often high rates of morbidity and mortality. Studies have demonstrated that risk prediction tools show a relatively poor predictive power for post-operative morbidity in liver and pancreas surgery. Whilst there may be some advantages to using them to in making high dependency bed-allocation decisions, it isn't clear whether scores such as P-POSSUM or dynamic tests such as cardiopulmonary exercise testing (CPET) offer any advantage over the decision making of an experienced clinician. The aim of this study was to evaluate whether a combination of the static and dynamic tests may help in identifying patients at risk of complications after major HPB surgery.
Methods: 281 consecutive patients undergoing major liver and pancreatic surgery at a tertiary HPB centre, were audited from a prospectively maintained database. Patients undergoing a palliative bypass were excluded from the results. Evaluation of P-POSSUM and CPET in predicting morbidity as defined by the Clavien-Dindo classification was done using univariate analysis. Observed to expected (O:E) ratios were calculated to assess goodness of fit of the model. Analysis was performed on the physiological and operative sub-scores, as well as the individual components of the P-POSSUM score to assess their value in predicting major postoperative complications.
Results: 122 pancreatic resections and 159 liver resections were performed over a 24-month period from January 2018 to January 2020. 62/281 (22.1%) of patients suffered a major complication, as defined by Clavien-Dindo severity of 3 or greater. P-POSSUM scores were not significantly different between patients suffering a complication and those who did not ($p=0.102$). Major liver resections (35.4%) and PPPD (26%) carried the greatest risk of severe complications. The O:E for major liver resections was 0.7 and for PPPD was 0.56, demonstrating a poor predictive fit for the highest risk surgeries. CPET was performed on 162 (58%) of patients but neither AT ($p=0.36$) nor VE/VCO2 ($p=0.57$) demonstrated statistical significance in predicting morbidity in pancreatic or hepatic surgery.
Conclusion: Complication rates for major HPB resections are high but similar to those reported by other centres. P-POSSUM scoring system over-predicts morbidity in both major pancreatic and hepatic resections. Furthermore, values attained through CPET testing failed to demonstrate any additional discriminatory power. The value of predicting complications lies in the ability to allocate sufficient resources to the highest risk surgical cases, with appropriate allocation of high-dependency beds when the risk is high. The current tools show limit predictive value and whilst repeat multivariate analysis of factors known to have an association with a poor outcome may give greater predictive power the models available continue to have limitations. Further work is needed to understand the factors that place patients at risk of complications and ultimately what could be done to reduce their incidence.

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Acknowledgements: Nothing to declare.

000869

How fresh is too old and how little is too much? Age and volume of perioperative red blood cell transfusions in major abdominal surgery and their effect on postoperative outcomes

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Intensive Care Medicine Experimental 2022, **10(2)**:000869

Introduction: Anemia is a modifiable risk factor for mortality and morbidity in many surgical populations. (1) Modern medicine offers many ways to correct preoperative anemia, but transfusions are still a cornerstone in its treatment. The potential benefits of perioperative red blood cell transfusion (PRBCT) should be weighed against its risks, as PRBCT has been identified as a risk factor for postoperative mortality, major adverse cardiovascular or cerebrovascular events (MACCE) and infection. (2–4) Surprisingly few studies evaluating the effects of PRBCT corrected for preoperative anemia.
Objectives: To ascertain whether the volume and age of PRBCTs are independent risk factors for mortality, MACCE and/or infection, taking into account preoperative anemia.
Methods: Multicenter observational cohort study using a nested cohort from the Myocardial Injury in Noncardiac Surgery in Sweden study (NCT03436238). (5) It included patients > 50 years of age undergoing elective major abdominal surgery at two hospitals in Sweden. Exposures were age (days) and volume (dL) of PRBCT. Old blood was defined as older than the median age of the oldest unit given each patient. The primary outcome was composite 30-day mortality, MACCE and infection. Secondary outcomes were individual MACCE and infection. A multivariable regression model adjusting for age, sex, ASA-class, length of surgery, number of comorbidities, intraoperative blood loss, preoperative anemia and volume or age of PRBCT was used to determine the independent effect of the exposures.
Results: We included 769 patients between April 2017 and December 2020. Overall, 153 patients (20%) received perioperative transfusion and 291 (38%) were anemic preoperatively. Median age of blood was 11 days. A total of 267 patients (35%) suffered complications in the 30 days following surgery. After adjustment, volume transfused significantly increased the risk of MACCE (OR 1.081; p = 0.029). Receipt of blood older than 11 days significantly increased the risk of infectious complications (OR 1.813; p = 0.024). (Table 1).
Table 1. Multivariable analysis of association between transfusion properties and outcomes.

	Volume PRBC		PRBCT > 11 days old	
Outcomes	**Adjusted OR (95% CI)**	***P*-value**	**Adjusted OR (95% CI)**	***P*-value**
Composite	1.034 (0.981–1.089)	0.216	1.524 (0.920–2.523)	0.102
MACCE	1.083 (1.010–1.160)	0.024	1.334 (0.659–2.698)	0.423
Infection	1.013 (0.960–1.070)	0.629	1.758 (1.054–2.935)	0.031

Conclusion: Every dL of PRBCT significantly increases the risk of postoperative MACCE with 8%. Receipt of blood stored longer than 11 days drastically increases the risk of postoperative infection. These findings further encourage the use of more restrictive transfusion regimes and raises the question whether current practice of storing blood for up to six weeks is safe.

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Acknowledgements: Funded by The Swedish Research Council (2019–02833), South Eastern Sweden Research Council (746981, 712291), and Linköping University-Region Östergötland ALF (687681, 792291).

000885

Nociception monitoring and pain management in the ICU: a multivariate analysis of pupillometry vs. standard clinical practice according (SCP) to the pain indicator behaviour scale (ESCID)

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Intensive Care Medicine Experimental 2022, **10(2)**:000885

Introduction: Patients admitted to ICU often receive basal analgesia to avoid pain, usually measured by behavioral scales. The Spanish Society of Intensive Care Medicine (SEMICYUC) recommends the Pain Indicator Behaviour Scale (ESCID). Nevertheless some procedures in the ICU may trigger painful situations. Pupillometry could be a validated nocioception evaluation method to assess the quality of the analgesia in ICU.
Objectives: To determine whether the protective effect on pain, diagnosed by ESCID (pain = ESCID ≥ 1) after endotracheal aspiration (ETA), in those patients in whom pupillometry-guided pre-analgesia is administered vs. standard clinical practice (SCP) is maintained after adjustment for possible confounding variables.
Methods: Control: Pre-AET analgesia according to SCH (nurse's subjective judgement). Experimental: Pre-AET analgesia with pupillary dilation reflex (PDR) 11.5% after 20 mA (cut-off point and intensity with best diagnostic performance, previous diagnostic test study). Preanalgesia: fentanyl 1 µg/kg ev bolus. AlgiScan®. Approved by CEIC Euskadi. Inclusion: > 18, analgesics in MV with BPS = 3, ESCID = 0, and RASS = -1-, -4. With informed consent. Exclusion: Myorelaxants, polyneuropathy, pupillary involvement, ECG < 6, clonidine, dexmedetomidine, tramadol, ketamine, adrenaline, and calcium antagonists, noradrenaline > 0.6 and/or dobutamine > 10 µg/kg/min. Description: Continuous: mean(SD). Categorical: N/%, Multivariate analysis by logistic regression. p < 0.05.
Results: N = 56 Control vs Intervention: % Reason for admission: ARDS 13.3 vs 21.2, Sepsis 15.8 vs 9.1, postQx 44.7 vs 54.5, trauma 13.2 vs 3, neuro 13.2 vs 6.1; Male: 57.9 vs 90.9; Age: 64.9(12.8) vs 66.7(13.0). Weight(kg): 72.5(12.8) vs 76.7(20.3), APACHE II: 15.9 (7.5) vs 16.3(7.4). ECG 13.9(2.6) vs 13.8(2.6). BIS 57.6 (17.2) vs 63.4 (12.8). RASS -3.2 (1.06) vs -2.9 (0.9). Sedatives: % Midazolam 13.5 vs 21.2; propofol 75.7 vs 69.7; None 10.8 vs 9.1; Analgesics % fentanyl 29.7 vs 39.4; remifentanil 61.1

vs 29.4; CIM 8.1 vs 15.2; BIS 66.2 vs 63.8. RASS -3.05 vs -2.92. Dose (mg/kg/h) Midazolam 0.22(0.43) vs 0.16(0.13), propofol 2.18 (0.74) vs 1.98 (0.89). (µg/kg/h) fentanyl 0.96(0.42) vs 0.99(0.60), remifentanil 8.5(2.48) vs 8.48(2.89). Experimental OR adjusted for; sex: 0.32 [0.09–1.06] ($p = 0.067$); APACHE ≥ 20: 0.22 [0.06–0.75] ($p = 0.016$); remifentanil: 0.23 [0.07–0.79] ($p = 0.020$); BIS ≥ 60 0.20 [0.06–0.68]($p = 0.010$).
Conclusion: The use of pupillometry for the detection of nociception to guide the prophylactic administration of analgesia prior to endotracheal aspiration has a protective effect on the development of ESCID-diagnosed pain, independent of severity level, level of sedation and baseline opioid.

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000896

Experience with ketamine use for sedoanalgesia protocol in critically ill COVID-19 patients needing mechanical ventilation in a medical ICU in a secondary-level university hospital: a global view from the first to the sixth wave of the pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000896

Introduction: To describe our experience with the use of ketamine (KET) for sedoanalgesia protocol in critically-ill COVID-19 patients with acute respiratory failure needing invasive mechanical ventilation.
Methods: Retrospective and descriptive study between March 2020 (first wave of the pandemic) and December 2021 (sixth wave) in critically-ill COVID-19 patients needing invasive mechanical ventilation. A total of 201 patients were admitted, 18 were excluded (transferred to another hospital: 5, and 13 transferred to the anesthetic department). The remaining 183 patients:79 needed non-invasive mechanical ventilation (NIMV) and 104 required invasive mechanical ventilation (IMV). In this group the following parameters were analyzed: gender, age group, severity scores, comorbidities. Deep sedation strategy (PaO2/FiO2 ratio < 150 mmHg, prone position and/or neuromuscular blockade(NMB)): midazolam (MDZ) + fentanyl (FNT);combination with propofol (PF) was used: if MDZ > 0.25 mg/kg/h or tolerance; ketamine was added if propofol dose > 4.5 mg/kg/h and/or continuous neuromuscular blockade needed. Superficial sedation strategy (SSS) to achieve RASS score -2 and + 1. Dynamic SSS type: Propofol + remifentanil (RF): need for neurological evaluation, acute kidney injury, and/or BMI > 30 kg/m^2 or cooperative SSS type: PF + KET (previous respiratory disease and/or hemodynamic instability) or PF + FNT (pain and/or psychiatric disorder).
Results: 104 patients were analyzed. Gender 67 male/37 female, age group: > 60: 27 patients, 60–70: 54 and > 70 years old: 23, APACHE II score: 26 ± 7.6, SOFA: 7.1 ± 2.6, comorbodities: hypertension: 29, diabetes: 21, BMI > 30 kg/m^2: 18, COPD/asthma: 16 and 11 were immunocompromised. 104 patients needed deep sedation strategy (DSS) with MDZ + FNT, MDZ + FNT + PF was needed in 85 patients and the combination MDZ + FNT + PF + KET was used in 71 patients (40 of them needed continuous NMB). In the Dynamic sedation strategy group: PF + KET was used in 71 patients and PF + FNT in 52 patients.
Conclusion: With deep sedation strategy, ketamine was used in 68% of the patients, 56% of them requiring continuous NMB. With superficial sedation strategy, ketamine was used in the cooperative type in 68% of the patients.

000903

Perioperative extracorporeal membrane oxygenation for severe COPD patients undergoing lung volume reduction surgery

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Intensive Care Medicine Experimental 2022, **10(2)**:000903

Introduction: Lung volume reduction surgery (LVRS) is an adequate treatment for selected COPD patients with severe emphysema resulting in improvements in lung function, quality of life and long-term mortality. Compared to non-surgical standard therapy, patients undergoing LVRS are at significant risk for perioperative complications with a sixfold increased chance for short-term mortality (1). Especially patients with severely impaired lung function and poor diffusing capacity (DLCO) have a high likelihood of perioperative death. Venovenous extracorporeal membrane oxygenation (VV-ECMO) may secure perioperative gas exchange, enable lung-protective ventilation, and promote rapid postoperative spontaneous breathing. Data on safety and benefit of the use of VV-ECMO in patients undergoing LVRS, however, is still limited.
Objectives: To assess safety and benefit of VV-ECMO during LVRS in patients with advanced emphysema.
Methods: This retrospective analysis included patients undergoing LVRS with elective perioperative VV-ECMO between January 2021 and April 2022 at Charité—Universitätsmedizin Berlin. To assess its safety profile, perioperative complications associated with VV-ECMO were evaluated. In order to identify potential beneficial effects, intraoperative ventilation and time until postoperative extubation were investigated.
Results: In total data from 12 patients were eligible for analysis. Preoperative forced expiratory volume in one second (FEV1) was 26% of predicted value (IQR, 20–30), residual volume 205% (IQR, 164–223), and DLCO 22.5% (IQR, 20–28), respectively. Robot-assisted lobectomy or atypical lung resection were the performed procedures. Seven patients (58%) received dual-lumen and 5 patients (42%) femorojugular or femoro-femoral cannulation. Anticoagulation was not used after ECMO initiation or during surgery. The circuit did not have to be changed during the perioperative course in any of the cases. No major bleeding at cannula insertion site or occluding cannula thrombosis occurred. The use of VV-ECMO allowed protective one-lung ventilation with an appropriate PEEP (8 cmH2O [IQR, 7–8]), a low tidal volume (2.1 ml/kg predicted body weight [IQR, 1.7–2.8]), and a low driving pressure (9 cmH2O [IQR, 7–11]). Median time until post-surgical extubation was 20 min (IQR, 10–32). The median duration of VV-ECMO after surgery was 17 h (IQR, 9–19). The ICU and hospital length of stay was 7 days (5–15) and 22 days (16–31), respectively. None of the patients died during the perioperative course.
Conclusion: In patients with severe lung emphysema undergoing LVRS, the perioperative use of VV-ECMO proved itself to be safe, allowed protective one-lung ventilation, and rapid postoperative spontaneous breathing. While our analysis suggests that VV-ECMO in emphysema patients might be beneficial and reduce perioperative complications, selection criteria for patients need to be defined, and prospective trials are warranted.

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Acknowledgements: None.

Anaesthesia & Peri-operative Medicine 7

000921

Analysis of thrombin generation test in critically ill patients with COVID-19 and comparison with healthy volunteers

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Intensive Care Medicine Experimental 2022, **10(2)**:000921

Introduction: COVID-19-associated coagulopathy (CoAC), mainly thrombotic complications, is a recognized entity that determines morbidity and mortality (1, 2). However, the mechanics underlying CoAC are not completed understood (3). The thrombin generation (TG) and fibrin production may play an important role in CoAC. Another study showed that some TG assay parameters may be correlated with thrombo-inflammatory markers, and when analyzed with more common exams, such as D-Dimer (D-dimer/ETP ratio), it may predict major adverse events in COVID-19**.** (4).
Objectives: To evaluate the behavior of TG and its potential usefulness in assessing patients with COVID-19 and to correlate TG parameters with the severity of COVID-19.
Methods: P*ost-hoc* analysis of 28 critically ill patients with COVID-19 who had participated in a recent published study aimed to evaluate their coagulation profile (3). The plasma of participants was mixed with a recombinant human soluble thrombomodulin to assess the impact of the protein C anticoagulant pathway on TG assay, and analyses were done with the ST Genesia® Thrombin Generation System (Stago, Asnières-sur-Seine, France). We compared results from COVID-19 patients' TG exam on Day 0 and Day 3 and compared the results, on Day 0 from patients who had SOFA < 10 vs. patients who had SOFA > 10. Secondly, we compared the results from COVID-19 patients, on Day 0, vs. the results from 22 healthy volunteers. The following parameters were measured: lag time (ratio), peak height (%), time to peak (ratio), endogenous thrombin potential (ETP) (%), ETP inhibition (%), and velocity index (%).
Results: Comparing the TG exams of COVID-19 patients, between D0 and D3, the main results showed a statistically significant increase on lag-time [**1.47** (1.22–1.81) vs **1.58** (1.36–2.03), p < 0.001], peak height [**81.89** (66.30–101.05)% vs. **98.00** (78.81–111.10)%, p = 0.0267], and velocity index [**81** (52–107)% vs. **101** (47–128)%, p = 0.047] and an impaired ETP inhibition [**35.5** (19.6–54.1) vs. **33.8** (22.9–54.7)%, p < 0.001]. Among COVID-19 patients, those who were more severely ill (SOFA > 10) showed a greater impairment in the ETP inhibition (Table 1), which was also statistically significant when we analyzed COVID-19 patients vs. healthy volunteers [**35.5** (19.6–54.1)% vs **60.7** (49.2–67.8)%, p < 0.001] The lag time was also different between COVID-19 patients and healthy volunteers [**1.47** (1.22–1.81) vs **1.18** (1.04–1.31), p < 0.001].
Table 1. Results of COVID-19 patients on day 3 with SOFA < 10 X COVID-19 patients with SOFA > 10

Results	SOFA < 10 (*N* = 14)	SOFA > 10 (*N* = 11)	*p*-value*
Lag (ratio)	1.7 (1.4–2.1)	1.5 (1.3–1.6)	0.054
Peak height (%)	85.6 (70.1–114.1)	99.9 (86.9–107.9)	0.402
Time to peak (ratio)	1.6 (1.2–2.0)	1.2 (1.0–1.4)	**0.017**
ETP (%)	102.4 (88.0–116.4)	94.0 (75.5–102.0)	0.316
Velocity index (%)	57.8 (43.2–129.2)	110.2 (83.4–127.1)	0.089
Start tail (ratio)	1.2 (1.0–1.6)	1.0 (0.8–1.1)	0.052
Inib ETP (%)	48.9 (34.4–63.0)	24.2 (16.0–32.8)	**0.005**

Conclusion: In general, during hospitalization, patients with COVID-19 evolved with a TG assay showing a profile of greater hypercoagulability and decreased fibrinolysis. Moreover, when comparing patients with COVID-19 vs healthy volunteers, the main alteration on TG assay was the degree of ETP inhibition, whose impairment was more pronounced in the sicker group, which may represent less fibrinolysis activity during a state of hypercoagulability, and there must probably be a correlation between the degree of protein C deficit and the loss of ETP inhibition. We concluded that the routine use of TG assay is not yet recommended to evaluate patients with COVID-19 (5). However, according to our study, the use of TG test can help better understand the mechanism(s) underlying CoAC pathophysiology, and its follow-up can help predict the prognosis of patients infected with COVID-19.

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Acknowledgements: We thaks the support of the Stago® Laboratory Company that gave us the Thrombin generation assays to researches purposes.

000928

Experimental comparison of subanesthetic dose of propofol versus isoflurane in microcirculatory parameters of mouse dorsal skinfold chamber model

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Introduction: Currently, there is no definitive conclusion which anesthetic forms, intravenous or volatile, are beneficial especially in microcirculation level. Direct comparison studies are rare and few existing study results vary. Sepsis often accompanies microvascular endothelial injury and subsequently lead to organ damage and death. We queried if subanesthetic dose of propofol and isoflurane affects microcirculation in both healthy and septic mouse.
Objectives: The primary outcome was the difference of microvascular flow index frombaseline after 120 min of subanesthetic treatment.
Methods: Randomly assigned two groups of control and sepsis male, BALB/c mice were subdivided into propofol and isoflurane groups, 15 mouse for each group; propofol-control, isoflurane control, propofol-sepsis, and isoflurane-sepsis. After 72-h recovery period of dorsal skinfold chamber implantation, mice received either an intraperitoneal injection of sterile normal saline for control group or lipopolysaccharide for sepsis group. Each group was subjected to subanesthetic dose of propofol or isoflurane for 2-h period. Along with mean blood pressure and heart rate, microcirculatory parameters were measured from

incident dark-field microscop yof subcutaneous tissue in observational window at before sedation (T0), 30 min after sedation (T30), 120 min after sedation (T120). Subsequent blood extraction from right heart was for serum syndecan-1 measurement with enzyme linked immunosorbent assay analysis and lanthanum perfusion fixed dorsal skin tissue was obtained for electron microscopy of endothelial glycocalyx thickness evaluation.

Results: In healthy controls, anesthetics both resulted in blood pressure reduction, yet, in propofol and not in isoflurane, maintained microvascular flow thus creating significant agent difference inmicrovascular flow index at T120 ($p < 0.001$). Sepsis groups shared the same pattern but without statistical significance at T120 ($p = 0.023$). Glycocalyx thickness was similar in control groups, significantly thinner layer was observed in sepsis group. There were no syndecan-1 level difference between agents.

Conclusion: Subanesthetic dose of propofol and isoflurane both induced blood pressure reduction but only propofol may be capable of compensating microvascular flow with vasodilation. Such effect is more pronounced in healthy mouse but similar pattern exists in sepsis also.

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000959

Early extubation for liver transplant patients could reduce ICU demand

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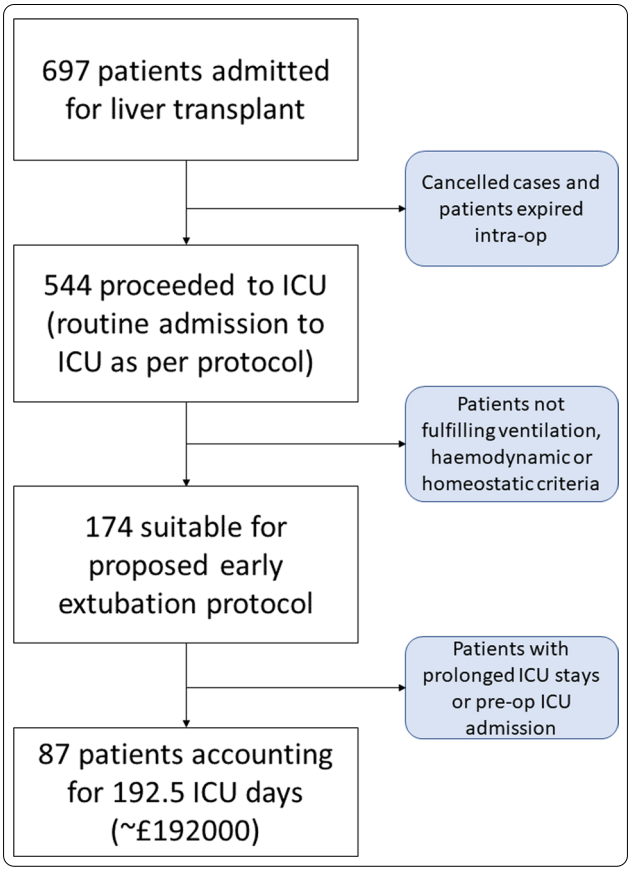
Intensive Care Medicine Experimental 2022, **10(2)**:000959

Introduction: Orthotopic liver transplantation is the gold standard treatment for selected patients with acute and chronic liver failure, some types of liver cancer and selected non liver failure conditions. UK liver transplantation has a 1-year survival of over 90% (1,2). Our transplant centre undertakes approximately 100 liver transplants annually, and these patients occupy a substantial number of ICU bed days. Early extubation after liver transplantation has been demonstrated to be safe and accelerates patient recovery (3). The development of an early extubation strategy in our centre has the potential to minimise unnecessary periods of sedation and ventilation and to free ICU capacity.

Objectives: To determine the number of OLTx recipients in our centre who could be considered for early extubation, their associated number of ICU admissions and ICU stay days that could be saved.

Methods: The study was conducted at a single centre tertiary teaching hospital with an active liver transplant service. Data from electronic patient records was used, collated and analysed using RStudio. All patients undergoing liver transplant as the first operation of their admission between 09/2014 and 08/2021 were included.

Results: We collected data from 697 individual liver transplant patients and excluded all that died within 24 h of admission. with a mean age of 54.5 years, mean length of hospital stay 19.4 days, mean length of stay in ICU 4.5 days. Using the established criteria(3) (saturations $\geq 95\%$ with $FIO2 \leq 0.5$, $Vt > 5$ ml/kg, $RR < 25$/min, normal pH, minimal use of vasopressor, normothermia) we identified 174 (25%) patients who could have been candidates for early extubation. To account for additional undetermined clinical and surgical factors we excluded patients with ICU stays longer than 3 days or pre-operative ICU admission. The remaining population contained 87 patients who had an average hospital length of stay of 17.5 days with an average of 2.2 days in ICU. The aggregate ICU stays accounted for 192.5 days.



Conclusion: Allowing for the limitations of retrospective data, early extubation for optimised patients could reduce the burden of ICU demand by liver transplant patients by allowing for admission to level 2 care or shorter length of stay in ICU. A reduction in ICU LOS by 50% with[ACM1] a proposed early extubation strategy could potentially save approximately £192,000 (€230,000) annually. With a recently implemented early extubation policy, we anticipate significant reductions in ICU length of stay and will be evaluating the actual impact of this policy in future work.

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Acknowledgements

1. KK is supported by an Academy of Medical Sciences Clinical Lecturer Starter Grant (AMS/SGL023/1048)
2. ACM is supported by a Clinician Scientist Fellowship from the Medical Research Council (MR/V006118/1)

000985

Sodium abnormalities before and after cardiac surgery and the role of urinary sodium

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Intensive Care Medicine Experimental 2022, **10(2)**:000985

Introduction: Patients undergoing cardiac surgery frequently display sodium abnormalities, both before surgery and post-surgery[1]. Since dysnatremia is associated with a worse outcome [2], measures to timely detect or predict the course plasma sodium might improve the quality of care.
Objectives: To assess to incidence of hyponatremia and hypernatremia and their persistence after cardiac surgery patients are admitted to the ICU, as well as the predictive value of urinary sodium obtained in the ICU.
Methods: Subsequent adult patients admitted to our ICU during a 2-year period were studied. In the operating room and ICU plasma sodium was determined with an ion-selective method with ABL-90 Flex Radiometer blood gas analyzers. Daily mean plasma sodium was determined on the day before the operation (D-1) up to 7 days after surgery. All urine produced post-surgery on the day of ICU-admission was analyzed for sodium. Except for the impact of mannitol used in the heart–lung machine, diuretics were typically not administered in this phase. Hyponatremia (Na < 135), normonatremia, and hypernatremia (Na > 145) were determined at baseline and from the last available measurement for the first 7 days post-surgery. Pre-operative sodium was correlated with post-operative sodium and the predictive power of urinary sodium was examined.
Results: We evaluated 1025 patients, of whom 470 underwent coronary artery bypass grafting, 244 aortic or valvular surgery, and the remainder combinations thereof or other surgery. At baseline, 8% had hyponatremia and 0.4% hypernatremia. Post-surgery, 17% had hyponatremia and 2% hypernatremia. In 95% of the patients urinary sodium was available on day 0. Median (IQR) urinary sodium concentration was 41 (25–65) mmol/L, with a range of 10–196 mmol/L. Sodium on day 0 had a poor correlation with post-surgery sodium ($R^2 = 0.14$) and day 0 urinary sodium was not related with post-operative sodium.
Conclusion: Hyponatremia regularly occurs after cardiac surgery and appears mainly determined by factors present after ICU-discharge. Targeted post-operative measures to monitor sodium and to modify infusions and drugs to reduce hyponatremia may be warranted.

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001039

Pain assessment during noxious procedures with videopupillometry in deeply sedated intensive care patients: an observational study

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Intensive Care Medicine Experimental 2022, **10(2)**:001039

Introduction: Pupillometry has shown promising results for diagnosing pain in ICU deeply sedated patients (1,2), but it has not been explored in deeply sedated patients who are unable to express pain through behavioural testing in response to a noxious procedure, particularly when they are paralysed.
Objectives: The objectives of the study were to compare automated pupil dilation reflex (PDR) responses during non-noxious and noxious procedures, and to measure the diagnostic performance of PDR using recommended cut-off points to detect pain.
Methods: A prospective observational study was conducted in a medical-surgical ICU population without brain injury of a tertiary hospital. A 30-s videopupillometer reflex (PDR) measurement was performed once a day at three time points (before-during-5′ after) of a non-noxious and a noxious procedure up to 7 days of deep sedation. The non-noxious procedure consisted of a gentle touch on each shoulder and was performed when the patient had no stimulation for at least 20 min. The noxious procedures were endo-tracheal tube suctioning or patient turning onto the side. The bedside nurse according to the patient's clinical needs and care organization determined the timing and the type of procedure. The unit analyses were the number of measurements.
Results: A total of 915 pupil measurements in 60 patients were performed. PDR was higher during noxious procedures than before. After adjusting for age, noxious procedures remained the only predictive factor for higher PDR (coefficient = -15.14 (95%CI = -20.17–-15.52, $p = 0.000$). The diagnosis performance analyses showed that a PDR > 12% had a sensitivity of 65% and a specificity of 94% for pain detection, with an area under the receiver operating curve of 0.828 (95%CI = 0.779–0.877).
Conclusion: In conclusion, PDR is a valid measure to assess pain in deeply sedated ICU-patients. A PDR value of > 12% has a good performance in detecting pain related to patient's usual care procedures.

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Acknowledgements: Supported by grants from the Swiss National Science Foundation (to MO).

001079

Perceived vs. observed adherence to delirium screening: a secondary analysis of data from the prospective, multicenter EuMAS study

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Introduction: Guidelines recommend the frequent assessment of delirium using validated delirium screening instruments. Previous studies, however, have shown implementation gaps in routine care, which may be due to ICU staff's misperception of guideline adherence at local ICUs.
Objectives: To compare the perceived and observed adherence to routine delirium screening across European ICUs.
Methods: This is an exploratory, preplanned, secondary analysis of the Enhancing European Management of Analgesia, Sedation, and Delirium (EuMAS) study (ClinicalTrials: NCT03553719), which assessed delirium, pain, and sedation (PAD) management for patients across 12 European centers at 3 cross-sectional time points. Between the first and second time point, centers received a structured, 6-week PAD training. At the first time point, we asked ICU staff members about the delirium screening practices at their local ICUs. For this analysis, we compared the delirium screening practices as perceived by ICU staff with the actual frequency of delirium screenings that patients at local ICUs received.
Results: We received responses from 26 ICU staff members from 8 centers. A share of 38% (10/26) were nurses, 31% (8/26) were residents, and 31% (8/26) were consultants. The centers' ICUs had a median of 17.5 [range 8–51] beds and were either surgical, medical, mixed, or neurological. Most centers (7/8) had delirium screening protocols in place, but the quantity of recommended daily delirium assessments varied from one to at least three (Table 1). ICU staff members estimated that 57.6% [center-level median; range 27.1–95] of patients at their local ICU were screened for delirium on the day of the cross-sectional assessment. According to our observations, 76.4% [center-level median; range 0–100] of ICU patients were screened for delirium in each center on the same day. ICU staff members estimated the share of patients that was screened for delirium at their local ICU either too high (up to 95%) or too low (up to 63.2%) (Table 2).
Table 1. Delirium screening practices in centers according to ICU staff

Center (number of respondents)	ICU beds	Specialization	Delirium screening protocol	Daily delirium screenings as per protocol
Center 1 (4)	51	Surgical	Yes	At least 3 times
Center 2 (3)	36	Mixed	Yes	Twice
Center 3 (3)	8	Medical	Yes	Once/twice
Center 4 (3)	16	Surgical	Yes	At least 3 times
Center 5 (3)	24	Surgical	Yes	At least 3 times
Center 6 (3)	13	Surgical	Yes	At least 3 times
Center 7 (4)	10	Neurological	No	-
Center 8 (3)	19	Mixed	Yes	At least 3 times/twice

Table 2. Perceived vs. observed delirium screening practices in 8 participating centers

Center	ICU patients screened for delirium (%)		Absolute difference
	Staff reported	Observed	
Center 1	28.4	91.7	+63.2
Center 2	58.3	75	+16.7
Center 3	41.7	25	− 16.7
Center 4	27.1	0	− 27.1
Center 5	56.9	85.7	+28.8
Center 6	87.2	77.8	− 9.4
Center 7	95	0	− 95.0
Center 8	66.7	100	+33.3

Conclusion: ICU staff members' perception of the frequency of routine delirium screenings at their local ICU substantially deviated from observed clinical practice. This discrepancy underscores the need for PAD guideline implementation strategies, even if ICUs are convinced to already adhere to these guidelines.

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Acknowledgements: Funded by the European Society of Intensive Care Medicine (ESICM) with the NEXT Start-up Grant.

001082

The impact of small volume resuscitation with hypertonic saline after cardiac surgery on total body water distribution—Results of a post hoc analysis of the HERACLES randomized controlled trial

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Intensive Care Medicine Experimental 2022, **10(2)**:001082

Introduction: Perioperative fluid overload contributes to mortality in cardiac surgery (CS) [1, 2]. In the HERACLES trial, we evaluated whether small volume resuscitation with a single bolus of 5 ml/kg of hypertonic saline (7.3% NaCl) (HS) versus isotonic saline (0.9% NaCl) (control) over 60 min after cardiac surgery reduces cumulative perioperative fluid intake [3]. We noted a decreased overall fluid balance and an increased urinary output in the HS-group compared to controls. Controversly, some investigations indicate increased fluid accumulation in patients receiving large sodium loads through intravenous fluid administration [4, 5]. Currently, the impact of excess sodium loading on water and salt distribution in critically ill patients is still unclear.
Objectives: The primary objective was to assess the influence of HS infusion on body water distribution measured by bioelectrical impedance analysis (BIA) in patients after cardiac surgery. Secondary outcomes were changes in urinary sodium, potassium and chloride excretion.
Methods: Pre-defined post-hoc analysis of the HERACLES trial [3], a single-center randomized controlled double blind clinical trial conducted at Bern University Hospital, Bern Switzerland (NCT03280745). All patients randomized were eligible for this analysis. Exclusion criteria: i) patients without BIA on pre-operative day (d-1) and post-operative days 1 and 2, patients with general contraindications to BIA. BIA measurements (BIACORPUS RX 4000, MEDI CAL HealthCare GmbH; Karlsruhe, Germany) were performed at d-1 and post-operatively (d0), on the first post-operative day (d1), 48-72 h after surgery (d3) and on post-operative day 6 (d6). Urinary electrolytes (sodium, potassium, chloride) were measured at d-1, d0, d3 and d6.
Results: Out of 165 patients, 136 patients were included (49 HS-group, 87 controls). Patients received comparable median total peri-operative fluid volumes (HS: 7,846 ml, interquartile range [IQR] 5,831–9,095 ml vs. controls: 8,187 ml, IQR 6,063–9,791 ml; $p = 0.2$). Median sodium load in the HS-group was 11.8 g, IQR 10.4–14.3 g (controls: 0.94 g, IQR 0–1.4 g; $p < 0.001$). The cumulative dose furosemide

equivalent patients received until d6 was higher in controls (200 mg, IQR 90-340 mg vs HS: 130 mg, IQR 40-220 mg; p = 0.02). Peri-operative change in total body water (TBW) did not differ between groups (HS: mean change 29%, standard deviation [SD] 23% vs. control: mean change 27%, SD 19%; p = 0.47). We noted no peri-operative change in additional BIA parameters (all p > 0.05). Higher TBW and intracellular water levels were noted in the HS vs. control group over time (p = 0.01 and p = 0.006, adjusted for cumulative dose furosemide equivalent). Urinary electrolyte excretion over time were comparable between the HS and control groups (all p > 0.05).

Conclusion: A single HS bolus after cardiac surgery may induce delayed but temporary water accumulation. This may suggest redistribution of excess sodium into the extravascular space.

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Acknowledgements: n.a.

001087

Immunosuppressive phenotypes and theragnostic targets following major surgery: a prospective cohort study

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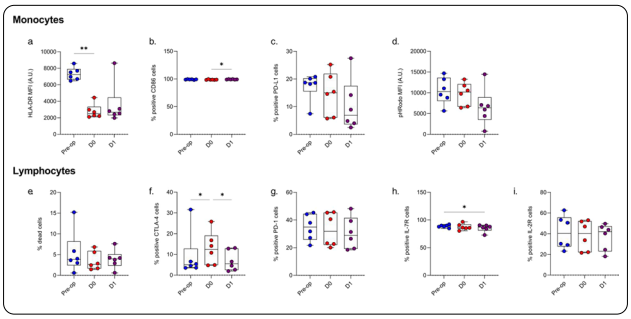
Intensive Care Medicine Experimental 2022, **10(2)**:001087

Introduction: Post-operative infections are a significant morbidity amongst patients undergoing surgery. The immune response to significant (sterile) inflammation associated with surgery may be contributary. Following an initial pro-inflammatory response, an anti-inflammatory 'resolution' phase ensues. *We hypothesise that the immune response to an infection during the latter resolution phase may be impaired, posing an 'at risk period' for patients.*
Objectives: Characterise immunosuppressive changes over 48 h in patients who undergo major surgery.
Methods: Surgical patients' immune phenotypes were characterised pre-operatively at induction (Pre-op), following 24 h (D0), and at 48 h post-operatively (D1). Flow cytometry panels assessed monocyte antigen presentation (HLA-DR, CD86, CD80), phagocytosis (opsonised pHRodo bioparticles), and lymphocyte cell signalling and senescence (CTLA-4, PD-1, IL-7RA, IL-2RA).
Results: Six patients were recruited. Surgery was associated with suppressed HLA-DR (a.) and CD86 expression (b.). PD-L1 expression (c.) and phagocytosis (d.) may also be reduced. CTLA-4 expression (f.) was increased, while PD-1 (g.) and IL-7RA (h.) expression was decreased. There was no change in cell death (e.) or IL-2RA (i.) expression. (**Figure 1**).



Conclusion: Surgical patients develop several features of immunosuppression in monocytes and lymphocytes within 24 h of surgery. Further work is required to ascertain the timecourse of immunosuppression and recovery, and its association with infectious complications.

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Acknowledgements: ESICM Next Start Up (2018).

001094

Severe thrombocytopenia in critically ill COVID-19 patients: More of a thrombotic rather than a hemorrhagic phenotype? A single-center retrospective study

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Introduction: As COVID-19 disease is characterized by vasculopathy and a higher risk of thromboembolic events, pharmacological thromboprophylaxis has been a cornerstone of medical treatment. Unfortunately, thrombocytopenia is a common finding in COVID-19 patients occurring in up to 36% of these patients being associated with disease progression and poor outcome. Subsequently, the decision on anticoagulation in COVID-19 patients with severe thrombocytopenia sometimes proves a difficult task to perform.
Objectives: To assess the incidence of thrombocytopenia in our ICU COVID-19 patient population and record the presence of thrombotic and hemorrhagic complications during their ICU stay.

Methods: We have performed a retrospective single-center study from 03/2020 to 04/2021 including all consecutively critically ill mechanically ventilated PCR SARS-COV-2 positive patients. Patients' demographics, comorbidity, laboratory values, ICU length of stay, complications like thrombotic or hemorrhagic events during ICU stay and mortality were recorded for each patient. Two patient groups, i.e., with and without thrombocytopenia (PLTs < 150,000/µL), were compared.
Results: Altogether 97 patients were included in our study (mean age 68.2 ± 10.1 years) 67 (69%) men and 30 (33%) women. During the first 10 days of ICU admission thrombocytopenia occurred in 41 patients (42.3%). Of these, 18 patients developed mild (PLTs < 150,000/µL), 15 moderate (PLTs < 100,000/µL) and 8 patients severe thrombocytopenia (PLTs < 50,000/µL). Comparison of group A and group B showed no difference in gender, comorbidity and length of ICU stay. Patients with thrombocytopenia were older (72 vs 66 years old, p = 0.015) and had a higher mortality (48.7% vs 25%, p = 0.015). Interestingly, 6/8 (75%) of patients with severe thrombocytopenia eventually died during ICU stay, 5/8 (62.5%) of them having previously developed venous thromboembolism (VTE), and 3/8 (37.5%) being tested positive for Heparin-induced thrombocytopenia. Also, no hemorrhagic events occurred during the period of severe thrombocytopenia.
Conclusion: Thrombocytopenia seems to be common in COVID-19 patients and associated with increased ICU mortality. In our study, patients presenting with severe thrombocytopenia during the first 10 days after ICU admission had a high incidence of VTE and mortality.

Anaesthesia & Peri-operative Medicine 8

001154

Fluid administration guided by inferior vena cava ultrasound before spinal anaesthesia may reduce post-procedural hypotension rate

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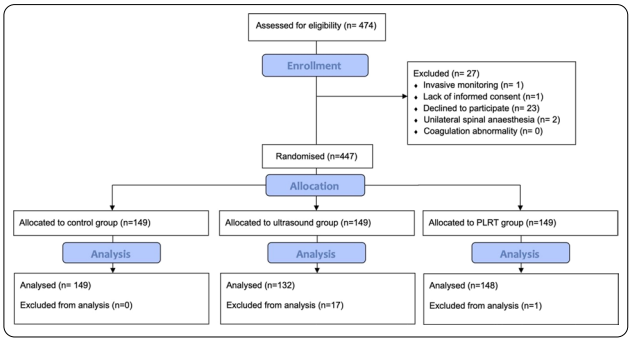
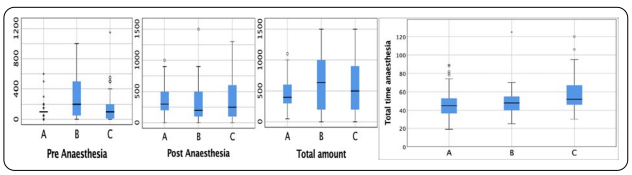
Intensive Care Medicine Experimental 2022, **10(2)**:001154

Introduction: Spinal anesthesia (SA) is safe and used for a variety of surgical procedures. Arterial hypotension is one of the most frequent adverse events. Transient hypotensive episodes are generally well tolerated in patients without special comorbidities. However, these episodes can lead to serious complications in elderly emergency situations and patients at high cardiovascular risk or those taking medications such as beta blockers, angiotensin-converting enzyme inhibitors, selective serotonin-recapture inhibitors, or monoamine oxidase inhibitors.
Objectives: This study was conducted to estimate the incidence of hypotension after spinal anesthesia after ultrasound-guided inferior vena cava volemic optimization (IVCUS) compared with a control group in patients undergoing elective surgery.
Methods: A prospective, controlled, randomized, three-arm, parallel-group study was conducted in our tertiary hospital from May 2014 to February 2019. In the IVCUS group (I, 132 patients) and the passive leg lift test group (L, 148 patients), pre-anesthesia volume optimization was performed following a fluid response protocol. In the control group (C, 149 patients), no specific intervention was performed. According to ESICM guidelines, hypotension was defined as two measures of systolic blood pressure (SAP) < 80 mmHg and/or mean arterial pressure (MAP) < 60 mmHg, or a decrease in SAP of more than 50 mmHg or more than 25% from baseline, or a decrease in MAP of more than 30% from baseline, and/or clinical signs/symptoms of inadequate perfusion. The primary outcome was the rate of hypotension after SA following fluid optimization therapy guided by IVCUS and PLRT testing or no intervention. Secondary outcomes were an analysis of the amount of fluids administered, the amount of vasoactive drugs used, and the time required to perform the entire anesthetic procedure.



Results: 474 patients were collected. In group I, the rate of hypotension was 35%. In group L, the rate of hypotension was 44%. In group C, the rate of hypotension was 46%. A hypotension reduction rate of 11% (95% CI -1 to -24%, P = 0.047) was observed between group I and group C. A rate of reduction in hypotension of 2% (95% CI -3 to -5%, P = 0.428) was observed between group L and group C. The total amount of fluid administered was greater in group I than in group C (593 mL versus 453 mL, P = 0.015) and greater in group L than in group C (511 mL versus 453 mL, P = 0.11).



Conclusion: The incidence of arterial hypotension after SA is extremely frequent. This study provides encouraging evidence that IVCUS combined with a fluid protocol may decrease the incidence of arterial hypotension after SA.

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001119

Use of the modified VExUS scale as an indicator of acute kidney injury and acute-on-chronic kidney injury in patients undergoing coronary artery bypass graft

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Intensive Care Medicine Experimental 2022, **10(2)**:001116

Introduction: Acute kidney injury (AKI) is one of major complications in critically ill patients and it can be multifactorial (p.e septic or cardiogenic shock), but it can be due to venous congestion which worsens tissue perfusion in favour of organic failure. Determining venous congestion is not easy. Central venous pressure (CVP), accumulated fluid balance or presence of peripheral edema are not error-free [1, 2]. Beaubien-Souligny et al. proposed the VExUS system based on the combination of ultrasound findings in suprahepatic, portal and intrarenal veins. The greater the venous congestion, the greater the ultrasound changes [3]. Inferior vein cava diameter was used as the first parameter to differentiate patient at risk of venous congestion, so they assumed that patients with IVC < 20 mm did not have congestion. Since IVC is not an infallible method to assess the patient's blood volume [4, 5], we propose a new classification (modified VExUS –mVExUS) to classify venous congestion. Our aim is to demonstrate whether severe venous congestion determined by mVExUS is associated with a higher incidence of AKI in patients undergoing CABG.
Methods: Observational and prospective study. Inclusion criteria: patients undergoing CABG. We analyzed venous flows by ultrasound at the level of the suprahepatic, portal and intrarenal veins during their stay in the ICU. Statistical analysis: quantitative variables in means (SD) and medians (min–max) according to their normality. Bivariate analysis: khi-square and anova test.
Results: 12 patients (83.3% male). Median age was 71.5 years (45–77). EUROSCORE II at admission was 4.9 (2.5). They stayed in the ICU for 3 days (1–6) and 10.5 days (8–18) in the hospital. None of them died at the ICU or hospital.

	mVExUS 0	mVExUs 1	mVExUS 2	mVExUS 3
SAMPLE % (*n*)	50 (6)	8.3 (1)	33.3 (4)	8.3 (1)
EUROSCORE II mean (SD)	6.5 (2.5)	5	3.25 (1.2)	2
AKI % (*n*)	50 (2)	25 (1)	25 (1)	0
CRRT*/DIALYSIS	0	0	0	0
CVP** in mmHg median (min–max)	10 (7–17)	4	7.5 (6–8)	10
USE OF INOTROPES % (*n*)	33.3 (2)	0	50 (2)	0
USE OF VASOPRESSORS % (*n*)	16.7 (1)	100 (1)	25 (1)	0
ICU STAY median (min–max)	2 (1–4)	3	4 (3–6)	3
HOSPITAL STAY median (min–max)	10 (8–18)	12	11 (10–15)	9

*CRRT: continuous renal replacement therapy

**CVP: central venous pressure

Conclusion: 1. We have not found significant differences ($p < 0.05$) in the presence of AKI between patients with mVExUS 3 and mVExUS 0, 1 and 2. 2. We have not found significant differences between patients with mVExUS 3 and mVExUS 0, 1 and 2 for the following variables: days of admission to the ICU, days of hospital admission, PVC levels, need for inotropes, need for vasopressors, renal resistance index or weight gain.

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001167

Use of heparin grafted membrane reduces the need for anticoagulation in post-operative dialysis

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Intensive Care Medicine Experimental 2022, **10(2)**:001167

Introduction: Post-operative hemodialysis (HD) can be complicated by bleeding. Reduction of anticoagulation in this set of circumstances is crucial. Use of heparin grafted membrane has been reported as safe to achieve this goal and appears easy to apply.We report the results of combination of low dose unfractionated (UH) heparin and heparin grafted membrane (HGM) to minimize anticoagulation level during post-operative HD in the intensive care unit (ICU).
Methods: 21 chronic dialyzed patients age: 53 (42; 65) (median (Q1;Q3) with a SAPS II: 27 (23; 32) admitted in the ICU for clinical monitoring and HD after sleeve gastrectomy.Because of post-operative bleeding risk and the need to use UH for thromboprophylaxis, tight heparinization (UH bolus of 25 IU/kg at the start of HD) combined with HGM (Evodial, Baxter) was chosen as anticoagulation method.The first post-operative HD session was studied in all the 21 consecutive patients.
Results: HD sessions length (hours) was 4 (4; 4) median (Q1; Q3).Blood flow ml/min) was 300 (250; 350)Net ultrafiltration (ml) was 1800 (500; 2450)A median bolus of 2500 (2450; 2750) UI of heparin was adminstred in only 11 patients, the others 10 receiving no bolus at all.Clotting events leading to premature termination of the dialysis session (after 3 h) were observed in only 2 cases (both of them in the absence of UH bolus). The use of HGM and tight anticoagulation(or even no anticoagulation) led to 90. 4% of blood circuit patency at the fourth hour during early post operative HD in our population.Furthermore, ultrafiltration did not seem to be an obsatcle to achieve this result.
Conclusion: In this specific population HGM combined with tight or no anticoagulation is a safe and efficient method for HD in the early post-operative period. It usefulness in wider ICU populations and clinical situations deserves additional studies.

001172

Predictive value of SAPS II and APACHE II in intensive care surgical patients admitted after a Whipple procedure

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Introduction: A Whipple procedure is one of the most complex abdominal surgeries, commonly prescribed as first line therapy for pancreatic head cancer. It is associated with a high morbidity rate and significant potential for perioperative mortality, which frequently justifies postoperative care in an intensive care unit (ICU) after surgery.
Commonly used ICU prognostic scoring models include the Simplified Acute Physiologic Score II (SAPS II) and the Acute Physiology and Chronic Health Evaluation II (APACHE II). However, their predictive value in patients after Whipple procedure is not well studied.
Objectives: The aim of this study is to identify possible predictors of intensive care unit mortality, following Whipple procedure, and to compare the predictive value of APACHE II and SAPS II scores in this population.
Methods: Retrospective cohort study from consecutive patients (P) admitted in a 10-bed mixed ICU, after elective duodenopancreatectomy, between January 2015 and July 2021. The chi-square test was used for categorical variables, and analysis of variance for continuous variables. Binary logistic regression was used to control for confounding. The accuracy of the SAPS II and APACHE II scores for predicting in-hospital mortality was evaluated using the receiver operating characteristic (ROC) curve and computation of the area under the curve (AUC).
Results: A total of 81 P were included, 53.1% of male sex, with a mean age of 67 ± 9 years-old. Smoking habits was present in 28.4% of patients and alcohol consumption in 11.1%. The mean APACHE II score was 14.9 ± 6 and the mean SAPS II score was 36.5 ± 13. In this cohort, the mean length of stay in the ICU was 4.1 ± 3 days, with 1.9 ± 3 days of mechanical ventilation. In 34.6% of patients vasoactive amines were used. The mortality rate during ICU stay was 8.6% (7 patients) and in-hospital mortality was 13.6% (11 patients). After a logistic regression, that controlled for potential confounding factors, the predictors of ICU mortality in this cohort were previously diagnosed heart failure ($p = 0.023$), mechanical ventilation days ($p = 0.001$), APACHE II score ($p = 0.024$), need for vasoactive medication ($p = 0.020$) and days with vasoactive medication ($p = 0.001$). For the predictive value of APACHE II and SAPSII, using the ROC curves, the APACHE II score was a good predictor of mortality in the ICU (AUC 0.752, $p = 0.028$), but not the SAPS II score (AUC 0.579, $p = 0.491$). When it comes to in-hospital mortality, both scores have a good predictive power in this cohort (SAPS II with AUC 0.690, $p = 0.043$; APACHE II with AUC 0.763, $p = 0.005$).
Conclusion: Heart failure, high APACHE II score and use of vasoactive medication are predictors of ICU mortality in patients after a Whipple procedure. SAPS II score is not a good predictor for mortality in the ICU in this patients, but both APACHE II and SAPS II have a good predictive power when it comes to in-hospital mortality in this cohort.

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001173

Impact of combined anaesthesia in overall survival of patients admitted for Whipple procedure

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Introduction: Regional anaesthesia (RA) is hypothesized to reduce cancer recurrence by reducing surgical stress response and the associated immunosupression, minimizing volatile anaesthesia (VA) and reducing postoperative pain and opioid analgesic requirements. Results from retrospective studies are conflicting about the benefits in overall survival with combined anaesthesia (CA) versus VA.
Objectives: The objective of this study is to compare the overall survival of patients submitted to elective Whipple procedure with combined anaesthesia (RA and VA) versus those with only volatile anaesthesia (VA).
Methods: Retrospective, longitudinal, comparative study from consecutive patients (P) submitted to an elective duodenopancreatectomy, admitted in the ICU between January 2015 and July 2021. We compared 2 different groups (G1: P submitted to CA; G2: P submitted to VA). The chi-square test was used for categorical variables, and analysis of variance for continuous variables. Overall survival was estimated using the Kaplan–Meier analysis with a log-rank test.
Results: A total of 134 P were analyzed, with 81 included (G1: n = 52; G2: n = 29), 44% of male sex, with a mean age of 67 ± 9 years-old. In this cohort, 46,9% had 3 or 4 ASA score. AC was used in 64,2% of P. The mean length of stay in hospital was 27 ± 18 days, with in-hospital mortality of 13.6% (11 patients). There was no significative difference between G1 and G2 in terms of sex ($p = 0,48$), age ($p = 2,06$), ASA score(0,22) and general comorbidities. The drug most used in AC (G1) was Ropivacaíne (49%) and Sevoflurane was used in 66,7% of P. The Kaplan Meier analysis observed no significant difference in overall survival between the CA group and the VA group ($p = 0.716$).
Conclusion: In our cohort there was no benefit in AC over VA in terms of overall survival, in P submitted to Whipple procedure as approach to cancer of pancreatic head.

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001223

The effect of Nefopam on postoperative pain and patients' satisfaction in geriatric patients with spinal stenosis undergoing spinal surgery: A double-blind, randomized study

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Introduction: Lumbar spinal stenosis is a degenerative disease of the lumbar spine. If surgery is performed for this disease, most of them

show a good clinical course after surgery, but it is reported that about 30% of patients have residual symptoms after surgery. Nefopam is a centrally acting analgesic agent and is known to have analgesic and anti-hyperalgesic effects through the NMDA receptors. We investigated effects of nefopam on postoperative pain and patients' satisfaction in patients with spinal stenosis undergoing spinal surgery.
Methods: A total of 69patients were randomly divided into two groups: the control group (n = 30) received 20 ml of normal saline and the nefopam group (n = 39) received 20 mg of nefopam 1 h before the end of the operation. Total intravenous anaesthesiawas administered under bispectral index monitoring during anaesthesia induction and maintenance. Rocuronium was administered beforeintubation and during surgery when the train-of-four count was 2 or more. After operation, patient-controlled analgesia with a solution of fentanyl and ramosetron was used and the consumption of this solution was recorded. Surgical site pain score, dysesthesia scores of the legs at rest were evaluated at postoperative 12 h, 24 h, 48 h and 72 h. The overall satisfaction with postoperative pain management was investigated at postoperative 72 h using numerical rating scale 1 to 5.
Results: There was no statistically significant difference between the two groups in terms of leg dysesthesia and back pain before surgery (6.5 ± 1.3 vs. 6.7 ± 2.1, 4.2 ± 3.2 vs. 3.1 ± 2.4, respectively, P = 0.752, P = 0.317). The severity of dysesthesia of leg in the nefopam group was significantly lower than that in the control group at postoperative 12, 24, 48, and 72 h (4.2 ± 2.3 vs. 1.7 ± 2.0, 4.2 ± 1.7 vs. 1.6 ± 1.5, 3.4 ± 2.0 vs. 1.6 ± 1.5, and 3.2 ± 1.8 vs. 1.6 ± 1.5, respectively, P = 0.004, P < 0.001, P = 0.009, and P = 0.015). However, there was no statistically significant difference in the severity of pain of surgical site between the two groups at postoperative 12, 24, 48, and 72 h (4.6 ± 3.3 vs. 2.9 ± 2.2, 3.9 ± 3.1 vs. 2.9 ± 1.5, 3.2 ± 2.4 vs. 1.9 ± 1.2, and 2.4 ± 1.7 vs. 1.6 ± 1.3, respectively, P = 0.107, P = 0.231, P = 0.064, and P = 0.138). The overall satisfaction with postoperative pain management in the nefopam group was significantly lower than that in the control group at postoperative 12, 24, 48, and 72 h (2.7 ± 0.8 vs. 3.9 ± 0.6, respectively, P < 0001).
Conclusion: Administration of nefopam effectively reduces lower extremity dysesthesia within 72 h after surgery in geriatric patients. However, there was no statistically significant effect on pain at the surgical site. The significantly higher satisfaction with postoperative pain control in the nefopam group than in the control group is thought to be due to a significant decrease in leg dysesthesia.

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Acknowledgements: None.

001245

Cyclic heating and cooling of an anesthetic reflector considerably improves its efficiency

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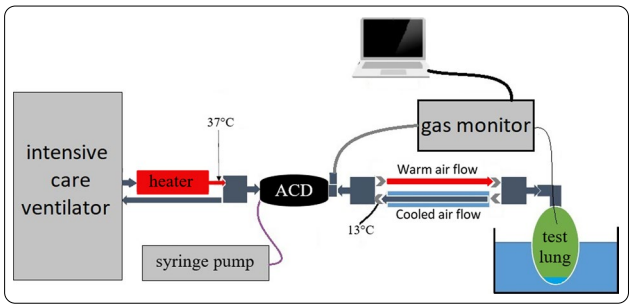
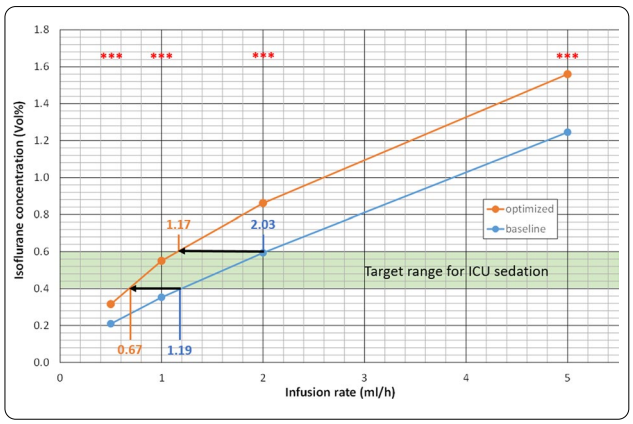
Introduction: In view of global warming, reducing consumption of volatile anesthetics (VAs) seems eminent. This can be achieved by rebreathing from a circle system, but also by anesthetic reflection[1]: The Sedaconda-ACD-S (ACD,Sedana Medical, Danderyd, Sweden), connected between ventilator and the patient, retains approx. 80% of exhaled isoflurane during expiration and releases it back to the patient during the next inspiration[2], thereby reducing consumption compared to low flow anesthesia[3]. We tested whether consumption could be further reduced by warming the reflector during inspiration and cooling during expiration.



Methods: The isoflurane concentration C was measured inside the test lung after equilibration over 5 min and averaged,repeated three times on different days. Settings: 500 ml tidal volume, 10 bpm, 21% O, Isoflurane infusion rates (IR): 0.5,1.0, 2.0 and 5.0 mL/h. Under "optimized conditions", the ACD was exposed to 37 °C dry air during inspiration and to 14 °C cold air during expiration. C was compared with T-tests for each IR.
Results: Cyclic heating and cooling the ACD considerably increased the achieved CISO for all IR studied (Fig.. 2, all P < 0.001).Interpolation of data showed that for achieving 0.4 (0.6) Vol% isoflurane, IR can be reduced by 44% (42%).



Conclusion: Cyclic heating and cooling considerably increases the efficiency of the anesthetic reflector and reduces consumption of VAs by almost half in a test lung model. With a miniaturized set up for cooling, this method carries apotential for further saving VAs in clinical practice in the OR as well as for inhaled sedation in the ICU.

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001258

Use of military anti-shock trousers in resuscitation of acute circulatory failure patients in intensive care unit

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Intensive Care Medicine Experimental 2022, **10(2)**:001258

Introduction: Military anti-shock trousers (MAST) was used for augment venous return (VR) in combat casualty care. Basically, it improves hemodynamic by increased mean systemic pressure (Pms) cause increase in MAP and suggested in septic shock patients when pharmacologic venous thromboembolism is contraindicated. No study of

hemodynamics effect and clinical outcome compared with flat position in patients with shock during resuscitation.
Methods: Randomized, single blind, prospective cohort and comparison study on experimental design. 60 patients with shock were included in this analysis. 30 patients were performed MAST by use of pneumatic leg compression pressure 40 mmHg during and until finish resuscitation compared with the flat position and measured for hemodynamic variables immediately after finish resuscitation. Primary outcome was difference in hemodynamic variables and secondary outcome was mean days in ICU stay.
Results: There was no difference in baseline characteristics in hemodynamic variables. MAST significantly increased all hemodynamic variables after resuscitation. Compared to the flat position, MAST significantly increased CO [3.29 (2.64, 3.93) vs. 0.34 (0.26,0.42) L/min, $p = < 0.001$], SV [9.87 (8.68, 11.05) vs. 1.91 (1.15, 2.67) L, $p < 0.001$], MAP [7.9 (5.8, 10) vs. 1.67 (0.82, 2.52) mmHg, $p < 0.001$], SVR [26.87 (21.13, 32.6) vs. 11.13 (8.99, 13.27) dyn.s/cm5, $p < 0.001$], FTc [43.23 (37.15, 49.32) vs. 10.93 (7.96, 13.9), $p < 0.001$], SD [2 (1.76, 2.24) vs. 0.7 (0.57, 0.83), $p < 0.001$] and PV [11.07 (9.41, 12.73) vs. 5.57 (4.27, 6.87), $p < 0.001$] and MAST was significantly less mean days in ICU than flat position [4 ± 1.29 vs. 6 ± 1.11, $p < 0.001$].
Conclusion: In patients with acute circulatory failure, MAST significantly increased all hemodynamic variables during resuscitation and associated with less mean days in ICU.

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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.

001276

Early primary hemostasis dysfunction during Extracorporeal Life Support. A rapid diagnostic approach with therapeutical guidance intentions

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Introduction: The use of extracorporeal life supports (ECLS) for cardiac and respiratory failure has increased in recent years, specially during the SARS-CoV-2 pandemic, improving outcomes in selected patients. However, major bleeding remains one of the main complications leading to increased morbidity and mortality in this population. Acquired von Willebrad disease (aVWD) has been described during long-term mechanical circulatory support. However, there is little evidence on its development during short-term support.
Objectives: To investigate the primary hemostasis alterations profile in patients with short-term ECLS and its potential treatment in case of bleeding complications.
Methods: Patients who received ECLS from June 2020 to May 2022 in the Cardiovascular and Medical intensive care unit (ICU) of a University Hospital in Barcelona were prospectively included. Primary hemostasis was evaluated by: i) VWF antigen (VWF:Ag) and activity (VFW:GPIbM) measurement (immunoturbidimetry); ii) VWF multimers analysis (agarose-gels and immunoblotting); iii) Platelet functional analysis (PFA-200) and iv) Platelet activation (CD62P and CD63 expression by flow cytometry). Studies were performed 24 h after implant, every 7 days, and in the first week after ECLS explant. T-TAS® was used for hemostasis analysis in samples from bleeding patients, before and after in vitro addition of purified VWF.
Results: Twenty-five patients were included: 20 patients received venovenous and 5 patients venoarterial ECLS. After 24 h of ECLS implant, all patients showed increased VWF:Ag levels and prolonged PFA occlusion times, independently of platelet counts. In 60% of patients, altered VWF:GPIbM/VWF:Ag ratio (< 0.7) and loss of VWF high molecular weight multimers (HMWM) were observed. No significant changes in CD62P expression were detected in platelets from patients with ECLS compared to control (mean ± SD of 4.34 ± 2.2 vs. 3.27 ± 0.6, respectively; $p = 0.3$). Thirteen patients presented bleeding events; In vitro addition of purified VWF to their samples significantly reduced the T-TAS occlusion time (776 s ± 207 s vs. 1161 s ± 251 s, Mean ± SD, post vs. pre, respectively; $p < 0.05$). All patients showed normalization of VWF:GPIbM/VWF:Ag ratio (> 0.7), HMVM and PFA values after ECLS removal.
Conclusion: ECLS caused primary hemostasis alterations, leading to aVWD and platelet activation, solved early after support removal. Hemostatic efficiency in ECLS bleeding patients was corrected in vitro by providing functional purified VWF.

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Anaesthesia & Peri-operative Medicine 9

001297

Proteome analysis of COVID-19 patients in intensive care with and without delirium

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Intensive Care Medicine Experimental 2022, **10(2)**:001297

Introduction: Coronavirus disease 2019 (COVID-19) involves different organs [1]. Here, proteome analysis can offer a precise method to analyze a wide range of proteins providing further insight to different metabolic, immunologic and inflammatory pathways [2]. In the intensive care unit (ICU) around 50% of patients with COVID-19 suffer from delirium [3]. Thus, protein profiling may eluate new biomarkers or specific protein pattern.
Objectives: To assess the protein profile of COVID-19 patients with and without delirium at admission treated in the ICU.

Methods: In this prospective observational cohort study (ethics approval EA2/066/20; DRKS00021688) SARS-CoV-2 infected patients treated at the ICU from March 2020 to June 2020 were eligible for inclusion. Delirium at admission was diagnosed by positive delirium screening with the Confusion Assessment Method for Intensive Care Unit (CAM-ICU) or by oversedation defined as a Richmond Agitation Sedation Scale (RASS) < -2. From all patients three biosamples for proteome measurement were taken per week. The proteome measurements were done by mass spectrometry-based analysis and the log2-based transformed concentrations were further analyzed.
Results: We included 70 ICU-patients in our final analysis, 42 patients with delirium and 28 patients without delirium. Patients with delirium at admission had higher SOFA-score without Glasgow-Coma-Scale [8 (7–12) vs. 5 (3–6), p = 0.01] and were more often invasively ventilated at admission [30 (71.4%) vs. 1 (3.6%), p = 0.01]. Mortality did not differ between groups [4 (9.5%) vs. 4 (14.3%), p = 0.82]. Out of 284 proteins, 18 were significantly different between patients with delirium and without delirium. The abundance of proteins (median; IQR) involved in lipid metabolism [APOC3 (11.3; 11–11.8 vs. 10.9; 10.5–11.3), APOE (9.7; 9.4–10.6 vs. 9.4; 9.2–9.6), AZGP1 (10.3; 10–10.6 vs. 9.9; 9.7–10.1)], in impaired kidney function [CST3 (6.5; 5.9–7.1 vs. 5.9; 5.4–6.6)], in immunological and inflammatory function [PIGR (6.7; 6.1–7.1 vs. 6; 5.6–6.4), AMBP (10.9; 10.6–11.2 vs. 10.6; 10.5–10.8), C2 (8.1; 7.9–8.3 vs. 7.9; 7.6–8), B2M (8; 7.3–8.8 vs. 6.4; 6.1–7.5), SERPINF1 (8; 7.8–8.2 vs. 7.7; 7.5–7.9), LYZ (5.7; 5.3–6.2 vs. 5; 4.8–5.7)] as well as in retinol metabolism [RBP4 (8.9; 8.3–9.5 vs. 8.3; 7.7–8.8)] were elevated in patients with delirium vs. those without. Conversely, concentration of somatotrop [CLEC3B (5.6; 5.4–6 vs. 6.1; 5.8–6.5)], immunological protective proteins [HPX (12.7; 12.4–13 vs. 13; 12.8–13.2)], IGHG2.IGHG3.IGHG4 (12.3; 12–12.7 vs. 12.8; 12.6–13.1), IGLV2.8 (7.9; 7.2–8.4 vs. 8.3; 8–8.9), IGHM (11.5; 10.8–11.9 vs. 12; 11.5–12.3)] as well as proteins involved in anticoagulation (LPA.PLG (6.4; 6–6.6 vs. 6.6; 6.4–6.8), CD5L (9.2; 8.6–9.5 vs. 9.8; 9.1–10.2)] were reduced in patients with delirium vs. those without.
Conclusion: ICU patients with COVID-19 and delirium at admission demonstrated a higher rate of organ impairment and showed different protein patterns involving different pathways compared to patients without delirium.

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001321

Effect of noradrenaline on propofol-induced mitochondrial dysfunction in human skeletal muscle cells

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Intensive Care Medicine Experimental 2022, **10(2)**:001321

Introduction: Mitochondrial dysfunction is a hallmark of both critical illness and propofol infusion syndrome [1, 2] and may be aggravated by noradrenaline.
Objectives: We investigated the effects of noradrenaline on mitochondrial biology in human skeletal muscle cells with and without propofol-induced mitochondrial dysfunction.
Methods: Human skeletal muscle cells were isolated from vastus lateralis biopsies from patients undergoing elective hip replacement surgery (n = 14) or healthy volunteers (n = 4). After 96 h exposure to propofol (10 μg/mL), noradrenaline (100 μM), or both, energy metabolism was assessed by extracellular flux analysis and substrate oxidation assays using [14C] palmitic and [14C(U)] lactic acids. Mitochondrial mass, membrane potential, morphology and reactive oxygen species production were analysed by confocal laser scanning microscopy.
Results: Propofol moderately reduced mitochondrial mass and induced mitochondrial dysfunction including profound inhibition of exogenous fatty acid oxidation and a reduction of maximum electron transfer chain capacity and ATP synthesis. Noradrenaline exposure increased mitochondrial network size and turnover in both propofol treated and untreated cells as apparent from increased co-localisation with lysosomes. After adjustment to mitochondrial mass, noradrenaline did not affect mitochondrial functional parameters in naïve cells, but it significantly reduced the degree of mitochondrial dysfunction induced by propofol co-exposure, including restoration of fatty acid oxidation capacity. Both propofol and noradrenaline reduced mitochondrial membrane potential and increased reactive oxygen species production, but their effects were not additive.
Conclusion: Noradrenaline prevents rather than aggravates propofol-induced impairment of mitochondrial functions in human skeletal muscle cells. Its effects on bioenergetic dysfunctions of other origins, such as sepsis, remain to be demonstrated.

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Acknowledgements: Supported from Grant AZV NU21J-06–00,078.

001331

Perioperatively acquired weakness (POAW): an observational trial

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Intensive Care Medicine Experimental 2022, **10(2)**:001331

Introduction: Intensive care unit-acquired weakness (ICUAW) is a phenomenon seen in many critically ill patients, causing prolonged intensive care unit (ICU) stay and overall hospitalization period as well as increased morbidity and mortality and an impaired long-term outcome. Perioperatively risk factors are likewise and may cause muscular impairment. Our published pilot trial "Perioperatively Acquired Weakness" (POAW) (1) showed significant weakness and decreased functional independent measures in non-ICU patients undergoing elective surgery for the first time. Our goal was to confirm our earlier results and expand the knowledge about POAW.
Objectives: Evaluation of a perioperatively acquired muscle weakness with decreased functional capacity due to the risk factors during perioperative process.
Methods: In this prospective, clinical, observational trial a total of 100 patients undergoing elective surgery were included and examined preoperatively, at postoperative day one (POD1), and at hospital discharge or latest at postoperative day seven (POD7/D). We measured hand grip strength by dynamometry and strength assessment using the MRC scale. The patient´s muscle function was assessed by functional independence measure (FIM). Ethics vote Charité EA2/221/17, trial registration www.drks.de DRKS00015637.

Results: We included 100 patients. Age (53 [39/62]) with 54% male and 46% female. In our study cohort, we see a hand grip strength in decreased range preoperative with median 95% [83%/108%] compared to standard values published by Dodds et al.(2). At POD1 we see a significant weakness compared to preoperative with median 89%[79%/105%] (p = 0,02) and at POD7/D median 90%[79%/112%] (p = 0,034). Additionally the strength assessment of 12 muscle groups on the upper and lower extremities using the MRC score showed significantly decreased scores on POD1 compared to the preoperative assessment (p < 0,001) and did not reach initial values at POD7/D (p = 0,001). This significance is even more impressive because of the short duration of anaesthesia (median duration 102 min) while duration of anaesthesia shows a significant correlation with the development of muscle weakness, where a longer duration was more likely to cause muscle impairment (p = 0,006). The results from the FIM questionnaire showed no significant difference in our cohort when comparing preoperative to postoperative scores of patients (POD7/D) (p = 0.072). So although we can show a clinically measurable weakness, this has no significant effect on patient´s overall functional outcome.
Conclusion: We can confirm the development of perioperatively acquired weakness from our pilot trial as indicated by significant decreased handgrip strength and significant decreased MRC-scores on POD1 as well as POD7/D in this new cohort. Duration of surgical procedure seems to be a risk factor.

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001338

Changes in sleep quality among ICU survivors

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Intensive Care Medicine Experimental 2022, **10(2)**:001338

Introduction: Poor sleep quality in the intensive care unit (ICU) is known to be associated with increased morbidity and mortality. Both environmental and physiological factors are thought to play an important role. However, little is known about the changes in sleep quality in patients recovering from critical illness.
Methods: Patients admitted to the medical ICU of a university-affiliated hospital between July 2017 and April 2021 were enrolled in a prospective cohort study. ICU survivors who completed Korean Richards-Campbell Sleep Questionnaire (K-RCSQ) at two-time points; ICU discharge and hospital discharge (or the 28th day from ICU discharge) were included. Participants with an increase of 10 or more total K-RCSQ scores after ICU discharge were grouped as improvement in sleep quality group and others were classified as lack of improvement in sleep quality group.
Results: A total of 52 participants were included in this study. The mean total K-RCSQ score at the time of ICU discharge and hospital discharge was 48.0 ± 8.5, and 54.3 ± 23.2, respectively. Of the K-RCSQ subscales, RCSQ 2 (the falling asleep domain) was significantly higher at the time of hospital discharge compared to at the time of ICU discharge (56.7 ± 27.8 vs. 46.3 ± 32.8; $p = 0.04$). The perceived noise assessment score was also significantly higher in the ICU, compared to general wards (35.3 ± 28.6 vs. 24.6 ± 25.5; $p = 0.03$). Among the 52 participants, 27 (51.9%) showed improvement in sleep quality. The improvement group were given less antipsychotics during their stay in the ICU compared to the lack of improvement group (1 [3.7%] vs. 8 [32.0%]; p = 0.01).
Conclusion: Although the mean total K-RCSQ score was not different, ICU survivors reported significant improvement in falling asleep after ICU discharge. Improvement in sleep quality after ICU discharge may be associated with the use of antipsychotics during the ICU stay.

001340

A comparison of the total intraoperative fluid administered by goal directed fluid therapy and conventional fluid therapy in isolated traumatic brain injury patients undergoing early decompressive craniectomy—a prospective randomized controlled trial

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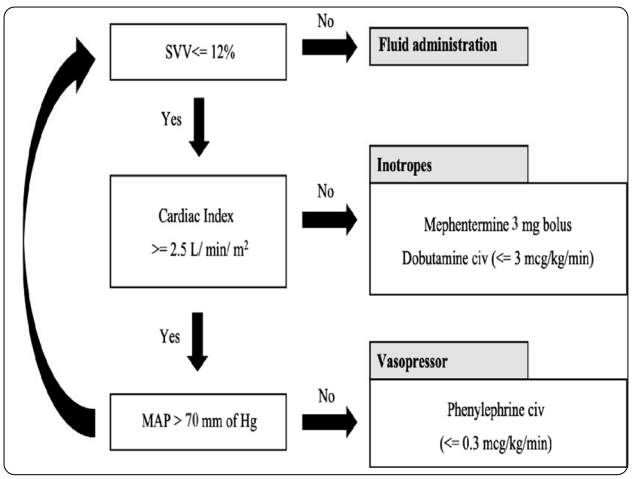
Introduction: Traumatic brain injury patients are prone to osmotic and electrolyte disturbances1 and hence require a unique approach to fluid management2.
Objectives: To compare goal-directed therapy and conventional hemodynamic based therapy on total intra-operative fluid administered during decompressive craniectomy.
Methods: Prospective randomized controlled trial was accruing 64 adult patients with TBI undergoing decompressive craniectomy. Goal directed fluid therapy (GDT): Flo Trac, EV-1000 device (Edwards Lifesciences, Irvine, CA) to monitor Stroke volume variation, Cardiac index and mean arterial pressure.Conventional fluid therapy: Crystalloid infused at a rate of 2 ml/kg/hour with target MAP > 70 mm of Hg.



Results: There was a numerical difference in total fluid administered between both the groups but did not prove to be statistically significant (p = 0.511). No significant difference in intraoperative blood loss,urine output,lactate levels, haematocrit levels, total ventilator days (p = 0.115), total ICU days (p = 0.294), total hospital days (p = 0.311), Average FOUR score (p = 0.172), GCS at discharge (0.663) and GOS at 3 months post-discharge (p = 0.589). Overall mortality was 4 patients in group A (12.5%) and 7 patients in group B (21.8%) died.

Parameter	Group A (GDT) (n=32) mean±SD	Group B (CHT) (n=32) mean±SD	P value
Total Intraoperative fluid Input	2567.81±534.6749	2670.62±698.7589	0.511
Total intraoperative blood loss	496.87±221.044	512.50±216.6459	0.776
Total intraoperative urine output	558.59±353.1316	466.56±243.8350	0.230
Haematocrit			
Before incision	30.59±6.1506	30.08±4.4422	0.705
End of surgery	27.07±4.7675	27.14±4.6871	0.958
Δ Haematocrit	3.73±5.2067	3.02±4.7694	0.572
P value	0.000	0.000	
Lactate		1.64±1.1176	0.284
Before incision	2.00±1.4620	1.57±0.9695	0.777
End of surgery	1.65±1.2766	0.06±0.7079	0.069
Δ Lactate	0.35±0.4918	0.001	
P value	0.000		
Total ventilator days	3.03±4.4684	4.50±4.7519	0.208
Total ICU days	1.75±4.7110	3.37±6.0734	0.236
Total hospital days	6.09±6.1137	7.46±6.7917	0.398
GCS at discharge	10.03±3.8460 (n=30)	9.56±4.3840 (n=30)	0.663
GOS at 3 months post discharge	4.43±1.135	4.10±1.539	0.589

Conclusion: No statistically significant difference between the total intraoperative fluid administered between both the groups was observed. Quest for ideal fluid regime in traumatic brain injury patients it still ongoing.

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Acknowledgements: To Dept of Anaesthesia & Intensive care,PGIMER.

001348

Inhalation sedation with sevoflurane is safe and effective in critical patients with COVID-19 pneumonia and ARDS

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Intensive Care Medicine Experimental 2022, **10(2)**:001348

Introduction: Volatile sedation is unknown for most of the intensive care units. However, it could be useful to minimize sedation drugs, adverse events and provide pulmonary benefits. In this study, we describe our experience using sevoflurane in a third level Spanish hospital during COVID-19 pandemic.
Objectives: To clarify Sevoflurane inhalation sedation safety and efficacy severe COVID-19 critical patients.To clarify Sevoflurane inhalation sedation safety and efficacy severe COVID-19 critical patients.
Methods: 15 patients with severe COVID-19 sedated with inhaled sevoflurane were studied for safety and efficacy. Sedation was administered by ANACONDA® device (same filter in all ventilators). Pulmonary mechanics (peak pressure, plateau pressure, delta pressure and compliance), ventilation data by arterial gasometry (CO2) and hemodynamic repercussion (Norepinephrine in mcg/Kg/min pre-administration, one hour, 12 h and 24 h after starting sevoflurane infusion) were collected. Sedation target, renal repercussion and the need of adjuvant sedation was also collected. 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. Pearson`s correlation was used to assess interrelation between quantitative variables.
Results: Age 60.6 ± 6.7 years. Men 66,6%. SOFA 4.1 ± 1.1. Pre-sevoflurane Invasive mechanical ventilation 5.4 ± 3.4 days. Sevoflurane dose 6.6 ± 1.5 ml/h. Tidal volume 6 ml/kg. Pearson's correlation was adequate for sedation target, monitored by BIS (parameters analysed at one, twelve and 24 h after starting sevoflurane and BIS data) in 100% of our patients, without adjuvant sedation. Renal failure was not observed.

	Pearson´s correlation	*p*
Peak pressure Pre ßà peak pressure 1 h	0.94	< 0.00
Peak pressure Pre ßà peak pressure 12 h	0.63	< 0.05
Peak pressure Pre ßà peak pressure 24 h	0.26	0.3
Plateau pressure Pre ßàPlateau pressure 1 h	0.65	< 0.05
Plateau pressure Pre ßàPlateau pressure 12 h	0.75	< 0.00
Plateau pressure Pre ßàPlateau pressure 24 h	0.73	< 0.00
Compliance pre ßà compliance 1 h	0.95	< 0.00
Compliance pre ßà compliance 12 h	0.96	< 0.00
Compliance pre ßà compliance 24 h	0.86	< 0.00
Delta pressure pre ßà Delta pressure 1 h	0.93	< 0.00
Delta pressure pre ßà Delta pressure 12 h	0.93	< 0.00
Delta pressure pre ßà Delta pressure 24 h	0.67	< 0.03
Norepinephrine pre ßà norepinephrine 1 h	0.98	< 0.00
Norepinephrine pre ßà norepinephrine 12 h	0.89	< 0.00
Norepinephrine pre ßà norepinephrine 24 h	0.89	< 0.00
pCO2 pre ßà pCO2 1 h	0.83	< 0.00
pCO2 pre ßà pCO2 12 h	0.8	< 0.00
pCO2 pre ßà pCO2 24 h	0.55	0.034

Conclusion: Inhalation sedation with sevoflurane is safe and effective in patients with severe COVID-19. Using ANACONDA® device, an increase in Peak pressure and pCO2 was observed.

001401

The first four pandemic waves of SARS-COV-2 in patients admitted to intensive care unit and association with outcome

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Intensive Care Medicine Experimental 2022, **10(2)**:001401

Introduction: Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) related pneumonia and the associated systemic complications are responsible for still high mortality in patients admitted to the intensive care unit (ICU).
Objectives: The aim of this single-center observational, retrospective study was to describe clinical characteristics and laboratory parameters of critically ill patients with severe Coronavirus Disease 2019 (COVID-19) during the first ten days of ICU admission and their association with outcome.
Methods: Local Ethic Committee approved the study protocol. Adult critically ill patients consecutively admitted to our university ICU with severe COVID-19 pneumonia from March 2020 to September 2021 were enrolled in the study. Data were divided according to the four registered pandemic waves. Demographic data, comorbidities, physiological variables, ICU length of stay (LOS), and laboratory parameters during the first ten days of ICU admission were collected. Clinical data were evaluated in univariate analysis according to ICU mortality as measure of outcome. In multivariable logistic regression model, we entered in the model variables which reached 0.1 level of significance.
Results: A total of 268 adult patients were enrolled. Mortality was 60, 88, 74 and 77% in the four waves ($p = 0.05$) and ICU-LOS was 34,13, 9 and 9 days, respectively ($p = 0.001$). Univariate analysis showed that non-survivors were older (73 ± 10 vs 60 ± 12 years; $p = 0.001$), had higher incidence of diabetes (34 vs 16%; $p = 0.004$) and chronic respiratory disease (14 vs 9%; $p = 0.014$). ICU-LOS was longer in survivors

(27 (IQR 30) vs 9 (8) days; p = 0.001). At admission, non-survivors had higher LDH (679 vs 446 mU/ml; p = 0.001), IL-6 (73 vs 32 pg/ml; p = 0.001), d-dimer (2.28 vs 1.42 µg/mL; p = 0.002), Troponin T (38 vs 11 pg/ml; p = 0.001), creatinine (1 vs 0.7 mg/dL; p = 0.002), BUN (73 vs 50 mg/dL; p = 0.001), myoglobin (171 vs 64 ng/ml; p = 0.002) and glycemia (166 vs 139 mg/dL; p = 0.001) than non-survivors. In multivariable analysis, age [OR1.10; C.I. 1.065–1.135], diabetes [2.345; 1.011–5.441] and LDH [1.002;1.001–1.003] remained predictors of ICU mortality. Temporal profile of laboratory data showed: higher but decreasing procalcitonin level in the first wave and low but increasing levels in the following ones; low and decreasing albumin levels in all the studied waves; high BUN and myoglobin levels in all the waves; higher IL6 levels in first wave than in the others; high d-dimer level in all the waves, and increasing trend in the fourth wave.
Conclusion: In severe COVID-19 ICU patients, age, diabetes and LDH are significant predictors of outcome.

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Acknowledgements: None.

001402

Retrospective analysis Undertaken for the Patients Treated for Unexplained Retroperitoneal/ abdominal pain in the Emergency Department (RUPTURED)—Abdominal Aortic Aneurysm (AAA) arm RUPTURED-ARM

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Intensive Care Medicine Experimental 2022, **10(2)**:001402

Introduction: Acute abdominal pain is one of the commonest reasons for presentation to ED. The older individuals carry a higher mortality rate, with complex pathologies. Amongst the different acute abdominal presentations, abdominal aortic aneursym carries considerable mortality in the older population. This lead to the National AAA Surveilance Programme (NAAASO) for men over the age of 65 years for AAA screening. The use of ultrasound by emergency physicians is becoming increasingly popular in the UK. The immediacy and availability of bedside ultrasound in the emergency department means that critical management decisions can be made earlier.
Objectives: Primary outcome: To study the prevalence of AAA in patients presenting to our emergency department with abdominal pain, renal colic and back pain Secondary outcome: To assess the common presentation pattern of AAA, course in hospital, all cause mortality, re-presentation rates and vascular referral rates.
Methods: Retrospective assessment of patients presenting to BVH emergency department over 6 months from January 2021 to June 2021 was collected. Any patient over the age of 50 presenting with abdominal pain, renal colic or back pain was deemed suitable for the study. We further assessed the patient groups on their presentation for the need to be indicated for a bedside USS as follows Inclusion criteria included unexplained abdominal pain, renal colic and back pain in individuals over 50 years. Exclusion criteria was age < 50,known AAA but asymptomatic / abdominal pain attributable to alternate diagnosis, Pregnant women, documented evidence of recent AAA.
Results: Between January 2021 and June 2021, around 920 patients presented with abdominal pain, renal colic and back pain (as triaged at first point of contact). There were about 42 renal colics, 65 flank pains and 179 back pains and 636 other abdominal pain. Of the 920 patients, the prevalence of Abdominal aortic aneurysm was 20 patients (2.1%). Of the 20 patients, 15 were male and 5were female. Diagosis had been obtained by bedside USS in only 6 patients (30%), 6 patients (30%) went straight to CT scanner and no imaging performed at all in 8 patients (60%). The 8 patients were identified on subsequent investigations in the community or specilaity review.4 cases had discussion with the tertiary vascular centre and all 4 were arranged for transfer to the same center from AE. There was 4 patients (20%) with an all-cause mortality within 30 days. Of the 4 patients, 3 (15%) succumbed to the current illness, while 1 patient had died of complications from heart failure. Meanwhile, the overall all-cause mortality in the 920 patients was around 56.3%
Conclusion: The prevalence of AAA between January 2021 and December 2021 was about 2.1%, which is higher than the prevalence reported in NAASP. The mortality due to AAA was 15% compared to 5.63%

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001409

Comparing routine with expert delirium screening in critically ill patients: a secondary analysis of data from the prospective, multicenter EuMAS study

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Intensive Care Medicine Experimental 2022, **10(2)**:001409

Introduction: Routine screening for the presence of delirium in critically ill patients is a recommendation found in multiple international guidelines and expert statements [1,2]. Previous data have suggested discrepancies between the results of routine bedside delirium screening compared to an evaluation by a trained expert [3,4]. This has significant potential implications for targeted qualityt improvement projects aiming at optimal detection of delirium in an intensive care unit (ICU) cohort.
Objectives: To assess the performance of routine delirium screening as compared to screening by a trained expert in a large European cohort and to evaluate the effects of a delirium teaching module on this performance.
Methods: This is an exploratory, preplanned, secondary analysis of the Enhancing European Management of Analgesia, Sedation, and Delirium (EuMAS) study (ClinicalTrials: NCT03553719), which assessed delirium, pain, and sedation (PAD) management for patients across 12 European centers at 3 cross-sectional time points. Between the first and second time point, centers received a structured, 6-week PAD training. At each time point, delirium screening results documented in the patient chart were collected and included patients were screened for the presence of delirium by a study expert using the Confusion Assessment Method for the ICU (CAM-ICU). Results of the documented screening exam and the expert assessment were subsequently compared for congruency.
Results: We analyzed 158, 127, and 100 expert and routine CAM-ICU delirium screenings for patients with at least one rating in assessment periods 1, 2, and 3, respectively across 12 ICUs. There were no significant differences in baseline characteristics between timepoints. Cohen's kappa κ, which was used to quantify the interrater reliability, was 0.694 (95% CI 0.511–0.886) for assessment period 1, which could be quantified as *substantial* interrater reliability [5]. In assessment periods 2 and 3, Cohen's kappa κ was 0.526 (95% CI 0.316–0.736) and 0.545 (95% CI 0.329–0.762), respectively, corresponding to *moderate* interrater reliability [5] (Table 4).
Table 4. Interrater reliability of routine and expert delirium assessments, by assessment period.

Assessment period	Cohen's kappa *κ* [95% CI]	Standard error	*n*
1	0.698 [0.511; 0.886]	0.095	158
2	0.526 [0.316; 0.736]	0.106	127
3	0.545 [0.329; 0.762]	0.109	100

Cohen's kappa κ was calculated without the use of weights, by using all available cases (all subjects with at least one rating) to determine the expected agreement, and by constructing design-based confidence intervals. Using deterministic benchmarking, 0.41–0.60 can be described as *moderate*, and 0.61–0.80 as *substantial* interrater reliability [5].
Conclusion: In this cohort of 12 European hospitals, the agreement between routine delirium screening and the screening performed by a trained expert were compared. The interrater reliability was overall moderate to substantial and did not improve significantly throughout the course of the study and across training periods. Future studies will need to assess methods to improve the quality of bedside delirium screening in critically ill patients.

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Acknowledgements: Funded by the European Society of Intensive Care Medicine (ESICM) with the Next Start-up Grant.

001424

Application of the ABCDEF bundle in patients with covid-19 pneumonia and its consequences in survivors one year after discharge

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Intensive Care Medicine Experimental 2022, **10(2)**:001424

Introduction: in patients admitted to the ICU and especially in those who survived COVID-19, serious sequelae have been observed in the physical, mental and cognitive spheres (1)(2). As a preventive measure to reduce the impact of these conditions, it has been shown that the application of the ABCDEF bundle during the stay in the ICU allows us to reduce the involvement of these 3 levels in our patients.(3)(4).
Objectives: to analyze risk factors, clinical course, and outcome, including annual neuropsychological, cognitive, and physical post-ICU discharge in pts. with coronavirus disease 2019 (COVID-19) infection admitted to an ICU where the ABCDEF bundle is implemented as a routine standard of care for all patients.
Methods: A retrospective, descriptive study for 12 month (Jan-Dec.20) of pts. with COVID-19 admitted to a 16 beds intensive care unit (ICU). Exclusion criteria: pre-existing mental illness, pts. who required transfer to another ICU, and pts. who were died during ICU stay. The data we collected from the patients were: age, sex, body mass index, prognostic severity scales (Apache-II and Saps-3), underlying diseases, need for mechanical ventilation (IMV) and its duration, use of muscle relaxants (MR), need to prone position, complications, maximum dose of midazolam (MDZ) and other neuroleptics. We used pain-indicating behavior scale (ESCID), Richmond Agitation-Sedation Scale (RASS) to identifie levels of agitation and sedation and Confusion Assessment Measure for ICU(CAM-ICU) to measure Delirium. We collected whether rehabilitation had begun during the ICU stay and the start date, in addition to indicating whether there had been a family presence. The relationship with the presence of physical, cognitive or affective alterations after hospitalization discharge, were analyzed. Values are presented as percentage, mean, and medians with interquartile range (IQR). The independence of the variables was established with a significance level of $p < 0.01$, using the chi-square test or the Student's test, depending on their category. All analyses were done with IBM SPSS Statistics for macOS, version 25.
Results: A total of 100 pts., out of a total of 159 pts. with COVID-19 admitted to the unit during this period, were analyzed. General characteristics: 67% males, mean age: 58 years (34–79), mean admission APACHE II: 12 points (2–22), median admission SAPS3: 50 points (IQR: 21–58), 78% pts. needed for IMV, duration of IMV: 19 days (IQR: 8–33), median ICU stay in intubated pts.: 24 days (IQR: 11–39), median hospital stay in intubated pts: 36 days (IQR:21 -54). CAM ICU resulted positive for delirium (CP) in 56% pts., all of them were intubated pts. There is a correlation between the presence of delirium duration of coma, 11 days (IQR: 6–21), 8 days (IQR: 7–16), presented (CP)Vs nonpresented (CN)(95% CI, $P < 0.001$), maximum dose of midazolam, 192 mg (IQR: 120–331), 70 mg (IQR: 46–168), CP vs CN (95% CI, $P < 0.001$), and duration of administration, 15 days (IQR: 10–26), 6 days (IQR: 3–8), CP vs CN

(95% CI, P < 0.001), presence of complications, need prone, RASS and ESCID, and affective sequela (all 95% CI, P < 0.001). 87% of our patients receive rehabilitation during their ICU stay with a median start time of 20 days (IQR 9–31) All our relatives had family support throughout their stay in the ICU. We have not found statistical significance in the rest of the variables analyzed (p > 0.05).
Conclusion: Despite the difficulty of applying the ABCDEF bundle in the ICU and especially during the pandemic, we have seen in our unit a great commitment in the measures we adopted, such as family presence or the starting of rehabilitation, as well as measuring the values of daily scales for the evaluation and early detection of pain and delirium. Detecting in the later correlation its presence and the duration of the coma, the dose and duration of benzodiazepines dispensed. So, we have found a significant relationship between the presence of delirium and the days of sedation, daily dose and duration of benzodiazepines in continuous perfusion.

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Acute Respiratory Failure 1

000021

Outcomes of critically ill patients with COVID-19 hypoxic respiratory failure. Is non-invasive mechanical ventilation a wise choice?

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Intensive Care Medicine Experimental 2022, **10(2)**:000021

Introduction: The choice between invasive mechanical ventilation (MV) and non-invasive mechanical ventilation (NIV) in COVID-19 patients has been a topic of discussion during the current pandemic. After 2 years, the fear of aerosolization has decreased and there is a trend towards a more conservative use of MV in these patients. However, there are very little studies reflecting patient results.
Objectives: To analyze the results of patients with acute respiratory failure caused by COVID-19 pneumonia hospitalized in an Intensive Care Unit (ICU) with the necessity of ventilatory support, and compare the results of the patients treated with MV and NIV.
Methods: Retrospective observational study comparing patients admitted to a polyvalent ICU with a diagnosis of COVID-19 pneumonia, between August 2020 and May 2021, who received ventilatory support. Patients were divided into 3 groups: (G1) MV upon admission (G2) treatment with NIV only and (G3) failure of NIV after a period of more than 24 h, with subsequent need for MV. The demographic and clinical characteristics of the 3 groups were compared. Results were adjusted by modeling to control the effect of confounding variables. Patients with limitation of life-sustaining care were excluded from the study.
Results: A total of 183 patients were included (n G1: 41, G2: 104 and G3: 38), 28.4% were men, with a mean age of 61.5 ± 12.1 years, APACHE II of 11.6 ± 5.8 and Barthel of 96.8 ± 7.15. As relevant comorbidities, we found obesity 46.4% (BMI: 30.3 ± 5.5), hypertension in 51.9%, diabetes in 23% and respiratory pathology in 19.3% of patients. At admission, 13.6% of patients had mild ARDS, 71% moderate, and 15.3% severe.
Conclusion: In our series, no significant differences were found in the days of MV between patients treated with MV in the first 24 h of admission and patients with NIV failure and subsequent need for MV. The NIV failure rate was 26.7%. According to our results, an initial NIV test does not increase the days of MV, on the other hand, it avoids a considerable percentage of intubations and, consequently, their complications.

000035

Impact of extra-respiratory stimulations on dyspnea in critically ill mechanically ventilated patient: the sensopnea 2 study

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Introduction: Half of patients undergoing mechanical ventilation (MV) in the intensive care unit report a dyspnea of moderate to severe intensity, which causes immediate suffering and post-traumatic stress disorders. Dyspnea has two distinct components, a sensory component and an emotional component. Our objective was to evaluate and to compare the respective impact of a modulation of the sensory component (respiratory afferents) and the emotional component (extra respiratory auditory and sensory stimulations) on the intensity of dyspnea in critically ill patients undergoing MV, either invasive or non-invasive.
Methods: Patients MV for more than 48 h with a dyspnea intensity ≥ 40 mm on a visual analog dyspnea scale (Dyspnea-VAS) were included. We studied the following interventions: 1) increase of pressure support level by 5 cmH2O vs. baseline ventilator settings as a control (sensory component), 2) a relaxing standardized music piece vs. a "pink" noise as a control (emotional component), and 3) fresh air directed toward the face vs. the thigh as a control (emotional component). A washout period separated each condition. Dyspnea was assessed with the Dyspnea-VAS and the A1 score of the Multidimensional Dyspnea Profile. The respiratory drive was assessed by the P0.1 and electromyographic activity of the Alea Nasi and parasternal muscles.
Results: We included 46 patients, 19 tracheostomized, 18 intubated and 9 under non-invasive ventilation. Median (interquartile range) age was 63 years (54–73) and duration of mechanical ventilation was 33 days (7–49). Compared to their respective control group the three intervention decreased Dyspnea-VAS: 1) pressure support increment 20 [20–40] mm vs. 70 [60–80], p < 0.0001, 2) auditory stimulation 40 [20–40] vs. 70 [60–80], p < 0.0001 and 3) sensory stimulation 40 [30–50] vs. 60 [50–80], p < 0.0001). Compared to their respective control group the three interventions decreased A1: 1) pressure support increment 5 [4–6] vs. 7 [6–8], p < 0.0001, 2) auditory stimulation 2 [0–2] vs. 7 [6–8], p < 0.0001 and 3) sensory stimulation 3 [2–4] vs. 7 [6–8], p < 0.0001. The electromyographic activity of Alea nasi and parasternal muscles decreased significantly after pressure support increment (p < 0.0001 for both) but did not change during auditory and sensory stimulation. P0.1 decreased more markedly with pressure support increment (3.7 [2.7–5.1] cmH2O vs. 6.5 [6.0–8.1], p < 0.0001) than with auditory (6.0 [5.7–7.4] vs. 6.3 [6.0–7.7], p = 0.002) and sensory (6.0 [5.3–7.6] vs. 6.5 [5.7–7.7], p = 0.001) stimulation.
Conclusion: In critically ill MV patients, auditory and sensory extra-respiratory stimulations decreased dyspnea without decreasing respiratory drive, suggesting a mechanism involving a modulation of the emotional component.

000037

Impact of emotional stimulations on thirst in critically ill mechanically ventilated patient

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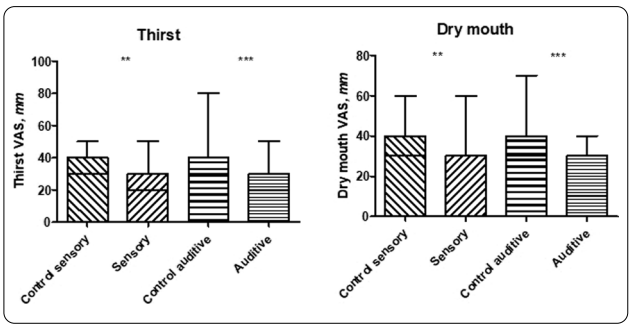
Intensive Care Medicine Experimental 2022, **10(2)**:000037

Introduction: Up to 70% of intensive care unit patients report thirst. Thirst provokes the urge to drink fluids. This multidimensional symptom is described in terms of intensity and dry mouth. Few studies have investigated thirst relief in intensive care unit patients and none has focused on mechanically ventilated (MV) patients Relieving thirst usually involves giving the patient something to drink; unfortunately, in this population, it is difficult to meet this need and alternative interventions are needed. Our objective was to evaluate and to compare the impact of auditory and a sensory stimulations on the intensity of thirst in critically ill patients undergoing invasive or non-invasive MV. This is an ancillary study of the "Sensopnea 2" study.
Methods: Patients MV for more than 48 h with a dyspnea intensity $\geq$ 40 mm on a visual analog dyspnea scale (Dyspnea-VAS) were included (inclusion criteria of the Sensopnea 2 study). Two visual analog scales (Thirst-VAS and Dry mouth-VAS) assessed thirst and dry mouth sensation. We studied the following interventions: 1) a relaxing standardized music piece vs. a "pink" noise as a control (auditory stimulation), and 2) fresh air directed toward the face vs. the thigh as a control (sensory stimulation). A washout period separated each condition.
Results: We included 46 patients, 19 tracheostomized (41%), 18 intubated (39%) and 9 under non-invasive ventilation (20%). Median (interquartile range) age was 63 years (54–73) and duration of mechanical ventilation was 33 days (7–49). Figure 1 shows Thirst-VAS and Dry mouth-VAS during sensory stimulation and auditive stimulation with their control. Compared to their respective control group the two intervention decreased Thirst-VAS: 1) auditory stimulation 20 [0–30] vs. 30 [0–40], p = 0.0004 and 2) sensory stimulation 30 [20–50] vs. 40 [30–50], p = 0.0025). Compared to their respective control group the two intervention decreased Dry mouth-VAS: 1) auditory stimulation 30 [10–40] vs. 40 [30–70], p = 0.0002 and 2) sensory stimulation 30 [0–60] vs. 40 [30–60], p = 0.0013).



Conclusion: In critically ill dyspneic MV patients, auditory and sensory stimulations decrease thirst and dry mouth sensation.

000068

Improvement of interobserver agreement of ARDS diagnosis by adding additional imaging and a confidence scale

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Introduction: Acute respiratory distress syndrome (ARDS) is often not recognised in clinical practice, largely due to variation in the interpretation of chest X-ray (CXR) leading to poor interobserver reliability (Sjoding). Two approaches seem to improve agreement:the aggregation of multiple images and scoring by multiple experts (Sjoding, Meade). The inclusion of the rater's confidence in the diagnosis rather than dichotomising the judgements can increase the uniformity between raters and facilitate a more consistent diagnosis.
Objectives: We hypothesized that the agreement in interpretation of chest imaging for the diagnosis of ARDS in invasively ventilated intensive care unit patients between experts improves when using an 8-grade confidence scale compared to using a dichotomous assessment, and that the agreement increases after adding chest computed tomography (CT) or lung ultrasound (LUS) to CXR.
Methods: A panel of three experts scored ARDS based on clinical and imaging (CXR, LUS and CT) data from an observational cohort study (Hagens) using a dichotomous assessment and an 8-grade confidence scale (Figure 1). The intra class correlation (ICC) was calculated per day, imaging modality, and scoring method and were compared using bootstrapping. Patients were classified as having ARDS or not based on the combined confidence grades of the experts, followed by a consensus meeting for conflicting scores. Diagnostic accuracy was compared between individual experts, a team of researchers and the team of treating clinicians.

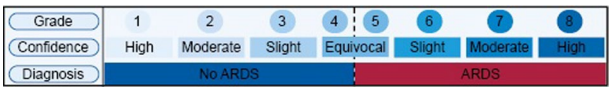

Figure 1. The 8-grade confidence scale. The expert scored a certain grade for each available image. The upper row displays the grades the expert scored, where the middle row indicates how the confidence of this grade should be interpreted. The row below indicates the corresponding diagnosis.

Results: 401 patients were included in the analysis. The best ICC was found using an 8-grade confidence scale for LUS (ICC: 0.49; 95%-CI: 0.29 to 0.63) and CT evaluation (ICC: 0.49; 95%-CI: 0.34 to 0.61) (Figure 2). When 8-grade was compared to dichotomous assessment, on day 1 the ICC of CXR increased by 0.022 and of CT by 0.065. Adding LUS to CXR increased the ICC with 0.25 while adding a CT increased ICC with 0.25 for the confidence assessment. The diagnostic accuracy for ARDS of the individual experts ranged from 0.72 to 0.86, while the research team had an accuracy of 0.80 and the clinical team of 0.57.

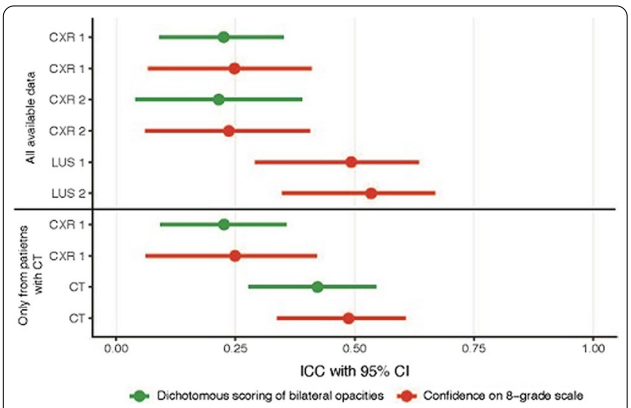

Figure 2. Agreement on scoring ARDS for all imaging modalities. ICCs with 95% confidence interval displaying the agreement for dichotomous scoring of bilateral opacities to diagnose ARDS and scoring of confidence for ARDS diagnosis on an 8-grade scale. Abbreviations: CI: confidence interval, CXR = chest X-ray, ICC = intra class correlation coefficient, LUS = lung ultrasound.

Conclusion: Agreement on diagnosis of ARDS can increase substantially by adapting the scoring system from dichotomous to an 8-grade confidence scale and by adding additional imaging modalities such as LUS or chest CT. This suggests that a simple assessment of ARDS presence by a chart review of one assessor is insufficient to define ARDS in future studies.

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Acknowledgements: LDJB reports Consultancy for Sobi and Scailyte paid to institution and Grants from Longfonds, Health Holland, IMI and Amsterdam UMC paid to institution. LAH, FLIMV, NFLH, HAG, MRS, SCG, MJS, DCJJB, and RMS have no conflict of interest regarding this manuscript.

000080

Predictors of effectiveness of HFNC oxygenation in severe SARS-COV2 pneumonia in non-ICU hospital wards

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Intensive Care Medicine Experimental 2022, **10(2)**:000080

Introduction: SARS-CoV2 pneumonia requiring hospitalizationin can icrease ICU occupant beds due to the need for invasive mechanical ventilation (IMV). High Flow Nasal Canula (HNFC) oxygenation could avoid supplementary IMV and subsequent ICU hospitalization.
Objectives: To identify factors associated with failure of HFNC oxygenation in unvaccinated patients hospitalized in non-ICU wards for severe SARS-CoV2 pneumonia.
Methods: A prospective cohort study of consecutive hospitalized patients in non-ICU wards requiring intensive oxygenation with HFNC for severe SARS-CoV2 pneumonia (WHO scale 5), March–May 2021 during the predominance of B.1.17 strain. All patients received standard-of-care treatment with remdesivir, dexamethasone and enoxaparine. COVID-19 pneumonia was confirmed by lung CT scan lesions and nasopharyngeal RT-PCR test. ROX index was calculated 2, 4 and 6 h after HFNC initiation. Logistic regression analysis evaluated in-hospital outcome (IMV and mortality). ROX values for IMV were assessed by ROC analysis.
Results: Demographics: 69 patients;male (72.5%), mean age(SD±): 57(12)years, mean BMI (SD±):29.6(5.9)Kg/m2, mean(SD±) Charlson Comorbidity Index(CCI):1.9(1.7). Symptoms started 8 (±3)days before hospitalization. PaO2/FiO2 (SD±) at admission was 170(71). All patients had extensive lung infiltrates. A 33.3% (n = 23) failed HFNC oxygenation with sustained severe hypoxemia (PaO2/FiO2 below 100) requiring IMV and ICU hospitalization. A 26.1% (n = 18) under HFNC oxygenation deceased. ROX index remained lower in patients who failed HNFC and those who died compared to patients with clinical success (Fig. 1) and non-survivors (Fig. 2). ROX index at 6 h was the only independent factor for HFNC failure (cutoff 4.79, AUC 0.869(0.778–0.960; p < 0.001, sensitivity 63%, specificity 80%),need for IMV(adjOR 0.26[95%CI 0.12–0.55]) and mortality (adjORrox 0.34[95% CI 0.16–0.70]) both with CCI > 2 (adjORcci 10.22 [95% CI 2.28–45.90).

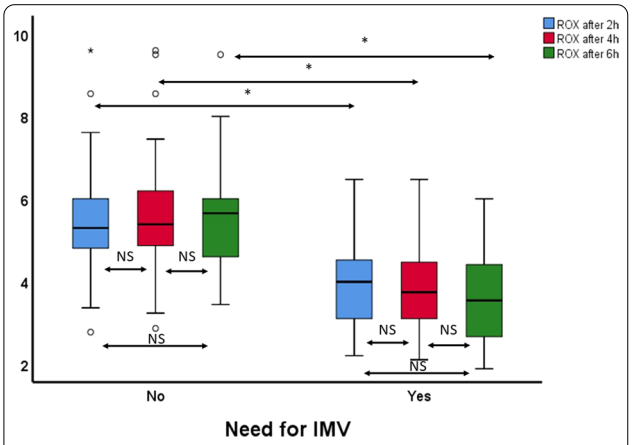

Figure 1.

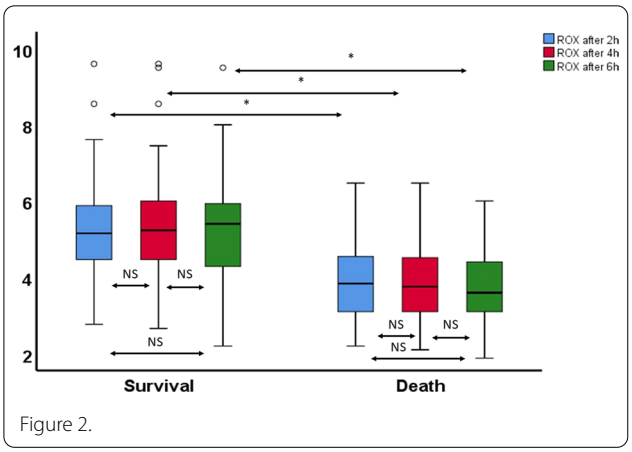

Figure 2.

Conclusion: HFNC oxygenation was successful in 40.8% of patients with severe SARS-CoV2 pneumonia saving 28 patients from IMV and ICU hospitalization. A higher ROX score at 6 h after HFNC implementation is the best predictor of success and in-hospital survival.

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Acknowledgements: None.

000095

Benefits of the intellectual mechanical ventilation modes in patients with obesity

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Intensive Care Medicine Experimental 2022, **10(2)**:000095

Introduction: The number of surgical patients with obesity is increasing.Obesity alters respiratory anatomy and physiology and, therefore, requires an adaptation of ventilator settings during mechanical ventilation[1].To date, no guideline about ventilatory strategies in obese patients undergoing surgery under general anesthesia has been developed[2]. There are no data about using intellectual full closed

loop modes in this patients. There is an ability to personalize respiratory support and reduce workload for physicians without compromising patient's safety with using intellectual modes of mandatory ventilation[3].
Objectives: To compare the effect(s) of intellivent-ASV and conventional ventilation modes in patients with obesity (BMI > 30 kg/m2) after uncomplicated cardiac surgery.
Methods: In this trial 40 adult patients were ventilated with full closed loop ventilation and oxygenation mode (INTELLiVENT-ASV®) and 40 with conventional ventilation modes after uncomplicated cardiac surgery. Hamilton G5 ventilators were used and 8 physicians were involved into the study. All physician's actions, ventilator settings and changes were monitored and recorded during mechanical ventilation and weaning. Care of both groups was standardized, except modes of postoperative ventilation. We compared:

- the physician's workload, through accounting number of manual ventilator settings and time they spent near the ventilator in every group;
- duration of tracheal intubation in ICU;
- evaluation of ventilation safety by considering driving pressure, mechanical power, PEEP, tidal volume and FiO2 level;
- the frequency of undesirable events, postoperative complications.

Results: In Intellivent group the number of manual ventilator settings and physician's time spent near the ventilator before tracheal extubation were significant lower: 0 (0–2) vs 5 (4–7), and 40 (2–75) sec vs 183 ± 60 s respectively ($p < 0.0001$ in both cases). There were significant differences in the duration of respiratory support in ICU: 240 ± 55 min (Intellivent group) vs 283 ± 79 min (control) ($p = 0.0059$). Intellivent-ASV mode was more protective compared to conventional mode through significant reduction in the driving pressure, mechanical power, tidal volume, FiO2 and PEEP levels, but without difference between paO2/FiO2 ratio. ΔP and Vt were significantly lower in Intellivent group—ΔP on mechanical ventilation was 7 (6–8) cm H2O vs 9 (8–10) cm H2O ($p < 0.0001$); Vt on mechanical ventilation was 6.4 ± 0.7 vs 8.6 ± 1.3 ml/kg/PBW ($p < 0.0001$), MP—9.3 ± 2.9 vs 12.1 (8.3–18.9) J/min ($p < 0.0001$). PEEP and FiO2 level were also significantly lower in Intellivent group: PEEP on mechanical ventilation was 7 (5–11) cm H2O vs 10 (7–12) cm H2O and FiO2 level was 28 (24–30) % vs 35 (30–39) %. There were no significant differences between the groups in frequency of undesirable events and duration of ICU and hospital stay.

	Intellivent—ASV	Conv. modes	*p*
Body mass index (BMI), kg/m2	33.5 (32–40)	33.5 ± 2	0.5006
Respiratory support in ICU, min (CI95%)	240 ± 55 (223–257)	283 ± 79 (258–308)	0.0059
FiO2	28 (24–30)	35 (30–39)	< 0.0001
Ratio paO2/FiO2 (CI95%)	332 ± 51 (316–349)	316 ± 58 (297–334)	0.1746
Tidal volume (Vt), ml/kg/PBW (CI 95%)	6.4 ± 0.7 (6.2–6.6)	8.6 ± 1.3 (8.1–9.0)	< 0.0001
Δ*P* (driving pressure) cmH2O	7(6–8)	9(8–10)	< 0.0001
Recruitment maneuvers	3 (7.5%)	8(20%)	0.12
NIV after extubation of trachea	4 (10%)	9(22.5%)	0.2254

Conclusion: Intellivent-ASV mode in obese patients after uncomplicated cardiac surgery allows to personalize respiratory support, provides more protective mechanical ventilation and reduces the physician's workload without compromising the quality of respiratory support and safety of patients.

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000128

Inhaled nitric oxide use in mechanically ventilated COVID-19 ARDS patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000128

Introduction: Patients with SARS-CoV2 (COVID-19) admitted with acute respiratory distress syndrome (ARDS) frequently have refractory hypoxemia. Prior studies have described improved oxygenation in acute lung injury. There is limited research on the impact of inhaled nitric oxide (iNO) on mechanically ventilated patients for COVID-19 ARDS.
Objectives: In this study, we investigate the short-term, in-hospital outcomes of mechanically ventilated COVID-19 ARDS patients receiving iNO.
Methods: A retrospective cohort study was conducted on patients admitted with COVID-19 to an intensive care unit (ICU) who were mechanically ventilated at Rush University System for Health in Illinois between March and October 2020. Patients were subdivided within the cohort based on the administration of iNO during admission. The primary end point was in-hospital mortality. Secondary endpoints included changes in oxygenation as defined by PaO2/FIO2 Ratio (P/F), changes in ventilation (PaCO2), changes in peak and plateau pressure, and ICU length of stay (LOS). Changes in pre- and post-iNO outcomes were compared using paired t-tests. Categorical outcomes were compared using chi-square tests or Fisher's exact test when appropriate.
Results: Three hundred and fifteen patients were admitted to the ICU with COVID-19 ARDS requiring mechanical ventilation. Twenty-one patients (6.6%) were placed on iNO during their admission. There was no difference in the baseline demographics between the two groups (Table 1). Patients in the iNO group required more vasopressin, epinephrine, phenylephrine ($p < 0.05$ each, Table 2). iNO was started at a mean of 28.57 (10.14) parts per minute (ppm) with a maximum dose of 31.43 (10.14) ppm. The average time from intubation to initiation of iNO was 4.48 days with an average duration of iNO use of 3.57 days. Average time from iNO start to either ICU discharge or death was 8.24 days. Patients who received iNO had higher in-hospital mortality (71.4%) in comparison to patients who did not receive iNO (41.8%). P/F ratio improved after initiation of iNO (74.8 (32.7) vs. 99.7 (43.2), $p < 0.05$). Peak pressure was increased after iNO initiation (31.1 (6.7) vs. 34.1 (6.4), $p < 0.05$). There was no change in PaCO2 or plateau pressure. Patients in iNO group had longer median LOS but this was not a significant difference (17.4 vs. 14.9 days, $p = 0.508$).

Table 1: Baseline patient demographics

	iNO Group	No iNO Group	p
Age (mean (SD))	58.29 (11.60)	59.78 (14.26)	0.639
Sex (%)			0.08
Female	4 (19.0)	112 (38.1)	
Male	17 (81.0)	182 (61.9)	
BMI (mean (SD))	32.78 (5.56)	33.38 (8.81)	0.76
Race (%)			0.194
American Indian or Alaskan Native	0 (0.0)	1 (0.4)	
Asian	0 (0.0)	6 (2.2)	
Black or African American	3 (14.3)	91 (33.5)	
Native Hawaiian or Other Pacific Islander	0 (0.0)	3 (1.1)	
Other	14 (66.7)	103 (37.9)	
White	4 (19.0)	68 (25.0)	
Smoking Status (%)			1
Current	0 (0.0)	7 (3.0)	
Former	4 (22.2)	59 (25.5)	
Never	14 (77.8)	165 (71.4)	
Atrial Fibrillation (%)	5 (23.8)	78 (26.7)	0.771
Coronary artery disease (%)	11 (52.4)	119 (40.8)	0.296
HTN (%)	14 (66.7)	216 (74.0)	0.464
COPD (%)	1 (4.8)	35 (12.0)	0.487
Diabetes Mellitus (%)	9 (42.9)	158 (54.1)	0.318
Asthma (%)	1 (4.8)	37 (12.7)	0.489
Cancer (%)	2 (9.5)	30 (10.3)	1
Hx of Ventricular arrythmia (%)	3 (14.3)	35 (12.0)	0.729
Stroke (%)	2 (9.5)	49 (16.8)	0.546
Peripheral artery disease (%)	0 (0.0)	29 (9.9)	0.238
Hx of Myocardial Infarction (%)	8 (38.1)	95 (32.5)	0.6
Hx of Venous thromboembolism (%)	6 (28.6)	84 (28.8)	0.985
Hx of life threatening arrythmia (%)	0 (0.0)	12 (4.1)	1
Heart Failure (%)	1 (4.8)	34 (11.6)	0.489
Hyperlipidemia (%)	12 (57.1)	152 (52.1)	0.652
Obstructive sleep apnea (OSA) (%)	1 (4.8)	48 (16.4)	0.218
Pacemaker/ICD (%)	1 (4.8)	10 (3.4)	0.54
Interstitial Lung Disease (%)	0 (0.0)	13 (4.5)	1
HIV (%)	0 (0.0)	2 (0.7)	1
Dementia (%)	0 (0.0)	10 (3.4)	1
Peptic Ulcer Disease (%)	0 (0.0)	16 (5.5)	0.612
Cirrhosis (%)	1 (4.8)	14 (4.8)	1
Pulmonary Hypertension (%)	3 (14.3)	14 (4.8)	0.096
Chronic Kidney Disease (%)	2 (9.5)	61 (20.7)	0.27

Table 2: Vasopressor-inotrope requirements

	iNO Group	No iNO Group	p
n	21	294	
Any Vasopressor (%)	20 (95.2)	258 (87.8)	0.4876
Norepinephrine (%)	20 (95.2)	258 (87.8)	0.4876
Vasopressin (%)	17 (81.0)	134 (45.6)	0.0017
Phenylephrine (%)	8 (38.1)	47 (16.0)	0.0167
Epinephrine (%)	13 (61.9)	91 (31.0)	0.0036
Dopamine (%)	2 (9.5)	8 (2.7)	0.1378
Any Inotrope (%)	2 (9.5)	26 (8.8)	1
Dobutamine (%)	2 (9.5)	25 (8.5)	0.6982
Milrinone (%)	1 (4.8)	4 (1.4)	0.2934

Conclusion: In this cohort, although the salvage use of iNO improved hypoxemia in the short-term, patients who required iNO were more critically ill and had higher mortality. More data is needed to evaluate the efficacy of inhaled nitric oxide in severe ARDS due to COVID-19 and to determine the most beneficial time to administer inhaled nitric oxide after ICU admission.

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Acknowledgements: None.

000161

Safety and feasibility of high-flow nasal oxygen therapy for severe COVID-19 outside the ICU setting

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Intensive Care Medicine Experimental 2022, **10(2)**:000161

Introduction: High-flow nasal oxygen (HFNO) therapy may improve outcome in severely hypoxic patients due to Coronavirus Disease 2019 (Covid-19) (1, 2). HFNO is predominantly applied in the Intensive Care

Unit (ICU) setting, but also on respiratory wards to preserve ICU capacity. As data on HFNO therapy outside the ICU setting are scarce, the aim of this study was to assess the safety and feasibility of HFNO therapy outside the ICU setting.

Methods: We conducted a prospective observational study in 11 hospitals in the Netherlands. Adult patients who were hospitalized and treated with HFNO for severe hypoxemic respiratory failure due to COVID-19 were included. Local practice of HFNO therapy outside ICU setting was assessed. Detailed clinical data were collected, including respiratory parameters, tolerability and time course of HFNO treatment (feasibility endpoints), complications and clinical outcomes (safety endpoints).

Results: In 7 out 11 hospitals HFNO could be initiated on the ward. Monitoring on the wards (SpO2, respiratory rate, blood pressure, heart rate) was done at regular time points (mostly at 0, 0.5,1,2,4,6, 12 h after initiation and 3 times daily thereafter). The average nurse: patient ratio was 1:3. Between December 1st, 2020, and July 1st, 2021, 608 patients were included. HFNO was initiated at the ward in 379 (62%), at a median ROX index of 6.5 (IQR 5.0–8.5; Table 1). HFNO was discontinued for discomfort in 12 (2%) patients. Pneumothorax/-mediastinum or facial decubitus were observed in 5 (0.9%) and 1 (0.2%) patients during HFNO therapy, respectively. Selected data on HFNO time-course, intubation complications and outcome are depicted in Table 1/ Figure 1. 186 (49%) patients were referred to ICU. Median ROX index on ICU referral was 4.0 (IQR 3.45–4.92). Of those, 139 (75%) patients were invasively ventilated. None of the patients died prior to or during intubation.

Table 1. Summary characteristics of patients

	Overall (n=608)	Ward-initiated (n=379)	ICU-initiated (n=229)	P-value[1]
Age	61 (53 - 68)	61 (53 - 68)	61 (52 – 67.5)	0.61
SaO_2-FiO_2 ratio on hospital admission	232 (123 – 288)	249 (211 – 291)	125 (116 – 238)	<0.001
ROX index on HFNO initiation	5.1 (3.9 – 7.5)	6.5 (5.0 – 8.5)	3.9 (3.4 – 4.7)	<0.001
Time admitted until HFNO initiation (h)	16 (2 – 45.5)	17 (3 - 42)	12 (1 - 58)	0.28
Duration of HFNO therapy (h)				
Until weaning[2]	110 (70 - 116)	112 (75.5 – 171.5)	104.5 (51.5 – 148.25)	0.04
Until ICU referral	-	20 (6 – 43.5)	-	NA
Until IMV[3]	29 (12 - 60)	37 (14.5 – 75)	23.5 (9.25 – 51)	0.01
Total	71 (28 – 125)	88 (41 – 139)	41 (15 - 104)	<0.001
Intubation	277 (45.6)	139 (36.7)	138 (60.3)	<0.001
Complications during intubation[3]				
Hypoxemia <80%	35 (12.6)	24 (17.3)	11 (8.0)	0.02
Hypotension <90 mmHg	19 (6.9)	9 (6.5)	10 (7.2)	0.80
CPR	1 (0.4)	0	1 (0.7)	NA
In-hospital mortality	58 (9.5)	23 (6.1)	35 (15.3)	<0.001

Continuous data are presented as median with interquartile range (IQR). Categorical variables are reported as number with percentages. [1]Groups were compared by using Mann-Whitney-U tests for continuous variables and chi-square test for categorical variables. [2]Non-intubated patients only. [3]Intubated patients only. HFNO: High-flow nasal oxygen. IMV: invasive mechanical ventilation. NA: Not applicable. CPR: cardiopulmonary resuscitation

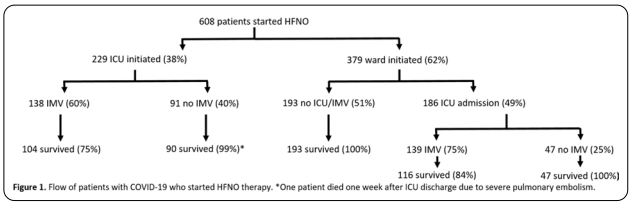

Figure 1. Flow of patients with COVID-19 who started HFNO therapy. *One patient died one week after ICU discharge due to severe pulmonary embolism.

Conclusion: Our detailed study in a large cohort of patients with COVID-19 on HFNO therapy outside the ICU indicated that HFNO can be applied safely and is feasible under the circumstances and measures implemented during this study.

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Acknowledgements: This study was funded by an unrestricted grant from Indorama Ventures Europe B.V.

000230

Influence of patient's position on esophageal and transpulmonary pressure

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Intensive Care Medicine Experimental 2022, **10(2)**:000230

Introduction: Intubated patients with the acute respiratory distress syndrome (ARDS) are usually treated with protective ventilation limiting plateau pressure below 30 cmH2O and, if possible, a driving pressure under 15 cmH2O. However, these airway pressure might not reflect the actual pressure applied to the lung. Transpulmonary pressure is the difference between airway pressure and pleural pressure, the latter estimated by the esophageal pressure. This technique and measurements had been validated, initially, in healthy patients in half-sitting position, and then confirmed in different positions. Few studies have evaluated the impact of patient positioning on pleural pressure and transpulmonary pressure in intubated patients with ARDS.

Objectives: We aimed to assess the changes in esophageal and transpulmonary pressures at different positions (supine at 0° and semi-recumbent at 45°) in intubated patients with ARDS.

Methods: In this single-center, prospective study performed in a medical ICU of a tertiary care center, all patients diagnosed with ARDS in the study period were monitored with an esophageal catheter, if no contraindication (esophageal varicose, severe coagulopathy), and included. In all patients, we collected end-expiratory and end-inspiratory esophageal pressures, airway pressures and intra-abdominal pressure at the two positions. Inspiratory transpulmonary pressure was calculated using the elastance ratio method. Positive end expiratory pressure (PEEP) was not modified and remained at the level set by the clinician in charge of the patient. Comparisons of values at 0° and 45° were performed using paired Wilcoxon tests.

Results: We included 14 patients admitted from January to April 2022. Ther median (IQR) age, SOFA score and SAPS II were 63 years (58–72), 7 (5–12) and 46 (27–60) respectively and 57% were men. Eleven of them (79%) were intubated for pneumonia including four positives to SARS-CoV2 (29%). Their median PaO2/FIO2 on the day of intubation was 104 (78–181) mmHg and 12 (86%) had moderate or severe ARDS. At the time of measurement, set and total PEEP were 10.0 [10.0;12.0] and 13.0 [11.2;15.0] cm H20 respectively. Comparisons of the airway pressures, esophageal pressures and transpulmonary pressures are shown in Table 1. Intra-abdominal pressure also significantly increased from 12.2 [7.5;12.9] to 20.4 [17.7;26.5] cmH2O when changing position from 0° to 45° (p = 0.004).

Table 1: Comparison of pressures at supine at 0° and semi-recumbent 45°

	At 0°	At 45°	p-value
Airway			
Plateau pressure (cmH_2O)	24.0 [22.2;26.8]	26.5 [25.0;33.2]	0.0495
Driving pressure (cmH_2O)	10.0 [9.3;14.2]	14.0 [9.3;21.8]	0.0495
Compliance (cmH_2O)	32.5 [27.2;49.0]	25.5 [18.5;39.0]	0.0634
Esophageal			
Plateau pressure (cmH_2O)	15.0 [13.2;18.6]	12.6 [11.0;13.9]	0.0013
End expiratory pressure (cmH_2O)	11.6 [9.9;13.8]	7.4 [6.0;9.7]	0.0011
Driving pressure (cmH_2O)	3.1 [2.2;4.7]	4.6 [3.6;6.1]	0.0030
Transpulmonary			
Plateau pressure (cmH_2O)	16.5 [15.0;21.0]	19.0 [14.2;23.8]	0.6596
End expiratory pressure (cmH_2O)	-0.5 [-1.0;4.5]	5.0 [2.3;8.3]	0.0009
Driving pressure (cmH_2O)	7.5 [6.0;11.0]	9.5 [5.3;14.5]	0.3410

Values are expressed as median [IQR]

Conclusion: Keeping PEEP stable and changing position from supine at 0° to semi-recumbent at 45° significantly increases all airway pressures and decreases esopageal pressures. The relative changes led to a non-significant increase in transpulmonary plateau pressure but a significant increase in end-expiratory transpulmonary pressure resulting in a stable transpulmonary driving pressure.

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Acute Respiratory Failure 2

000022

Non-invasive ventilation trial in patients with ARDS caused by COVID-19. Are we harming our patients by trying?

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Introduction: The use of and non-invasive mechanical ventilation (NIV) in COVID-19 patients has been a topic of discussion during the pandemic. There is still no clear evidence of the outcomes of an initial approach with NIV.
Objectives: To analyze the results of patients that required invasive mechanical ventilation (IMV) because of ARDS caused by COVID-19 pneumonia and compare the patients that were initially treated with non-invasive mechanical ventilation (NIV) vrs patients treated exclusively with MV.
Methods: Retrospective observational study comparing patients admitted to a polyvalent Intensive Care Unit (ICU) with a diagnosis of ARDS due to COVID-19, between August 1, 2020 and May 31, 2021, who received IMV. The patients were divided into 2 groups: (G1) patients who received IMV in the first 24 h of treatment and (G2) patients initially treated with NIV who needed IMV after more than 24 h of treatment. Demographic characteristics, days of admission to the ICU, days of hospital admission, hospital mortality and mortality at 28 days were compared between both groups. Results were adjusted by modeling to control the effect of confounding variables.
Results: A total of 79 patients (n G1 = 41 and n G2 = 38) were included, 29.1% were men, with a mean age of 62.5 ± 10.2 years, APACHE II of 15.2 ± 5.8 and Barthel of 96.2 ± 10.9. Among the comorbidities that stood out, 53.1% were obese (BMI: 31.3 ± 5.5), 58.2% had hypertension, 24.1% diabetes mellitus and 79.5% had a history of respiratory pathology. On admission, 11.4% of patients had mild ARDS, 59.5% moderate, and 29.1% severe. The mean ICU stay was 25.4 days (G1: 26.1 ± 24.2 days, G2: 24.6 ± 18.9 days). No statistically significant differences were found between both groups ($p = 0.261$). The average number of days of hospital admission was 38.6 (G1: 38.9 ± 35.5 days, G2: 38.4 ± 35.5 days). There were no statistically significant differences according to the patient group ($p = 0.417$). The death rate was 27.8%. No statistically significant differences were found between hospital mortality ($p = 0.972$) or 28 days after admission ($p = 0.155$) between the groups.
Conclusion: In our series, there were no significant differences in ICU stay, hospital stay or mortality, between patients whose initial treatment was IMV and those who had previously received NIMV. According to our results, an initial NIMV attempt with subsequent failure does not imply a worse outcome for the patient. Larger studies would be necessary to confirm this hypothesis.

000058

HucMSCs derived exosomal LINC02154 alleviates acute lung injury and fibrosis through interacting with FTO to promote PTEN degradation

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Introduction: Acute lung injury (ALI) is a serious respiratory disease with inflammatory response, lung injury, and fibrosis. Mesenchymal stem cells (MSCs) have great application prospects in the progression of ALI.
Objectives: The purpose of this study was to investigate the role and mechanism of human umbilical cord MSCs (hucMSCs) on inflammation and pulmonary fibrosis in ALI.
Methods: Human fetal lung fibroblast 1 (HFL-1) cells, hucMSCs, exosomes derived from hucMSCs (hucMSCs-exo), or exosomes derived from HFL-1 cells (HFL-1-exo) were intratracheal instillation to the lipopolysaccharide (LPS)-induced mice or treated to LPS-induced human pulmonary alveolar epithelial cells (HPAEpiC) cells. Hematoxylin–eosin (HE) staining, TUNEL assay, lung wet to dry (W/D) weight, and bronchoalveolar lavage fluid (BALF) protein concentration were used to assess lung injury. Enzyme-linked immunosorbent assay (ELISA) showed the levels of inflammatory cytokines in the BALF. Masson staining, hydroxyproline assay, RT-qPCR, and western blot assays were performed to detect pulmonary fibrosis. The cell apoptosis was detected by flow cytometry. Subsequently, high throughput sequencing was used to assess the expression profiles of long non-coding RNAs (lncRNAs) of hucMSCs-exo and HFL-1-exo. RNA pull-down and RNA immunoprecipitation (RIP) assays were used to evaluate the interaction of LINC02154 with FTO. The n6-methyladenosine (m6A) methylation levels of LINC02154 and PTEN in HPAEpiC cells were detected by m6A RIP (Me-RIP) assay. The mRNA stability of PTEN was detected by Actinomycin D (ActD) assay.
Results: hucMSCs attenuated LPS-induced injury, inflammatory cytokine levels, and fibrosis through transporting exosomes to alveolar epithelial cells (AECs) in ALI. Furthermore, LINC02154 was significantly up-regulated in hucMSCs-exo. hucMSCs derived exosomal LINC02154 suppressed LPS-induced injury, inflammatory cytokines levels, and fibrosis in vitro and in vivo. Mechanically, LINC02154 interacted with m6A methylation-associated RNA binding protein FTO to suppress PTEN expression and mRNA stability. Lastly, the LINC02154/FTO/PTEN axis inhibited LPS-induced AECs injury and fibrosis.
Conclusion: Our findings suggested that hucMSCs derived exosomal LINC02154 played protective roles through interacting with FTO, leading to the down-regulation of PTEN. The study provided a promising therapeutic target in the treatment of ALI.

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Acknowledgements
1. The National Key Clinical Specialty Construction Projects of China
2. Scientific Research Project of Hunan Provincial Health Commission, No.: 202103020704
3. Natural Science Foundation of Hunan Province, No.: 2021JJ30963

000088

Pre-hospital inhaled corticosteroids use and hospital mortality of COVID-19: results from the international viral infection and respiratory illness universal study (VIRUS)

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Introduction: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes acute respiratory failure leading to widespread morbidity and mortality. Randomized trial of a short-term inhaled corticosteroid (ICS) vs placebo has shown decreased need for hospitalization from COVID-19. In vitro data has shown that ICS inhibits SARS-CoV-2 replication in infected epithelial cells and lung injury may be attenuated in animal models.
Objectives: To compare hospital mortality in admitted COVID-19 patients with and without pre-hospital use of ICS.
Methods: Adult patients admitted with COVID-19 in 183 hospitals from 23 countries between March 2020, and December 2021 were enrolled into the Society of Critical Care Medicine's Discovery Viral Infection and Respiratory Illness Universal Study (VIRUS) COVID-19 registry. Patients' characteristics and comorbidities that were associated with increased mortality in the univariate analysis were included into multivariate regression analyses to assess the association between pre-hospital use of ICS and the primary outcome of in-hospital mortality. History of asthma and COPD, the most frequent clinical indications for outpatient therapy with ICS, were included as pertinent predictor variables in multivariate analyses. As disease severity was strongly correlated with the use of systemic steroids, we included hospital use of systemic steroids and not disease severity in the multivariate analysis.
Results: A total of 29,972 adult patients were included in the study. Of these, pre-hospital use of ICS was identified in 2208 (7.4%). Patients with pre-hospital use of ICS, compared to those without ICS use, were older [median 67 (IQR 56–77) vs 62 (IQR 49–74) years], more likely to be female (52.2% vs. 43.9%), and had higher rates of asthma (33.9% vs 7.5%), COPD (35.1% vs. 9.1%), hypertension (68.2% vs. 55.2%), as well as all other pertinent comorbidities. The ICS group had higher unadjusted hospital mortality rate of 19.1% vs. 15.3% compared to the non-ICS group. After adjustments for demographic characteristics and pertinent comorbidities in the multivariate analysis (Table), patients receiving pre-hospital ICS had significantly lower odds of mortality (OR 0.73, 95% CI 0.61 to 0.87, p = 0.0005). There was no significant interaction between prehospital ICS and hospital use of systemic steroids in the multivariate analysis (p = 0.44).

Term	Odds ratio	Lower 95%	Upper 95%	Prob > ChiSq
Age	1.042	1.038	1.046	< 0.0001*
Female	0.666	0.602	0.737	< 0.0001*
BMI > 30	1.008	1.001	1.015	0.0221*
Race	1.032	1.006	1.058	0.0147*
Ethnicity	1.264	1.178	1.357	< 0.0001*
Coronary artery disease	1.369	1.202	1.559	< 0.0001*
Hypertension	0.945	0.845	1.057	0.3249
Congestive heart failure	1.470	1.268	1.704	< 0.0001*
COPD	1.319	1.123	1.549	0.0008*
Asthma	0.781	0.635	0.961	0.0173*
Chronic kidney disease	1.127	0.986	1.287	0.081
Diabetes mellitus	1.107	0.997	1.228	0.057
Inpatient systemic steroids	1.572	1.423	1.736	< 0.0001*
Pre-hospital inhaled corticosteroids	0.729	0.610	0.870	0.0004*

Conclusion: In this large international cohort, pre-hospital use of inhaled corticosteroids was associated with lower odds for adjusted mortality despite the higher burden of pertinent comorbidities and older age. This effect was independent of the subsequent, in-hospital use of systemic steroids.

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Acknowledgements: This study was supported by NIH/NCRR/NCATS CTSA Grant Number UL1 TR002377. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. The registry is funded in part by the Gordon and Betty Moore Foundation, and Janssen Research & Development, LLC. They did not influence the analysis, interpretation, and reporting of pooled data.

000159

WIND classification open compared to ICC classification for weaning outcome in COVID-19 patients

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Introduction: Although the WIND (Weaning according to a New Definition) classification based on duration of ventilation after the first separation attempt has been validated in clinical practice, it has not been tested in COVID-19 population.
Objectives: Although the WIND (Weaning according to a New Definition) classification based on duration of ventilation after the first separation attempt has been validated in clinical practice, it has not been tested in COVID-19 population.
Methods: In the OmeLEtte trial, 60 severe ARDS patients due to COVID-19 infection under invasive mechanical ventilation that meet criteria for prone position between March and September 2021 were randomized to reduced prone position sessions versus prolonged sessions.. In this secondary analysis, patients were classified into simple, difficult, or prolonged weaning group according to ICC classification and WIND classification.
Results: During the study period, 260 patients were admitted to the ICU, and 60 patients were included in the study. These patients were classified by the WIND classification as follows: Group Never weaned = 12 (20%), Group 1 = 29 (48%), Group 2 = 11 (18%), and Group 3 = 8 (14%). However, only 34 (56%) patients were classified by ICC classification as follows: simple weaning = 26 (76%), difficult weaning = 5 (15%), and prolonged weaning = 3 (9%). There were no differences between baseline characteristics. Clinical outcomes were significantly different across weaning groups by WIND classification but not according to ICC classification (table 1).

Variables	WIND classification				ICC classification			
	Group 1 (29/60)	Group 2 (11/60)	Group 3 (8/60)	*p*	Simple (26/34)	Difficult (5/34)	Prolonged (3/34)	*p*
Age	53.5 (44.25–62.75)	47 (31.5–62.5)	52 (37–67)	0.61	54 (44–64)	45 (28.35–61.65)	61 (51–71)	0.6
Sex male	14	6	7	0.14	14	3	2	0.89
BMI	31.8 (27.3–36.3)	31.95 (26.2–37.7)	31.82 (25.2–38.4)	0.760	31.6 (25.6–37.6)	29.76 (25.76–34.76)	37 (25–49)	0.73
Apache II	11 (7.5–14.5)	12 (8–16)	14 (10.5–17.5)	0.38	12 (9–15)	9.5 (6–13)	15 (6–24)	0.30
UCI LoS	10 (7.5–12.5)	21 (13–29)	32 (12–42)	0.000	15 (6.5–23.5)	8 (6–10)	17 (12–22)	0.24
Hosp Los	19.5 (14.5–24.5)	31 (17.5–44.5)	44.5 (25–64)	0.001	26 (12.5–39.5)	14.5 (11–18)	17 (11–23)	0.07
MV days	6.5 (3.5–9.5)	18 (10–26)	31.5 (15–28)	0.000	11 (0.5–21.5)	5.5 (3.5–7.5)	17 (5–29)	0.35
VFDs	21.5 (18.5–24.5)	10 (2–28)	0 (0–1)	0.000	17 (6.5–27.5)	22.5 (20.5–24.5)	0 (0–4)	0.32
Tracheostomy	3	6	8	0.000	10	0	1	0.24
Mortality	0	1	3	0.003	3	0	2	0.023

Conclusion: The WIND classification could be a better tool for predicting weaning outcomes than the ICC classification in severe ARDS patients due to COVID-19. A larger confirmatory study would be valuable to validate these findings.

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Acknowledgements: None.

000208

Ultra-Lung-Protective multimodal Ventilation does not decrease Biotrauma in Severe ARDS patients on veno-venous ECMO: a Prospective Randomized Controlled Study.

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Intensive Care Medicine Experimental 2022, **10(2)**:000208

Introduction: Ultra-Lung-Protective (ULP) ventilation may be useful during veno-venous Extra Corporeal Membrane Oxygenation (vv-ECMO) for severe Acute Respiratory Distress Syndrome (ARDS) to minimize ventilator-induced lung injury (VILI) and to facilitate lung recovery.
Objectives: Firts objective was to compare pulmonary and systemic biotrauma evaluated by numerous biomarkers of inflammation, epithelial, endothelial injuries and lung repair according two ventilation strategies. Second objective was to assess safety of ULP strategy.
Methods: Prospective unblinded randomized controlled study. Patients received either Lung Protective (LP) ventilation (ventilation protocol of early ECMO arm of the EOLIA study [1]) in the control group or ULP ventilation in the interventional group which is a multimodal strategy using a low tidal volume (1–2 mL/kg of predicted body weight), a low respiratory rate (5–10 cycles/min), positive expiratory transpulmonary pressure and at least 12 h of prone position. Each ventilation strategy was applied during 48 h.
Results: The primary outcome was the alveolar concentrations of interleukin (IL)-1-beta, interleukin-6, interleukin-8, surfactant protein D and blood concentrations of serum advanced glycation end products and angiopoietin-2 48 h after randomization. Enrollment was stopped

for futility after inclusion of 39 patients. Thirty-eight patients (20 in the ULP group and 18 in the LP) were included in primary analysis. Tidal volume, respiratory rate, minute ventilation, plateau pressure and mechanical power were significantly lower in the ULP group during the ventilation protocol. PEEP, driving pressure and respiratory system compliance were not different between groups as well as ECMO blood flow, sweep gas flow and membrane FO2. Concentrations of pre specified biomarkers of the primary and secondary outcomes were not different in ULP and LP groups 48 h after randomization. Concerning safety, during the 48 h of the ventilation strategies, occurrences of barotrauma, right ventricular dysfunction, pressure sores and tracheal tube obstruction were unfrequent and not different between ULP and LP groups.
Conclusion: Despite reduced minute ventilation, plateau pressure and mechanical power, a multimodal ultra-lung-protective ventilation does not decrease biotrauma as compared with a lung-protective ventilation.
Clinical trial registered with www.clinicaltrials.gov (NCT03918603).

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Acknowledgements: The study was supported by a Grant of 138 K. Euros from the French Ministry for Solidarity and Health.

000257

Technical performances of ventilators during noninvasive ventilation: a bench study

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Introduction: A large choice of recent ventilators, dedicated or not, are available to perform noninvasive ventilation (NIV) in intensive care units (ICU). We conducted a bench study to compare the technical performances of different ventilators for NIV, and particularly their impact on patient-ventilator asynchrony (PVA) according to different respiratory conditions.
Methods: Ventilators have been evaluated on a previously validated bench test for NIV consisting of a 3D mannequin head connected to an ASL 5000® lung model (Ingmar Medical, Pittsburgh, PA) via a dual-limb circuit with a Quattro FX NV® (Resmed) facial mask. Five ICU ventilators with the NIV algorithm activated (Evita XL®, Dräger / Evita 500®, Dräger / Evita 800®, Dräger / Servo-U®, Maquet / Monnal T75®, Air Liquide), 2 dedicated NIV ventilators (Trilogy Evo®, Philips Respironics / Astral 150®, Resmed) and 1 transport ventilator (Monnal T60®, Air Liquide) were tested according to 3 patient profiles simulated with the lung model (normal,obstructive,and restrictive lung) and different respiratory conditions: 3 levels of non-intentional leak (0, 15 and 30L/min), 2 levels of pressure support (8 and 14cmH2O) and 2 respiratory rates (15 and 25c/min).
Results: Median total leak was not different between all ventilators ($p = 0,09$). The asynchrony index (AI), defined as the [number of asynchrony events/(ventilator cycles + wasted efforts) × 100], was higher with ICU ventilators than with dedicated NIV ventilators (4%[0;76] vs 0%[0–15], respectively; $p < 0.05$). The global AI was also significantly different between all ventilators ($p < 0.001$). The AI was higher with ICU ventilators for the normal and restrictive profiles as compared to dedicated NIV and transport ventilators ($p < 0.01$) but not different between ventilators for the obstructive profile. The overall median AI was correlated with the mean total leaks ($p < 0.01$), but several ventilators had a better adaptation to an increase of the level of leaks, the AI increasing less than for others ($p < 0.01$). Auto-triggering represented 43% of overall PVAs. The AI was higher, all ventilators confounded, with a pressure support of 14 cmH2O as compared to 8 cmH2O, whereas no significant difference was observed according to the respiratory rate used. Triggering delay, cycling delay, pressure–time product, pressure rise time and pressure in the mask were different between all ventilators ($p < 0.01$). There was no difference between ventilators for minute ventilation ($p = 0.21$) and peak pressure ($p = 0.24$). Dedicated NIV ventilators induced a lower pressure–time product than ICU and transport ventilators ($p < 0.01$). The rising time was found higher with dedicated NIV ventilators than with others ($p < 0.01$).
Conclusion: Despite the implementation of NIV algorithm, the most recent ICU ventilators appear to be less efficient than dedicated NIV ventilators, particularly in terms of PVA and work of breathing. These performances could however change according to the underlying respiratory disease and/or the amount of leaks.

000262

Talc pleurodesis for recurrent pneumothorax in COVID-19 requiring mechanical ventilation: a case series

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Introduction: Barotrauma, including pneumothorax, pneumomediastinum, and subcutaneous emphysema, is a common complication of severe COVID-19 requiring invasive mechanical ventilation (IMV). The incidence of barotrauma in these patients was estimated to be 18.4% in a recent meta-analysis. Pneumothorax, the most common form of barotrauma seen in COVID-19, is often difficult to manage in this setting due to an estimated recurrence rate of 9.3%. Here we present our local experience using talc pleurodesis to prevent recurrent pneumothorax in severe COVID-19 requiring prolonged IMV complicated by recurrent pneumothorax.
Methods: We identified 3 patients with COVID-19 with recurrent pneumothoraces while receiving IMV for > 4 weeks at the University of New Mexico Hospital Medical ICU. Due to the severity of their respiratory failure and ongoing IMV requirement, these patients were not considered candidates for VATS. In each patient, we performed talc slurry pleurodesis by injecting 1–4 g of sterile talc in 50–100 mL of sterile saline through a previously placed thoracostomy tube. The chest tube was clamped in one patient, while in the other two the drainage system (Atrium) was elevated above the patient so the talc slurry would remain in the pleural space. After an hour, the tube was either unclamped or the Atrium placed back on the floor below the patient to allow excess slurry to drain out.
Results: All 3 patients tolerated the pleurodesis without bleeding or other major complications. The only adverse effect documented was pain, which was controlled in each case with analgesic agents. The chest tube drains were removed in all 3 patients approximately 24 h after talc pleurodesis. In one patient, before the tube was removed, a second pleurodesis was repeated after 48 h due to residual pneumothorax. As of the time of this report, none of the patients have had a recurrent pneumothorax at 3 weeks, 6 months, and 9 months post-procedure, respectively. All 3 patients were ultimately discharged from the ICU to a long-term acute care hospital.
Conclusion: Current guidelines recommend surgical consultation for pleurodesis by video-assisted thoracoscopic surgery (VATS) after a first or second spontaneous pneumothorax. However, patients with pneumothorax secondary to COVID-19 are often not surgical candidates due to severity of illness, and different therapeutic options

are therefore needed. The use of medical pleurodesis for recurrent pneumothorax in other settings has been shown to result in a lower recurrence rate than chest tube drainage alone in patients who are not surgical candidates. In this small series of patients with COVID-19 requiring prolonged IMV and recurrent pneumothorax, talc pleurodesis resulted in successful short-term prevention of further recurrence with no adverse effects. Though additional prospective data are needed, our series suggests that talc pleurodesis can be an effective therapeutic option to prevent recurrent pneumothorax in this challenging patient population.

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000285

Electron microscopy study of postmortem biopsies of COVID-19 patients in a tertiary ICU in Spain

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Introduction: COVID-19 has affected almost every country. Autopsies remain the gold standard for understanding the pathogenesis of new and emerging diseases. The current rate of autopsies is low. Therefore, performing postmortem biopsies for the study of structural alterations by electron microscopy is important. To answer many questions that remain unanswered.
Objectives: To describe the histopathological findings by electron microscopy of post-mortem lung biopsies from patients who died of SARS-CoV-2 infection.
Methods: A prospective observational study of post-mortem lung biopsies was performed in patients who died of COVID-19 in the ICU of the Fundación Jiménez Díaz in Madrid. Biopsies are being obtained by 14G tru-cut from March 15, 2020 until now. The material obtained is being studied at the Anatomic Pathology Service for histological and IHC analysis, and at the CNME for observation by Transmission Electron Microscopy (TEM) on a JEOL JEM 1400 plus microscope at 100 kv. Epidemiological, severity, analytical and respiratory mechanics data were collected on the last day of admission.
Results: 12 patients (92%H) were studied. The median age was 68 years (IQI 60–74 years). The most frequent antecedents were: LD58%, HT 50% y DM 50%. Median APACHE II 14. The median number of days in the ICU was 32 (range 22–41). The median number of days in MV was 32. Tracheostomy was performed in 92%. The ventilatory modality was volume control in 83%, with a mean tidal volume adjusted to ideal weight of 5.8 ml/kg. This resulted in a plateau of 28 cmH20, a driving pressure of 20 and a static compliance of 19. At the gasometric level: ph of 7.35 (CI of 7.26–7.38), a pCO2 of 70 (CI 54–84) a pafi of 80 (CI 54–122). Mean laboratory values were: D(DD) 1648 µg/L, lymphocytes 9351 (abs), platelets 207,500 µl, Hb 8.0 g/L, creatinine 0.63 mg/dl, CRP 30.2 mg/dl, ferritin 958 ng/mL. Percutaneous bedside biopsies were performed in the first hour after death. Ultrastructural findings with TEM were diffuse alveolar damage (DAD) and frequent hyaline membrane formation in 100% and cryptogenic pneumonia in 44%. In general, loss of the characteristic lung structure and a high degree of cell lysis and vacuolization, corresponding to pneumocytes of both types, were observed. In type II pneumocytes, images with morphology and size compatible with coronavirus viral particles included inside vesicles, and other extracellular particles close to the remains of membranes similar to the virus itself were identified. Although all patients received heparin prophylaxis. Even so, numerous fibrin microthrombi were identified in 92% of the pulmonary samples, in the alveolar capillaries, showing no signs of vasculitis. In addition, IHC showed intense expression of CD163 + macrophages as well as CD8. The frequent presence of CD163 + macrophages represent the histopathological substrate of macrophage activation syndrome in these patients.
Conclusion: DAD and hyaline membrane formation were frequently observed in all patients. Subsequent TEM study revealed severe cellular damage in both type II pneumocytes and endothelial cells, which is highly consistent with the presence of viral particles in both cell.

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000292

Impact of non-invasive ventilatory support strategy used during acute respiratory failure by SARS-COV-2

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Intensive Care Medicine Experimental 2022, **10(2)**:000292

Introduction: Avoiding invasive mechanical ventilation (IMV) by using non-invasive ventilatory support became widespread practice during the Covid-19 pandemic. However, limited data are available regarding the clinical effectiveness of non-invasive ventilatory support strategies for the management of acute respiratory failure (ARF) in the setting of Covid-19.
Objectives: The aim was twofold: First, to determine whether high flow nasal cannula (HFNC) or non-invasive ventilation (NIV) were associated with clinical failure measured as the need for IMV or death among intensive care unit (ICU) admitted patients with Covid-19. Second, the risk factors associated with clinical failure among Covid-19 patients requiring non-invasive ventilatory strategies.
Methods: This multicentric, observational, prospective study in 73 Spanish ICU using data obtained from SEMICYUC's registry (Feb20-Jun21) enrolled all consecutive patients admitted to the ICU due to ARF with confirmed SARS-COV-2 infection who were treated with non-invasive ventilatory support. Two independent groups were classified according to the first ventilatory strategy used at admission: HFNC or NIV. The primary outcome was defined as clinical failure when the

patient required IMV or died during the ICU stay. Data included demographics, comorbidities, severity at admission, respiratory parameters, biomarkers, and clinical failure. The statistics included Chi-square distribution, t-test, Mann–Whitney and logistic regression with significative p value ≤ 0.05. Approved by Ethical Committee with study number: 2020/9050.
Results: There were 3889 patients enrolled, of which 1692 were treated with non-invasive ventilatory support at admission, 75% (n = 1275) with HFNC and 25% (n = 417) with NIV. Patients initially receiving HFNC had lower severity scores and were presented with less shock at admission compared to patients with NIV. In addition, HFNC patients had lower inflammatory parameters at admission (total leukocyte count, lactate dehydrogenase and D-dimer) and were less likely to receive corticosteroids, tocilizumab, and hydroxychloroquine. HFNC patients had lower rates of clinical failure compared to NIV (61.6% vs 68.1%, p = 0.016). The main reason of clinical failure was the need for IMV in both groups (97% [HFNC] vs 96% [NIV], p > 0.05). Patients who failed (n = 1066, 63%) were older, had higher body mass index (BMI) and higher severity scores at admission. Clinical failure patients had more comorbidities (COPD, cardiac failure, hematologic disease, diabetes mellitus, hypertension), higher levels of lactate dehydrogenase, creatine phosphokinase (CPK), urea levels, and shock at admission. Risk factors independently associated to clinical failure were APACHE [1.096 (1.049–1.145), p ≤ 0.001], SOFA [1.456 (1.273–1.664), p ≤ 0.001], CPK [1.001 (1.000–1.002), p = 0.024)] and shock at admission [4.085 (1.959–8.520), p ≤ 0.001].
Conclusion: Clinical failure was associated with initial NIV therapy compared to HFNC in patients with ARF due to Covid-19 patients. Other risk factors related to disease severity at ICU presentation were independently associated with clinical failure.

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000314

Sub-phenotype identification in SARS- COV-2 infected adult patients with ARDS by latent profile analysis: a retrospective study

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Intensive Care Medicine Experimental 2022, **10(2)**:000314

Introduction: SARS-Cov-2 virus associated pneumonia and ARDS was often associated with hyperinflammation and elevation of several serum inflammatory markers but usually less than what is observed in non-COVID ARDS [1]. An elevated inflammatory markers such as c-reactive protein, IL-6 etc.was associated with severe infection [2]. Previous studies have found existence of two distinct sub phenotypes in non-COVID ARDS patients [3].
Objectives: In this study, sub phenotypes of COVID-19 ARDS patients were identified by latent profile analysis in a cohort of Indian patients.
Methods: Data of n = 233 adult (aged more than 18y) Indian patients with laboratory confirmed SARS-CoV-2 infection, admitted in a tertiary care teaching hospital, were analysed in this retrospective study. Only patients with acute respiratory failure (defined by PaO2/FiO2 ratio < 200 mm Hg) and chest x-ray showing bilateral infiltrates were included. Latent profile was analysed by '*tidyLPA*' package in R (R studio, version 1.2.5033) and age adjusted distal outcome was analysed in *Jamovi version 2.3.0*.
Results: Mean (SD) age of the patients was 53.3 (14.9)y and 62% patients were male. On the basis of lowest Bayesian information criterion, a two sub phenotypic model was formulated. Neutrophil to lymphocyte ratio (NLR) and serum IL-6 was used as latent variable in that model (entropy 0.91). The second phenotype (hyperinflammatory) had lower platelet count (p = 0.02), higher serum creatinine (p = 0.004), higher c-reactive protein (p = 0.001), higher ferritin (p < 0.001) and serum LDH (p = 0.009). Age adjusted hospital mortality was significantly higher in the second sub-phenotype [odds ratio (95% confidence interval) 6.2 (3.3–11.6); p < 0.001]. However, significant overlap was observed in this sub-classification.
Conclusion: Two distinct but overlapping sub-phenotypes were identified in SARS-CoV-2 associated respiratory failure. Hyperinflammatory sub-phenotype was associated with significantly poor short-term outcome. Similar findings were previously reported in other acute respiratory distress syndrome patients also. Further studies are required to know the effect of anti-inflammatory drug treatment on these two sub-phenotypes.

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Acknowledgements: No funding received.

Acute Respiratory Failure 3

000036

Increasing sweep gas flow through the membrane lung reduces dyspnea and respiratory drive in veno-arterial ECMO patients: the DysCO 2 study

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Intensive Care Medicine Experimental 2022, **10(2)**:000036

Introduction: Patients with severe heart failure may benefit from veno-arterial extracorporeal membrane oxygenation vaECMO, which preserves systemic blood flow. In addition, the vaECMO oxygenation membrane ensures blood oxygenation and CO2 removal. In clinical practice, vaECMO patients may exhibit dyspnea despite adequate blood flow and the absence of blood gas abnormalities. Our objective was to evaluate, in vaECMO patients exhibiting significant dyspnea, the impact of an increase in sweep gas flow through the vaECMO membrane on dyspnea.
Methods: Patients with 1) vaECMO for cardiogenic shock and 2) a dyspnea ≥ 40 mm on a visual analog dyspnea scale (Dyspnea-VAS)

from zero to 100 mm were included. Four conditions were studied: on inclusion and after three sweep gas flow increments of two liters per minute each. Dyspnea was assessed with the Dyspnea-VAS, the A1 score of the Multidimensional Dyspnea Profile and the Intensive Care Respiratory Distress Operating Scale (IC-RDOS). The respiratory drive was concomitantly assessed by the measure of the electromyographic activity of the Alea Nasi and parasternal muscles.

Results: We included 21 non-mechanically ventilated patients. Median (interquartile range) age was 40 years (30–55), 62% male and duration of ECMO was 3 days (2–4). Dyspnea-VAS was 50 (45–60) mm. Weinberg radiological pulmonary oedema score was 3 (0–5). Gas flow at inclusion was 1 L/min (0.5–2). Table 1 shows respiratory rate, PaCO2, Dyspnea-VAS, A1 score and IC-RDOS across the four conditions. PaCO2 decreased in response to the 2-L-per-minute increase in sweep, but it ceased to decrease after 6 L. Dyspnea did not decrease immediately but was significantly lower after 6 L of increased sweep regardless of the assessment score. The electromyographic activity of Alea nasi and parasternal muscles decreased significantly after sweep gas flow increment. There was a significant inverse correlation between the Dyspnea-VAS and the sweep gas flow (Rho = –0.68, $p < 0.0001$) but not between Dyspnea-VAS and PaCO2 (Rho = 0.136, $p = 0.236$).

	Baseline	+2 L/min	+4 L/min	+6 L/min	p
Sweep gas flow					
Sweep gas, *L.min⁻¹*	1 (0.5-2)	3 (2.5-4)	5 (4.5-6) *$	7 (6.5-8) *$	<0.0001
Clinical parameters					
RR, *min⁻¹*	23 (21-25)	21 (18-22)	19 (16-20) *	15 (13-17) *$	<0.0001
Blood gases					
$PaCO_2$ *mmHg*	37 (31-40)	33 (28-38)	32 (29-37) *	34 (31-39)	0.004
Dyspnea					
Sensory D–VAS, mm	50 (45-60)	50 (40-50)	40 (30-40) *$	20 (10-30) *$	<0.0001
A1	50 (50-60)	50 (50-60)	50 (40-60)	40 (30-50) * $ £	<0.0001
IC–RDOS	5.0 (3.8-6.6)	4.8 (3.0-5.8)	3.3 (2.7-5.1)	2.9 (2.7-4.6) *	<0.0001
Electromyography					
Alea Nasi EMGmax	1 (1-1)	0.94 (0.67-0.99)	0.86 (0.63-0.99) *	0.78 (0.50-0.99) *	0.0002
Parasternal EMGmax	1 (1-1)	0.99 (0.93-1.00)	0.94 (0.87-0.99) *	0.87 (0.75-0.98) *$	0.0001

Conclusion: In critically ill patients with vaECMO, incrementation of sweep gas flow through the oxygenation membrane decreases dyspnea. It might be mediated by a decrease in respiratory drive, as suggests the concomitant decrease in respiratory rate and electromyographic activity of respiratory muscles.

000113

Alternatives to conventional invasive ventilation in viral acute respiratory distress syndrome: a systematic review and meta-analysis

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Intensive Care Medicine Experimental 2022, **10(2)**:000113

Introduction: SARS-CoV2 can produce a wide range of diseases, including Acute Respiratory Distress Syndrome (ARDS) as well as many other respiratory viruses. In the case of SARS-CoV2 is a highly contagious disease and as reported at the beginning of the pandemic from the China Center for Disease Control, 81% of patients would be mild, 14% would be severe and 5% are critical [1]. Those critical cases would require critical care in Intensive Care Units (ICU) especially ventilatory management as the principal cause of death from COVID-19 is ARDS [2]. But SARS-CoV2 generated a great shortage of respiratory ventilators in the first months of the COVID-19 global pandemic [3]. Because of this is necessary to study alternatives for Invasive mechanical Ventilation (IMV) that can be suitable for ARDS cause by SARS-CoV2 or other Respiratory virus.

Objectives: To determine the efficacy and safety of alternative ventilation strategies compared with conventional invasive mechanical ventilation in patients with ARDS caused by a respiratory virus.

Methods: A systematic review was conducted following the PRISMA flowgram and recommendations [4]. The terms with each MERSH term were "acute respiratory distress syndrome" (Disease), "High Flow Nasal Cannula (HFNC)" OR "Continuous Positive Airway Pressure (CPAP)" OR "Non-invasive ventilation (NIV)" OR "Ventilators splitters (VS)" OR "Low-cost ventilator (LCV)" (Therapy) and "SARS" OR "SARS-CoV2" OR "H1N1" OR "Influenza" OR "MERS" (Pathogen). The search was done on Medline and Embase for Index literature and regulatory agencies for gray literature. Studies included could be randomized clínical trials (RCT) or non-randomized studies (NRS) that compare at least one ventilatory alternative (HFNC, NIV CPAP, VS or LCV) to IMV in patients with ARDS due to respiratory virus and mortality as an outcome. If enough studies per ventilatory alternative were found, a meta-analysis in Revman5 was performed by determining the OR by Random effects model of mortality compared to IMV. Subgroup analysis was performed to explore possible heterogeneity, bias evaluation for included studies and GRADE evaluation was also performed [5,6].

Results: 36 Studies fulfilled the inclusión criterias, of which 29 of them were NRS, 2 were studies on trial and 5 were abstract congress with results, while RCTs were not identified. From those 29 NRS and 5 abstract congress studies, 13 were for NIV, 8 for CPAP, 6 for HFNC, 3 have simultaneously evaluated multiple interventions and 5 did not properly distinguish between interventions. No studies of LCV were found, 1 study on trial for SV and 1 for NIV were identified. NIV evidence OR = 0.41 [0.29, 0.60; $I^2 = 74\%$], HFNC shows OR = 0.31 [0.15, 0.67; $I^2 = 78\%$] and CPAP has a OR = 0.39 [0.15, 1.06; $I^2 = 90\%$]. Subgroups analysis reduces heterogeneity and GRADE evaluation shows evidence of very low quality.

Conclusion: NIV and HFNC reduce mortality in ARDS of viral origin, while CPAP does not. High heterogeneity between studies and because there are only NRS indicated the necessity to conduct RCTs.

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Acknowledgements: There was no funding for this study. but this research is being used as a thesis for Master's degree in Epidemiology.

000242

Mechanical power at study-end correlates with neuroinflammation in moderate-ARDS pigs ventilated for 12 h

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Intensive Care Medicine Experimental 2022, **10(2)**:000242

Introduction: In clinical studies, increased morbidity and mortality have been associated with mechanical power (MP) generated by mechanical ventilation (MV). MV and acute respiratory distress syndrome (ARDS) have been also linked to neuroinflammation. Hippocampal inflammation, which can be measured by microglia percentage, has been associated with both MV and ARDS. Temporary transvenous diaphragm neurostimulation (TTDN) has been shown to mitigate hippocampal inflammation in a juvenile, healthy lung, porcine model. Currently, no study has demonstrated an association between hippocampal inflammation and MP in an ARDS porcine model.
Objectives: This study investigates any potential correlation between microglia percentage and MP in an ARDS porcine model.
Methods: Juvenile pigs (4–5 months, 50–87 kg) underwent protective MV (volume control, PEEP 5 cmH2O, tidal volume 8 ml/kg) for 12 h, with moderate ARDS (PaO2/FiO2 between 100 and 200). ARDS was induced by injecting oleic acid into the pulmonary artery. Subjects were assigned to three groups (n = 6 per group): lung injury with MV only (LI-MV), lung injury with MV and with TTDN every other breath (LI-MV + TTDN50%), and lung injury with MV and with TTDN every breath (LI-MV + TTDN100%). Diaphragm neurostimulation was delivered according to methods published previously, via a central line catheter embedded with electrodes (LIVE Catheter, Lungpacer Medical, Inc.), targeting a neurostimulation-induced reduction of 15–20% in ventilator pressure–time product. After the study, the hippocampus was harvested, and an ionized calcium-binding adapter molecule-1 (IBA-1) assay was used to stain microglia. Microglia were identified using machine-learning software (ImageJ) and microglia percentages were determined. MP was calculated as MP = 0.098*RR*VT*(PIP-½(driving pressure)). The Kruskal–Wallis test and Spearman's correlation were used for statistical analyses. P-values < 0.05 are considered statistically significant.
Results: MP at study-end and microglia percentage were both significantly lower in the LI-MV + TTDN100% group than in the LI-MV group ($p = 0.008$ and $p = 0.0004$, respectively). MP at study-end and microglia percentage were, respectively: 14.8 J/min (13.2–16.5) and 18.0 (17.0–32.2) for the LI-MV group, 11.4 J/min (9.9–13.8) and 12.7 (11.6–13.8) for the LI-MV + 50%TTDN group, and 8.6 J/min (6.2–11.9) and 8.8 (7.7–10.3) for the LI-MV + TTDN100% group. Differences in MP at study-end and in microglia percentage between the LI-MV + TTDN50% group and both of the other groups were not statistically significant ($p > 0.05$). MP showed a linear, positive, and moderate correlation with hippocampal microglia percentage, ($r = 0.55$, $p = 0.0188$).
Conclusion: In a porcine moderate-ARDS model, TTDN on every breath significantly mitigates hippocampal inflammation and significantly reduces MP at study-end. Mechanical power at study end moderately correlates with hippocampal inflammation.

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Acknowledgements: Lungpacer Medical USA Inc.

000272

Trends in mortality, treatment, and costs of management of acute respiratory distress syndrome in South Korea: analysis of data between 2010 and 2019

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Intensive Care Medicine Experimental 2022, **10(2)**:000272

Introduction: Despite recent advances in the understanding and management of acute respiratory distress syndrome (ARDS), trends in treatment, mortality, and healthcare costs following these advancements remain to be identified.
Objectives: In the present study, we aimed to investigate these trends using real-world data from a national cohort database in South Korea.
Methods: Using the National Health Insurance Service database, we collected and analyzed data for critically ill adult patients with ARDS who were admitted to intensive care units in South Korea between 2010 and 2019.
Results: The final analysis included 25,431 patients with ARDS. The 30-, 90-, and 365-day mortality rates in 2010 were 43.8%, 56.5%, and 68.2%, respectively. These rates had gradually decreased to 36.6%, 49.8%, and 58.8%, respectively, by 2019. Extracorporeal membrane oxygenation support for patients with ARDS started in 2014 at a rate of 5.1% (118/2,309), which gradually increased to 8.3% (213/2,568) in 2019. The rate of neuromuscular blockade treatment gradually increased from 22.6% (626/2,771) in 2010 to 30.9% (793/2,568) in 2019. The renal replacement therapy rate gradually increased from 5.7% (157/2,771) in 2010 to 12.0% (307/2,568) in 2019. The mean total cost of hospitalization increased from 5,986.7 USD in 2010 to 12,336.4 USD in 2019.
Conclusion: Real-world data for 2010–2019 indicate that patients with ARDS in South Korea have experienced changes in mortality, treatment, and healthcare costs. Despite the increased financial burden, mortality among patients with ARDS has decreased due to advances in disease management.

000294

Lung injury scores are correlated with mechanical power in a moderate-ARDS preclinical model

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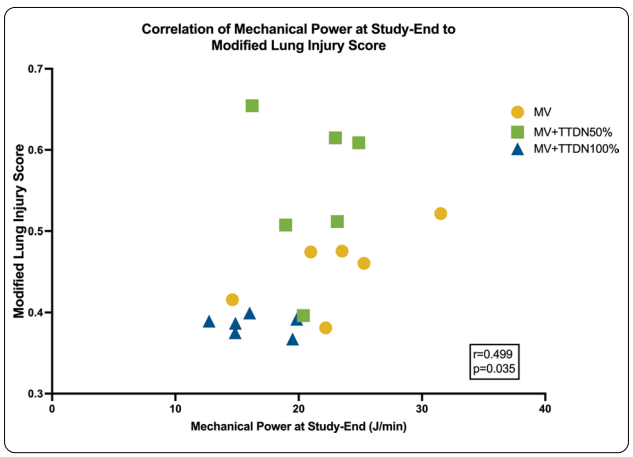
Intensive Care Medicine Experimental 2022, **10(2)**:000294

Introduction: Mechanical power quantifies the energy released to the respiratory system based on tidal volume, frequency, and flow, and is associated with increased ventilator-induced lung injury (VILI) and mortality.1,2 The additional occurrence of lung injury, such as acute respiratory distress syndrome (ARDS), further increases the risk of iatrogenic VILI.3 Reducing mechanical power is a target for reducing the sequelae of VILI in critically ill patients.
Objectives: We propose that temporary transvenous diaphragm neurostimulation (TTDN), synchronously combined with volume-control mode of MV, reduces mechanical power in a moderate-ARDS pig model, resulting in lower lung injury scores.
Methods: Deeply sedated, large pigs were ventilated using volume-control: 8 ml/kg, PEEP 5 cmH2O, with rate and FiO2set to achieve normal arterial blood gases. ARDS was induced using oleic acid via the pulmonary artery until PaO2/FiO2 < 200.4 The pigs were then ventilated for 12 h post-injury. Two groups received TTDN synchronized to

inspiration, targeting a reduction in ventilator pressure–time product of 15–20%. The MV+TTDN100% group received TTDN on every breath and the MV+TTDN50% group received TTDN on every second breath. A third group received volume-control ventilation only (MV group). Mechanical power was calculated as: MP = 0.098*RR*Vt*(Peak inspiratory pressure–½ driving pressure)0.5 Lung tissue was scored using a published scoring system, which was modified, as pigs have smooth muscle fibers that mimic hyaline membranes, and interstitial thickness was omitted, as postmortem lung inflation was not performed.6

Results: Median (IQR) mechanical power at study-end was lowest in the MV+TTDN100% group: 16 J/min (14–20) MV+TTDN100% group vs. 22 J/min (18–24) MV+TTDN50% group vs. 23 J/min (19–27) MV group (p = 0.028). Lung injury scores were also lowest in the MV+TTDN100% group: 0.39 (0.37–0.39) MV+TTDN100% group vs. 0.56 (0.48–0.62) MV+TTDN50% group vs. 0.47 (0.40–0.49) MV group (p = 0.002). Mechanical power at study-end is moderately correlated to lung injury scores (r = 0.4985, p = 0.035).



Conclusion: Mechanical power and lung injury scores were lowest in MV+TTDN100%. A consistent increase in risk of death in humans has been reported when mechanical power > 17.0 J/min for the first 48 h, as well as increased in-hospital mortality for every 5 J/min increase.2 In our study, MV+TTDN100% required mechanical power < 17 J/min at study-end, which was 7 J/min lower than MV. This demonstrates that MV+TTDN100% delivered safe mechanical power during the post-injury ventilation period, further supported by the moderate correlation between mechanical power and modified lung injury scores. TTDN on every breath offers a new way to reduce mechanical power during ventilation. If these results translate to human patients with ARDS, then TTDN has the potential to further reduce the relative risk of death in sedated ARDS patients receiving lung-protective mechanical ventilation.

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Acknowledgements

1. Royal Columbian Hospital Foundation
2. TB Vets Foundation
3. MITACS
4. Lungpacer Medical Inc.
5. BC Lung Association (Grant in Aid)

000339

Risk factors for intubation after more than one attempt in critically ill patients: Spanish prospective multicenter study on intubation in critically ill patients (INTUPROS)

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Intensive Care Medicine Experimental 2022, **10(2)**:000339

Introduction: Intubation in the critically ill is a high-risk procedure because of the clinical conditions of patients and the reasons for intubation. The INTUPROS study (NCT03916224) was made in Spain to evaluate the incidence and risk factors for major complications in the intensive care setting.

Objectives: To evaluate the risk factors for intubation after more than one attempt in a cohort of critically ill patients.

Methods: Prospective multicentre study in 43 Spanish ICU (6 months from april-2019 to october-2020) including only adult intubations and excluding patients with cardiac arrest Variable analysed: demographics, comorbidities, body mass index, APACHE II, SOFA and MACOCHA scores, reason for intubation, cardiovascular and respiratory conditions peri-procedure, patient position, use of Sellick manoeuvre, oxygenation method, devices and accessories used or intubation, first operator, Cormack score, used drugs, first pass intubation, major complications, and mortality. Continues variables are expressed as median (percentile 25–75) and continuous variables as percentages. Ethical committees approved the study protocol. An univariant analysis with U-Mann–Whitney or chi-square tests as appropriate and a multivariate analysis with logistic regression using a two-tailed p < 0.05 were used.

Results: A total number of 1837 patients were included. In 39 cases (2,1%) a previous difficult airway was registered. MACOCHA score was > 2 in 353 cases (19,3%). First operator was a resident physician in 1156 cases (63.3%) and a videolaryngoscope (VL) was used in the first attempt in 206 cases (11.2%). Cormack score was III-IV in 292 cases (15.9%) and there were pharyngeal secretions, blood or flood in 528 (28.9%). Intubation in the first pass was achieved in 1300 patients (70.8%), and 6 were can't intubate-can't oxygenate cases. A MACOCHA score > 2 OR 1.70 (CI 95% 1.26–2.30), respiratory failure as the reason for intubation OR 1.33 (CI 95% 1.04–1.69), a Cormack score III-IV OR 7.37 (CI 95% 5.34–10.18), presence of pharyngeal secretions, blood or flood OR 1.64 (CI 95% 1.28–2.10), ant the first attempt by resident OR 1.69 (CI 95% 1.31–2.17), were independently associated with a higher risk of intubation after more than one attempt, while the use of VL at the first attempt OR 0.46 (CI 95% 0.30–0.71) reduced the risk. The

number of laryngoscopy attempts was independently associated with the development of major complications OR 1.16 (CI 95% 1.01–1.33), but not with mortality.
Conclusion: Risk scores, respiratory failure, pharyngeal occupation, and less expertise of the operator are associated with a higher rate of failure in the first pass intubation, increasing the incidence of peri-procedure complications. The use of videolaryngoscope at first attempt increases the rate of intubation in the first attempt.

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000354

Non-invasive electromagnetic phrenic nerve stimulation to generate diaphragm contraction with effective Tidal volume in anesthetized patients—a proof-of-concept study

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Intensive Care Medicine Experimental 2022, **10(2)**:000354

Introduction: Mechanical ventilation (MV) is a life-saving intervention in critically ill patients. MV has side effects such as ventilator-induced diaphragm dysfunction (VIDD), with 80% prevalence in critically ill patients [1]. VIDD results in longer ICU and hospital length of stay (LOS) [2]. Diaphragmatic training by repetitive non-invasive bilateral electromagnetic phrenic nerve stimulation could prevent or ameliorate VIDD [3]. We have demonstrated that magnetic stimulation technology can be safely used near medical equipment in an ICU setting [4].
Objectives: We hypothesized that non-invasive electromagnetic stimulation of the phrenic nerves is feasible and results in a diaphragm contraction with an adequate tidal volume. Primary endpoint was the mean tidal volumes of at least 10 stimulations with the same intensity.
Methods: The present single center, proof-of-concept study was performed in five ASA I/II normal weighed patients scheduled for elective surgery with general anesthesia and planned intubation. After induction of anesthesia, intubation and reversal of the muscle relaxant, patients received non-invasive electromagnetic stimulation of the phrenic nerves, while the mechanical ventilator was set on spontaneous breathing mode with zero PEEP. For the stimulation, the STIMIT-exclusive *PMR35 dual coils* in combination with a standard clinical magnetic stimulator were used bilaterally with different stimulation intensities (10%, 20%, 30%, 40%).
Results: Patients were 30 [IQR 21–33] years old, 60% (n = 3) females, with a BMI of 22.6 [IQR 21.5–23.5] undergoing elective ear-nose-throat surgery. The mean tidal volume was 0.00 ± 0.00 ml/kg ideal body weight (IBW), 1.66 ± 1.58 ml/kg IBW, 5.11 ± 1.74 ml/kg IBW and 8.07 ± 2.31 ml/kg IBW for 10%, 20%, 30% and 40% stimulation intensity, respectively (Figure 1). There was a linear relationship between dosage (stimulation intensity) and effect (tidal volume) ($p < 0.001$; r2 0,63). The optimal stimulation intensity to achieve 3–6 ml/kg IBW was between 20 and 30% intensity in most cases (Table 1).

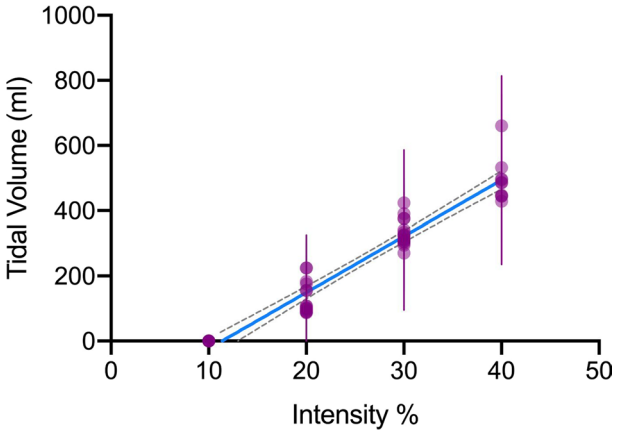

Figure 1—Tidal volume generated by bilateral non-invasive electromagnetic phrenic nerve stimulation in ml per ideal body weight with different intensities (10%, 20%, 30%, 40%) of the magnetic stimulator. Linear correlation with 95% CI ($p < 0.001$; r2 0,63).

Conclusion: Non-invasive bilateral phrenic nerve stimulation with an stimulation intensity of 20–30% seems to be able to non-invasively generate a tidal volume of 3–6 ml/kg IBW in pulmonary healthy normal-weighed anesthetized patients. Whether this non-invasive technique can prevent or attenuate VIDD has to be assessed in critically ill patients.

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Acknowledgements: This investigator initiated study was partly funded by STIMIT AG, Biel, Switzerland.

000361

Temporal trends of representation and outcomes of racial minorities in therapeutic clinical trials of acute respiratory distress syndrome

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Intensive Care Medicine Experimental 2022, **10(2)**:000361

Introduction: Heterogeneity of acute respiratory distress syndrome (ARDS) might be, in part, due to race. The racial minority of Black patients was previously (almost 15 years ago) found to be under-represented and to have higher mortality than Whites in therapeutic clinical trials of ARDS [1].

Objectives: We attempted to assess whether under-representation of Black patients in ARDS trials persisted over time, and to examine temporal trends of their outcomes.
Methods: We performed a secondary analysis of patient-level data from patients with ARDS enrolled in six randomized controlled trials performed by the United States of America ARDS Network, namely ARMA (published in 2000), ALVEOLI (2004), FACTT (2006), ALTA (2011), EDEN (2012), and SAILS (2014) [2–7]. We classified race into three mutually exclusive categories: "White/non-Hispanic", "Black", and "other". The group "other" included Hispanic, Asian, American Indian or Alaska Native, and Pacific Islanders. Prevalence and 60-day mortality of Black patients were the primary outcomes of the study.
Results: The overall prevalence of Black patients in ARDSNet trials was 17.0% (742 of 4,361 patients) without change over time (Figure); 17.2% in ARMA [2] versus 14.3% in SAILS [7] ($R^2 = 0.094$; $p = 0.555$). Black patients had higher 60-day mortality compared to Whites (29.9%, versus 25.9%, $p = 0.024$). After adjusting for age, body mass index, baseline immunosuppression and oxygenation at screening, Black patients still had higher mortality than Whites (hazard ratio = 1.27; 95% confidence intervals 1.09–1.48).

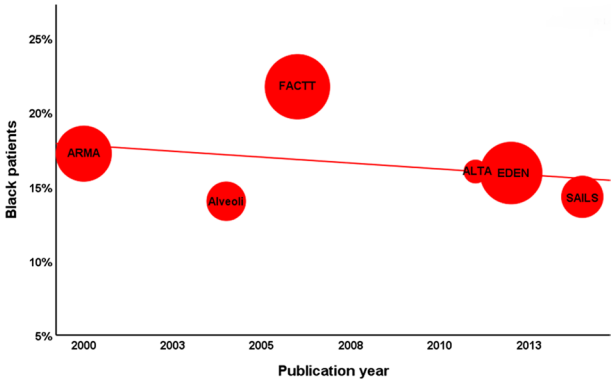

Figure. Representation of Black patients in ARDS Network randomized controlled trials over time. Each circle represents an ARDS Network trial, and circle size is proportional to study sample size.

Conclusion: Neither representation nor outcomes of Black patients in ARDS therapeutic trials improve over time.

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Acknowledgements: This study was supported by a grant to IIS from the Hellenic Foundation for Research and Innovation (80–1/15.10.2020). This analysis was prepared using ARMA, ALVEOLI, FACTT, ALTA, EDEN and SAILS research materials obtained from the Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) of the National Heart, Lung and Blood Institute (NHLBI) and does not necessarily reflect the opinions or views of the ARMA, ALVEOLI, FACTT, ALTA, EDEN, SAILS, ARDSNet, or the NHLBI.

000381

The use of inhaled nitric oxide (iNO) in Covid-19 ARDS patients: a French retrospective registry

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Intensive Care Medicine Experimental 2022, **10(2)**:000381

Introduction: Inhaled Nitric Oxide (iNO) has been widely used all over the world during COVID19 pandemia1. Previous studies reported conflicting results on the effect of iNO on oxygenation improvement.
Objectives: The objective of this registry was to describe the use of iNO in a large cohort of Covid19 ARDS (CARDS) patients.
Methods: Multi-center, retrospective cohort registry conducted in 12 French hospitals in 2020 on CARDS patients treated with iNO.
Patients characteristics, clinical respiratory support, nitric oxide therapy safety and efficacy parameters and patients clinical outcomes were collected. iNO response was defined as PaO2/FiO2 ratio improving by > = 20% after iNO initiation.
Results: From march to december 2020, 300 CARDS patients (22.3% female) were included in the registry. At ICU admission, their median (IQR) age, SAPS II, and SOFA scores were 66 (57–72) years, 37 (29–48), and 5 (3–8), respectively. Patients were still hypoxaemic despite protective ventilation (in all patients) and prone positioning sessions (in 68%). At iNO initiation, 2%, 37%, and 61% patients had mild, moderate, and severe ARDS, respectively. Median (IQR) delay between iNO therapy initiation and ICU admission, ARDS diagnosis, and intubation were 7 (3–12), 6 (2–11) and 4 (1–10) days respectively. The median duration of iNO was 2.8 (1.1–5.5) days with a median dosage of 10 (7–13) ppm at initiation. Responders were analyzed at different stages: 45.7% of patients were responders within 6 h following iNO initiation, 56.9% based on the best PaO2/FiO2 ratio within 24 h after iNO initiation and 70.3% patients had at least one response during iNO administration. The severity of ARDS is the only predictive factor associated with iNO response considering the best PaO2/FO2 ratio obtained within 24 h (Table 1).

Table 1: Severity of ARDS at iNO initiation in iNO responders and non responders.

		iNO non responders (N = 106)	iNO responders (N = 140)	p-value
Severity of ARDS before iNO initiation	N	105	139	0.004 [Fisher exact test]
	Missing	1	1	
	Mild	4 (3.8%)	1 (0.7%)	
	Moderate	49 (46.7%)	43 (30.9%)	
	Severe	52 (49.5%)	95 (68.3%)	

A post hoc analysis was performed on 62 patients who fulfilled EOLIA ECMO criteria2 (PaO2/FiO2 < 80 mmHg OR (PaCO2 < = 60 mmHg and pH < 7.25) before initiation of iNO therapy.After 6 h of NO,32 patients (51.6%) lost the criteria for ECMO, ie, they had PaO2/FiO2 > = 80 mmHg and (PaCO2 < 80 mmHg or pH > = 7.25). Among patients eligible for ECMO, those who lost ECMO criteria under iNO had a lower mortality rate (60%vs 84%); Adjusted OR: 0.23 (95% CI: 0.06, 0.89), p = 0.03] than their counterparts, even after adjusting for parameters such as age, total SOFA score, duration of ventilation before NO initiation and wave of COVID-19 concerned. Regarding safety aspects, renal replacement therapy was initiated in 23.5% patients during iNO administration, without a formal causal link with iNO.

Conclusion: This registry confirmed the benefits of iNO for arterial oxygenation improvement in severe ARDS patients. This effect seems more relevant in the most compromised population. In patients with ECMO criteria, an iNO-driven improvement in gas exchanges is associated with better survival. These promising results must be confirmed in well designed studies.

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Acknowledgements: This study was sponsored by Air Liquide Santé International.

000407

Withdrawing life-support treatment in critical ill due to COVID-19

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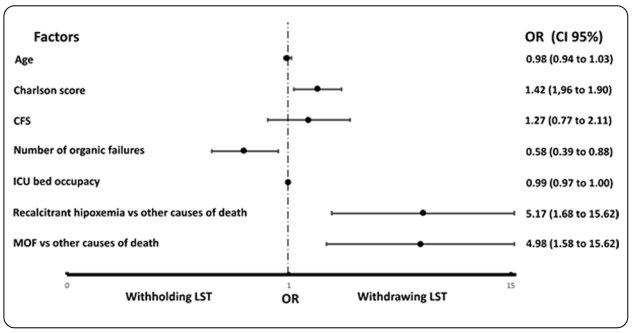
Introduction: Withdrawing life-support treatment (WLST) is defined as the therapeutic adecuacy of life-support to a patient´s clinical situation. During the COVID 19 pandemic this decision was considered in a large number of patients admitted to intensive care units (ICU) due to the lack of response to treatment, a decision that involved an even greater emotional burden.

Objectives: To analyze the different factors that lead to WLST in COVID-19 patients admitted to ICUs.

Methods: Retrospective observational study of COVID 19 patients admitted to the ICU between March 2020 and September 2021. Demographic, severity, and outcome variables of patients admitted to the ICU were reviewed and categorized for cases in which WLTS was decided and cases where it was not. Categorical variables are expressed in frequency and percentages form and are compared using a $\chi 2$ test; continuous variables are expressed as median and interquartile range (IQR) values and are compared using the student's t-test. A significance level of 5% (two-tailed) was used. A multivariate analysis was performed using logistic regression to estimate the effect size and adjust for confounding factors. The analysis was performed using STATA version 13 ® (StataCorp LCC).

Results: There were a total of 631 ICU admissions with COVID-19 during the study period, with a mortality rate of 31.85% (n = 201). 93,03% (187) were admitted for respiratory failure and required invasive mechanical ventilation. WLST was decided in 122 cases (65,24%), the majority of them (131, 70,05%) were male. Median age were 67 (61–72) years old, being older those who WLST (68 [61–72] vs no WLST 66 [58–71] years old). There were no statistically significant differences regarding comorbidities between both groups. In multivariate analysis, age, clinical frailty scale, and ICU bed occupancy on the day of death did not influence the WLTS decision. Charlson score at admission (3 [2–4] vs 2 [2–3]; OR: 1,42 [IC95%: 1,06 to 1,90]) and recalcitrant hypoxemia (59,84% vs 36,92%; OR: 5,17 [IC95%: 1,68 to 15,89]) influenced the WLST. The sum of organic failures (number of organic failures) at the time of death influenced withholding life-support treatments (2 [1–3] vs. 3 [2–3]; OR: 0,59 [IC95%: 0,39 to 0,88]) (Figure 1). Length of stay in-ICU was similar in both groups (p = 0.259).



Conclusion: Charlson score and the clinical situation at the time of death influence the WLST decision. It should be noted that this decision was made mainly in those who presented recalcitrant hypoxemia and that the addition of organic failures led to withholding the treatment. Age, ICU bed occupancy and the different waves of the pandemic did not influence the WLST.

Acknowledgements: ICU Department of Hospital Universitario de Toledo.

Acute Respiratory Failure 4

000069

Should we routinely use NIV/CPAP or HFNO post TAAA surgery to reduce the incidence of PPCS? Single-centre observational study

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Intensive Care Medicine Experimental 2022, **10(2)**:000069

Introduction: The gold standard approach for descending thoracic aorta (DTA) repair and thoracoabdominal aortic aneurysm (TAAA) repair is open thoracoabdominal surgical repair (Lopez-Marco et al., 2020) DTA and TAAA repair requires lung isolation and single lung ventilation usually achieved with a dual lumen endotracheal tube (Cooper, 2011). This type of procedure is associated with high incidence of postoperative pulmonary complications (PPCs) approximately 45–62%, associated higher mortality rate and overall increased hospital length of stay and subsequent financial costs (Pasin et al., 2017, Mamo et al., 2019 and Griffiths et al., 2018).

Standardised postoperative respiratory management of this cohort has not been established. However, there is some evidence to suggest the routine use of non-invasive ventilation (NIV), continuous positive airway pressure (CPAP) and or high flow nasal oxygen (HFNO) in the immediate postoperative phase could reduce the incidence of PPCs (Mamo et al., 2018 and Kindgen-miles et al., 2005).
Objectives: The objectives of this observational study include:

- Identify the number of patients receiving post operative NIV/CPAP or HFNO following elective TAAA
- To identify the criteria indicating the need for NIV/CPAP of HFNO post elective TAAA

Methods: Adults admitted to ICU following elective TAAA surgery from Jan 2020 to Dec 2021 were included. Baseline characteristics were collected, surgery statistics and primary and secondary outcomes.
Results: A total number of n23 patients underwent elective TAAA surgery. n20 patients survived and were included in the analysis. 70% of patients underwent surgery for Crawford Classification extent II TAAA. The most common reported co-morbidity was hypertension (60%). Average left heart bypass time was 226 (±83) mins. Patients received on average 39L of blood and fluids peri-operatively and 100% received cryoablation of intercostal nerves. 35% (n7) of patients required NIV or CPAP during the post extubation phase and with some crossover to HFNO, 70% of patients received HFNO in the post operative extubation phase. Reasons for escalation to NIV/CPAP or HFNO predominantly were post operative atelectasis (70%), pneumonia confirmed by physician requiring antibiotics (75%) and a P/F ratio of < 200 (55%).
Conclusion: Patients receiving elective surgery for TAAA repair are high risk of developing post-operative complications due to the nature of single lung ventilation. This observational study found 35% of patients receiving surgery for extent II Crawford Classification TAAA repair required NIV or CPAP during the post extubation phase and a total of 70% of patients required HFNO to support recovery. Due to the small sample size of this data it is not clear whether the routine use of NIV/CPAP or HFNO would reduce the incidence of PPCs for this cohort. Further investigation comparing CPAP/NIV or HFNO to no intervention is required to impact on local guidelines and clinical practice.

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000259

The effects of anti-C5a antibody vilobelimab on several biomarkers: an explorative study

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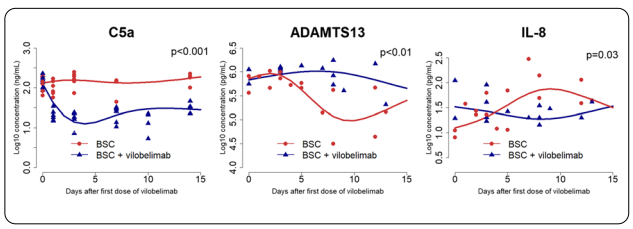
Intensive Care Medicine Experimental 2022, **10(2)**:000259

Introduction: Complement 5a (C5a) is an important contributor to the innate immune system and has the potency to activate the coagulation system [1, 2]. High C5a levels have been reported in severely ill COVID-19 patients and correlate with disease severity and mortality [3–5]. Accumulating evidence shows an association between complement activation in severe COVID-19 and markers of endothelial injury, hypercoagulation and inflammation [5, 6]. Subsequently, complement and neutrophil extracellular traps (NETs) have been identified as key drivers in COVID-19 immunothrombosis [7]. Previously, we assessed the potential benefit and safety of selectively blocking C5a in severe COVID-19 patients with the monoclonal antibody vilobelimab [8]. Here, we report a sub-study of the PANAMO phase 2 trial.
Objectives: To explore the effect of vilobelimab on various biomarkers.
Methods: Between March 31 and April 24, 2020, 17 patients with a severe COVID-19 pneumonia (PaO2/FiO2 ratio 100–250 mm Hg) were enrolled in an exploratory, open-label, randomised phase 2 trial in the academic hospital Amsterdam UMC, location AMC. Patients were randomized between treatment with best supportive care (BSC) plus vilobelimab (on days 1, 2, 4, 8, 15 and optionally days 11–13 and 22) and BSC only. Biomarkers including, but not limited to, complement activation, inflammation, coagulopathy, endothelial activation and NET formation were measured on several time points longitudinally. Biomarker concentration in the first fifteen days after inclusion between the two groups were compared over time with linear mixed-effects models (LMMs) with spatial splines. Beyond day 15, sampling was considered too sparse to be representative.



Results: Eight patients were randomized to the vilobelimab group and nine patients to the BSC group. Baseline characteristics were comparable between the two groups. A significant decrease over time was seen in the vilobelimab group for C5a compared with the BSC group ($p < 0.001$). Although sampling was scarce, ADAMTS13 levels decreased over time in the BSC group compared with the vilobelimab group ($p < 0.01$) and IL-8 levels seemed increased in the BSC group ($p = 0.03$). The LMMs are plotted in the figures above. All three biomarkers remained significantly different when tested over 28 days. Biomarker concentrations did not differ significantly for complement markers C3a, MASP-2, factor Bb nor for the aforementioned biomarkers.
Conclusion: In this small, exploratory sub-study, patients treated with vilobelimab showed a significant decrease of C5a over the first fifteen days, compared with the BSC group. ADAMTS13 decreased over time in the BSC group compared with the vilobelimab group, potentially indicating a protective effect of vilobelimab on thrombotic complications [9]. Il-8, which can be induced by C5a, seemed more supressed in patients treated with vilobelimab [10]. A larger sample size is needed to further substantiate our findings, however, these results can give

a first direction why inhibition of C5a could be beneficial in severe COVID-19.

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000327

Dexamethasone versus methylprednisolone in COVID19 critically ill patients: a multicenter propensity score matching study

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Intensive Care Medicine Experimental 2022, **10(2)**:000327

Introduction: Dexamethasone has a mortality benefit in COVID-19 patients, particularly those requiring invasive mechanical ventilation (MV). However, it is uncertain if another corticosteroid, such as Methylprednisolone, may be utilized to obtain a superior clinical outcome.
Objectives: We conducted a study to compare Dexamethasone's clinical and safety outcomes versus Methylprednisolone in COVID-19 critically ill patients admitted to the intensive care units (ICUs).
Methods: A multicenter, retrospective cohort study includes COVID-19 critically ill adult patients admitted to ICUs from March 2020 to July 2021. Patients were categorized into two groups based on the type of corticosteroid received within 24 h of ICU admission, the active group for patients who received Methylprednisolone and Dexamethasone as the control group. The primary outcome was the progression of multiple organ dysfunction (MOD) score at day three of ICU admission. The secondary outcomes were respiratory failure requiring MV, mortality, ICU and hospital length of stay (LOS), ventilator-free days (VFDs) at 30 days, and complications during ICU stay. Propensity score (PS) matching was used (1:3 ratio) based on patient's age, and multiple organ dysfunction score within 24 h of ICU admission.
Results: A total of 1385 patients were screened during the study period; 526 patients were eligible after applying the study exclusion criteria. After PS matching, 264 patients were included according to the selected criteria. Of these patients, 198 were given Dexamethasone therapy, while 66 patients were given Methylprednisolone within 24 h of ICU admission. In regression analysis, patients who received Methylprednisolone compared to Dexamethasone had a higher MOD score at day #3 of ICU admission (beta coefficient: 0.17 (95% CI 0.02, 0.32), P = 0.03). Moreover, hospital-acquired infection was higher in the Methylprednisolone group (OR 2.17, 95% CI 1.01, 4.66; p = 0.04). However, other complications during the stay were similar between the two groups. The 30-day and the in-hospital mortality were similar in both groups on multivariable cox proportional hazards regression analysis.
Conclusion: In critically ill patients with COVID-19, the use of methylprednisolone compared to dexamethasone resulted in a higher MOD score on day three of ICU admission with a similar mortality rate.

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000358

Diaphragmatic thickness in patients receiving PRVC ventilation and SIMV: a randomized controlled trial

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Intensive Care Medicine Experimental 2022, **10(2)**:000358

Introduction: Ventilator induced diaphragmatic atrophy is of utmost clinical importance as diaphragmatic function is a major determinant of successful weaning from mechanical ventilation. We designed this study to compare the effect of assist/controlled mode (PRVC) and assisted mode (SIMV) with pressure support on diaphragmatic atrophy in patients with acute respiratory failure.
Objectives: The primary endpoint of the study was to compare the change in diaphragmatic thickness at day 3 between patients on PRVC ventilation & SIMV-PS ventilation.
Methods: Seventy adult patients with acute respiratory failure requiring invasive mechanical ventilation, were recruited. Diaphragm thickness was measured at the zone of apposition between the eighth or ninth intercostal spaces on the right side in the mid-axillary line using B mode ultrasound.

Results: Diaphragmatic thickness was reduced irrespective of the ventilation mode used and percentage of decline in end-inspiratory diaphragmatic thickness was significantly higher in PRVC ventilation group than SIMV group at day 2 [median [IQR] 8 [0–9.1] in PRVC versus 4.35[0–6.9] in SIMV group; p = 0.0010] and day 3 [median [IQR] 13.6 [12–17.4] in PRVC versus 10.5[5.3–13.6] in SIMV group; p = 0.0010]. No difference was obtained in the diaphragmatic thickness fraction at the time of extubation (p = 0.48), number of SBTs required (p = 0.37), duration of mechanical ventilation (p = 0.09), length of ICU stay (p = 0.10) and survival to ICU discharge (p = 0.61).
Conclusion: The use of SIMV PS mode maintaining assisted spontaneous ventilation, compared to assist control mode may the reduce rate of diaphragmatic atrophy in mechanically ventilated patients with acute respiratory failure.

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Acknowledgements: No grant received.

000403

Increased mortality in patients with acute respiratory failure of undetermined etiology

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Introduction: In patients with acute respiratory failure (ARF), early adequate therapy is associated with good prognosis. There are many possible etiologies for acute respiratory failure, but diagnosis is often unclear. In this study, we investigated the effect of undetermined etiology on the prognosis of patients with ARF.
Methods: This is a prospective multicenter cohort study that included 165 adult patients with ARF admitted to the intensive care unit (ICU) from June 2020 to February 2021. Relationship between ARF etiology and hospital mortality was assessed using a multivariable regression model adjusting for confounding factors.
Results: Among the 165 patients, a bronchoalveolar lavage (BAL) was performed in 66 (40.0%). Etiologies of ARF were classified into 10 categories: bacterial pneumonia (47.3%), viral pneumonia (3.6%), septic shock related (13.9%), invasive fungal infection (13.3%), aspiration pneumonia (20.0%), airway disease related (3.0%), drug-induced pneumonitis (0.6%), cardiogenic pulmonary edema (3.0%), disease-related infiltrates (3.0%), undetermined (17.0%). By multivariable analysis, factors associated with hospital mortality were high SAPS3 score (OR 1.05 [95% CI 1.02–1.09]; p = 0.003), invasive fungal infection (OR 5.15 [95% CI 1.41–18.80]; p = 0.013), and undetermined etiology (OR 22.56 [95% CI 4.69–108.52]; p < 0.005).

Table 1. Mortality according to different etiology of acute respiratory failure

Etiology (n, %)	Survived (n = 87)	Died (n = 78)	P-value
Bacterial infection	48 (55.2)	30 (38.5)	0.047
Viral infection	2 (2.3)	4 (5.1)	0.580
Sepsis-related	9 (10.3)	14 (17.9)	0.237
Invasive fungal infection	7 (8.0)	15 (19.2)	0.060
Aspiration pneumonia	24 (27.6)	9 (11.5)	0.017
Airway disease-related	5 (5.7)	0 (0.0)	0.090
Drug induced pneumonitis	1 (1.1)	0 (0.0)	1.000
Cardiogenic pulmonary edema	5 (5.7)	0 (0.0)	0.090
Disease-related infiltrates	1 (1.1)	4 (5.1)	0.301
Unknown etiology	4 (4.6)	24 (30.8)	< 0.001

Conclusion: In patients with ARF, up to 17% remain with undetermined ARF etiology despite comprehensive diagnostic workup. Undetermined ARF etiology is independently associated with hospital mortality. Rapid and noninvasive noble diagnostic strategies for ARF patients are warranted.

000411

Biotrauma and organ dysfunction caused by driving pressure, mechanical power and other ventilator-induced lung injury parameters

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Introduction: In patients with Acute Respiratory Distress Syndrome (ARDS) the extrapulmonary organ dysfunction is a major cause of mortality. Ventilator-induced Lung Injury (VILI) parameters such as Driving pressure (DP) and Mechanical Power (MP) are related to an increased mortality risk. However, the physiological mechanisms leading to death are not known.
Objectives: To analyze the associatoin between DP, MP as well as other VILI parameters with systemic inflammation, pulmonary epithelial and endothelial injury, coagulation disorders and organ dysfunction.
Methods: Prospective observational study of patients presenting with ARDS in which we evaluated the association of DP, MP and other VILI parameters to pulmonary and extrapulmonary dysfunction (pulmonar and non-pulmonary SOFA) as well as Interleukin (IL)-6, IL-8, IL-10, IL-17, TNFa, TNFa solube receptor (RS), Tissue factor, Angiotensin, CCL2, CCL7, VGEF, Von Willebrand factor, Protein C, Plasminogen activator inhibitor, Angiopoietin, RAGE, Factor IX and Protein C.
Results: 30 patients with ARDS. The cause of ARDS was pulmonary sepsis/bronchoaspiration in 70% of patients. Median age (IQR) was 62 (45; 69) and 58% were male. Median APACHE at ICU admission was 21 (17; 28). P/F ratio and ventilatory ratio were 118 (91; 175) and 2.1 (1.7; 2.4) upon ARDS diagnosis.
Median DP, MP, tidal volume, positive-end inspiratory (plateau) pressure and PEEP were 14 (12; 16) cmH2O, 25 (18; 29) J/min; 7 (6.2; 7.9) ml/kgIBW; 24 (22; 26) cmH2O and 10 (9; 12) cmH2O respectively.
Positive end-inspiratory (plateau) pressure and DP upon ARDS diagnosis were associated to worse pulmonary SOFA at day 1 and 3 and higher biomarkers of pulmonary epithelial dysfunction at the same time points. However, these variables were not associated to systemic inflammation, coagulation disorders, endothelial dysfunction and non-pulmonary organ dysfunction.
Tidal volume normalized to ideal body weight and PEEP were not related to either epithelial and endothelial pulmonary dysfunction, systemic inflammation, coagulation disorders or multiorgan dysfunction.
Mechanical power was associated with higher RsTNFa and lower Angiotensin.
Respiratory system compliance and inspiratory resistance were related to higher IL-8 and RsTNFa, respectively.

Conclusion: DP and plateau pressure are related to pulmonary epithelial dysfunction and worse pulmonary SOFA, but not with extrapulmonary organ dysfunction or systemic biotrauma. This suggests that the pathway to death realted to these variables is due to lung dysfunction and its consequences.
MP is associated with higher systemic inflammation and endothelial dysfunction. However, compliance and inspiratory resistance, two non-modifiable components of the respiratory system, are related to systemic inflammation and are components of the MP equation. Therefore, we can not assure whether a causal relationship between systemic inflammation, endothelial dysfunction and MP exists.

000432

Role of veno-arterial-venous extracorporeal membrane oxygenation as a bridge to lung transplantation

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Introduction: Extracorporeal membrane oxygenation (ECMO) is widely used as a support therapy in patient with end-stage heart or lung diseases. As a bridge to lung transplantation, veno-venous (VV) ECMO has been preferred. However, prolonged waiting times lead to right heart dysfunction.
The purpose of this study was to find the role of veno-arterial-venous (VAV) ECMO in patients with right heart failure(RHF) waiting lung transplantation.
Methods: A retrospective review was performed of 86 patients supported with ECMO before lung transplantation (LTx) from December 2012 to September 2020 in a single institution. The cases had applied VAV ECMO as a bridge were reviewed.
Results: Of 86 patients bridged with ECMO to lung transplantation, total seven patients were supported with VAV ECMO. Four patients were placed on VAV ECMO from the start because of severe pulmonary hypertension. The three other patients were changed from VV to VAV type ECMO due to RHF while waiting for LTx. The average age of patients was 55.1 years and mean ECMO support days was 18 (range 5–38). When VAV ECMO supported, mean value of right ventricular systolic pressure was 75.2 mmHg (range 50.0–107.0). Conversions from VV ECMO to VAV ECMO were performed at the mean of 20 days of VV ECMO. In one patient, sudden cardiac arrest due to RHF occurred on day 25 of VV ECMO that led him to undergo a urgent mode change to VAV ECMO. There was no major complication related to ECMO during patients were supported with VAV ECMO. Right heart function of all seven patients improved after receiving LTx successfully. One patient expired 7 months after LTx due to lung cancer diagnosed after transplantation and one patient died of intracranial hemorrhage at day 28 after transplantation. Five patients are still alive at a median of 34.9 months (range 27.5–76.7) after LTx.
Conclusion: Our experience with ECMO as a bridge to lung transplantation, cardiac function evaluation is required on a regular basis and VAV ECMO could be a useful for patient with right heart failure waiting lung transplantation.

000445

May the antigen-based test predict COVID-19 patients' outcome?

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Introduction: Individuals can test positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by antigen-based (as) and molecular assays (ms): while the first are likely to be positive early in the disease course, when there is an increased likelihood of high levels of infectious virus, the second can be positive following the resolution of their clinical disease. Little data are available about the prognostic value of the persistent positivity at the antigen-based assays.
Objectives: To evaluate any prognostic value of antigen-based assays in critically ill SARS-CoV-2 positive patients.
Methods: Retrospective observational study of COVID-19-confirmed critically ill patients (pts), treated in our ICU (AR B BR, AOUI-University Hospital Integrated Trust) of Verona from 1st Jan to 1st May, 2021. We collected demographic, clinical data, as well as data on organ failure and outcome on D1, D3, D7 of ICU stay.
Results: 117 pts were included, the median age was 64 years, 90 (76.9%) were male and the median BMI was 29.69 kg/m^2. 85 pts (72.6%) had cardiovascular disorders, 22 (18.8%) had dyslipidemia, 20 (17%) had diabetes and 11 (9.4%) had a history of asthma. 28 days ICU mortality was 11.9%, 14 died during hospitalization, of which 12 in the ICU. Median APACHE II score was 10 for survs and 19.50 for non survs. On D1, among survs (103 pts), we recorded 43 positive antigenic swabs (as) and 60 negative as; among non survs (14 pts) we recorded 12 positive as and 2 negative as. On D3 (114 pts) among the survs (101 pts), we recorded 27 positives as and 74 negatives as; among non survs (13 pts) 10 positive and 3 negatives as. On D7 (85 pts) among survs (76 pts), we recorded 16 positive as and 60 negative as; among non survs (9 pts) 6 positive and 3 negative as. Most of these pts needed mechanical ventilation; the rate of intubated patients in survs and non survs was 34.3% and 78% on D1, 56.1% and 70% on D3 and 77.9% and 100% on D7, respectively. We analyze the SOFA score without the neurological component (SOFA-N) on D1, 3, 7. On D1 median SOFA-N for surv and non survs was 3.5 and 4.5, respectively, on D3 3 and 5, while on D7 3 and 4. The median of ICU LOS was 9.5 days (1–147) for survs and 6 days (1–28) for non survs.
Conclusion: Our preliminary data support the hypothesis that in critically ill COVID-19 patients the persistent positivity to the SARS-CoV-2 antigenic-based assays may be used as a prognostic tool.

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000449

Airway pressure release ventilation (APRV) versus Biphasic positive airway pressure ventilation (BPAP) in Coronavirus disease-19 (COVID-19) associated ARDS: Should transpulmonary pressure-monitoring be mandatory?

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Intensive Care Medicine Experimental 2022, **10(2)**:000449

Introduction: Airway pressure release ventilation (APRV) is a time-cycled, pressure-controlled mode of ventilation. It can improve oxygenation in patients with acute respiratory distress syndrome (ARDS) by increasing mean airway pressure, resulting in alveolar recruitment and maintenance of an open lung.[1] COVID-19 associated ARDS (CARDS) seems to differ from ARDS caused by other pathophysiology. So far, little is known about the benefits and harms of APRV compared to lung protective biphasic positive airway pressure ventilation (BPAP) in CARDS.[2, 3].
Objectives: Mechanical ventilation can be guided by esophageal/transpulmonary pressure (TPP), which can detect signs of baro- and atelectrauma.[4] This study aimed to compare potential benefits and harms of APRV vs BPAP in CARDS patients by monitoring TPP.

Methods: This retrospective cohort study focused on adult COVID-19 positive patients, admitted to an Intensive Care Unit of a German quaternary care hospital from March 2020 to October 2021. All patients included in this study were suffering from CARDS ($PaO2 \leq 300$ mmHg), initially ventilated in BPAP-mode and consecutively in APRV-mode (in supine position) under TPP-monitoring. BPAP was set as per ARDSnet recommendations for lung protective ventilation.[5] APRV was set according to previous BPAP settings: High pressure ≤ 30 mbar, low pressure ≤ 5 mbar and the time on the lower pressure-level adjusted to an end-expiratory flow equal to 75% of the peak expiratory flow rate (≤ 0.5 s). Ventilator-settings, airway-pressures, TPP, arterial blood gas results, sedation requirements and hemodynamic stability were compared in all patients by three different measurements (1-2 h apart) in BPAP vs consecutively three measurements (1-2 h apart) in APRV.
Results: Twenty patients (65% male, mean age: 60.59 ± 13.04 years, mean body mass index: 33.63 ± 7.77 kg/m2, mean APACHE Score: 21.50 ± 10) were included in the study. Median endexpiratory TPP was negative in APRV vs positive in BPAP (-1.20 mbar; IQR: -4.88/+4.53 vs +3.45 mbar; IQR: +1.95/+8.57; $p < 0.04$), indicating a risk of atelectasis. Neither in APRV nor in BPAP, TPP-monitoring revealed signs of barotrauma (endinspiratory TPP ≥ 25 mbar). Mean tidal volumes per ideal body weight (7.16 ± 1.12 ml vs 5.23 ± 0.69 ml; $p < 0.01$) and mean airway pressures (27.12 ± 1.68 mbar vs 22.68 ± 2.62 mbar; $p < 0.01$) were higher in APRV vs BPAP. There was no significant difference in mean peak-, plateau-, driving-pressures, compliance/resistance, oxygenation/decarboxylation, sedation requirements or hemodynamic stability in APRV vs BPAP.
Conclusion: APRV vs BPAP did not show any benefit regarding oxygenation or decarboxylation. In contrast, APRV vs BPAP in CARDS patients without TPP-monitoring carries the risk of unwitnessed atelectrauma. Intrinsic PEEP, measured by the ventilator, is an unsafe predictor of atelectrauma in APRV. Consequently, TPP-monitoring is a useful tool in APRV to avoid ventilator-associated lung-injury in CARDS patients.

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Acknowledgements: This Study and its authors received no financial support.

000468

COVID-19 associated coagulation abnormalities in patients treated with VV-ECMO support as assessed by viscoelastic methods: a sub-cohort of the HEMOCOV study

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Introduction: Venovenous extracorporeal membrane oxygenation (VV-ECMO) for severe respiratory failure has been widely used for severe COVID-19 disease. In these patients, COVID-19-associated coagulopathy (CAC) has been implied as a pathophysiologic mechanism contributing to severity, although little data has been published regarding the profile and type of coagulation disorders in this subset of patients.
Methods: HEMOCOV study was an open-label, prospective observational study, conducted in patients with COVID-19-related acute respiratory failure (ARF) admitted in intensive care unit (ICU) of an academic tertiary care hospital. Coagulation tests, including thromboelastometry, biochemical analysis and clinical performance evaluation were analyzed at ICU admission, at 5-day interval until discharge, day 30 of admission or death.
Results: 145 patients with ARF related to COVID-19 were included in this study, of whom 27 have been treated with VV-ECMO support. Median age was 40 years (IQT 22–74), 26 have been submitted to invasive mechanical ventilation (IMV). The mean SAPS II (*Simplified Acute Physiology Score*) was 34.8 and mean SOFA score was 6.2. At admission, median platelet level was 205×109 cel/L, mean hematocrit was 44.7%, coagulation factor VIII was 291%, vWF:RCo was 47%. As reported in complementary study (data not shown), LI30-INTEM and CFT-FIBTEM has been associated with risk of death. In this subgroup of patients, values were 100% and 796 s, respectively. Clinically significant thrombotic events occurred in 42.3% and hemorrhage in 57.7% of patients. ICU mortality was 30.7%.
Conclusion: Our study suggest that hypercoagulability and hypofibrinolysis may be important pathophysiological mechanisms in patients with severe COVID-19 treated with VV-ECMO support. Longitudinal viscoelastic testing may be useful for better assessment of thrombotic and hemorrhagic risk in these patients.

Acute Respiratory Failure 5

000177

Clinical characteristics, treatments and mortality during the first four waves: a nationwide comparative cohort study of critically ill COVID-19 patients in the Netherlands

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Intensive Care Medicine Experimental 2022, **10(2)**:000177

Introduction: Up to date four waves of COVID-19 patients have been identified in the Netherlands, resulting in over 22.000 deaths. Despite the introduction of novel treatments the mortality among patients with severe COVID-19 remains high.
Objectives: We aim to describe to changes in characteristics, treatments and outcomes for COVID-19 patients admitted to the ICU in the Netherlands during the four pandemic waves.
Methods: In this cohort study among 10 large academic and teaching hospitals adult patients who were admitted to the ICU for COVID-19 were included between 27 February 2020 and 31 December 2021. Study groups were compared over the waves with Chi-square for trend for categorical data and with Kruskal–Wallis test for numerical data. In-hospital mortality was defined as mortality either on the ICU or on the ward.
Results: 1414 critically-ill patients with COVID-19 were included; the mean age was 64 years [IQR, 56–72] and 72% were male. 44.7% was admitted directly to the ICU, the other 55.3% first to the ward. The median length of hospital stay was 17 days [IQR, 11–28] and the ICU-stay 9 days [IQR, 4–18]. ICU-mortality was 24% and in-hospital mortality 32%. See Table 1 for the clinical characteristics, treatments and outcomes per wave. The percentage of males decreased over the waves (from 76% in wave 1 to 66% in wave 4), as well as the median age (from 65 to 60 years). The median length of ICU-stay decreased over time, as well as the ICU-mortality (28% in wave 1 to 17% in wave 4).

Table 1. Clinical characteristics, treatments and outcomes.

	Wave 1 Mar–Jun 2020	Wave 2 Jul 2020–Jan 2021	Wave 3 Feb–Jun 2021	Wave 4 Jul–Dec 2021	*p* value
n	623	393	247	151	
Demographics					
Sex—male (no. (%))	473 (75.9)	279 (71.0)	167 (67.6)	100 (66.2)	**0.002***
Age, years (median [IQR])	65 [58, 72]	65 [57, 72]	63 [53, 70]	60 [51, 68]	**<0.001^**
Patients with comorbidities (no. (%))	447 (78.4)	313 (83.2)	187 (81.3)	108 (72.0)	0.502*
Treatments					
Hydroxychloroquine (no. (%))	410 (65.8)	3 (0.8)	2 (0.8)	1 (0.7)	**<0.001***
Remdesivir (no. (%))	13 (2.1)	67 (17.0)	5 (2.0)	1 (0.7)	0.870*
Steroids (no. (%))	139 (22.3)	352 (89.6)	231 (93.5)	150 (99.3)	**<0.001***
IL-6 antagonist (no. (%))	5 (0.8)	3 (0.8)	118 (47.8)	110 (72.8)	**<0.001***
Monoclonal antibodies (no. (%))	0 (0)	0 (0)	0 (0)	26 (17.2)	**<0.001***
Invasive ventilation (no. (%))	539 (87.1)	280 (71.8)	175 (71.1)	94 (62.3)	**<0.001***
Outcomes					
Length of hospital stay, days (median [IQR])	18 [10, 30]	17 [11, 26]	15 [11, 31]	17 [10, 25]	0.411^
Length of ICU stay, days (median [IQR])	11 [5, 21]	8 [3, 16]	7.00 [4, 16]	6 [2, 13]	**<0.001^**
ICU mortality (no. (%))	175 (28.1)	88 (22.4)	54 (21.9)	26 (17.2)	**0.002***
In-hospital mortality (no. (%))	213 (34.2)	124 (31.6)	68 (27.5)	43 (28.5)	**0.046***

*Chi-square for trend for categorical data and ^Kruskal–Wallis test for numerical data

Conclusion: The in-hospital mortality, ICU-mortality and length of ICU-stay of COVID-19 patients admitted to the ICU decreased during the four pandemic waves in the Netherlands. Furthermore we found an increased use of anti-inflammatory drugs and monoclonal antibodies, and a decreased use of invasive ventilation.

Acknowledgements

1. This work was supported by the Talud Foundation for the Amsterdam UMC Corona Research Fund and the Netherlands Organisation for Health Research and Development (ZonMw; TURN-COVID grant number 10430142110001).
2. This work was done on behalf of the COVID-PREDICT study group.

000342

Use of lung ultrasound for assessment of lung recruitment in patients with ARDS

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Intensive Care Medicine Experimental 2022, **10(2)**:000342

Introduction: Positive pressure mechanical ventilation is a non-physiological intervention that saves lives but is not free of important side effects. It invariably results in different degrees of collapse of small airways. Recruitment maneuver (RM) aims to resolve lung collapse by a brief and controlled increment in airway pressure while positive end-expiratory pressure (PEEP) afterward keeps the lungs open. Therefore, ideally RM and PEEP selection must be individualized and this can only be done when guided by specific monitoring tools since lung's opening and closing pressures vary among patients with different lung conditions.
Objectives: The aim of this study was to explore the clinical value of ultrasonic monitoring in the assessment of pulmonary recruitment and the best PEEP.
Methods: This study was conducted on 120 patients, 30 were excluded as in whom lung collapse cannot be confirmed then the rest were 90 patients from whom another 25 patients excluded as they were hemodynamically unstable the rest 65 patients were divided into two groups: Group A: Included 50 mechanically ventilated patients with ARDS, underwent lung recruitment using lung ultrasound and Group B: Included 15 mechanically ventilated patients with ARDS, underwent lung recruitment using oxygenation index. This prospective study was held at many critical care departments around Egypt.
Results: We noticed that lung recruitment in both groups significantly increased Pao2/Fio2 ratio immediately after recruitment compared with basal state and also significantly increase dynamic compliance compared with basal state. The increase in PF ratio immediately was significantly more in ultrasound group than in oxygenation group. Furthermore, we noticed that that P/F ratio 12 h after recruitment decreased compared with P/F ratio immediately after recruitment but significantly increased compared with basal state before recruitment and also we found that the increase in P/F ratio 12 h after recruitment was more significantly in lung ultrasound group than in oxygenation group. Furthermore, we noticed that lung recruitment (both lung ultrasound and oxygenation group) significantly increase RV function using TAPSE compared with basal state. Both opening pressure and optimal PEEP were significantly higher in lung ultrasound group than in oxygenation group. In our study, opening pressure was 37.28 ± 1.25 in lung ultrasound group and was 36.67 ± 0.98 in oxygenation group and optimal PEEP was 14.64 ± 1.08 in lung ultrasound group and was 13.13 ± 0.74 in oxygenation group.
Conclusion: Lung US is an effective mean of evaluating and guiding alveolar recruitment in ARDS. Compared with the maximal oxygenation–guided method, the protocol for reaeration in US-guided lung recruitment achieved a higher opening pressure, resulted in greater improvements in lung aeration, and substantially reduced lung heterogeneity in ARDS.

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000409

Impact of veno-venous ECMO blood flow on transpulmonary thermodilution measures during acute respiratory distress syndrome

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Intensive Care Medicine Experimental 2022, **10(2)**:000409

Introduction: Although parameters provided by transpulmonary thermodilution (TPT) may be of interest in patients affected with acute respiratory distress syndrome (ARDS), their accuracy in patients equipped with veno-venous extracorporeal membrane oxygenation (VV-ECMO) has been poorly reported to date. The aim of this study was to evaluate the impact of VV-ECMO blood flow on TPT results.
Objectives: The aim of this study was to evaluate the impact of VV-ECMO blood flow on TPT results.
Methods: In this single center cohort study conducted from April 30, 2020 to September 30, 2021, all patients equipped with both thermodilution catheters and VV-ECMO and referred for VV-ECMO explantation had TPT measurements during a gradual decrease of VV-ECMO blood flow from 5 L/min to 0 L/min (VV-ECMO clamped). Parameters (extravascular lung water index (EVLWi), cardiac index, and pulmonary vascular permeability index (PVPi)) were averaged from 2 injections and indexed on the estimated dry weight of the patients. The primary endpoint was the variation of EVLWi measured by TPT according to VV-ECMO flow. The secondary endpoints were variation of other TPT parameters according to VV-ECMO flow.
Results: Twenty patients were included. EVLWi and PVPI were significantly affected by high blood flows on the VV-ECMO system compared to their measure without VV-ECMO. They showed minimal variations for blood flows below 2 L/min (Figure 1). Bland–Altman analysis revealed a correct agreement between measurements of EVLWi with VV-ECMO blood flows at 2 or 1 L/min, and its reference measurement at 0/min (respectively biases of -0.21 ± 0.68, 95% limits of agreement [-1.55–1.12] and -0.16 ± 0.59 [-1.32–0.99] ml/kg). VV-ECMO blood flows up to 5 L/min did not affect the determination of cardiac index.
Conclusion: High VV-ECMO flows overestimated EVLWi and PVPI, but were accurate for blood flows below 2 L/min. TPT determination of cardiac index was not impacted by the presence of VV-ECMO.

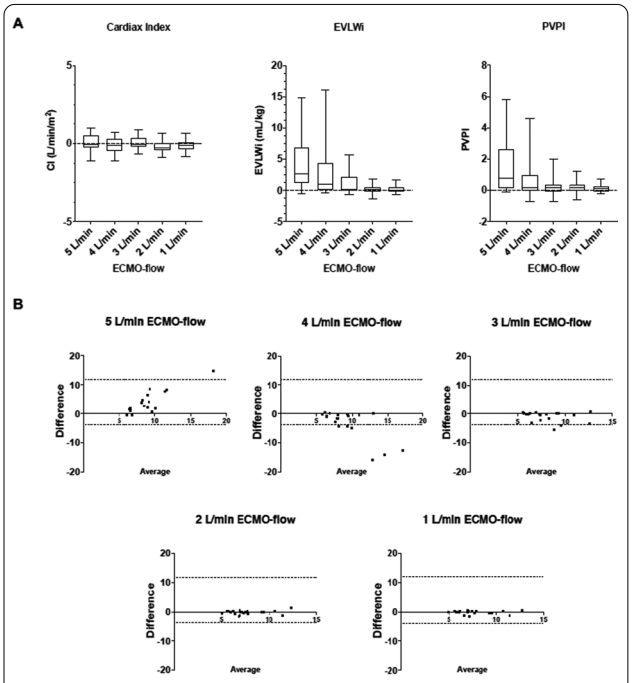

Figure 1. Influence of veno-venous ECMO blood flow on cardiac index, EVLWi, and PVPI measured by transpulmonary thermodilution. (A) Difference between measure at each level of ECMO blood flow and the measure performed with the ECMO blood flow at 0 L/min. **(B)** Bland-Altman analysis of the agreement between measurement of EVLWi at various ECMO blood flow, and its determination with ECMO blood flow at 0 L/min. EVLWi, Extra-Vascular Lung Water index; PVPI, Pulmonary Vascular Permeability Index.

000437

Characteristics of the continuously recorded mechanical power and its associated clinical outcomes in medical patients with respiratory failure (CORE POWER) study. (A pilot study)

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Introduction: The amount of energy delivered from the ventilator applied to the lungs within a given timeframe is defined as mechanical power (MP). Recently, low MP is one of the new concepts in lung-protective ventilation strategies that may associate with survival benefits. Up to now, the safety MP threshold remains unclear. However, measuring MP requires additional calculations not being carried out in usual clinical care and the reports about MP were mostly cross-sectional data. The real-time dynamic data of MP using the geometric method were scarcely reported, particularly in non-sedated and paralyzed patients [1,2].
Objectives: This study primarily aimed to determine the association between the continuously-recorded MP and the clinical outcomes of medical patients with respiratory failure.
Methods: This was a prospective, pilot study performed in a single center. Adult patients admitted to medical intermediate and intensive care units who require invasive mechanical ventilation had been consecutively enrolled. The patients' ventilators were connected to the specific investigator's computer system (DRACO software) for continuously real-time data recording for at least 24 h after intubation. The lung mechanics were measured and real-time MP was automatically computed using the geometric reference method. The primary outcome was in-hospital mortality.
Results: There were 337 eligible patients from 18 October 2021 to 28 February 2022. A total of 63 patients with acute respiratory failure requiring mechanical ventilation were analyzed. 51 patients survived (81%) and 12 (19%) patients died before hospital discharge. The patients had a mean age of 69 years. Demographic and anthropometric baseline data for all populations were not different, except SOFA score had a significantly high in non-survivors (7, 3.5–8 VS 4, 2–6). There were no significant differences between survivors and non-survivors in terms of baseline values of MP (12.9 [3.6] VS 14.3 [4.7], $p=0.391$) or other ventilator variables. Interestingly, mechanical power of ≥ 19 J/min was significantly associated with higher in-hospital mortality (2 [100%] VS 5 [14.7%], $p=0.033$). In addition, there was a trend toward higher mortality for patients who spent a long time in the range of high MP (≥ 19 J/min). There was no difference in other clinical outcomes between the high and low MP groups, including ICU mortality, ICU length of stay, duration of intubation, duration of mechanical ventilation, and respiratory complications associated with mechanical ventilation.
Conclusion: Our study demonstrated that higher intensities of mechanical power at 19 J/min and above were associated with increased hospital mortality. Limiting exposure to high MP using real-time continuous MP monitoring may serve as novel guidance for lung-protective ventilator settings in critically ill patients.

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000465

Influence of nasotracheal versus orotracheal intubation on sedation and ventilation: a retrospective cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000465

Introduction: Nasotracheal intubation (NTI) may be used for long term ventilation in critically ill patients, although this concept has been widely abandoned in favor of tracheostomy approximately 25 years ago. However, therapy concepts in intensive care have changed since then and recent data indicate potential benefits [1]. Compared to orotracheal intubation (OTI), patients receiving NTI may require fewer sedatives and thus be more alert and with fewer depression of respiratory drive.
Objectives: To study the influence of NTI and OTI in critically ill patients regarding sedative medication, scores on the Richmond-Agitation-Sedation-Scale (RASS), and rate of assisted ventilation.
Methods: We retrospectively included adult patients admitted to twelve ICUs (140 beds) of the University Medical-Center Hamburg-Eppendorf, who received tracheal intubation and were ventilated > 48 h. According to the route of intubation patients were assigned to the OTI or NTI group. Data were extracted from the electronic database. We compared doses of sedative drugs, fraction of time with RASS 0 or -1 (RASSopt) for day 1 to 3 after intubation, and percentage of assisted ventilation for day 1 to 10. Data are given as mean ± standard deviation.
Results: From January 1, 2018, to December 31, 2020, 1192 patients with 329 NTI and 1298 OTI instances were included. Patients were (NTI vs. OTI) 66 ± 13 vs. 63 ± 15 years old, $p=0.001$, with 67% vs. 65% males, and an APACHEII of 31 ± 8 vs 31 ± 7, $p=0.107$. On average, while sedated patients received: 1077 ± 1355 mg/d vs. 1768 ± 1473 mg/d propofol, $p<0.001$, 395 ± 547 µg/d vs. 693 ± 639 µg/d sufentanil, $p<0.001$, and 3.6 ± 20.6 mg/d vs. 6.5 ± 23.8 mg/d midazolam, $p=0.029$. RASSopt was attained for day 1 to 3 in (NTI vs. OTI) 39 ± 35%

vs. 17 ± 25%, p < 0.001. The average percentage of assisted ventilation for day 1 to 10 was (NTI vs. OTI) 43 ± 29% vs. 29 ± 25%, p < 0.001. The mean length of intubation was (NTI vs. OTI) 134 ± 87 h vs. 160 ± 109 h, p < 0.001.
Conclusion: Patients in the NTI group received fewer sedative drugs, spent a higher percentage of time in the recommended RASS range, and received less controlled ventilation. We suggest further studies to evaluate if these findings influence outcome parameters.

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000478

A pilot randomized controlled trial for ozanimod therapy in hospitalized COVID-19 patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000478

Introduction: Sphingosine-1-phosphate (S1P) receptor ligands reduce lung damage and endothelial activation in models of virus-induced pneumonia. Feasibility of initiating S1P receptor ligand therapy during pneumonia needs confirmation.
Objectives: Evaluate safety/efficacy outcomes of ozanimod therapy in COVID-19 patients.
Methods: In a prospective multicentric open-label pilot trial, adult patients with COVID-19 requiring O2 were recruited (3 Canadian centres, starting Sept. 2020). Patients were randomized to standard of care (SOC) or SOC + ozanimod (*per os*). Modified WHO-adapted 6-points ordinal scale for clinical improvement was computed daily and adverse events were recorded.
Results: As of March 2022, 43 patients (out of 48) were enrolled and 20 received ozanimod. Stratification at randomization balanced groups for risk factors of poor outcome and initial O2 requirement. No serious drug reaction was reported. Asymptomatic bradycardia occurred with ozanimod in most patients during first 2 days. So far, 37 patients completed the study-ending phone call (day 90). Ordinal scale-related outcomes are shown in Table 1.

Main outcomes in both study arms

	SOC (n = 23)	SOC + Ozanimod (n = 20)
Age, yr—median (IQR)	62 (48–69)	65 (61–68)
Male—no. (%)	17 (74)	12 (60)
Ordinal scale -related measures		
O2 therapy—days, median (IQR)	9 (4–12)	6 (3–10)
Nasal High Flow—days, median (IQR)	4 (0–7)	3 (0–6)
Intubation—no. (%)	5 (22)	2 (10)
Hospitalization– days, median (IQR)	10 (7–17)	9 (6–13)
Serious Adverse Event—no	7	4
Adverse Event—no	19	21

Conclusion: This small scale trial provides the very first evidence supporting the possibility of initiating S1P receptor ligand therapy during COVID-19 pneumonia.

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Acknowledgements: Supported by an unrestricted grant from Brystol Myers Squibb, which also provided the study medication.

000488

Non-invasive electromagnetic phrenic nerve stimulation: the role of the distance to the initial stimulation points in generating a tidal volume

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Intensive Care Medicine Experimental 2022, **10(2)**:000488

Introduction: Phrenic nerve stimulation leads to diaphragm activation and contraction, and has the potential to prevent diaphragmatic atrophy in mechanically ventilated patients [1]. Its implementation in clinical practice might consequently reduce Ventilator-induced diaphragmatic dysfunction (VIDD) and possibly reduce the duration of mechanical ventilation or mortality [2, 3]. However, non-invasive techniques of electromagnetic phrenic nerve pacing have not yet been established.
Objectives: Using non-invasive electromagnetic phrenic nerve stimulation we investigated the relationship of coil distance from the predetermined ideal stimulation site and the generated tidal volume.
Methods: Subsequently to induction of anesthesia, endotracheal intubation and reversal of the muscle relaxant, five ASA I/II patients scheduled for elective surgery with general anesthesia received bilateral non-invasive electromagnetic stimulation of the phrenic nerves using a magnetic field intensity of 20%. The ideal stimulation site was located using ultrasonography and by comparing the stimulator-induced tidal volumes. The coil positioning was changed in two directions: (i) medio-laterally at 5 mm, 10 mm and 15 mm distance from the optimal stimulation point, and (ii) cranio-caudally at 5 mm, 10 mm and 15 mm if anatomically feasible. Tidal volumes generated were measured via the ventilator.
Results: The difference between anatomical (identified using ultrasonography) and the used stimulation site was 10 ± 3 mm and 8 ± 3 mm for the left and right side, respectively. The medio-lateral displacement was feasible in all patients. Tidal volume declined linearly ($r2 = 0.199$; $p < 0.0001$, Figure 1) as the distance from the used stimulation point was increased anterior to posterior. The mean tidal volume declined by -0.42 ± 1.33 ml/kg, -1.23 ± 1.69 ml/kg and -1.75 ± 1.35 ml/kg for 5 mm, 10 mm and 15 mm distance as a function of moving the coils away from the initial identified stimulation point, respectively. Due to the clavicle bone as well as the mandible bone, maneuvering the coils more cranially or caudally was only feasible in two patients and limited to a maximum of 10 mm. The resulting mean tidal volume declined by -0.68 ± 0.32 ml/kg and -1.08 ± 0.35 ml/kg for 5 mm and 10 mm distance, respectively.

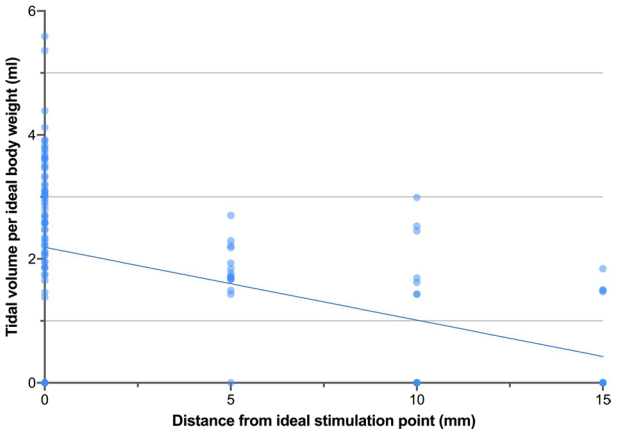

Figure 1 Tidal volume depends on medio-laterally distance to the ideal stimulation site.

Conclusion: The effectiveness of non-invasive electromagnetic phrenic nerve stimulation declines linearly with increasing medio-laterally distance to the ideal stimulation site, which therefore should be determined prior to any intervention.

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Acknowledgements: This investigator-initiated study was partially funded by STIMIT AG, Biel, Switzerland.

000497

A silver bullet? The HACOR score may predict CPAP failure in COVID-19 disease

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Intensive Care Medicine Experimental 2022, **10(2)**:000497

Introduction: In patients with COVID-19 respiratory failure, continuous positive airway pressure (CPAP) reduces the likelihood of requiring invasive ventilation or death; however, there remains no reliable method for identifying which patients will benefit from CPAP. Using a validated scoring system to identify those unlikely to benefit has great appeal for both individuals and healthcare systems trying to manage resources under surge conditions. The HACOR score (Duan et. al.) combines heart rate, acidosis, conscious level, oxygenation and respiratory rate to predict CPAP failure in hypoxaemic respiratory failure. We aimed to assess the HACOR score as a method to predict CPAP failure in COVID-19.
Methods: Ethical approval was granted (WoS REC 4 21/WS/0091). A retrospective note review of all patients who received non-invasive ventilation for COVID at our hospital between 1st March 2020 and 30th April 2021 was performed. Baseline demographics, physiological data were captured alongside HACOR scores before commencement of CPAP, at 1 h, 6 h, 12 h and 24 h after commencement. HACOR scores were assessed for predicting the combined primary outcome of tracheal intubation or death.
Results: Seventy patients who received CPAP for COVID during the review period were identified, 26 (37.1%) commenced CPAP in ICU and 44 (62.9%) in medical HDU. The overall mortality rate was 38.6% (n = 27). Twelve patients had a documented ceiling of treatment of CPAP of which seven (58.3%) died. Of those considered for intubation, twenty-nine (50.0%) improved on CPAP and twenty-eight (48.2%) proceeded to tracheal intubation; one patient (1.7%) considered for intubation died during CPAP treatment. Of those intubated, 19 (67.9%) died. HACOR score was best at predicting the combined outcome of tracheal intubation or death at 12 h after CPAP initiation; here it could predict failure with an accuracy of 77.4% (AUROCC 0.811) [p = 0.005].
Conclusion: While recognising its limitations, namely a small sample from a single centre, this review suggests the HACOR score may be able to accurately predict CPAP failure in COVID-19 respiratory failure. This conclusion is supported by another small and recently published study (Guia et. al.) which showed the HACOR score at one hour after commencing CPAP predicted CPAP failure in COVID-19 respiratory failure with an accuracy of 82.03%. A larger multicentre retrospective review may help further elucidate this.

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000506

Assessing respiratory mechanics during assisted mechanical ventilation: the "sinking iceberg" effect

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Introduction: In pressure support ventilation (PSV), a brief inspiratory occlusion maneuver may unveil the inspiratory effort generated by the patient.[1] In a retrospective study, we reported that, in PSV, the difference between Plateau pressure (*Pplat*)—measured by the estimation of the inspiratory effort using the pressure muscle index (PMI)—and the positive end-expiratory pressure (PEEP), i.e. driving pressure (ΔP), is associated with outcome in patients with acute respiratory distress syndrome (ARDS).[2] The ongoing prospective ICEBERG STUDY (NCT05203536) aims at validating these findings. However, a systematic assessment of the response of the patient's inspiratory drive and effort across different levels of PS is lacking.
Objectives: The aim of this physiologic study is to assess how patients in PSV modulate their drive, inspiratory effort and respiratory mechanics across different levels of PS. Since across these levels the pressure generation moves from the patient to the ventilator and viceversa, we used the metaphor of a sinking iceberg.
Methods: We performed a single-center observational prospective study in adult patients with diagnosis of acute hypoxemic respiratory failure, intubated or tracheostomized, undergoing PSV. We cross-randomized patients to four steps of PS level, each one lasting 10 min, above (i.e. + 3 and + 6 cmH2O) or below (i.e. -3 and -6 cmH2O) the clinically set PS level. At the end of each step an inspiratory hold and an expiratory occlusion maneuvers were performed to calculate respiratory mechanics parameters such as *Pplat*, ΔP, respiratory system static compliance (*Cpl,rs*), PMI and P0.1. Neural activity of both the diaphragm (Costmar) and the intercostal inspiratory muscles (Intercost) was continuously monitored via surface electromyography (sEMG).

Differences between continuous variables were tested across PS levels using one-way ANOVA.

Results: 17 patients on PSV were enrolled. Results are presented as means ± standard deviation and one-way ANOVA significance level (P). sEMG results are shown as percentage variation of the signal measured at clinical PS (%clin). *Pplat* (from 16.6 ± 3.0 to 20.7 ± 3.4 cmH2O, P < 0.001), *ΔP* (from 8.6 ± 2.5 to 12.7 ± 2.4 cmH2O, P < 0.001) and tidal volume (from 0.41 ± 0.11 to 0.61 ± 0.17 L, P < 0.001) increased linearly from -6 to + 6 cmH2O of PS. Inversely, PMI decreased (from 6.8 ± 3.3 to -1 ± 2 cmH2O, P < 0.001) together with P0.1 (from 2.6 ± 1.4 to 0.9 ± 1.0 cmH2O, P < 0.001), Costmar (from 192 ± 81 to 70 ± 31%clin, P < 0.001) and Intercost (from 160 ± 56 to 71 ± 37%clin, P < 0.001). *Cpl,rs* did not significantly vary through the steps (P = 0.136).

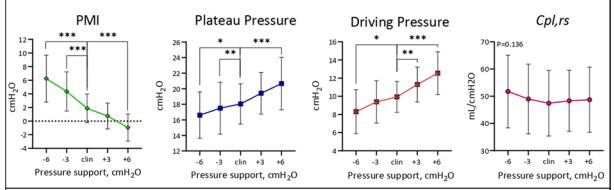

Fig 1. Respiratory mechanics at varying levels of pressure support.

Legend: *Cpl,rs*, respiratory system static compliance; PMI, pressure muscle index; clin, clinical pressure support; P, one-way ANOVA significance level; *, ** and *** stand for Holm-Sidak test significance level respectively <0.05, <0.01 and <0.001.

Conclusion: Inspiratory effort (i.e. PMI) varies according to different levels of PS. The higher the PS the higher the *ΔP*, while PMI decreases and *Cpl,rs* does not significantly change (Fig..1). Accordingly, the neural inspiratory drive (i.e. sEMG signals) gradually decreases when PS increases. Further studies may provide information on the potential risk of high tidal volume ventilation at high PSV.

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Acute Respiratory Failure 6

000290

Effectiveness of vibratory physiotherapeutic methods for respiratory rehabilitation after cardiac surgery

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Intensive Care Medicine Experimental 2022, **10(2)**:000290

Introduction: Postoperative respiratory complications in cardiac surgery patients occur in 20–30% cases, and the most of them can be associated with ineffective cough and bronchial mucus evacuation**.** One of the main causes of its development is microatelectasis, which can cover a significant part of the lung tissue as a result of impaired lung drainage function and tracheobronchial patency.

Objectives: a comparative assessment of the effectiveness of methods for stimulation the of mucus passage in the early postoperative period of cardiac patients using oscillatory PEP therapy, stimulation of cough with a mechanical insufflator-aspirator, vibroacoustic lung massage, and the traditional method of manual percussion of the chest.

Methods: 160 patients were randomized in the study and divided into 4 groups, 40 in each. Inclusion criteria: age over 18 years, spontaneous breathing after tracheal extubation, the ability to maintain adequate gas exchange against the background of oxygen inhalation, clear consciousness and productive contact with the patient, adequate anesthesia (≤ 2 points) according to a 10-point visual-analog pain scale. Exclusion criteria: the need for re-intubation and mechanical ventilation, non-invasive mask ventilation, acute cerebrovascular accident, shocks of various etiologies, ongoing bleeding, extracorporeal detoxification methods, any neuromuscular diseases, pneumothorax, hydro- or hemothorax. All procedures were performed 10–12 h after tracheal extubation. The efficiency of mucus discharge was assessed, gas exchange indices on room air breathing and maximum inspiratory lung capacity (MILC) were measured.

Results: Before intervention ineffective bronchial mucus evacuating in the early period after tracheal extubation was observed in 86.7% of the patients. A single procedure of both PEP-therapy (group 1) and mechanical cough stimulation (group 2) led to an improvement in sputum passage, as evidenced by an increase in the number of patients with productive cough by 4.25 times (p < 0.0009) and 5.3 times (p < 0.0007), respectively. In patients of groups 1 and 2, an increase in MILC was observed (by 42.2% and 60.0%, respectively, p = 0.00000). In the control group 3, with manual physiotherapy, the average increase in MILC was only 11.6%. Mechanical respiratory therapy procedures led to a significant improvement in gas exchange variables, as evidenced by an increase in SpO2 in groups 1 and 2 (P = 0.000009 and 0.000001, respectively) and a decrease in the proportion of patients with impaired oxygenating lung function (SpO2 level below 92%) by 11 and 12 times, respectively (P < 0.01). The arterial SaO2 in group 2 significantly increased after the procedure (P = 0.017), and PaCO2 decreased (P = 0.00048).The most significant effect in gas exchange parameters were revealed after vibroacoustic lung massage. In group 3 the number of patients with productive cough increased 12.3 times (p < 0.0001). There was an increase in SpO2 from 91 to 93% (p = 0.000000) and MILC from 950 to 1150 ml (0.000000). Vibroacoustic lung massage was accompanied by improvement of gas exchange indices, as evidenced by statistically significant increase PaO2 and p/f index with simultaneous decrease of PaCO2.

Changes in gas exchange and maximum inspiratory lung capacity indicators when using various technologies (n = 160)(M ± σ; Me[10:90])

Indicators	Acapella	Comfort Cough Plus	Vibrolung	Manual percussion
MILC, ml	900[475:1650]	1000[500:1750]	950[300:2400]	700[400:1100]
Before	1200[600:2500]	1600[1400:2800]	1150[575:2650]	776 ± 249
After	P = 0,00,000	P = 0,00,000	P = 0,000,000	P = 0.007
SpO2, %	93.1 ± 2.2	92.0 ± 3.4	91[90:93.5]	95[91.9:97]
Before	94.9 ± 1.8	96.0 ± 2.4	93[90:96]	94.5[91:97.1] P = 0,667
After	P = 0,000,009	P = 0,000,001	P = 0,000,000	

Conclusion: Mechanical vibratory methods have significant advantages over classical manual chest massage. Their positive effect on mucus passage, ventilatory parameters and gas exchange was noted. There were no complications associated with procedures.

000413

Changes in Diaphragm Thickness during Mechanical Ventilation: A Comparison of Covid-19 versus non-Covid-19 Patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000413

Introduction: Diaphragm atrophy and dysfunction have been reported in humans during mechanical ventilation, and both are associated with longer Intensive Care Unit (ICU) length of stay and worse outcomes (1). However, to the present days, research aimed at studying anatomical changes of diaphragm in critically ill patients did not include those infected by Covid-19, who were extensively submitted to mechanical ventilation, which makes unclear if the same changes can occur with this group of patients.
Objectives: The aim of this study was to quantify with ultrasound the changes on diaphragm thickness (Tdi) in a population of critically ill mechanically ventilated patients with and without diagnosis of Covid-19 at two different times: after intubation and after extubation.
Methods: We performed a prospective observational single-center study in the general ICU and Covid-19 ICU, in Albert Einstein Hospital (São Paulo, Brazil). The study protocol was approved by the ethics committee of our institution and written informed consent was obtained from the patients or his/her relative. Study subjects were included if they were ventilated for more than 24 h. Exclusion criteria were as follow: palliative care, patients previously under mechanical ventilation, age less than 18 years, expected time under mechanical ventilation less than 24 h, and associated neuro-muscular diseases. The right diaphragm thickness was accessed by ultrasound in the first 24 h of mechanical ventilation and after extubation at the zone of apposition (ZOA), defined as the region where the diaphragm is apposed to the rib cage. Once the diaphragm was identified, its Tdi was measured at the end of the expiration phase, when the thickness is at its minimum value, by Bidimensional mode (B-mode). Diaphragmatic thickness was calculated as the distance between the inner edges of the hyperechogenic layers at end expiration. Ultrasound was performed by two senior Physiotherapists with 6 years experienced in diaphragm as well as lung and peripheral muscle ultrasonography. Data are presented as mean and standard deviation or median and interquartile range.
Results: In total, 51 patients were enrolled (25 Covid-19 and 26 non Covid-19). Time of Mechanical Ventilation was higher in Covid-19 patients [7.3 ± 3.7 days vs. 3.5 ± 2.6 days; $p < 0.001$)], but ICU length-of-stay were not different [(12.7 ± 9.00 days vs. 12.5 ± 11.4 days); $p = 0.865$]. Covid-19 patients had a similar SAPS III score those non Covid-19 [47 (44–56) vs. 50 (40–57); $p = 0.546$]. The values of Tdi after intubation was similar in Covid-19 and non Covid-19 patients [(0,20 ± 0.06 mm vs. 0.20 ± 0.08 mm); $p = 0.903$]. After extubation, both groups had decreased Tdi [0.160 ± 0.04 mm (-20,7%) vs. 0.164 ± 0.05 mm (-18%); $p = 0.780$) in Covid-19 and non Covid-19, respectively.
Conclusion: Despite the longer time in Mechanical Ventilation in Covid-19 patients, changes in Diaphragm Thickness were not different from non Covid-19 patients.

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000471

Awake prone position in COVID-19 patients with helmet CPAP: effects on gas exchange, respiratory mechanics, and distribution of ventilation

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Intensive Care Medicine Experimental 2022, **10(2)**:000471

Introduction: Awake prone positioning in awake subjects has been demonstrated to be feasible and effective in increasing oxygenation in association with CPAP (1).
Objectives: We aimed to assess respiratory mechanics and the distribution of ventilation in Covid-19 patients undergoing awake prone positioning at different levels of positive end expiratory pressure (PEEP).
Methods: The study was conducted in a Covid-19 ICU of a university hospital (Ospedale Luigi Sacco, Milan). We enrolled awake, spontaneously breathing patients with confirmed infection by novel coronavirus 2019 (SARS-CoV-2) and a diagnosis of moderate to severe ARDS according to the Berlin definition (PaO2/FIO2 < 200 mmHg). Exclusion criteria were age < 18, pregnancy, contraindications to helmet CPAP or prone positioning, pneumothorax or pneumomediastinum, severe COPD (GOLD 3–4).The protocol consisted of 2 steps: PEEP 5 and 10 cmH2O delivered by helmet CPAP in the supine and prone positions. The sequence of PEEP steps and position were randomized. Patients were equipped with a nasogastric tube designed for esophageal pressure measurement (Nutrivent) and a 16-electrode belt placed around the chest for the acquisition of intrathoracic impedance variations (Pulmovista).At the end of each 20 min step, arterial blood gas analysis was performed, and the esophageal pressure (PES) swing and electrical impedance tomography (EIT) tracings were recorded. We calculated the modified pressure time product (mPTP), work of breathing (WOB) and the dynamic transpulmonary driving pressure (dTPP) as previously described(2).The EIT tracings were analyzed offline to determine the Global Inhomogeneity Index (GI), Centre of ventilation (COV) and dorsal fraction of ventilation. Statistical analysis was performed by means of two-way ANOVA for repeated measures.
Results: A total of 16patients were studied. Prone positioning induced significant increase in PaO2/FIO2 (161.1 ± 50.2 vs 255.0 ± 99.6 $p < 0.001$); this effect was more pronounced with PEEP 10 compared to PEEP 5. There was no significant impact of PEEP level or position on delta PES, dTTP, mPTP or WOB. EIT analysis demonstrated a significant increase in the dorsal fraction of ventilation attributable to prone positioning (Fig. 1) but no difference in GI or the COV.
Figure 1: Data are presented in Box Plot (median, 25th-75th).
Conclusion: In this population helmet CPAP provided in the prone position induced a significant increase in oxygenation that was not associated to improvement in other indices of "protective" ventilation, such as delta PES or inhomogeneity index.

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000489

The Effect of INTELLiVENT–ASV on Oxygenation, FiO2 and PEEP in Critically Ill Invasively Ventilated Patients

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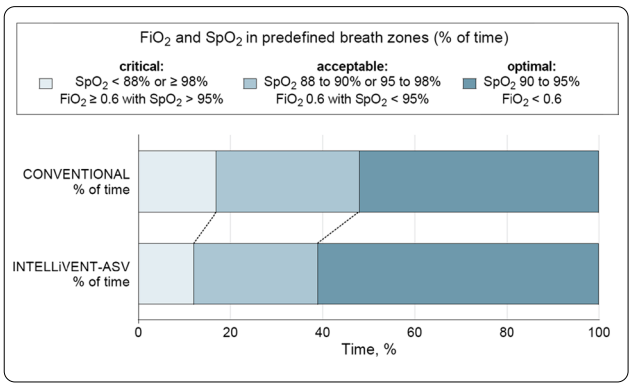
Intensive Care Medicine Experimental 2022, **10(2)**:000489

Introduction: Hyperoxia can have deleterious effects and hypoxemia is associated with higher mortality. There is need for economic use of oxygen. INTELLiVENT–ASV is an automated closed–loop ventilation mode, that performs automated titrations of FiO2 and PEEP based on a set SpO2 target range.
Objectives: To compare oxygenation, FiO2 and PEEP with INTELLiVENT–ASV *vs* conventional ventilation in critically ill invasively ventilated patients. We hypothesized that INTELLiVENT–ASV improves oxygenation with an optimal SpO2, at lower FiO2 and with less PEEP.

Methods: Substudy of a multicenter, randomized crossover study that includes patients within 24 h of start of ventilation. Patients were randomized to start with 3 h INTELLiVENT–ASV or 3 h conventional ventilation, after which they crossed– over. SpO2, FiO2 and PEEP was collected for each breath. Oxygenation was categorized in 3 predefined zones with combination of SpO2 and FiO2 (see Figure).
Results: This study included 18 critically ill patients; we collected data for a total of 134,051 breaths; 66,329 breaths under INTELLIVENT–ASV and 67,722 breaths under conventional ventilation. With INTELLiVENT–ASV, the duration within optimal oxygenation was 61% of time, compared to conventional ventilation, which was 52% ($p < 0.001$). Time spent with acceptable oxygenation was 27% vs 31% ($p < 0.001$) and INTELLiVENT-ASV spend less time in the critical zone (12% *vs.* 17%, $p < 0.001$). PEEP was not different.
Conclusion: INTELLiVENT–ASV applies ventilation with more optimal oxygenation.



000520

Development and Validation of a Prediction Model for Acute Respiratory Distress Syndrome in Coronavirus Disease-2019: Updated Lung Injury Prediction Score

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Intensive Care Medicine Experimental 2022, **10(2)**:000,520.

Introduction: Early recognition of patients at risk of developing acute respiratory distress syndrome (ARDS) is crucial for implementing and evaluating preventive strategies in both clinical practice and research. Patients who develop ARDS due to severe acute respiratory syndrome coronavirus 2 infection (*c*-ARDS) have distinct characteristics compared to ARDS caused by other underlying etiologies.
Objectives: To develop and validate an updated lung injury prediction score (c-LIPS) tailored for predicting acute respiratory distress syndrome in coronavirus disease-2019.
Methods: This was a Registry-based cohort study using data from the Viral Infection and Respiratory Illness Universal Study: COVID-19 Registry. The development cohort consisted of patients enrolled from 5 participating Mayo Clinic sites. The validation analyses were conducted on the remaining patients enrolled from more than 120 hospitals in 15 countries. Hospitalized adult patients with coronavirus disease-2019 (COVID-19) between January 2020 and January 2022 were screened. Patients who developed ARDS within the first day of admission were excluded. The original LIPS was calculated with and without enhancement using reported COVID-19 specific laboratory risk factors (c-LIPS). Additional points were derived using coefficients from a multivariate logistic regression model. The main outcome was ARDS development and secondary outcomes included hospital mortality, invasive mechanical ventilation, progression on the World Health Organization scale, and discharge disposition. The area under the curve (AUC) was used to assess the model's discrimination.
Results: The derivation cohort consisted of 3710 patients, of whom 28% developed ARDS. The c-LIPS discriminated patients who developed ARDS with an AUC of 0.79 (95% Confidence Interval: 0.77–0.81) compared to original LIPS (AUC 0.74, 0.72 -0.76, P = < 0.0001). The model was well calibrated (Hosmer–Lemeshow p = 0.50). Despite the different characteristics of the two cohorts, the score's performance was comparable in the validation cohort of 5426 patients (16% ARDS), with an AUC of 0.74 (0.73–0.76). The c-LIPS's performance in predicting the requirement for invasive mechanical ventilation in derivation and validation cohorts had an AUC of 0.74 (0.71–0.78) and 0.72 (0.70–0.74), respectively.
Conclusion: In this large patient sample c-LIPS was successfully tailored to predict ARDS in COVID-19 patients. Though having an overall modest performance for clinical use, it could inform enrollment in future ARDS prevention clinical trials.

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Acknowledgements

1. This study was supported by the Mayo Clinic Critical Care Independent Multidisciplinary Program (IMP) Research Subcommittee.
2. HY receives funding from National Heart, Lung, and Blood Institute grant number K23HL151671.
3. RK receives funding from the National Institutes of Health/National Heart, Lung and Blood Institute: R01HL 130,881, UG3/UH3HL 141,722; Gordon and Betty Moore Foundation, and Janssen Research & Development, LLC; and royalties from Ambient Clinical Analytics.inc. They had no influence on acquisition, analysis, interpretation and reporting of pooled data for this manuscript.
4. OG receives funding from the Agency of Healthcare Research and Quality R18HS 26,609–2, National Institutes of Health/National Heart, Lung and Blood Institute: R01HL 130,881, UG3/UH3HL 141,722; Department of Defense DOD W81XWH; American Heart Association Rapid Response Grant—COVID-19; and royalties from Ambient Clinical Analytics.inc

5. AJW receives funding from the National Institutes of Health/National Heart, Lung and Blood Institute grants R01HL151607, R01HL139751, R01HL136660, Agency of Healthcare Research and Quality, R01HS026485, Boston Biomedical Innovation Center/NIH/NHLBI 5U54HL119145-07 and royalties from UptoDate.
6. The VIRUS Registry was supported, in part, by the Gordon and Betty Moore Foundation, and Janssen Research & Development, LLC.

000538

A portable, non-invasive platform based on near-infrared optics to assess endothelial and microvascular health at the intensive care: the VASCOVID platform

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Introduction: Critical requirements for COVID-19 patients' intensive care [1] have emphasized the pressing need for personalized intensive care unit (ICU) treatment. Previous studies have shown the possibility to consider endothelial health as a biomarker for the stratification of COVID-19 patients [2], which are often affected by vascular system anomalies and endothelial dysfunctions. The same is true in other pathologies such as sepsis and acute respiratory distress syndrome. Near-infrared spectroscopy (NIRS) has been exploited, combined with a vascular occlusion test (VOT) in patient stratification and in predicting weaning failure from mechanical ventilation in different respiratory diseases [3–6].
Objectives: The European Project VASCOVID [7] aims to develop a portable non-invasive platform to assess the endothelial health at the ICU. VASCOVID aims to solve the shortcomings of commercial NIRS devices by combining new time-domain (TD) NIRS [8] and diffuse correlation spectroscopy (DCS) [9] instruments to provide more accurate and precise measurements of tissue oxygen saturation (StO2, %) and additional biomarkers such as absolute haemoglobin concentration (tHb, uM), blood flow index (BFI) and oxygen metabolism. In this work we studied different VOT protocols on healthy subjects to optimize the measurement settings, aiming to more reliable data before moving to the ICU.
Methods: The thenar eminence's haemodynamic response to three repeated VOTs has been recorded on 19 healthy subjects, placing the cuff in three different locations: forearm near the wrist, forearm near the elbow and on the arm. Each VOT consisted in 2 min of baseline, 3 min of occlusion and 5 min of recovery.
Results: The results, averaged among the subjects, are presented in Fig.. 2. During the occlusion, an increase in tHb was observed, being more pronounced when the cuff was placed on the wrist and the elbow positions, closer to the probed area, suggesting that this effect might be due to vein congestion. Vein congestion also affects deoxygenation rate since differences were retrieved in the three cuff positions. BFI shows unexpected oscillations before and after the occlusion. A key finding is that the location of the cuff alters the results. Furthermore, the oscillations appear only on the end-point organs, such as the thenar muscle.

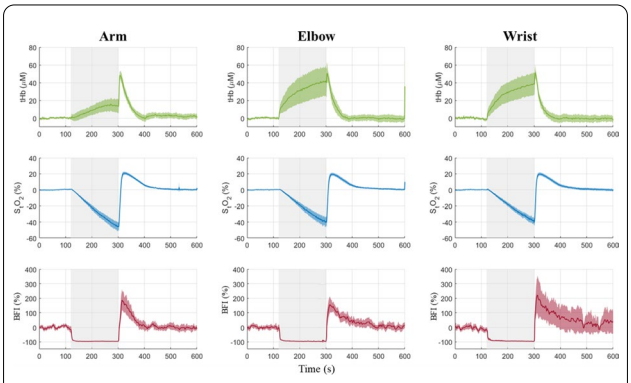

Fig.. 2: tHb, StO2 and BFI retrieved during VOT protocols on the thenar eminence, averaged among 19 subjects.Occlusion periods is in grey.

Conclusion: The optimization of the VOT strategy is crucial for the success of hybrid TD-NIRS and DCS devices combined with VOT for the upcoming usage on ICU patients. VASCOVID platform will provide a unique approach to obtain rich data linking tissue metabolism and microvascular reactivity to challenges and pathophysiology with modern data analysis methods.

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Acknowledgements: This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101016087.

000556

Impact of the body mass index (BMI) in patients with COVID-19 acute respiratory distress syndrome (CARDS) in the intensive care unit (ICU)

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Intensive Care Medicine Experimental 2022, **10(2)**:000556

Introduction: Obesity is becoming a top priority problem, requiring more complicated hospital management (difficult intubation, ventilation, mobilization, and transportation, among others). Data on the relationship between individuals with obesity and COVID-19 prognosis are complex. This article describes our experience in managing obese patients with COVID-19 acute respiratory distress syndrome (CARDS) in the intensive care unit (ICU).
Objectives: Analyze the impact of the body mass index in the evolution of CARDS patients.
Methods: We conducted a retrospective study of adult ICU admissions due to CARDS between March 2020 and September 2021. We reviewed demographic and severity variables, complications, and the need for advanced support. We organized the patients into three groups according to BMI: average weight (BMI > 25), overweight (BMI between 25–30), obesity type I (BMI between 30–35), obesity type II (BMI between 35–40) and obesity type III (BMI > 40). Descriptive statistics included median and interquartile ranges for continuous variables and numbers and percentages for categorical variables. Continuous data were compared with the Kruskal–Wallis test and categorical variables with Fisher's exact test. Two-sided $p > 0.05$ was considered statistically significant. The analysis was performed using STATA version 13® (StataCorp LCC).
Results: A total of 547 patients were admitted. According to BMI, 73 patients (13%) had average weight, 209 (38%) were overweight, 137 (27%) had obesity type I, 69 (12,8%) had obesity type II, and 59 (11%) had obesity type III. A summary of the patient's demographics, severity, complications, and medical support is shown in Table 1. CARDS was more frequent in men in all BMI ranges, but in obesity type II and III, the sex gap was significantly reduced (p 0.03). There were no differences regarding comorbidities between BMI groups. Regarding respiratory failure, oxygenation index was worst as BMI increased (ß: -2 $r = 0.06$; $p > 0.001$), as well as respiratory SOFA was higher in those with higher BMI ($p = 0.01$), an association we did not observe when analyzing the complete SOFA score ($p = 0.56$). APACHE-II did not show differences between groups ($p = 0.21$). Regarding respiratory support, there were no differences between the need for invasive mechanical ventilation (IMV) ($p = 0.55$) or its duration ($p = 0.56$) across BMI groups. Besides, patients with BMI > 35 required more often proning manoeuvres ($p = 0.02$). There were no differences regarding tracheostomy need ($p = 0.21$) or ECMO support ($p = 0.89$). ICU and in-hospital length of stay did not differ, and complications did not increase with BMI.
Conclusion: At admission, obese patients showed the worst oxygenation index. However, in our cohort, we did not observe an impact between obesity and mortality, days of invasive mechanical ventilation or ICU stay.

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000576

Diagnosing ARDS in COVID–19 Patients Under High–flow Nasal Oxygen

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Introduction: High–flow Nasal Oxygen (HFNO) has been increasingly used in hypoxemic patients with a COVID–19 pneumonia which typically presents with bilateral pulmonary infiltrates on a chest X–ray or lung computed tomography (CT). It has been suggested to replace the minimum of 5 cm H2O PEEP with a minimum of 30 L/min airflow in patients under HFNO, to allow a timely diagnosis of acute respiratory distress syndrome (ARDS) for these patients who fulfill all the other Berlin criteria. It is uncertain if this results in comparable patient cohorts with respect to epidemiology and outcome.
Objectives: To determine and compare the epidemiology and outcomes in COVID–19 patients under HFNO with a minimum 30 L/min airflow with COVID–19 patients receiving invasive ventilation with a minimum of 5 cm H2O PEEP.
Methods: We applied the classic Berlin definition for ARDS in invasively ventilated patients, and the adjusted definition, in which we replaced a minimum of 5 cm H2O PEEP with a minimum of 30 L/min airflow, in patients under HFNO. The primary endpoint was 28–day mortality. Secondary endpoints included ICU– and hospital–mortality. Hazard ratios were calculated for 28–day mortality using an adjusted Cox proportional hazard model. A P value < 0.05 was considered statistically significant.
Results: Of 109 patients, 33 patients were under HFNO and 76 patients received invasive ventilation. All patients fulfilled the (classic or adjusted) Berlin definition for ARDS. FiO2 was typically set higher in patients under HFNO at the moment of ARDS diagnosis. The two patient groups were not significantly different with respect to the epidemiological characteristics, except for a higher SAPS II in patients under invasive ventilation. The two groups had comparable outcomes, including 28–day mortality (Table 1). In the HFNO group 23 patients were intubated.

Patient characteristics	HFNO N = 33	invasive ventilation N = 76	*p*-value
Age, years (median [IQR])	66 [61–72]	66 [58–72]	0.961
Male gender, N (%)	24 (72.7)	57 (75.0)	0.991
BMI, kg/m2 (median [IQR])	27.9 [25.4–32.3]	26.8 [24.6–31.2]	0.368

Patient characteristics	HFNO N = 33	invasive ventilation N = 76	*p*-value
SAPS II score (median [IQR])	46 [45–50]	54 [50–60]	< 0.001
Comorbidities, N(%)	29 (87.9)	61 (80.3)	0.491
Arterial hypertension, N (%)	16 (48.5)	26 (34.2)	0.233
Cardiovascular disease, N (%)	8 (24.2)	11 (14.5)	0.337
Heart failure, N (%)	1 (3.0)	3 (3.9)	1.000
Chronic pulmonary disease*, N (%)	4 (12.1)	10 (13.2)	1.000
Diabetes mellitus, N (%)	13 (39.4)	22 (28.9)	0.395
Chronic kidney disease, N (%)	6 (18.2)	7 (9.2)	0.314
Malignancy, N (%)	2 (6.1)	10 (13.2)	0.450
Neuromuscular disease, N (%)	1 (3.0)	1 (1.3)	1.000
Obstructive sleep apnea, N (%)	1 (3.0)	1 (1.3)	1.000
Outcomes			
28–day mortality, N (%)	13 (39.4)	27 (35.6)	0.75
ICU mortality, N (%)	15 (45.5)	31 (40.8)	0.70
Hospital mortality, N (%)	15 (45.5)	31 (40.8)	0.70
ICU LOS, N (%)	11 [6–21]	12 [7–27]	0.52
Hospital LOS, N (%)	15 [11–25]	19 [12–28]	0.36

Conclusion: An adjustment in the definition for ARDS, in which a minimum of a minimum of 5 cm H2O PEEP is replaced with a minimum of 30 L/min airflow in patients under HFNO, results in comparable groups with respect to epidemiology and outcomes in critically ill COVID–19 patients.

000584

Ventilation of the right lung determines the extent of injury to the contralateral non-ventilated lung in pigs

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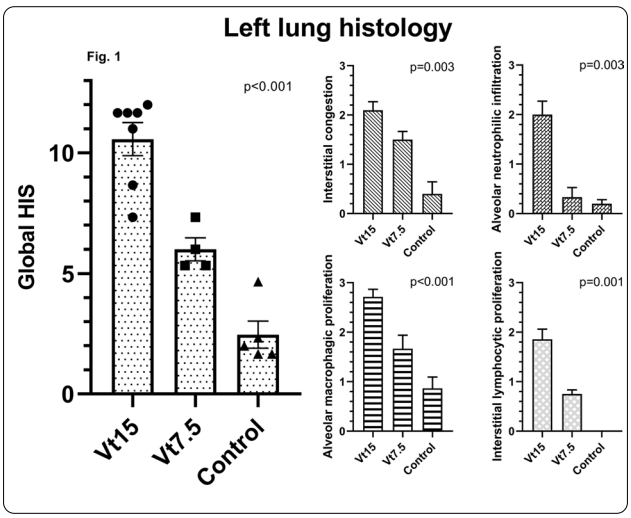
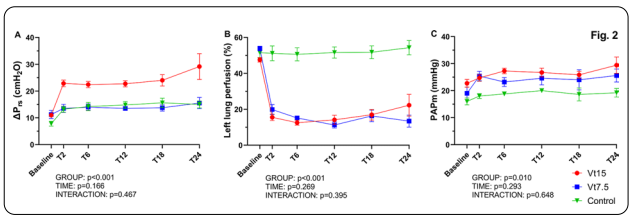
Intensive Care Medicine Experimental 2022, **10(2)**:000584

Introduction: Non-ventilated lung regions are common in acute hypoxemic respiratory failure. As they don't receive tidal ventilation, these regions should be spared from ventilator-induced lung injury (VILI). However, regional crosstalk (Elliot et al., 1991) and redistribution of perfusion (Zeng et al. 2020) might extend VILI even to non-ventilated areas.

Objectives: To verify whether different ventilation of the right lung determines the extent of injury to the contralateral non-ventilated lung in previously healthy mechanically ventilated pigs.
Methods: 16 sedated, paralyzed healthy pigs (35 ± 6 kg) were randomized into 3 groups. After baseline measurements, in 7 pigs the right lung was ventilated with 15 ml/kg tidal volume (Vt), while the left lung wasn't ventilated and left open to room air through double-lumen tube (Vt15 group); in 4 pigs, Vt to the right lung was 7.5 ml/kg and the left lung was non-ventilated and open to room air (Vt7.5 group); 5 pigs underwent two-lung ventilation with Vt 15 ml/Kg (Control group). No PEEP and a 15/min respiratory rate were employed. The study lasted 24 h in all animals. Hemodynamics, respiratory mechanics and perfusion (%) to each lung by electrical impedance tomography were assessed at baseline and at 2, 6, 12, 18 and 24 h. After sacrifice, three lung samples (apex, medium, basal) per lung were taken to measure mean wet-to-dry ratio and histological injury score (HIS, ranging from 0 to 33, 11 items, 0–3 points each) by a blinded pathologist. Data were analysed by one-way ANOVA or Kruskal–Wallis test (final measures) and by mixed effect two-way ANOVA (trends over time).
Results: The Vt15 group had higher HIS of the left non-ventilated lung in comparison to the other two groups (Figure 1). Among the 11 items composing HIS, the left lung of the Vt15 group showed more interstitial congestion and neutrophilic, macrophagic and lymphocytic infiltration as compared to Vt7.5 and control groups (Fig. 1). The wet-to-dry ratios of the left non-ventilated lung didn't differ between groups (p = 0.949).



The driving pressure measured along the experiment was higher in the Vt15 group, while Vt7.5 and controls had lower similar values (Fig.. 2A). A marked decrease of perfusion of the non-ventilated lung was evident both in Vt15 and Vt7.5 groups (Fig.. 2C), and was also associated with increased mean pulmonary arterial pressure in the same groups (Fig.. 2B). Arterial blood pressure and heart rate did not differ between groups at all timepoints.



The HIS and the wet-to-dry ratio of the ventilated right lung didn't differ between groups (p = 0.082 and p = 0.216).

Conclusion: The size of the tidal volume delivered to the ventilated right lung affects the extent of injury in the non-ventilated contralateral lung. Lung-to-lung crosstalk could be a key mechanism, while hypoperfusion and pulmonary artery pressure may play minor roles.

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Acknowledgements: "Ricerca finalizzata 2016" to T. Mauri.

000598

"Pulmonary histological material of patients who died from SARS COV2: description and association with clinical variables"

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Intensive Care Medicine Experimental 2022, **10(2)**:000598

Introduction: There is little information about histological manifestations of SARS Cov 2.
Objectives: The objective of our work was to describe the pulmonary histological characteristics of SARS Cov 2 in critical patients in MV who died from COVID, and their association with clinical variables of interest.
Methods: A prospective study was conducted during the months of September and October 2020. Informed consent was obtained from a family member. We included all patients who died in intensive care from Sars Cov2 and were on mechanical ventilation (MV). The sample was taken postmortem, within the next hour from death, by mini-thoracotomy at the level of the fifth anterior intercostal space. For the anatomopathologic analysis, a data collection sheet was prepared for the systematic evaluation of the variables of interest. The analysis of the collected samples was prospective and performed by 2 different doctors specialized in pulmonary pathological anatomy.
Results: We obtained 33 histological samples. The age of the patients was 72 (61–76) years, 7 (21%) were female. The Apache II was 16 [12–20], the SOFA 4 [3–6]. The median number of sick days was 17 [14–25], of which 11[5–17] days were in MV.

Pathological anatomical pattern n (%)	33 (100)
Diffuse alveolar damage n (%)	27 (81)
Exudative stage n (%)	7 (21)
Proliferative stage n (%)	0
Mixed stage n (%)	20 (60)
Insterstitial pathology	10 (33)
Hemorrhage n (%)	23 (70)
Insterstitial infiltrates n (%)	
Bronchial wall inflammation n (%)	7 (21)
Vascular wall thickening n (%)	18 (54)
Thrombi at the microvasculature level n (%)	13 (40)
Fibrosis n (%)	0 (0)
Co-infection	11 (33)

	Day 0	Death Day	P
Current volume (mL)	430 [400–450]	420 [400–475]	0,31
Respiratory rate (cpm)	26 [24–26]	28 [26–30]	0,42
PEEP (cmH2O)	12 [10–12]	12 [10–12]	0,44
Thoracopulmonary complacency (mL/cmH2O)	30 [26–44]	28 [20–35]	0,01
Ventilatory ratio	70 [47–100]	70 [45–73]	0,53
CO2 (mmHg)	39 [32–43]	54 [45–62]	0,01
ΔP (cmH2O)	12 [10–15,5]	15 [12–17,5]	0,06

After performing a binary logistic regression, the only variable that was independently associated with the development of thrombosis in histological samples was the thickening of the vascular wall ($p = 0.04$; OR 5 CI 95% 1.04–23.8) so, those who have thickening of the wall are 2.75 times more likely to have thrombosis than those who do not have it thickened. Regarding the development of hypercapnia on the day of death as a manifestation of vascular thickening, there was a tendency to have higher CO2 in patients with vascular thickening ($p = 0.06$; OR 1.05 95% CI 0.99–1.11) although this did not reach statistical significance.The only factor that was independently associated with the development of diffuse alveolar damage was elevated procalcitonin ($p = 0.01$; OR 0.81 95% CI 0.70–0.95).
Conclusion: The most frequent pathological pattern in these histological samples of patients who died of SARS COV 2 in MRA was the DAD; however; there was a significant rate of vascular thickening and thrombosis. Contrary to what we suspected, no fibrosis phenomena were observed yet in patients with persistence of severe and late ARDS with PaO2/FiO2 less than 150 mmHg and low thoracopulmonary complacency.

Acute Respiratory Failure 7

000365

FX06
to rescue acute respiratory distress syndrome during Covid-19 pneumonia. A randomized clinical trial

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Intensive Care Medicine Experimental 2022, **10(2)**:000365

Introduction: Vascular leakage is a major feature of SARS-CoV-2 induced acute respiratory distress syndrome (ARDS). Its level is associated with mortality, which remains as high as 50%. FX06, a drug under development containing fibrin-derived peptide beta15-42, stabilizes cell–cell interactions, thereby reducing vascular leak and mortality in several animal models of ARDS. It was successfully used as a rescue therapy in a patient exhibiting a severe ARDS following EBOLA virus infection. The aim of this study was to evaluate the efficacy of FX06 in reducing vascular leakage during SARS-CoV-2 induced ARDS.
Methods: We conducted a double-blinded placebo-controlled multicenter trial. Patients receiving invasive mechanical ventilation for less than 5 days for a SARS-CoV-2 induced ARDS were randomized to receive intravenous FX06, 400 mg per day during 5 days, or its placebo, on the top of usual care. The primary endpoint was the reduction of pulmonary vascular leakage from day 1 to day 7, evaluated by transpulmonary thermodilution-derived extra-vascular lung water index (EVLWi). All analyses were conducted on an intent-to-treat basis.
Results: After one consent withdrawal, 49 patients were enrolled and randomized, 25 in the FX06 group and 24 in the placebo group. Patients were very severe, with a median SAPS-II score of 57 [IQR 39; 66], a median PaO2:FiO2 ratio of 104 [69; 165], and a median static pulmonary compliance of 28 ml/cm of water [19–35]. One third of

them were equipped with veno-venous ECMO. Although EVLWi was elevated at baseline (15.6 ml/kg [13.5; 18.5]), the primary endpoint of its reduction from day 1 to day 7 was comparable between groups (-1.9 ml/kg [-3.3; -0.5] in the FX06 group *vs.* -0.8 ml/kg [-5.5; -1.1] in the placebo group, estimated effect -0.8 [-3.1; 2.4], p = 0.51). Cardiac index, pulmonary vascular permeability index, and fluid balance were also comparable between groups. PaO2:FiO2 ratio remained low and comparable between groups. Duration of mechanical ventilation and survival were also not affected by FX06 infusion, with 21 (84%) patients surviving at day 30 in the FX06 group and 17 (71%) in the placebo group (p = 0.27). Adverse events rates were comparable between groups, although patients receiving the drug experienced more ventilator-associated pneumonia (16/25 vs. 6/24, p = 0.009).
Conclusion: In this trial FX06 failed to reduce the level of SARS-CoV-2 induced pulmonary vascular leakage. Further studies are needed to evaluate its efficacy at earlier time points of the disease, or using other dosing regimens.

000484

"Characteristics and risk factors associated with mortality during the first cycle of prone secondary to ARDS due to SARS-CoV-2 pneumonia."

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Intensive Care Medicine Experimental 2022, **10(2)**:000484

Introduction: The prone position improves oxygenation and decreases mortality in patients with ARDS however, there is no definition of failure of this treatment.
Objectives: The objective was to describe the characteristics and behavior of oxygenation and pulmonary mechanics in patients with ARDS due to SARS-CoV-2 who required mechanical ventilation (MV) and in prone position (PP), during the pandemic. Secondary objectives were to identify independent determinants of mortality; particularly, if the number of cycles implemented in prone position was associated with a worse prognosis.
Methods: A prospective observational study. We included patients with ARDS due to SARS-CoV-2 and required PP due to PaO2/FiO2 ≤ 150 mmHg.
Results: Over an 18-month period a total of 273 patients were included for analysis. Age was 59 [49–67] years, with differences between survivors and non-survivors (52 [42–62] years in first wave versus 62 [55–69] years; p < 0.001); 62 (18%) of the patients belonged to the female sex. The scores APACHE II and SOFA were 13 [9–16] and 3 [2–5]. Regarding comorbidities, 113 (32%) had obesity, 112 (32%) high blood pressure, 52 (15%) type II diabetes, and 43 (12%) had COPD.

	All (n = 273)	Survivors (n = 100)	Non-survivors (n = 173)	Value "p"
Initial PaO2/FiO2 (mmHg)	116 [97–135]	115 [94–136]	117 [98–134]	0.53
Post-prone PaO2/FiO2 (mmHg)	181 [150–222]	207 [174–236]	170 [138–210]	< 0.001
PaO2/FiO2 increased after prone (%)	55 [26–102]	74[49–124]	42[17–77]	< 0.001
ΔP initial (Cmh_2O)	13 [11–15]	13 [11–14]	13 [11–15]	0.30
ΔP prone (Cmh_2O)	13 [11–15]	12 [11–14]	13 [12–15]	0.07
Initial Compliance (mL/cmH2O)	30 [25–38]	31 [25–38]	30 [25–38]	0.87
Initial compliance to the first prone cycle	32 [26–39]	33 [28–39]	32 [25–38]	0.10
Number of prone cycles (n)	1 [1–3]	1 [1–3]	2 [1–3]	< 0.001

Number of cycles (N = 273)	N (%)	Age	Mortality (%)	
1 cycle	127 (46)	61 [53–69]	70 (55)	< 0.00
2 cycles	57 (20)	60 [52–67]	40 (70)	
3 cycles	52 (17)	60 [50–68]	35 (70)	
4 cycles	17 (6)	57 [47–65]	14 (82)	
5 or more cycles	19 (7)	51 [35–57]	13 (70)	

Conclusion: After the first 24 h in the prone position the percentage in which paO2 / FiO2 increased over baseline, was independently associated with higher mortality. Patients who were unable to improve PaO2/FiO2 after 24 h in prone and who require more than 1 prone cycle may be candidates for other treatments for refractory hypoxemia.

000529

Comparison of clinical characteristics between respiratory failure patients who admitted to the ICU caused by COVID-19 and seasonal influenza

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Intensive Care Medicine Experimental 2022, **10(2)**:000529

Introduction: A new respiratory virus named coronavirus disease 2019 (COVID-19) sometimes causes respiratory failure that needs invasive mechanical ventilator application. There have been debates about the severity of seasonal influenza and COVID-19 infection.
Objectives: This study compared clinical characteristics of patients with respiratory failure which need Intensive care unit (ICU) care caused by COVID-19 and other respiratory virus, influenza.
Methods: This retrospective study was performed in a tertiary care hospital in South Korea. We recruited respiratory failure patients who needed ICU care due to influenza or COVID-19 from January, 2017 to April, 2021. Demographic and laboratory data were collected at baseline and analyzed.
Results: Sixty five patients with influenza and 135 patients with COVID-19 were enrolled. The mean age of COVID-19 patients was 66.0 compared to 68.9 of influenza patients (p = 0.112). There was no difference in sex, smoking history, diabetes mellitus, hypertension and chronic kidney disease between both groups. COVID-19 group showed significantly lower Charlson comorbidity index (1.1 vs. 2.6, p < 0.001, COVID-19 vs. Influenza), procalcitonin (1.1 vs. 18.56, p < 0.001, COVID-19 vs. Influenza), lactate levels (1.6 vs. 3.6, p = 0.017, COVID-19 vs.

Influenza), and acute physiology and chronic health evaluation II score (11.3 vs. 23.3, $p < 0.001$, COVID-19 vs. Influenza) than influenza group at intensive care unit (ICU) admission time. During ICU stay, influenza group required more invasive mechanical ventilation (81.5% vs. 30.4%, COVID-19 vs. Influenza) Between patients with respiratory failure who need invasive mechanical ventilation, the length of ICU stay was significantly higher in COVID-19 group (32.2 vs. 27.6, $p < 0.001$, COVID-19 vs. Influenza). In the survival analysis, COVID-19 group showed a higher overall survival than influenza group (log-rank $p = 0.001$).
Conclusion: When comparing respiratory failure who admitted to ICU due to COVID-19 and influenza, COVID-19 might need longer length of ICU stay but mortality rate might be lower than influenza.

000557

The role of EphA2/ephrinA1 pathway in hyperoxia-induced lung injury

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Intensive Care Medicine Experimental 2022, **10(2)**:000,557.

Introduction: Oxygen therapy is an essential treatment for patients with acute respiratory distress syndrome (ARDS). However, the inevitable development of hyperoxia-induced lung injury (HALI) may worsen patient prognosis. EphA2/ephrinA1 receptor-ligand signaling regulates the cytoskeleton and cell adhesion in various diseases and embryogenesis. According to several studies, the EphA2 receptor and ephrinA1 ligand affect inflammation via vascular endothelial injury. Therefore, the pathogenesis of HALI might be associated with the mechanism of action of Eph/ephrin signaling.
Objectives: To investigate whether EphA2/ephrinA1 expression can be affected by exposure to hyperoxia, and to explore the protective effect of the EphA2 monoclonal antibody (EphA2 mAb) on HALI mouse model and the survival benefit of the EphA2 mAb on HALI mice.
Methods: Male wild-type C57BL/6 J mice (20–24 g; Orient Bio) were exposed to > 95% O2 in a Plexiglass chamber. To evaluate the association between changes in EphA2/ephrinA1 signaling and exposure time on HALI, analysis was performed at 24 h, 48 h, and 72 h compared with normoxia (21% O2 room air). To analyze the effect of an EphA2 mAb (8 μg via tail vein, pretreatment), the mice were sacrificed at 72 h after hyperoxia exposure. Total cell counts, protein concentration measurements, and cytokine Luminex® assays (Biotech®, Minneapolis, USA) were performed on bronchoalveolar lavage (BAL) fluid. Western blotting, immunohistochemical (IHC), and immunofluorescence (IF) staining were performed on mouse lung tissue. To analyze the effect of the EphA2 mAb on survival, animal survival was observed by placing the mice in normoxic conditions after 72 h of hyperoxia exposure.
Results: With increasing exposure to hyperoxia, the expression of phosphorylated EphA2 in mouse lung tissue significantly increased, and protein leakage and cytokine activation (IL-1β, TNF-α, IL-6, and MIP-2) in BAL fluid were increased ($p < 0.05$). In addition, the expression of tight or adherens junctions proteins, such as ZO-2 and VE-cadherin, was disrupted due to hyperoxia. In the HALI mouse model, compared with phosphate-buffered saline (PBS), the EphA2 mAb attenuated cytokine activation (IL-10 and TNFα) in BAL fluid and lung injury scores ($p < 0.05$). The EphA2 mAb attenuated oxygen stress and abrogated the degradation of tight junction or adherens junction proteins, which was accompanied by a decrease in the expression of the antiapoptotic protein Bcl-2 ($p < 0.05$). Furthermore, the EphA2 mAb improved the survival of HALI mice ($p = 0.045$).
Conclusion: EphA2/ephrinA1 signaling is significantly associated with HALI. EphA2mAb treatment prevented alveolar-endothelial barrier damage and improved survival.

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Acknowledgements: This research was supported by Basic Science Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Science, ICT and Future Planning (NRF-2014R1A1A1038278).

000591

Practice of Awake Prone Positioning in Critically Ill COVID–19 Patients––insights from the PRoAcT–COVID study

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Intensive Care Medicine Experimental 2022, **10(2)**:000591
Introduction: It is unknown how awake prone positioning was practiced in patients with COVID–19 in the second wave of the national outbreak in the Netherlands.
Objectives: We studied the practice of awake prone positioning in COVID–19 patients admitted to the ICU because of acute hypoxemic respiratory failure, and determined associations with demographics and outcomes.
Methods: Investigator–initiated, national, multicenter study in 16 hospitals in the Netherlands. Patients that received awake prone positioning were compared to patients that did not receive this intervention. The primary endpoint was a composite of various aspects of awake prone positioning practice. The secondary endpoint was 'treatment failure', a composite of intubation for invasive ventilation and death before day 28. We used propensity matching to control for observed confounding factors.
Results: In 546 non–intubated patients, awake prone positioning was used in 88 (16.1%) patients, within median 1 [0 to 2] days after ICU admission, for median 1.0 [0.8–1.4] days and median 12.0 [8.4–14.5] hours per day. High–flow oxygen therapy was the most often used oxygen interface at start of awake prone positioning. Patients in the awake prone positioning group less often had a history of cardiovascular disease. In unmatched analysis, treatment failure occurred more often in patients that received awake prone positioning (HR, 1.80 [1.41–2.31]; $P < 0.001$); in matched analysis, differences remained present, but did no longer reach statistical significance (HR, 1.17 [0.87–1.59]; $P = 0.30$).
Conclusion: In this national cohort of COVID–19 patients in the second wave of the national outbreak, awake prone positioning was used in one in six patients. Awake prone positioning started early, but was often discontinued because of need for intubation. Patients that received awake prone positioning had higher risk for treatment failure.

Acknowledgements: Research time from W. Stilma was funded by a personal (PhD fellowship) grant from NWO Netherlands Organisation for Scientific Research, number 023.011.016.

000606

Evaluation of the performances of new generation of heated wire humidifiers

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Intensive Care Medicine Experimental 2022, **10(2)**:000606

Introduction: Heated wire humidifiers performances are influenced by ambient air temperature. When ambient temperature is high (> 25 °C), the humidification performances are significantly reduced, well below 30 mgH2O/L of absolute humidity with increased risk of endo-tracheal tube occlusion (1). These performances are partially improved with specific settings (increased chamber temperature to 40 °C or activation of compensation algorithm) (2).
Objectives: The aim of the study was to evaluate new generation heated wire humidifiers (FP950 and VHB 20) that adds parameters in their algorithm to maintain a stable humidity delivered to patients whatever ambient temperature.
Methods: We measured on bench the hygrometry of inspiratory gases delivered by (i) FP950 (Fisher&Paykel Healthcare, Auckland, New Zealand) (ii) VHB20 (Vincent medical, Hong Kong) (iii) MR850 with usual settings (37 at the chamber/40 at the Ypiece) (iv) MR 850 with no temperature gradient (40/40), and (v) MR850 with compensation algorithm activated. Hygrometry was measured with the psychrometric method (2) after at least one hour of stability while varying the room temperature from 20 to 30 °C.
Results: We present preliminary data based on 292 hygrometric measurements performed at the different conditions tested. The main results are shown in the figure. With the new heated wire heated humidifiers (MR950 and VHB20), the mean humidity delivered remained stable above 30 mgH2O/L of delivered absolute humidity even with ambient temperatures above 25 °C. With previous generation of HH, humidity delivered was adequate when no temperature gradient was set but with high risk of circuit condensation in this situation. There is currently no clinical experience with very high humidity delivered (> 40 mgH2O/L).

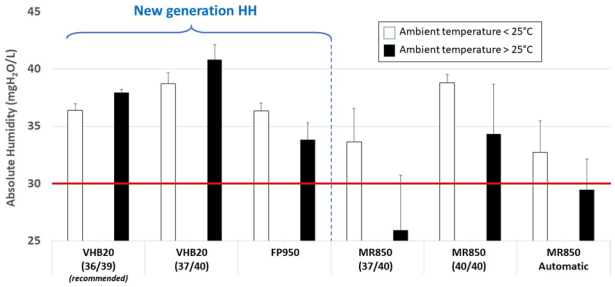

Figure: Absolute Humidity at different ambient temperatures (above and below 25 °C) delivered by new generation heated humidifiers (VHB20 and FP950) and previous generation (MR 850 at different settings: 37/40, 40/40 and with compensation activated). The minimum recommended absolute humidity (30 mgH2O/L) is represented by a red line.

Conclusion: The new heated wire heated humidifiers FP950 and VHB20 demonstrated stable performances while varying ambient temperature from 20 to 30 °C better than did the previous generation of heated humidifiers when ambient temperatures were high.

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Acknowledgements: Fisher&Paykel as well as Vincent Medical participated to cover the costs of the study and provided the tested devices.

000616

Utilization of automated oxygen titration in patients managed at the emergency department (ED) for suspected or confirmed COVID-19

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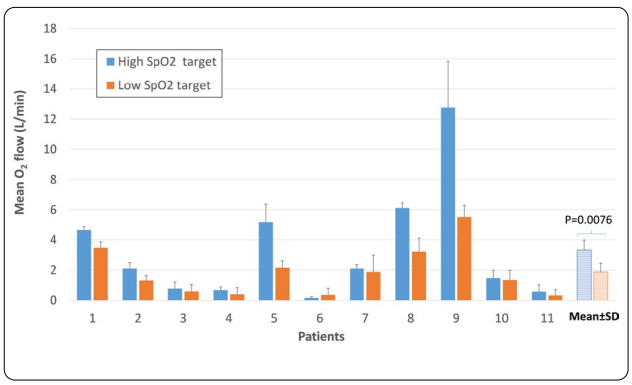
Introduction: During the COVID-19 pandemic, automated oxygen titration has been implemented at the ED to maintain the patients within the oxygenation targets and to reduce the interventions from healthcare workers.
Objectives: We report here our experience to manage patients with suspected or confirmed COVID-19 at the ED.
Methods: We retrospectively collected data from the automated oxygen titration device (O2 flow, SpO2, SpO2 target, respiratory rate and heart rate) in patients managed at the ED between April 2021 and February 2022. We analysed the time within the SpO2 target (set SpO2 ± 2%), with hypoxemia (SpO2 < target − 5%), with hyperoxemia (SpO2 > target + 5%). We analysed the whole population and the subgroup of patients with confirmed COVID-19. We evaluated the number of patients with oxygen weaning during the management. We evaluated separately the impact of the SpO2 target on oxygen flow when the target was modified by the clinicians by 2% or more. In this subgroup of patients, we evaluated the mean oxygen flowrate 15 min before and after the modification of the SpO2 target.
Results: We included 82 patients (mean age 72 ± 16 years, 57% were men) admitted at the ED with acute respiratory distress and suspected (n = 64) or confirmed (n = 18) COVID-19 requiring oxygen therapy. The mean duration of utilization of automated oxygen titration device was 14.3 ± 4.7 h. A SpO2 signal was present 91.9% of the time. Main SpO2 targets set by the clinicians were 90% (43%), 88% (27%), 92% (20%), 94% (4%). Oxygen weaning was possible in 35/82 patients (42%). For the whole population/COVID-19 patients, the time in the SpO2 target was 78/81%, time with hypoxemia was 3/3%, time with hyperoxemia was 2/0.6%. In a subgroup of 11 patients, the effect of modifying the SpO2 target was evaluated (Figure). The mean initial SpO2 target was 91.9% and the mean final target was 89.5%. The mean initial and final oxygen flow were 3.3 ± 0.6 and 1.9 ± 0.6 L/min respectively, P = 0.0076.



Conclusion: In patients with acute respiratory failure, the utilization of automated oxygen therapy was feasible to manage patients with suspected or confirmed COVID-19 with potential benefits. Similarly to other studies with automated oxygen therapy, the time in the oxygenation target was high, and oxygen weaning was potential in 1/3 of the patients. SpO2 target has a significant impact on oxygen flowrates and is a useful tool with this new device.

Acknowledgements: Conflicts of Interest: FL and ELH are co-inventors of FreeO2 and co-founder of Oxynov.

000623

Hygrometric performances of Heat and Moister Exchangers with low dead space

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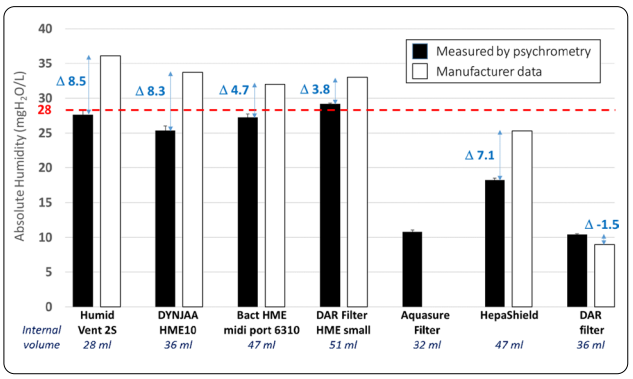
Intensive Care Medicine Experimental 2022, **10(2)**:000623

Introduction: In patients requiring lung-protective ventilation, HH is the first line humidification device to minimize dead space. When transporting these patients, it is important to use HMEs with low dead space and sufficient humidity delivered.
Objectives: In this study, we have evaluated hygrometric performances of low deadspace HMEs.
Methods: We tested on a bench, the hygrometric performances of ***4 HMEs***: BACT HME 6310 (47 ml), Pharma system—DYNJAAHME10 (36 ml), Medline—HUMID VENT 2S (28 ml), Teleflex Medical—DAR HME small (51 ml), Medtronic and ***3 Filters***: HEPASHIELD (47 ml), Flexicare—AQUASURE (32 ml), Bomimed—DAR filter (36 ml), Medtronic. We have used the psychrometric method to measure hygrometry at a steady state, with expiratory humidity of 35 mgH2O/L simulated as previously described (1). For each condition, 3 hygrometric measurements were performed with similar conditions for ambient air temperature 25 ± 0.5 °C, and ventilator settings. We compared with data provided by manufacturers.
Results:
Figure: Absolute Humidity according to manufacturer's (white bars) and to humidity measurements with the psychrometric method (black bars) with small dead space devices. The humidity of 28 mgH2O/L (red line) is indicated. The difference between manufacturers' data and psychrometric measurements is indicated for each device when manufacturers' data were available. AH: absolute humidity.



Conclusion: Several HMEs with small dead space provide sufficient gas humidity and may be used during transport for patients with lung-protective ventilation. However, important differences were found in terms of humidification performances for small dead space HMEs and filters. For prolonged utilization, humidity delivered should be above 28 mgH2O/L. For a few hours of utilization, it may be acceptable to use HMEs with humidity delivered above 25 mgH2O/L. Data provided by manufacturers obtained with the gravimetric method may not be reliable.

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000634

Risk factors for weaning failure in COVID-19 patients: a multicenter, observational study in Greece

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Intensive Care Medicine Experimental 2022, **10(2)**:000634

Introduction: Weaning failure is associated with prolonged intubation and patients who failed weaning trial may meet complications of long ICU stay such as infections, barotrauma and increased mortality [1]. Recognizing risk factors that are associated with weaning failure is of great importance especially in SARS-CoV-2 ARDS patients.
Objectives: Data regarding risk factors for mechanical ventilation (MV) weaning failure among SARS-CoV-2 ARDS patients are limited. We aimed to determine patients' characteristics of MV SARS-CoV-2 ARDS patients that could predestinate the outcome of weaning.
Methods: This was a multicenter (four centers) observational cohort study of SARS-CoV-2 ARDS patients during the SARS-CoV-2 pandemic period 2020–2021. Primary outcome was weaning success defined as spontaneous ventilation for > 48 h within the first 28 days from ICU admission.
Results: 96 SARS-CoV-2 ARDS patients were analysed. Chronic Obstructive Pulmonary Disease (COPD) and shock were independently associated with weaning outcome [odds ratio (OR) 0.80; (95% CI) -0.58-(-0.06), P = 0.01] and shock [0.67(-0.62-(-0.23), P = 0.00002] respectively.
Conclusion: The presence of COPD and shock are potential risk factors for adverse weaning outcome in SARS-CoV-2 ARDS patients.

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Acknowledgements: None.

000668

Design and Testing of a Novel, Low Cost, Non-invasive, Pediatric Bi-Level Positive Airway Pressure Ventilation Device

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Intensive Care Medicine Experimental 2022, **10(2)**:000668

Introduction: Lower respiratory tract infections account for > 2.6 million deaths globally. Lack of access to respiratory support affects these outcomes. Bubble CPAP (B-CPAP) is a simple respiratory support device effective in low- and high-income countries for infants but cannot be applied in larger children. CPAP is useful for spontaneously breathing patients with mild to moderate respiratory distress. Pressure applied during inspiration (Bi-PAP)

can augment ventilation and improve gas exchange for sicker patients.

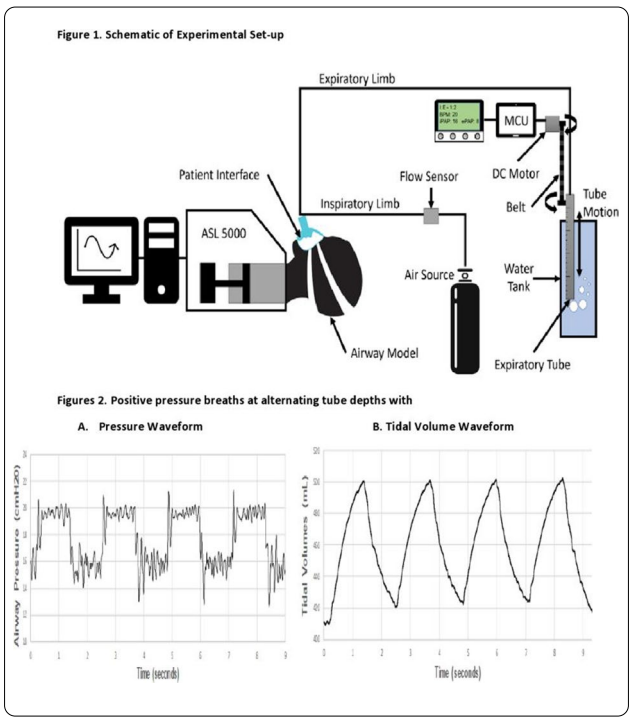
Objectives: To design a dual pressure device based on B-CPAP modification and assess if device reliably delivers pulmonary pressures in a test lung.

Methods: Experimental design consists of a linearly actuated dynamic expiratory tube (Fig.. 1). The position of the tube is alternated at different depths under water with a motorized belt providing timed delivery of intermittent positive pressure breaths. Device testing was conducted using pediatric models simulated by test lung ASL 5000 (Ingmar Medical, Pennsylvania), configured with healthy and diseased lung mechanics, with passive breathing. Varying PIP and PEEP settings with mask interface and endotracheal tube (ETT) were used, with respiratory rate set at 20 bpm, I:E ratio at 1:2. Breath data were extracted from ASL 5000 software and delivered pulmonary pressures and volumes analyzed with descriptive statistics using MATLAB (MathWorks, MA). Accuracy was compared between set and delivered pressures based on % Error calculation.

Results: Oscillations from bubbling were evident on pressure waveform (Fig.. 2). When device was set at 18/10cmH20, measured peak inspiratory pressures and PEEP had an error of 2% and 8% in healthy and 11% and 6% in ARDS test lungs respectively compared to set pressures. Mask interface resulted in lower delivered pulmonary pressures compared to ETT. Tidal volumes for healthy and diseased lungs were 167 mL and 108 mL respectively at settings of 18/10cmH20. This translates to volumes of 8 and 5 mL/kg for a 20 kg child. There was linear increase in tidal volumes with increasing delta pressures.

Conclusion: Bubble BiPAP is a novel device that can provide respiratory support for children up to 20 kg based on simulated models for mild to moderate respiratory illnesses. Respiratory rate, and cycle times can be set to achieve target support settings. More accurate delivery of inspiratory pressures requires further device optimization.

The effect of spontaneous breathing was not evaluated. In-vitro testing of physiologic effects of Bubble BiPAP in animals is planned as next step. With further modifications, Bubble BiPAP may provide additional respiratory support options for children in resource limited settings.



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Acknowledgements: This study is supported by the Seattle Children's Center for Clinical and Translational Research (CCTR) Pediatric Pilot Fund.

Acute Respiratory Failure 8

000446

Physiologic impact of increasing ECMO blood flow rate in severe ARDS patients

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Introduction: In patients with the acute respiratory distress syndrome (ARDS) undergoing veno-venous extracorporeal membrane oxygenation (VV-ECMO), higher blood flow rates can increase the arterial oxygen content (1) and decrease the mean pulmonary artery pressure (mPAP) (2) but may also require significant negative venous drainage pressure (Pdren) and worsen ventilation (V)—perfusion (Q) matching (3–5).

Objectives: We aimed to investigate the physiologic impact of 3 targeted ECMO blood flow rates while maintaining constant ventilation settings and acceptable arterial oxygenation.

Methods: Bi-centric, prospective, interventional study of patients with severe ARDS on VV-ECMO since < 7 days. During deep sedation and paralysis, ECMO blood flow was adjusted to target 3 ranges of mixed venous oxygen saturation in a randomized order: low (70–75%), intermediate (75–80%), and high (80–85%). Ventilation parameters, ECMO FdO2 and sweep gas flow were maintained constant. At the end of each study step (20 min), hemodynamics, respiratory mechanics and ECMO parameters were recorded, and arterial and mixed venous blood gases were obtained. The regional distributions of V and Q were measured using electrical impedance tomography (EIT) and analyzed offline using a custom software. One-way repeated measures ANOVA with Tukey's method for post-hoc pairwise comparisons were used to assess differences between steps.

Results: Data from 18 patients were analyzed. At enrollment, age and SOFA score were 52 ± 10 years and 7 ± 3. The respiratory system compliance was 23 [19–28] mL/cmH2O with a positive end-expiratory pressure of 15 ± 2 cmH2O and FiO2 of 85 [60–93] %. All patients had a diagnosis of pneumonia (78% COVID-19, 22% bacterial). Three distinct blood flow rates were obtained (1.62 ± 0.47 vs 2.39 ± 0.49 vs 3.36 ± 0.52 L/min, p = < 0.0001). Drainage cannulae were 25 ± 1 Fr. Increasing blood flow increased PaO2 (63 ± 9 vs 71 ± 12 vs 92 ± 31 mmHg, p = 0.0006) and the total pulmonary arterial compliance, decreased cardiac output and mPAP and did not alter PVR (Figure 1) or systemic

oxygen delivery (545 ± 150 vs 503 ± 126 vs 511 ± 95 mL/min/m2, p = 0.0795). Higher blood flow rate resulted in a decrease in Pdren (11 ± 21 vs 2 ± 29 vs -18 ± 29 mmHg, p = 0.0056) but was not associated with any worsening of Qva/Qt (54 ± 12 vs 54 ± 13 vs 56 ± 14%, p = 0.4167) or the EIT-based percentage of only ventilated (8.5 [4.7–15.2] vs 6.2 [3.8–11.7] vs 10.9 [5.2–20.7] %, p = 0.0606) or only perfused (16.1 ± 8.5 vs 17.6 ± 7.6 vs 16.6 ± 16.6%, p = 0.5758) lung units.

Conclusion: In severe ARDS patients receiving VV-ECMO, higher blood flow rate may decrease right ventricular workload and afterload with acceptable negative drainage pressure and no worsening of V/Q mismatch.

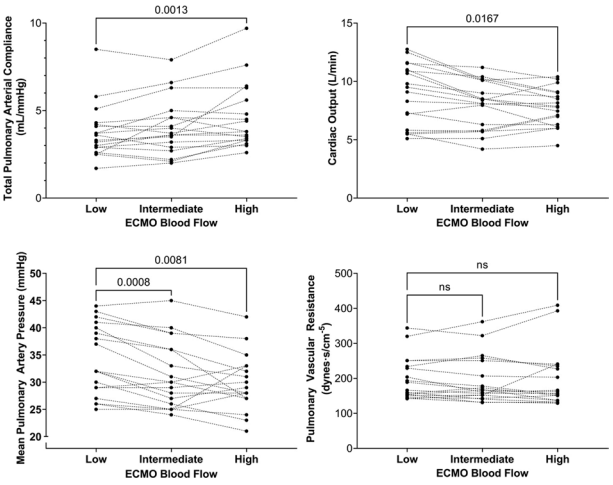

Figure 1: ANOVA p = 0.0006 for total pulmonary arterial compliance, p = 0.0027 for cardiac output, p = 0.0024 for mean pulmonary artery pressure, and p = 0.8175 for pulmonary vascular resistance. Tukey's correction is applied for multiple comparisons.

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Acknowledgements: ESICM Levi-Montalcini Biomedical Sciences Award (2020) to E. Spinelli.

000554

Occurrence and risk factors of major complication in critically adults requiring endotracheal intubation. A Nationwide, Prospective Study in Spain: INTUPROS study

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Introduction: Critically ill patients that require endotracheal intubation present almost always hemodynamic instability and/or severe hypoxemia, therefore intubation should be always considered as a high-risk procedure with a significant morbidity and mortality.

Objectives: to determine the frequency and associated factors for the appearance of major complications that occur in the intubation of critically ill patients.

Methods: prospective multicenter study (NCT03916224) in 43 Spanish ICUs (6 months from April 2019 to October 2020) including intubations in adults performed at the ICU excluding those due to cardiac arrest. Variables analysed: demographics, comorbidities, body mass index, APACHE II, SOFA, MACOCHA and Cormack scores, reason for intubation (including COVID 19 disease), peri-procedure cardiovascular and respiratory conditions, patient position, use of Sellick maneuver, preoxygenation method, devices and accessories used on intubation, first professional operator, induction drugs, first pass intubation, major complications and mortality. Major complications were considered: cardiac arrest requiring resuscitation, severe hypoxemia (saturation < 80% or decrease in saturation > 10% if previously was < 90%), severe hypotension (systolic blood pressure (SBP) < 65 mm Hg registered at least once or < 90 mm Hg lasting 30 min despite 1,000 mL crystalloid bolus or SBP decrease > 20% if < 65 mm Hg before intubation or requiring introduction or dose increase > 30% prior vasoactive support), cervical injury or death. The patients were followed up until hospital discharge or death. The ethics committee of the coordinating center (Virgen Macarena University Hospital, January 14, 2019) approved this study. This study was endorsed by the Spanish Society of Intensive Care Medicine (SEMICYUC). Bivariate analysis was made using chi-square or exact Fisher test as appropriate for qualitative variables and U Mann–Whitney test for quantitative variables. A multivariate analysis with logistic regression using variables with p < 0.05 in the bivariate analysis was performed to determine variables independently associated with major complications.

Results: a total number of 1837 patients were included. In 743 cases (40.4%), at least one major complication was registered. Overall, 973 major complications were observed: hypotension (487 patients; 26.5%), hypoxemia (373 patients; 20.3%). Cardiac arrest occurred in 35 cases (1.9%), with 20 died patients (1.1%). No cervical injury was recorded. Mortality in the ICU was higher in patients who suffered a major complication (43% vs 29.7%, p < 0.001) as well as hospital mortality (47.5% vs 35.8%, p < 0.001). The risk factors for major complications were: COVID 19 OR 2.17 (CI 95% 1.63–2.89), acute respiratory failure as reason for intubation OR 1.41 (CI 95% 1.07–1.86), MACOCHA scale score OR 1.08 (CI 95% 1.02–1.15), SOFA score at intubation day OR 1.05 (CI 95% 1.02-1.08), pre-intubation saturation < 90% OR 1.76 (CI 95% 1.41–2.20), pre-intubation MAP < 75 mmHg OR 1.70 (CI 95% 1.36–2.12), pre-intubation vasopressors infusion OR 1.45 (CI 95% 1.14–1.85), number of laryngoscopy attempts OR 1.16 (CI 95% 1.01–1.33). Coma as intubation reason OR 0.41 (CI 95%0.28–0.60) and the use of muscle relaxants OR 0.63 (CI 95% 0.47–0.86) were protective factors for major complications.

Conclusion: up to 40% of critically ill patients undergoing intubation present a major complication what is associated with a higher mortality. Not delaying the intubation and the use of muscle relaxants could reduce the occurrence of these events.

000604

Risk factors for deterioration and assessment of COVID-19 patients in a University Hospital—associations with clinical-laboratory features and outcome

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Introduction: COVID-19 pandemic is a public health emergency of international concern with a high mortality rate. It is imperative to identify COVID-19 risk factors associated with critical illness and increased mortality.
Objectives: This study aims to identify risk factors and prognostic factors for the deterioration of COVID-19 disease and mortality. Furthermore, the study intends to compare the characteristics and outcome indicators of patients hospitalized in COVID-19 Clinic (discharged from Clinic vs deteriorated and transferred to ICU) and COVID-19 ICU patients (survivors vs non-survivors).
Methods: This is a single-center, retrospective study conducted in the COVID19-clinic and COVID19-ICU of the University Hospital of Heraklion from January-October 2021. Demographic, clinical, laboratory, treatment data, and outcomes were recorded.
Results: Out of 184 patients from COVID-19 Clinic, 111 (57.6%) were fully treated and discharged from the Clinic (Clinic group) and 73 (39.7%) deteriorated and transferred to ICU (Clinic-ICU group). Clinic patients were noted to be younger (62.3 ± 13 vs 67 ± 13 years, $p = 0.008$), with less comorbidities (73% vs 89%, $p = 0.009$) with shorter hospital stay (8.6 ± 6 vs 29.4 ± 21 days, $p < 0.001$) and had lower mortality (4.5% vs 47.9%, $p < 0.001$). Clinic-ICU patients more frequently received high flow nasal cannula (HFNC) (90%vs20%, $p < 0.001$), were placed prone (58.3%vs14.7%, $p < 0.001$) and experienced complications ($p < 0.001$). Independent risk factors for deterioration were use the of HFNC (exp(B)0.255, 95%CI 0.087–0.749, $p = 0.013$), PF ratio on Day 1 (exp(B) 0.985, 95% CI 0.978–0.993, $p < 0.001$) and the existence of co-morbidity (exp(B) 0.176, 95%CI 0.050–0.622, $p = 0.007$). Predictive indicators of deterioration and transfer to ICU were determined to be the use of HFNC, PF ratio, ROX index, ROX-HR index on Day 1 as well as the high values of PT, INR and IL-6 (all $p < 0.001$). (Figure 1.A, 1.B). During the study period, 120 patients were hospitalized in ICU. Non-surviving ICU patients (55.8%) were, significantly, more likely to be older (73.2 ± 10.9 vs 60.7 ± 17.9 years, $p < 0.001$), male (71.7% vs 52.2%, $p = 0.023$), with longer duration of mechanical ventilation (MVD) (28.4 ± 21.9 vs 14.3 ± 13.5 days, $p < 0.001$) and longer ICU stay (28.1 ± 21.9 vs 12.3 ± 13.3 days, $p < 0.001$). Independent risk factors for mortality were age ($p < 0.001$), PF ratio on Day 1 ($p = 0.05$), MVD ($p = 0.001$) and WBC ($p = 0.013$). Prognostic indicators of mortality were age, PF ratio Day 3 and MVD.

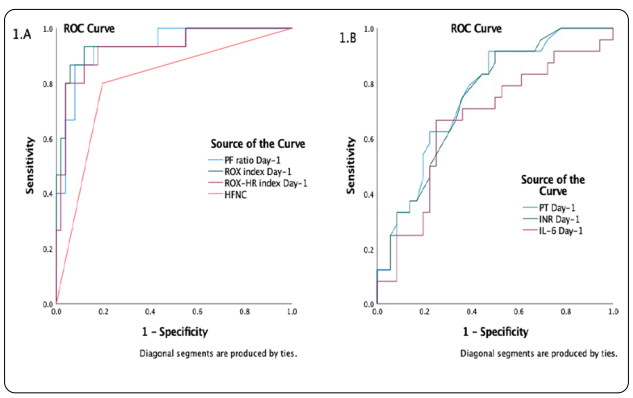

Figure 1. Prognostic factors for deterioration and ICU admission A. Clinical B. Laboratory.

Conclusion: Risk factors for deterioration of COVID-19 disease were found to be the use of HFNC, PF ratio, and the existence of co-morbidity. Predictive indicators of deterioration and transfer to ICU were the use of HFNC, PF ratio, ROX index, PT, INR, and IL-6. Risk factors for mortality in ICU patients were age, PF ratio, MVD, and WBC, whereas prognostic indicators of mortality were age, PF ratio, and MVD. Identified risk factors as well as patient data on admission might be used for best-performing algorithms, scoring systems, and predictive tools for decision-making in COVID-19 patients.

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000621

The effect of positive end-expiratory pressure on tidal volume distribution during assisted spontaneous breathing in a model of ARDS

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Introduction: Whether or not spontaneous breathing should be used in acute respiratory distress syndrome (ARDS) is disputed. Assisted spontaneous breathing may provide beneficial effects, such as improved oxygenation and diaphragm protection [1][2]. However, spontaneous breathing per se may also aggravate lung injury, possibly by the mechanisms deriving from the so-called patient self-inflicted lung injury [3]. During assisted spontaneous breathing (ASB) in patients with ARDS, the level of positive end-expiratory pressure (PEEP) is of great importance, as both protective and injurious lung phenomena may be induced [4]. However, the PEEP level chosen when assessing ASB in ARDS varies amongst studies and the optimal PEEP level is often unclear.
Objectives: The aim of the study was to estimate the effect of PEEP on the distribution of tidal volume throughout the lung during uninterrupted assisted ventilation.
Methods: 10 farm-bred pigs (28,4 ± 2,1 kg) were anesthetized and an ARDS-like condition was induced using repeated saline lung lavages. Spontaneous breathing was maintained and neurally adjusted ventilator assist (NAVA) initiated. Tidal volume distribution was assessed using electric impedance tomography (EIT) during an incremental and decremental PEEP protocol, reaching from 0 cmH2O to 15 cmH2O and back to 0 cmH2O, in steps of 3 cmH2O. Tidal volume distribution and degree of dependent lung volume ventilation was correlated to PEEP level.
Results: The increase of PEEP resulted in a homogenizing effect on the tidal volume distribution. As PEEP was increased, tidal volume was shifted from predominantly non-dependent to dependent lung regions. When PEEP was increased from 0 cmH2O to 15 cmH2O, the fraction of tidal volume reaching the dependent lung increased from 30 ± 8% to 59 ± 9% ($p < 0,0033$).
Conclusion: In this model of ARDS, when using assisted spontaneous breathing, increasing PEEP causes a more homogeneous distribution of ventilation and increases the ventilation of the dependent lung region. This study indicates the importance of PEEP level when using assisted spontaneous breathing during ARDS and indicates that homogeneity of ventilation must be taken into consideration when defining the criteria for identifying the optimal PEEP level.

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Acknowledgements: The study was supported by grants from the Swedish Research Council (2018-02438), the Swedish Heart Lung Foundation (numbers 20200877 and 20200825), and the Alvar Gullstrand research grant (ALF-938050).

000638

Continuous prone position and relationship with ventilatory mechanics in acute respiratory distress syndrome in SARS-CoV 2

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Introduction: Acute respiratory distress syndrome (ARDS) is a non-cardiogenic pulmonary edema associated with diffuse alveolar damage. It has an incidence of 150,000 cases per year in the United States, however, because of SARS-CoV-2, this incidence increased by 60%. Ventilatory support is the key in the treatment of severe ARDS and in recent years prone position ventilation (PPV) has become a therapeutic option in severe hypoxemia and the improvement in survival has been observed in patients with PaO2/FiO2 ratio of < 150 mmHg with a duration of 16 h per day, however few studies have documented benefit after this period.
Objectives: To analyze the ventilatory mechanics and oxygenation with prone position ventilation for a period over than 24 h, in patients with severe ARDS secondary to SARS-CoV-2 infection at the ICU of a thertiary hospital in Mexico City.
Methods: The study was a single-center retrospective and descriptive performed on severe ARDS patients secondary to SARS-CoV-2 infection. We analyzed PaO2/FiO2 ratio, Driving Pressure, ventilatory ratio and Mechanical Power before pronation (T0), during pronation (T1) and 24 h after pronation (Table 1). Standardized protocols were followed for each patient.
Table 1. Mechanic Ventilatory in the different periods, T0, T1 and T2.

Prono time	PaO2/FiO2 mmHg	Driving pressure cmH2O	Ventilatory ratio	Mechanical Power (J/min)
Before prone (T0)	101.44	19.93	2.04	26.65
30 min (T1)	141.50	17.73	1.74	20.80
24 h (T2)	177.11	17.03	1.70	18.40

Results: 395 patients were analyzed, 55 were excluded, a total sample remains was 340 patients with ARDS secondary to SARS CoV-2 infection with a median age of 51.6 years, 31.8% females and 68.2% males; mortality was 50.5%. We found a decrease in driving pressure of 14.5%, mechanical power of 30.9% and ventilatory ratio of 16.6%, as well as an increase in PaO2/FiO2 ratio (80% responders with 42% mortality, 20% non-responders with 63.2% mortality). The average of mechanical ventilation was 12.6 days and in the continuous prone position it was 10 days ($p < 0.0001$). Application of continuous PPV did not expose patients to an increased incidence of skin pression lesions, and other complications were not reported.
Conclusion: In this study, the improvement ventilatory mechanics after the prone position for more than 24 h is observed, which is associated with a decrease in mortality, and days of mechanical ventilation ($p < 0.02$), but not with the days of hospital stay ($p < 0.33$). The results obtained suggest that continuous PPV is safe and effective in patients with severe ARDS, however large sample are needed analyze other variables that may contribute to the success or failure continuous PPV.

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000687

What thresholds for invasive ventilation in hypoxemic respiratory failure are used in routine clinical care? A retrospective cohort study

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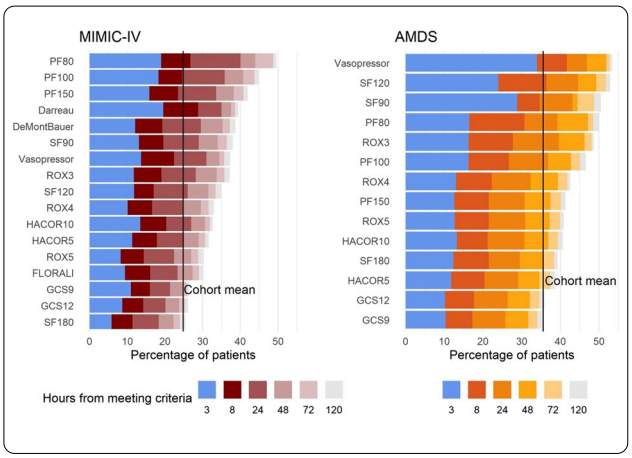
Intensive Care Medicine Experimental 2022, **10(2)**:000687

Introduction: No consensus exists on the optimal thresholds for the initiation of invasive ventilation in hypoxemic respiratory failure. To learn which thresholds are implied by clinical practice, we investigated whether existing candidate thresholds matched with usual care.
Methods: We conducted a retrospective cohort study of patients receiving inspired oxygen of 0.4 or more via non-rebreather mask, non-invasive positive pressure ventilation, or high-flow nasal cannula using patients from the Medical Information Mart for Intensive Care (MIMIC) IV (2009–2019) and Amsterdam Medical Data Sciences (AMDS) (2003–2016). We identified seventeen thresholds from a systematic review and observational studies, including the arterial-to-inspired oxygen (P:F) ratio, the saturation-to-inspired oxygen (S:F) ratio, and the criteria used in the Frat 2015 oxygen devices trial. We reported the probability of invasive ventilation within 3 h after meeting each threshold and the association of this outcome with covariates, using the odds ratio (OR) and 95% credible interval (CrI).
Results: We studied 4,660 patients (3,365 MIMIC, 1,295 AMDS). Invasive ventilation occurred in 28% (1,297) and mortality at 28 days was 21% (963). The probability of invasive ventilation within 3 h of meeting a threshold was generally 20% or lower. Thresholds with high probabilities of subsequent ventilation included a P:F ratio less than 80 mmHg (19% MIMIC, 16% AMDS), an S:F ratio less than 90 (13% MIMIC, 29% AMDS), and the initiation of vasopressors (16% MIMIC, 34% AMDS). Subsequent ventilation after meeting the Frat 2015 trial criteria was low (9% MIMIC). A ten-year increase in age (OR 0.81, CrI

0.77 to 0.85) and race/ethnicity of Black (OR 0.75, CrI 0.57 to 0.96) or Asian (OR 0.6, CrI 0.35 to 0.95) as opposed to White were associated with decreased probability of subsequent ventilation. At the time of meeting a threshold, a time of day outside the 12PM to 6PM interval, use of non-invasive ventilation (OR 2.41, CrI 1.89 to 3.01), and increased work of breathing (OR 3.11, CrI 2.47 to 3.88) were associated with increased probability of subsequent ventilation.



Caption: Stacked bar plot of the percentage of patients receiving invasive ventilation within increasing time intervals (x axis) after meeting different thresholds (y axis).

Conclusion: The probability of invasive ventilation after meeting prespecified thresholds was low and associated with non-physiologic variables. These results have implications for trial interpretation, study design, and equity of care.

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Acknowledgements: Dr Yarnell was funded by the Canadian Institutes for Health Research Vanier Scholar program, the Eliot Phillipson Clinician Scientist Training Program, and the Clinician Investigator Program of the University of Toronto.

000711

Use of ketamine in patients with refractory severe asthma exacerbations: systematic review of prospective studies

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Intensive Care Medicine Experimental 2022, **10(2)**:000711

Introduction: Asthma is a heterogeneous disease with wide range of symptoms. Severe asthma exacerbations (SAEs) are characterized by worsening symptoms and bronchospasm requiring emergency department visits. In addition to conventional strategies for SAEs (inhaled β-agonists, anticholinergics, and systemic corticosteroids), another pharmacological option is represented by ketamine. We performed a systematic review to explore the role of ketamine in refractory SAEs.

Methods: We performed a systematic search on PubMed and EMBASE up to August 12th, 2021. We selected prospective studies only, and outcomes of interest were: oxygenation/respiratory parameters, clinical status, need for invasive ventilation and effects on weaning.

PICOS

Participants	Adult and pediatric patients with severe asthma refractory to conventional therapy
Intervention	Ketamine
Comparison	Placebo or other pharmacological strategies
Outcome	Improvement in oxygenation parameters; amelioration of clinical conditions; reduction of escalation to invasive ventilation; facilitation in weaning from mechanical ventilation; decrease in peak inspiratory pressures and increase in lung compliance; evaluation of side effects
Studies included	Randomized controlled trials; prospective studies for sensitivity analysis only

Results: We included a total of seven studies, five being randomized controlled trials (RCTs, population range 44–92 patients). The two small prospective studies (n = 10 and n = 11) did not have a control group. Four studies focused on adults, and three enrolled a pediatric population. We found large heterogeneity regarding sample size, age and gender distribution, inclusion criteria (different severity scores) and ketamine dosing (bolus and/or continuous infusion). Of the five RCTs, three compared ketamine to placebo, while one used fentanyl and the other aminophylline. The outcomes evaluated by the included studies were highly variable. Despite paucity of data and large heterogeneity, an overview of the included studies suggests absence of clear benefit produced by ketamine in patients with refractory SAE, and some signals towards side effects.

First author, year, Design	N of patients Age (Range)	Inclusion Criteria	Ketamine dose(s) Comparison dose	Outcomes reported by the authors Side effects reported
Esmailian M, 2018; RCT	92 48 years (34 – 62)	-	- K: bolus 0.3 mg/kg (16.3%), 0.4 mg/kg (15.2%), and 0.5 mg/kg (17.4%) - Placebo	PEFR before and 1 h after treatment. No side effects reported.
Allen JY, 2005; RCT	68 6 years (2 – 10)	PIS> 8	- K: bolus 0.2 mg/kg + infusion 0.5 mg/kg/h (2 h) - Placebo	PIS score at 0, 30, 60, 90, and 120 minutes. No side effects reported.
Tiwari A, 2016; RCT	48 48 months (16 – 144)	PRAM ≥5 after 2 h of standard therapy	- K: bolus 0.5 mg/kg (20 min) + infusion 0.6 mg/kg/h (3 h) - Aminophylline: 5 mg/kg bolus (20 min) + infusion 0.9 mg/kg/h (3 h)	ΔPRAM in the first 24 h, Hypertension, Tachycardia. No side effects reported.
Nedel W, 2020; RCT	45 65 (51 – 79)	- Adults intubated for acute bronchospasm. -Rs_{tot}≥12 cmH_2O/L/s	- K: bolus 2 mg/kg + infusion 2 mg/kg/h - Fentanyl: bolus 1 mcg/kg + infusion of 1 mcg/kg/h	Rsmax, Cdyn, PEEPi, Duration of MV at baseline, 3h and 24h. No side effects reported.
Howton JC, 1996; RCT	44 33 (26 – 40)	-	- K: bolus 0.1 mg/kg + infusion at 0.5 mg/kg/h - Placebo	Respiratory rate, hemodynamic parameters, Borg Score, P/F ratio, FEV. before and after treatment. Side effects reported.
Petrillo TM, 2001; Prospective	10 8 (5 – 16)	CAS > 12	- K: bolus 1 mg/kg + infusion 0.75 mg/kg/h (1 h)	CAS, vital signs, PEFR before K administration, within 10 min after K administration, and 1 h after infusion. Side effects reported.
Heshmati F, 2003; Prospective	11 30 (15 - 40)	-	- K: bolus 1 mg/kg + infusion 1 mg/kg/h (2 h)	Ppeak, $PaCO_2$, PaO_2 before K administration, 15 min after administration and 2 h after infusion. No side effects reported.

Table 2. Summary of the included studies. RCT: Randomized Controlled Trial; K: Ketamine; MV: Mechanical Ventilation; PEEPi: Positive End Expiratory Pressure Intrinsic; Cdyn: Dynamic Compliance; Rsmax: Airway Resistance; PEFR: Peak Expiratory Flow Rate; Ppeak: Pressure Peak; FEV1:Forced Expiratory Volume in 1 second; PRAM: Pediatric Respiratory Assessment Measure; PIS: Pulmonary Index Score; CAS: Clinical Asthma Score.

Conclusion: Our systematic review does not support the use of ketamine in refractory SAE. A limited number of prospective studies with large heterogeneity was found. Well-designed multicenter RCT are desirable.

000735

Expiratory flow control and Ventilator induced lung injury

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Intensive Care Medicine Experimental 2022, **10(2)**:000735

Introduction: Mechanical power, which is the total amount of energy delivered by the ventilator in one minute, is a summary variable including all the mechanical factors known to induce lung damage during mechanical ventilation (VILI)[1]. Out of the total energy delivered in one breath, part of it is dissipated to win the inspiratory resistances, while the remaining amount is stored into the lung as elastic energy. This energy is then released during expiration: part of it is dissipated into the environment, while the remaining amount is dissipated into the respiratory system, being the putative cause of VILI. The distribution of dissipated energy between respiratory system and environment is influenced by the flow pattern[2].
Objectives: We investigated whether expiratory flow control could reduce the amount of energy dissipated into the lung parenchyma and, consequently, VILI.
Methods: We studied 22 female piglets (29 ± 2 kg). The animals were randomized into two groups: a control (n = 11) and a valve group (n = 11), where expiratory flow was controlled through a computer driven valve, acting as mechanical resistor. Both groups were ventilated prone for 48 h with similar mechanical power (~ 9 J/min), a level that has showed a consistent risk of VILI in our experience[3]. Electric Impedance Tomography was continuously measured. Measurements were taken at baseline, 30 min, and every 6 h. Expiratory energy distribution was directly computed from pressure–volume loops, being the hysteresis area of a P–V loop equal to the total amount of energy dissipated within the respiratory system throughout one respiratory cycle [2]. Lastly, lung weight, wet to dry ratios and histology were evaluated.
Results: The total mechanical power delivered was similar in the control and valve groups (8.49 ± 0.92 vs. 8.44 ± 0.56 J/min respectively, p = 0.88), as well as the fraction dissipated during inspiration (16.1 ± 3.5% vs. 16.9 ± 5.6%). The amount of energy/min dissipated within the respiratory system during expiration was remarkably different (2.9 ± 0.6 J/min, control, vs. 1.16 ± 0.4 J/min, valve, p < 0.001). Out of this energy/min, the amount dissipated into the lung parenchyma was higher in the control group than in the valve group (1.45 ± 0.5 J/min vs. 0.73 ± 0.16 J/min respectively, p = 0.008), while the remaining amount was dissipated into the main airways (Figure 1). The decrease of electrical impedance (a possible sign of lung damage [4]) was significantly greater in the control group (p = 0.02), primarily in the dorsal lung regions (Figure 2). Respiratory mechanics and gas exchange were similar in both groups, as well as the total lung weight, wet to dry ratios and histologic findings.

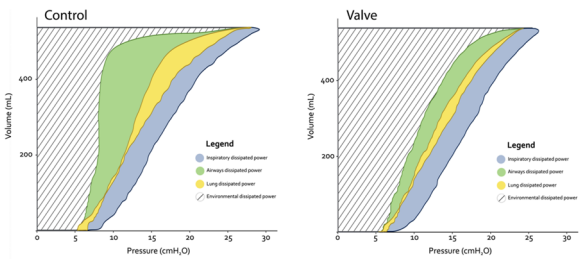

Figure 1: a visual model of energy dissipation distribution in the two experimental groups. As shown, the amount of energy dissipated to overcome inspiratory resistance was similar in the two groups (blue area), while the expiratory phase was remarkably different

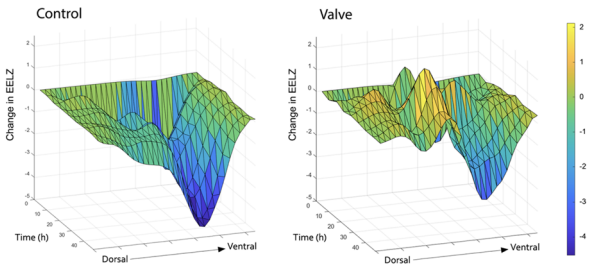

Figure 2: a tridimensional view of end-expiratory lung impedance (EELZ) change over time in the two groups. As shown, in the control group (panel A), the EELZ remained similar in the dorsal regions (green color) but sharply decreased with time in the most ventral ones (dependent regions, blue color). In contrast, in the valve group (panel B), the EELZ increased with time in the dorsal regions while it decreased in the ventral ones, albeit less than in controls. The two figures were built averaging all the impedance measured in the two groups.

Conclusion: Expiratory flow control causes different energy distribution. With our experimental setup, however, the lower amount of energy dissipated into the lung parenchyma in the valve group was insufficient to significantly decrease the lung damage vs. control.

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000770

Hygrometric performances of Heat and Moister Exchangers and Filters—comparison of the psychrometric method and manufacturers data

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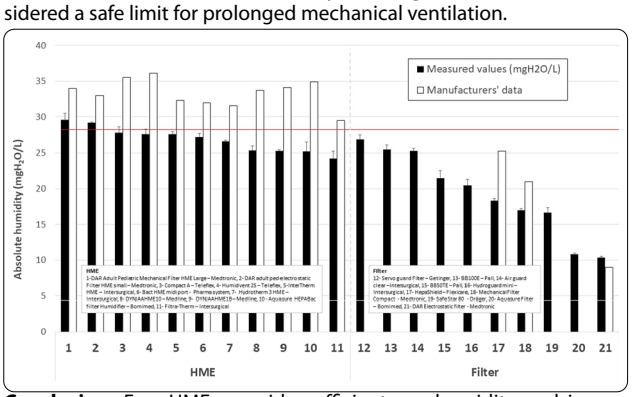
Intensive Care Medicine Experimental 2022, **10(2)**:000770

Introduction: Providing gas humidification greater than 28 mgH2O/L is mandatory for patients with prolonged intubation, with either heat and

moisture exchangers (HME) or heated humidifiers (HH). Several studies showed significant differences between independent measurements of the humidity delivered by the HME and manufacturers data (1–3).
Methods: We tested on a bench, the hygrometric performances of ***11 HMEs*** and ***10 Filters***: We used the psychrometric method to measure hygrometry at steady state, with expiratory humidity of 35 mgH2O/L simulated as previously described (2). For each condition, 3 hygrometric measurements were performed with similar conditions for ambient air temperature 25 ± 0.5 °C, and ventilator settings (respiratory rate 20/min, tidal volume 500 ml, FiO2 21%, PEEP 5 cmH2O, square flow 60 l/min). We compared data obtained on bench with data provided by the manufacturers.
Results: The mean measured absolute humidity in the group of HME and filters were 26.9 and 19.3 mgH2O/L respectively. For HME, mean humidity data provided by the manufacturers was 33.3 mgH2O/L ($P < 0.01$ in comparison with measured humidity). The mean differences between measured humidity and data provided by the manufacturers was 6.3 mgH2O/L, with 7/11 (63%) of devices with differences of 5 mgH2O/L or above.
The main results are presented on the figure.
Figure: Absolute Humidity according to manufacturer's (white bars, when available) and to humidity measurements with the psychrometric method (black bars). The humidity of 28 mgH2O/L (red line) is considered a safe limit for prolonged mechanical ventilation.



Conclusion: Few HMEs provide sufficient gas humidity and important differences were found in terms of humidification performances between HMEs and filters. Data provided by manufacturers obtained with gravimetric method may not be reliable.

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000781

Impact of exposure time in awake prone positioning on clinical outcomes of patients with COVID-19 related acute respiratory failure treated with high-flow nasal oxygen: a multicenter cohort study. Final Report

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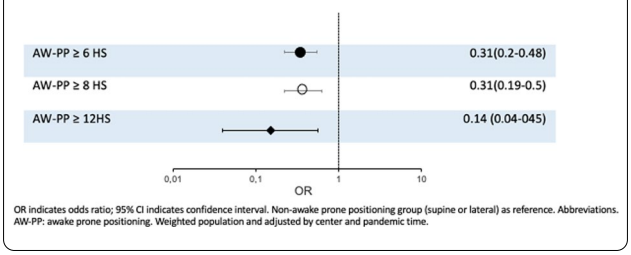
Intensive Care Medicine Experimental 2022, **10(2)**:000781

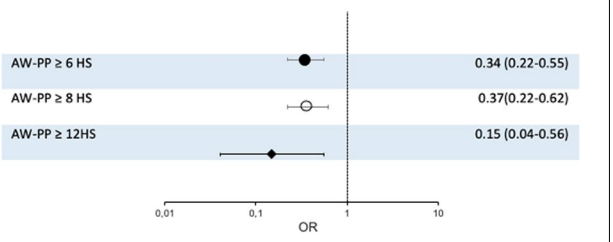
Introduction: In patients with COVID-19 related acute respiratory failure (ARF), awake prone positioning (AW-PP) reduces the need for intubation in patients treated with high-flow nasal oxygen (HFNO) (1,2). However, the effects of different exposure times on clinical outcomes remain unclear.
Objectives: We evaluated the effect of AW-PP on the risk of endotracheal intubation and in-hospital mortality in patients with COVID-19 related ARF treated with HFNO, and analyzed the effects of different exposure times to AW-PP.
Methods: This multicenter prospective cohort study in six ICUs of 5 centers in Argentine consecutively included patients > 18 years of age with confirmed COVID-19 related ARF requiring HFNO from June, 2020 to december, 2021. In the primary analysis, the main exposure was awake prone positioning for at least 6 h/day (3), compared to non-prone positioning (NON-PP). In the sensitivity analysis, exposure was based on the number of hours receiving AW-PP. Inverse probability weighting-propensity score (IPW-PS) was used to adjust the conditional probability of treatment assignment. Direct acyclic graph (DAG) was used to identify and select variables potentially associated with both awake prone positioning and study outcomes. The primary outcome was endotracheal intubation (ETI); and the secondary outcome was hospital mortality.
Results: During the study period 800 patients were screened and 669 were included; 379 (57%) tolerated AW-PP for [median (p25-75)] 14 (10–17) h/day during 5 (3–7) days; 290 (43%) patients served as controls. The balance between the characteristics of the study groups before and after IPW are shown in Fig. 1. After weighting by IPW, the values of all variables were balanced, showing a standardized difference of less than 0.1. Eighty-two (25%) patients in the AW-PP group and 117 (48%) in the NON-PP group were intubated. In the weighted population, the OR for endotracheal intubation was 0.31 (95% CI 0.2–0.48) (Fig. 1). In the sensitivity analysis for ETI, the OR was further reduced when the exposure increased ≥ 12 h/d. (Fig. 1). Fifty five patients in the AW-PP group (14%) and 93 (32%) in the NON-PP group died while being hospitalized. In the weighted population, the OR for hospital mortality was 0.34 (0.22–0.55) (Fig.. 2). In the sensitivity analysis for hospital mortality, the OR was further reduced when the exposure increased ≥ 12 h/d. (Fig.. 2).

Figure 1: Risk of intubation between groups in awake prone position and non-prone position.



OR indicates odds ratio; 95% CI indicates confidence interval. Non-awake prone positioning group (supine or lateral) as reference. Abbreviations. AW-PP: awake prone positioning. Weighted population and adjusted by center and pandemic time.

Figure 2: Risk of hospital mortality between groups in the awake prone position vs. non- prone position.



OR indicates odds ratio; 95% CI indicates confidence interval. Non-prone positioning group (supine or lateral) as reference. Abbreviations. AW-PP: awake prone positioning. Weighted population and adjusted by center and pandemic time.

Conclusion: In the study population, AW-PP for ≥ 6 h/day reduced the risk of endotracheal intubation and hospital mortality. This risk was further reduced with increasing exposure.

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Acute Respiratory Failure 9

000499

Performance of proportional assist ventilation plus (PAV+) after being challenged by a mechanical simulator

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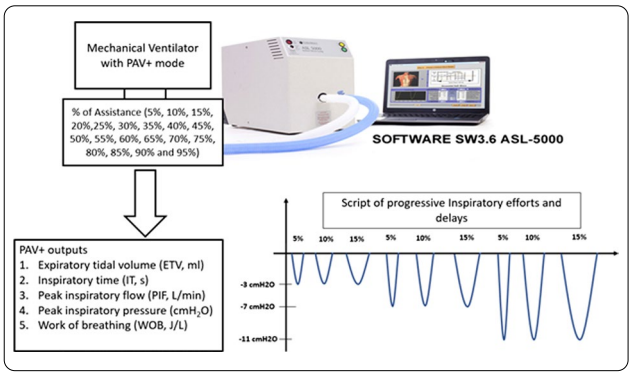
Intensive Care Medicine Experimental 2022, **10(2)**:000499

Introduction: In assisted mechanical ventilation, the work of breathing (WOB) should be shared by patient and ventilator. In PAV+, there is an association between respiratory muscle pressure and the pressure generated by the ventilator. There are still knowledge deficits about the influence of different types of inspiratory efforts on mechanical ventilator outputs during PAV+ assistance.
Objectives: Measure the four outputs of PAV+ ventilation: Expiratory tidal volume (ETV, mL), Inspiratory time (IT, s), Peak Inspiratory flow (PIF, L/min), Peak inspiratory pressure (PIP, cmH20) and Work of breathing (WOB, J/L) with a compliance of 100 ml/ cmH2O, a resistance of 10 cmH2O/L/sec and using a mechanical simulator (ASL-500 Ingmar Medical), in three different inspiratory efforts (-3, -7 and -11 cmH20) and three respective different inspiratory delays (5%, 10% and 15%) by 19 levels of PAV+ assistance (5 to 95%).
Methods: A mechanical simulator (ASL-5000 Ingmar Medical®) set with Compliance of 100 mL/cmH20 and resistance of 10 cmH20-L-s) was coupled to the Medtronic 980 (Purittan-Benett ®) mechanical ventilator in the Laboratory of Mechanical Ventilation of INCOR-Faculdade de Medicina Universidade de São Paulo, Brazil. We pre-programmed in the ASL5000 simulator software a sequential script of three different inspiratory efforts (-3, -7 and -11 cmH2O) and three different respective inspiratory delays (5%, 15% and 20%) (Figure A.1). Inspiratory effort was defined as the strength or capacity of the muscle to short and overcome a load (-3, -7 and -11 cmH20) and inspiratory delay was defined as % of the inclination to achieve the maximal peak inspiratory pressure effort (5%, 10% and 15%) (Figure 1).



The combinations started to run and there were triggered the ventilator 15 times for each of the 9 sequences, in 19 levels of PAV+ assistance (from 5 to 95%), totaling 2.565 combinations. The measured outputs from the ventilator were: Expired Tidal Volume (ETV: mL); Inspiratory time (IT: s); Peak inspiratory flow (PIF: cmH20); Peak inspiratory pressure (PP: cmH20); and Work of breathing (WOB) that were recorded in the ASL-5000_software and analyzed by R software for Windows, version 4.0.5.
Results: A exponential significant increase in ETV (from 88.46 mL to 1095.34 mL), IT (from 0.83 to1.64 s), PIF (from 10.88 to 125.53 L/min) and PP (from 7.53 to 33.23 cmH2O) were observed with the increase of both inspiratory efforts and PAV+ assistance. This increment was also amplified by the addition of 5%, 10% and 15% of inspiratory delays. There was a considerable increase in ETV with the increase of effort and delay, reaching a rise above 690% of the reference combination (effort of -3 cmH2O and delay of 5%, in level of assist by 10), that was the variable that had the most increase. The increase in IT occurred according to stronger or longer efforts, second one better than the first one, but less markedly than the other variables. PIF varied according to the changes in efforts combination. At PP, it is worth noting that for values of mode 10 and 50, the estimated medians growth a little with the delay (especially when the effort is -3 cmH2O), the inspiratory effort also has a greater influence on the PP gain than the inspiratory delay.
At % assistance of 10, the two works rise with minimal distances between them as the inspiratory efforts increased, meaning that the increase in the work of the "patient" was not fully compensated by the increase in the work of the ventilator. In % assistance of 50 and 80, the WOBpt and WOBtot evoluate with separation between the lines, revealing that the WOBpt was compensated by PAV+% of assistance increment as the inspiratory effort increase.
Conclusion: PAV+ responded promptly to increments of inspiratory effort and progressive increase of inspiratory assistance. Delaying the inspiratory muscle effort significantly booster PAV+' outputs proportionally to inspiratory efforts levels and PAV+% of assistance.

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Acknowledgements: The authors would like to thank Bruno de Castro Paul Schultze, Elisete da Conceição Quintaneiro Aubin, Rubens Santos Andrade Filho and Silvia Lopes de Paula Ferrari for performing statistical analyses.

000614

Corticosteroids for severe acute exacerbations of COPD in intensive care: from the French OUTCOMEREA cohort

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Intensive Care Medicine Experimental 2022, **10(2)**:000614

Introduction: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are a very frequent in intensive care unit (ICU). However, there are few data and conflicting results about corticosteroids therapy for critically ill patients with an AECOPD.
Methods: In this observational longitudinal cohort study, from OutcomeReaTM database with 32 french ICU centres participating, we assessed the impact of corticosteroid therapy for patients in ICU with a main diagnosis of AECOPD. The prescription of corticosteroids therapy at admission was defined as a daily dose $\geq$ 0.5 mg/kg of prednisone during the first 24 h after admission in ICU. We assessed the effect of corticosteroids on a main composite criteria including death and invasive mechanical ventilation (IMV) at day 28 after admission in ICU using an inverse probability of treatment weight (IPTW) estimator. Secondary outcomes were: survival analyse at D-28 and D-90, NVI failure, length of stay in ICU and in hospital, duration of ventilation and consumption of antibiotics and adverse effects of corticosteroids.
Results: We included 1,247 patients of which 31,4% was treated by a corticosteroid therapy at ICU admission. Corticosteroids administration at admission was significantly found as protector on the main composite outcome (RR = 0.693 [0.489; 0.98], p = 0.038). For the subgroup of patients with a very severe COPD, the protective effect of corticosteroid therapy on the primary composite outcome was not found (RR = 1,205 [0.577; 2.517], p = 0.6203). There was no significant impact of corticosteroids on failures of NIV, on lengths of stay in ICU and in hospital or on durations of ventilation. We did not observe statistical relation between the corticosteroid prescription at global prescription of antibiotics. However, corticosteroid therapy tended to be associated with longer duration of ATB treatment for patients in ICU at least 10 days (effect of corticosteroid therapy on antibiotic-free days at 10-day for the 395 patients with a length of stay in ICU $\geq$ 10 days: IRR = 0. 776[0.597; 1.009], p = 0.059)). Nosocomial infectious had the same prevalence in the two groups of patients. But the maximum systolic blood pressure and the levels of urea was higher and the glycemic disorders more frequent when patient received corticosteroids.
Conclusion: A corticosteroids administration at admission in ICU to patients with AECOPD had a protective effect on composite criteria including death or invasive mechanical ventilation at Day 28. Studies on doses to use or the profile of patients to treat are needed.

000678

Cohort study to evaluate the association between the time of starting early nutrition with days of invasive mechanical ventilation in patients with septic shock at the Dr. Mario Shappiro Critical Medicine Unit, ABC Medical Center, Mexico City

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Intensive Care Medicine Experimental 2022, **10(2)**:000678

Introduction: Mechanical ventilation (MV) refers to any artificial respiration procedure that uses a mechanical device to assist or replace ventilatory function and can also improve oxygenation and influence lung mechanics. MV is not a therapy, but rather a support that maintains the patient while the structural injury or functional alteration for which it was indicated is corrected. Severe sepsis causes diaphragmatic dysfunction and subsequent ventilatory failure, contributing to the respiratory failure seen in a large proportion of septic patients. Sepsis-induced diaphragmatic dysfunction and ventilator-induced diaphragmatic dysfunction share key signaling mechanisms, both processes involving the upregulation of proinflammatory cytokines and oxidative stress, which in turn can depress diaphragmatic function. However, few data are available on the interaction between sepsis and longer MV. It should be considered that there is a deterioration in the prognosis of life, deterioration in quality of life, increased medical care costs and increased care burden if there is difficulty in extubating the patient and prolonged ventilatory management is required. Nutritional support refers to the provision of enteral and/or parenteral nutrition. Although nutrition has been established as a mainstay of support and treatment in critically ill patients, despite the fact that no significant differences have been found in clinical outcomes, especially in terms of mortality, between patients with the highest and lowest levels of energy intake, the impact of this intervention on other endpoints being unknown, as most nutrition trials include all patients admitted to the ICU, but some implementations are restricted to patients with acute respiratory distress syndrome (ARDS) or those requiring mechanical ventilation.
Objectives: Verify the existence of an association between the start time of nutrition and the duration of invasive mechanical ventilation in patients with septic shock.
Methods: A prolective cohort study was carried out where patients with a diagnosis of septic shock and need for invasive mechanical ventilation (MVI) were included, the starting time was documented of nutrition regardless of the route of administration from their arrival,

this decision being independent of the study, according to the judgment of the treating physician. The severity of the current condition was estimated using prognostic scales such as SOFA, APACHE II and SAPS II, as well as the nutritional risk according to the NUTRIC Score since arrival. Daily follow-up of patients was given regarding the days requiring invasive mechanical ventilation and the provision of enteral or parenteral nutrition, and early start of nutrition was classified as those with start in the first 48 h after arrival at the unit or start late nutrition in those who started later. STATA was used for the statistical analysis, and it was carried out by means of Chi square and logistic regression test.

Results: One hundred and thirty-one patients with a diagnosis of septic shock were received under invasive mechanical ventilation, 110 patients were started on early nutrition and 21 patients were started on late nutrition. The average age was 69 years, 23% (31) of the total patients had DM, 42% (56) had SAH, and 51% (67) reported smoking. Regarding severity at admission, the median of SAPS II was 43 points, APACHE 17 points and SOFA 8 points, the average NUTRIC Score was 4 with no differences between both groups at the start of nutrition. The mean number of days of ventilation was 2 days for the total number of patients, with a longer IMV time in the late nutrition start group compared to both groups (2 days vs 5 days, $p = 0.012$). However, when adjusting for logistic regression, no statistically significant difference was found OR 0.13, CI (0.14–1.17) $p = 0.69$.

Conclusion: Although nutrition is considered a necessary support pillar in all critically ill patients with proinflammatory states such as sepsis, which influences pathophysiology in more than one way, according to our results, which are consistent with other primary points such as mortality, timing of start does not directly impact the days of invasive mechanical ventilation, so there is no evidence to refute the current recommendations.

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000724

Association between Integrated Pulmonary Index™ and ICU outcomes in patients under mechanical ventilation

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Intensive Care Medicine Experimental 2022, **10(2)**:000724

Introduction: Integrated Pulmonary Index™ (IPI) is an automatically calculated index which has demonstrated to predict the occurrence of respiratory compromise. However, its usefulness in critical care setting has not been evaluated.

Objectives: We aimed to evaluate the ability of IPI during the first 48 h after starting invasive mechanical ventilation (IMV) to predict outcomes (days on ventilator, extubation, reintubation, tracheostomy, intensive care unit (ICU) length of stay (LOS) and ICU mortality).

Methods: This is a prospective observational study in a polyvalent ICU. Patients needing IMV due to acute respiratory failure (ARF) who were monitored with capnography obtaining continuous IPI values during 24 h in a row were included. Two groups were done depending on the percentage of time in non-safe respiratory range (IPI ≤ 7): High Risk (HR, $\geq 50\%$) and Low Risk (LR, $< 50\%$). Demographic characteristics, chronic medical comorbidities, and a severity score at admission were recorded. At the first hour after starting IMV, parameters related with respiratory mechanics, ventilation, oxygenation, IPI value and related IPI parameters were also recorded. Defined outcomes were registered too.

Results: Data was analyzed from 53 patients, 36% in HR and 64% in LR. HR patients were older and presented COPD more frequently. PaO2/FIO2 ratio, EtCO2 and IPI value were higher in LR compared with HR who were extubated in a lower proportion (26% vs 38%, $p \leq 0.01$) and presented higher mortality (71% vs 19%, $p \leq 0.01$). IPI at one hour after starting IMV showed a good ability for mortality discrimination (AUC 0.688; 95% CI 0.539–0.837, $p = 0.027$). ICU LOS tended to be longer in LR than in HR [28 (11–47) vs 29 (15–55); $p > 0.05$]. A post-hoc analysis between survivors and non-survivors in both groups showed that while there were differences in the percentage of time spent in a non-safe respiratory range regarding IPI in HR group (70% vs 85%, $p = 0.029$), there were no differences in the LR group (17% vs 20%, $p = 0.719$). Only ventilatory ratio (VR) was significantly lower on LR non-survivors compared with HR non-survivors regarding respiratory mechanics. HR and LR non-survivors vs survivors presented less extubation rates.

Conclusion: IPI monitoring as an automatically calculated index, is useful in the first 48 h after starting mechanical ventilation to predict outcomes.

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000771

Behavior of Respiratory Drive and Muscular Pressure during Pressure Support Variation in COVID Patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000771

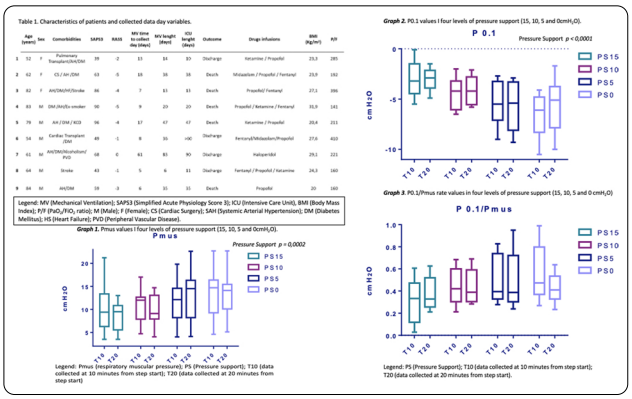
Introduction: The weaning phase in mechanically ventilated patients with COVID 19 seems to be more difficult when compared to other ARDS etiologies. Many patients seems to present an unappropriated muscular effort response to variation on pressure support.1,2 This fact can leads to self inflicted lung injury3 requiring high sedative doses4 resulting in a difficult in weaning process, long mechanical ventilation length and in a long period in Intensive Care Unit.

Objectives: Assess the variation of respiratory drive and muscular pressure during pressure support variation in COVID 19 patients.

Methods: This transversal study, approved by the institutional ethics committee, enrolled nine mechanically ventilated patients with ARDS due to COVID 19 during the weaning phase. (Table 1 – Population characteristics) The group was submitted to four levels of pressure support (15-10-5-0cmH2O). Respiratory muscular pressure was

measured using esophageal balloon, considering Baydur maneuvers, the relation Esophageal Pressure (Pes)/Air way occlusion pressure (Paw) were in an adequate range (0,8 – 1,2) 0.5,6 Pmus (muscular pressure) was considered as Delta Pcw (Chestwall pressure) – Pes. The respiratory drive was considered as P 0.1 value. The values were obtained at 10 and 20 min from the start of each level of Pressure Support (4 steps). The traces were analyzed with software LabVIEW. The measures of Pes were obtained from one minute mean cycle at 10 min from start of pressure support step and in the end of each pressure step. Two-way ANOVA test repeated measures was performed using GraphPad Prism version 6.00 for windows. P values < 0,05 was considered statistically significant.

Results: Nine patients traces were analyzed during weaning phase, at total 36 Pmus and P0.1 measures were performed. The median of all the measurements of Pmus were inversely proportional to PS decrease; Pmus median with PS15 was 9.45 (IQR 6.02–11.93); PS10 9.5 (IQR 8.15–12.85); PS5 12.55 (IQR 8.25–15.33) and PS0 14.4 (IQR 9.57–15.69) cmH2O. (p < 0,05)-Graph 1. P0.1 median values variated accordingly to the pressure support levels. P0.1 median with PS15 was -3.05 (IQR -4.07–-2.37); PS10 -4.2 (IQR -5.8–-3.27) PS5 -5.45 (IQR -7.12–-3.3). PS0 -5.35 (IQR -7.9–-4.55). (P < 0,05)-Graph 2. The P0.1/Pmus ratio was statistically different in each pressure support step. The median ratio in PS15 was 0.33 (IQR 0.22–0.48); PS10 0.41 (IQR 0.31–0.56); PS5 0.39 (IQR 0.32–0.69) PS0 0.46 (IQR 0.32–0.57). P0.1/Pmus was considered as a Respiratory drive/muscle effort ratio to characterize respiratory drive pattern response to pressure support variation. The P0.1/Pmus ratio median did not remain stable (p = 0,0047)-Graph 3.



Conclusion: An adequation and vigilance of Pressure Support by a good bed-side evaluation is essential to guide the mechanical ventilation settings to avoid respiratory muscles overload and poor outcomes.

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Acknowledgements: The authors received no financial support for the research.

000794

Physiologic effects of non-invasive ventilation compared to high flow nasal cannula postextubation in high-risk patients: Preliminary report of a randomized crossover study

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Intensive Care Medicine Experimental 2022, **10(2)**:000794

Introduction: Non-invasive ventilation (NIV) and high flow nasal cannula (HFNC) have been proposed as alternatives to prevent reintubation in patients at high-risk of weaning failure. However, these therapies have different mechanisms of action and their impact may vary accordingly. Although several trials have compared their clinical efficacy, no study has compared comprehensively their physiologic effects at the postextubation period.

Objectives: To compare the physiological effects of NIV versus HFNC in the post-extubation period in patients at high-risk of weaning failure.

Methods: This was a prospective randomized crossover study approved by the Institutional Scientific Ethics Committee of Pontificia Universidad Católica de Chile. Inclusion criteria were age > 18 years, mechanical ventilation (MV) for at least 48 h for an acute respiratory failure (PaO2/FiO2 < 300 mmHg), attending physician planned to perform a spontaneous breathing trial (SBT), and patients fulfilled criteria for high risk of weaning failure (age older than 65 years, MV more than 7 days, chronic lung or heart disease), and informed consent obtained. Before performing the SBT, a catheter with esophageal and gastric balloons, and electrodes to record the electrical activity of the diaphragm (Edi), was placed (Neurovent Research Inc). In addition, an electrical impedance tomography (EIT) belt was placed around the chest (Enlight, Timpel) and arterial and venous blood gases were analyzed, together with usual clinical signs. After extubation, patients were connected to NIV through full face mask with a single-limb noninvasive ventilator (Carina, Dräger) and to HFNC (AIRVO 2, Fisher and Paykel Healthcare) set at 50 L/min, for one hour each, in a random sequence. Throughout the study period patients were monitored with esophageal/gastric pressures, EAdi, EIT, arterial and central venous blood gases, and standard clinical variables.

Results: Ten patients (4 female) aged 57 ± 16 years were included. Patients had been on MV for 8.4 ± 2.6 days. Positive end-expiratory pressure and pressure support levels during NIV were 5.9 ± 1.1 and 6.7 ± 1.1 cmH2O, respectively. Compared with HFNC, NIV significantly increased tidal volume. However, no differences were observed in other ventilatory and hemodynamic variables and work of breathing.

Table 1. Physiological effects of HFNC and NIV

	HFNC	NIV	p-value
Heart rate, BPM	85 ± 10	85 ± 10	0.894
Mean arterial pressure, mmHg	93 ± 14	96 ± 17	0.106
Central venous pressure, mmHg	5 [0—6]	5 [1—7]	0.281
PaO2/FiO2, mmHg	269 ± 81	257 ± 47	0.830
PaCO2, mmHg	38 ± 4	37 ± 3	0.252
pH	7.44 ± 0.04	7.45 ± 0.04	0.214
Venous oxygen saturation, %	73 ± 8	75 ± 8	0.733
NT-proBNP, pg/mL	238 [104–666]	259 [104–736]	0.263

	HFNC	NIV	p-value
Troponin C, pg/mL	13.7 [6.85–21.9]	13.1 [6.9–21.3]	0.185
Respiratory rate, BPM	20 ± 3	19 ± 5	0.238
Tidal volume, ml	350 ± 129	426 ± 132	0.024
Minute volume, L/min	6.3 ± 3.1	7.09 ± 3.3	0.158
Ventilatory ratio	1.10 [0.79–1.29]	1.12 [1.04–1.29]	0.578
ΔEdi, μV	9.4 [7.9–12.5]	8.2 [6.9–16.2]	0.312
Neuroventilatory efficiency, ml/μV	36 [19–42]	34 [24–67]	0.468
ΔPes, cmH2O	6.6 [5.3–10.7]	6.9 [5.7–8.8]	0.425
PTP, cmH2O*s	6.8 [4.4–10.2]	6.0 [5.0–8.0]	0.312
PTP/min, cmH2O*s/min	115 [80–183]	114 [89–140]	0.744

Results are presented as median [interquartile range] or mean ± standard deviation. Paired t-test or Wilcoxon signed-rank test.

Conclusion: In the post-extubation period of patients at high risk of weaning failure, no differences were observed between NIV and HFNC in terms of gas exchange, work of breathing, or end-expiratory lung volume.

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Acknowledgements

1. FONDECYT N ° 1191709
2. CONICYT-PFCHA/Doctorado Nacional 2020-folio 2120175

000803

Assessment of the validity of Berlin definition of ARDS in patients with COVID-19-related respiratory failure and high-flow nasal oxygen requirement: A multicenter prospective cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000803

Introduction: The Berlin definition of acute respiratory distress syndrome (ARDS) was constructed considering feasibility, reliability, face and predictive validity (1). Patients with COVID-19-related acute respiratory failure (ARF) and high-flow nasal oxygen (HFNO) requirement who otherwise meet ARDS criteria are not included in this definition (2). Recent studies have evaluated the practical implications of extending the Berlin definition to these patients (3). However, the predictive validity of the definition as applied to this population has not been evaluated.

Objectives: Primary: to assess the predictive validity of the Berlin definition of ARDS in non-ventilated patients with COVID-related respiratory failure who require HFNO and otherwise meet ARDS criteria. Secondary: a) to assess the predictive validity of the definition in specific subgroups; b) to assess ventilator-free days at day 28 (VFD) in each severity group.

Methods: This multicenter prospective cohort study carried out in 6 ICUs of Argentina consecutively included patients > 18 years with confirmed COVID-19 related ARF requiring HFNO, from June, 2020 to December, 2021. It is part of the "Argentine Collaborative Group on High Flow and Prone Positioning Cohort" (4). The initiation, monitoring, and termination of treatment with HFNO and awake prone position were protocolized (5). Patients meeting the following criteria were included: a) arterial blood gas evaluation after initiation of HFNO; b) PaO2/FiO2ratio (P/Fratio) < 300 mmHg. in supine position; b) bilateral opacities on standard chest X-ray or computed tomography; c) worsening respiratory symptoms for < 1 week. We described patient characteristics, mortality according to ARDS severity (mild, moderate, and severe -P/Fratio < 300, < 200 and < 100 mmHg. respectively), and assessed the predictive validity using receiver operating characteristic curves (AUC). Additionally, the same analysis was restricted to the following subgroups: a) patients who subsequently required invasive mechanical ventilation (IMV); b) patients who performed awake-prone position > 6 h/d; and c) patients with moderate and severe ARDS categories.

Results: During the study period 565 were included. The characteristics of patients are shown in Table 1. 134 (23%) died within 28 days: 10 (16.6%) with mild, 60 (19.2%) with moderate, and 64 (31.5%) with severe ARDS. The AUC for mortality at day 28 in the overall population was 0.585 95%CI (0.535–0.635); when adjusted for age and sex the AUC value increased to 0.747 95%CI (0.701–0.793). One hundred ninety-nine patients (34%) required IMV, 330 patients (57.4%) tolerated > 6 h/d in the prone position and 515 (91%) were classified as moderate or severe ARDS. The AUC for each group was similar to the overall population. VFD for each category are shown on Table 1.

	Mild (n = 60)	Moderate (n = 312)	Severe (n = 203)
Age, years, median (p25,75)	56 (44–65)	59 (47–68)	62 (52–72)
Male, sex, n (%)	39 (65)	225 (72.1)	143 (70.4)
Diabetes, n (%)	20 (33.3)	73 (23.5)	48 (23.6)
Hypertension, n (%)	27 (45)	126 (40.5)	84 (41.4)
BMI, median (p25,75)	31.7 (28.4–35)	30 (27.7–35)	30 (27.2–33.6)
APACHEII, median (p25,75)	11 (8–15)	11 (7–15)	12 (8–17)
IMV, n (%)	19 (31.7)	91 (29.7)	89 (43.8)
VFD 28 d, median (p 25–75)	21 (15.5–24)	22 (16–25)	19 (10–23)

Conclusion: The predictive validity of the definition of ARDS in patients with COVID-19-related respiratory failure and HFNO requirement was similar to that of the population originally described in the Berlin Consensus AUC 0.577 95%CI (0.561–0.593). This validity was consistent across the different subgroups evaluated and improved when adjusted for age and sex. Assuming that the criteria of feasibility, reliability, and face validity are applicable to the population evaluated, these results support the use of this definition in these patients.

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000812

Characteristics and outcomes of critically ill pregnant/postpartum women with COVID-19 in The Republic of Srpska (B&H), single centre report

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Intensive Care Medicine Experimental 2022, **10(2)**:000812

Introduction: Coronavirus disease 2019 (COVID-19) is a novel infectious disease which spread worldwide. As of the March 5th 2020, COVID-19 pandemic has resulted in approximately 111,800 cases and 6330 deaths in the Republic of Srpska (Bosnia and Herzegovina).
Objectives: Our objective in the present study was to determine characteristics and outcomes of critically ill pregnant/puerperalwomen with COVID-19 in the Republic of Srpska.
Methods: The retrospective observational study of prospectively collected data included all critically ill pregnant/puerperal women with COVID-19 in university-affiliated hospital between April 1st 2020 and April 1st 2022. Infection was confirmed by real-time reverse transcriptase-polymerase chain-reaction (RT-PCR) from nasopharyngeal swab specimens and respiratory secretions. Patients' demographics, clinical and laboratory data, pharmacotherapy, and neonatal outcomes were analyzed.
Results: Out of 153 registered pregnant women with COVID-19 infection treated at gynaecology department of University Clinical Centre of the Republic of Srpska, 19 (12%) critically ill pregnant/puerperalwomen [median age of 36 (IQR, 29–38) years] were admitted to the MICU. Mortality rate was 21% (four patients) during study period. Of all patients (19), fourteen gave birth (74%) and four (21%) were treated with veno-venous extracorporeal membrane oxygenation (vvECMO). Fourteen infants were born prematurely and none of them died during hospitalisation.
Conclusion: High mortality rate was detected among critically ill pregnant/parturient patients treated in the MICU. Main predictors of mortality were the need of vvECMO and invasive mechanical ventilation. Preterm birth rate is high in patients who require higher level of life support (vvECMO and ventilatory support).

000822

Novel subgroups in acute respiratory failure based on the trajectories of three endotheliopathy biomarkers – a cohort study

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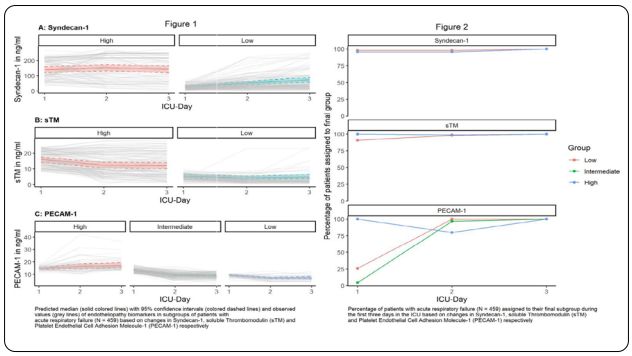
Introduction: Endotheliopathy at baseline is associated with worse outcomes in acute respiratory failure (ARF) (1), but the significance of the development in endotheliopathy during the first days of ARF is unknown.
Objectives: To determine if patients with ARF can be divided into subgroups with different prognoses based on the changes over time in Syndecan-1 (2,3), soluble Thrombomodulin (sTM) (4,5) and Platelet Endothelial Cell Adhesion Molecule-1 (PECAM-1) (6,7)?
Methods: Single-center prospective cohort including 459 patients with ARF requiring mechanical ventilation (MV). We measured Syndecan-1, sTM and PECAM-1 in plasma daily for three days and divided patients into subgroups using latent class mixed modelling (8). We correlated subgroups with clinical outcomes using Cox-regression.
Results: Based on Syndecan-1 and sTM, we identified two subgroups for each biomarker respectively (Figure 1). Based on PECAM-1, we identified three subgroups (Figure 1). Only for PECAM did the subgroup assignment change during ICU-Day 1–3 (Figure 2). Patients with persistent high levels of sTM were liberated from MV at a lower rate (Group High vs. Group Low, HR 0.66, 95% CI 0.50–0.88, p = 0.01) as were patients with persistent high levels of PECAM-1 (Group High vs. Group Low, HR 0.59, 95% CI 0.37–0.93, p = 0.02). Patients with persistent high PECAM-1 died on MV at a higher rate (Group High vs. Group Low, HR 3.48, 95% CI 1.21–10.06, p = 0.02). Patients with persistent high sTM had higher 30-day mortality (Group High vs. Group Low, HR 1.90, 95% CI 1.20–3.01, p = 0.01) as did patients with persistent high PECAM-1 (Group High vs. Group Low, HR 4.25, 95% CI 1.99–9.07, p < 0.01).



Conclusion: In ARF requiring MV, patients with persistent high levels of sTM and PECAM-1 had lower rates of liberation from MV and higher 30-day mortality. However, patients with persistent high levels of sTM were identifiable at baseline and only the trajectory of PECAM-1 added additional information.

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Acknowledgements
1. AP Møller Foundation
2. The Research Foundation at North Zealand's Hospital
3. Hindsgavl Symposium
4. Danmarks Frie Forskningsfond

001418

Effect of dexamethasone in patients with ARDS and COVID-19 (REMED trial) – prospective, multi-centre, open-label, parallel-group, randomized controlled trial

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Introduction: Since December 2019, SARS-Co-2 virus has infected millions of people worldwide. In patients with COVID-19 pneumonia in need for oxygen therapy or mechanical ventilation, dexamethasone 6 mg per day is currently recommended (1). However, the dose of 6 mg of dexamethasone is currently being reappraised as important therapeutic potential of higher doses of corticosteroids can be missed (2,3).
Objectives: To assess superiority of dexamethasone 20 mg (dexamethasone 20 mg on day 1–5, followed by dexamethasone 10 mg on day 6–10) vs 6 mg administered once daily intravenously for 10 days in adult patients with moderate or severe ARDS due to confirmed COVID-19.
Methods: A prospective, open-label, randomised controlled trial was conducted between February 2021 and March 2022. Primary endpoint was number of ventilator-free days (VFDs) at 28 days after randomisation. Secondary endpoints were mortality from any cause at 60 days after randomisation, dynamics of inflammatory markers, change in WHO Clinical Progression Scale at Day 14 and adverse events related to corticosteroid. REMED was registered in EudraCT No.:2020-005,887-70 and ClinicalTrials.gov: NCT04663555.
Results: 234 participants was enrolled. Results will be presented during the LIVES 2022 in Paris.
Conclusion: Results will be presented during the LIVES 2022 in Paris.

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Acknowledgements: Supported by the national budget through MEYS, RI CZECRIN (LM2018128) and from ERDF Project CZECRIN_4 PATIENTS (CZ.02.1.01/0.0/0.0/16_013/0001826) and by MH CZ - DRO (FNBr, 65269705) and Endowment fund Donatio Intensivistam (VAT No 0907206).

Acute Respiratory Failure 10

000579

Relation between lung ultrasound patterns and lung injury associated biomarkers in COVID-19 pneumonia

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Intensive Care Medicine Experimental 2022, **10(2)**:000579

Introduction: Lung ultrasound (LUS) has shown to be a valuable bedside tool to diagnose and monitor COVID-19 pneumonia. Moreover, markers of epithelial and endothelial cells, immunity markers and inflammatory markers have shown to be predictors of severity and mortality in patients with COVID-19 pneumonia. However, little is known about the relation between LUS patterns and these biomarkers. The aim of this study is to assess the relation between LUS patterns and distinct profiles of systemic and pulmonary lung injury markers. Another aim was to assess the relation between lung morphology and lung injury biomarkers.
Methods: A secondary analysis of three prospective observational studies of adult patients with laboratory-confirmed COVID-19 admitted to the general ward or ICU was conducted. Patients who have had a LUS examination at admission and whose biomarkers were available were included. The relation between LUS scores and lung injury biomarkers was assessed, as well as the difference between biomarkers concerning certain lung ultrasound patterns. Spearman's correlation, Wilcoxon Rank-Sum and ANOVA analyses were used in order to assess the study's objectives.
Results: Forty-three patients were included. LUS scores, lung aeration and pleural characteristics did not demonstrate a clear relation with lung injury biomarkers. In patients with non-focal lung morphology higher levels of various endothelial (sTM, vWF-A2), epithelial (SP-D), inflammatory (TNF-R1 and procalcitonin) and immune system (GAS6 and uPAR) biomarkers were found.

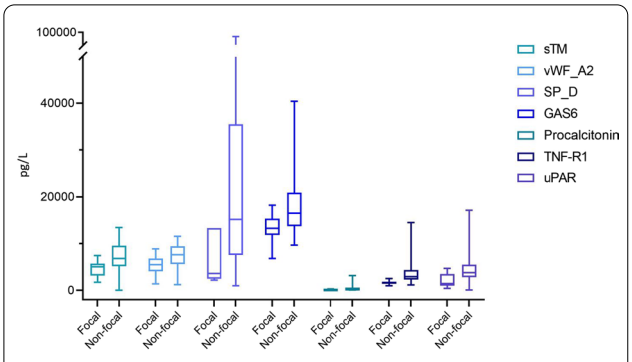

Figure 1: Boxplots of statistically signifcant ($p < 0.05$) differences of biomarker levels between lung morphology (focal and non-focal) groups.

Conclusion: LUS scores, lung aeration and pleural characteristics do not appear indicative of certain lung injury patterns. The classification of lung morphology as focal or non-focal through LUS exams might provide more insight in the ongoing pathophysiological process of lung injury in patients with COVID-19 pneumonia. However, no distinct pathophysiological pattern can be identified. These findings indicate the lack of a clear correlation between LUS imaging and lung injury biomarkers in these patients.

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Acknowledgements: Nothing to declare.

000704

Comparison of intubations in covid-19 versus non-covid-19. National multicenter study of intubation in critical ill patients (INTUPROS study)

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Intensive Care Medicine Experimental 2022, **10(2)**:000704

Introduction: In ICU, intubation should be always considered as a high-risk procedure (1) During Covid 19 pandemic some societies develop recommendations for airway management of these patients (2).
Objectives: To compare the characteristics of intubations in COVID-19 patients versus those of NON-COVID-19 in a cohort of critically ill patients.
Methods: Prospective, multicenter study (NCT03916224). 43 Spanish ICUs (6 months from April 2019 to October 2020). We include all intubations performed in adults, excluding those performed due to cardiac arrest. Some of the variables included were: demographic characteristics, comorbidities, body mass index, APACHE-II, the reason for intubation, the device used, method of pre-oxygenation, professional operator, drugs used, major complications, intubation at the 1st attempt, and mortality. Continuous variables are expressed as medians (25th-75th percentile) and categorical variables as %. Quantitative variables were analyzed with U-Mann–Whitney and qualitative variables with chi-square, $p < 0.005$. Ethics committees approval was obtained from each hospital.
Results: 1837 patients were included. 322 (17.5%) had COVID-19. COVID-19 patients intubated presented more obesity, fewer comorbidities, longer time until intubation, more prior use, and pre-oxygenation with HFNC, less previous use of vasopressors, more rate of intubation in the 1st attempt, more use of video laryngoscopy, more use of ketamine and NMBA, more intubation at the 1st attempt, less incidence of access difficult airway and more serious complications but less hospital mortality (Table 1).

	COVID-19 (n = 322)	No COVID-19 (n = 1515)	p
BMI	28.7 (25.5–32.8)	26.7(23.7–30.7)	< 0.001
Heart Failure	19 (5.9%)	194 (12.8%)	< 0.001
CKD	16 (5.0%)	141 (9.3%)	0.011
Cirrhosis	12 (3.7%)	109 (7.2%)	0.023
COPD	31 (9.6%)	223 (14.7%)	0.001
APACHE II on admission	16 (12–21)	20 (14–25)	< 0.001
SOFA on admission	5 (4–7)	6 (4–9)	< 0.001
SOFA intubation	5 (4–8)	7 (4–10)	< 0.001
Time until intubation	0 (0–1)	0 (0–3)	< 0.001
Previous use of HNFC	124 (38.5%)	375 (24.8%)	< 0.001
Previous use of NIV	64 (19.9%)	441 (29.1%)	0.001
Pre-oxygenation with HNFC	100 (31.2%)	224 (15.0%)	< 0.001
Pre-oxygenation with balloon	154 (48.7%)	1248 (83.4%)	< 0.001
Pre-oxygenation with NIV	39 (12.3%)	307 (20.5%)	0.001
Previous use of vasopressors	60 (18.6%)	499 (32.9%)	< 0.001
Secretions in the oropharynx	289 (89.8%)	1008 (67.1%)	< 0.001
First deputy operator	199 (61.8%)	882 (58.2%)	< 0.001
Use of stylet	208 (64.6%)	852 (56.5%)	0.008
Use of video laryngoscopy	118 (36.6%)	215 (14.2%)	< 0.001
Use of Frova Guide	26 (8.1%)	76 (5.0%)	0.030
Ketamine use	292 (90.7%)	1424 (94.0%)	0.030
Use of NMBA	311 (96.6%)	1258 (83.0%)	< 0.001
Intubation at 1st	243 (75.5%)	1057 (69.8%)	0.041
Difficult airway	28 (8.7%)	202 (13.3%)	0.022
Complications	188 (58.4%)	626 (41.3%)	< 0.001
Hospital mortality	102 (32.7%)	631 (41.9%)	0.003

Conclusion: COVID-19 patients have specific characteristics regarding intubation with a higher rate of complications, but lower hospital mortality. A differential management compared to non-COVID patients should be proposed.

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000788

Awake ECMO in COVID-19 – a proof of concept

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Intensive Care Medicine Experimental 2022, **10(2)**:000788

Introduction: Venovenous extracorporeal membrane oxygenation (VV-ECMO) was largely used to support patients with severe hypoxemia related to COVID-19. Usually, refractory acute respiratory failure (hypoxemia, hypercapnia, or both) under optimized mechanical ventilation (MV) are the most widely applied selection criteria for VV-ECMO. Awake ECMO strategy may limit perpetual ventilator induced injury and allow early rehabilitation.
Objectives: We aim to report the outcomes of two subgroups of VV-ECMO treated patients with severe COVID-19: conventional strategy vs. awake ECMO strategy.
Methods: Retrospective review of prospectively collected data from an ECMO referral centre. All COVID-19 patients treated with VV-ECMO were included. Baseline characteristics, outcome, VV-ECMO duration, mechanical ventilation days, delirium and ICU acquired weakness (AW) was collected. Two groups were defined: group 1 included patients treated with conventional strategy, in whom ECMO decannulation was performed before MV weaning; group 2 included patients with spontaneous breathing achieved before ECMO decannulation.
Results: 92 patients were treated with VV-ECMO support and included in this study (male: 71%). Mean age was 50 ± 12.1. Average SAPS was 35 ± 14, admission SOFA score 6 ± 3, and mean SOFA score on cannulation day was 6 ± 3. A total of 34 patients underwent awake ECMO, 2 were never on MV. 58 patients were treated with conventional approach, with extubation performed before ECMO decannulation. There was no significant difference regarding patient characteristics or severity among patients who were on awake ECMO strategy. Median time on awake ECMO was 9 days, ranging between 1 to 112 days. Overall mortality was 23.9% and only 2.9% (n = 1) in the awake ECMO group. Higher SOFA at cannulation (OR 0.786, CI 95% 0.651–0.950) and higher body mass index were predictors of lower probability of awake ECMO (OR 0.923, CI 95% 0.855–0.997). Considering only survivors in the two groups, awake ECMO was protective for delirium (OR:0.3, p = 0.03 CI 0.09 -0.911), even though time on neuromuscular blockage agents (NMBA) and ICU acquired weakness (AW) incidence was similar between the two groups. Overall, neuromuscular blockage agents (NMBA) (OR 1.16, CI 95% 1.06–1.27), AW (OR 0.04, CI 95% 0.005–0.26), PEEP at cannulation (OR 0.6219, CI 0.44–0.86) and running an awake ECMO course (OR 0.08, CI 95% 0.009 – 0.73) were mortality predictors in multivariable analysis.
Conclusion: Patients selected for awake ECMO were those with an improving condition that allowed for NMBA and sedation interruption, with lower likelihood in the obese and with higher SOFA at cannulation. The authors acknowledge bias due to lack of patient randomization. AW is unsurprisingly associated with survival because its diagnosis requires an awake patient, fit for rehabilitation. Our results show that awake ECMO is feasible with very low mortality in COVID-19 patients.

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000809

Timing of intubation and ICU mortality in COVID 19 patients. Retrospective preplanned analysis of 4198 critically ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000809

Introduction: Approximately 10% of patients with COVID 19 pneumonia can develop ARDS and require ICU admission. Although it has been demonstrated that delay intubation in patients with ARDS increase mortality, it is not so clear in case of COVID 19 pneumonia. Many patients present severe hypoxemia without symptoms of respiratory failure. This, added to the lack of mechanical ventilation devices, has made that some patients were not intubated as soon as guidelines indicate, showing that non invasive respiratory devices could avoid intubation and mechanical ventilation complications. However, some authors defend that delay intubation can produce self-induced lung injury and worsen the prognosis.
Objectives: Our objective is to evaluate if delay intubation in patients with COVID 19 pneumonia increase mortality risk.
Methods: Observational, retrospective, milticentre, preplanned study with prospectively collected data of COVID-19 patients admitted to ICU since February 2020 to March 2021. Adults admitted to ICU with COVID-19 pneumonia and acute respiratory failure were included. Patients with "do not intubate" order and those with missing data were excluded.
Demographic, clinical and laboratory variables were collected, as well as APACHE and SOFA scores, time to intubation, type of non invasive respiratory support at admission and outcomes.
Three cut-off were stablished for time to intubation: 1) Very early: patients intubated before or at ICU admission; 2) Early: within 24 h after ICU admission and 3) Late: beyond the first 24 h from ICU admission. We compared mortality, ICU length of stay and mechanical

ventilation days between groups. Chi square or U Man-Whitney test were used as appropriate. The impact of intubation time in mortality was assessed with binary logistic regression. It was considered significant $p < 0.05$.

Results: A total of 4198 patients were included, with a median of 63 years old (54–71), 70.8% male, with a medium SOFA of 4 (3–7), APACHE of 13 (10–18)] and PaO2/FiO2 of 131 (100–190) at admission. ICU mortality was 30.2% and ICU length of stay was 14 days (7–28).

A total of 2024 (48.2%) patients were intubated very early, 928 (22.1%) early and 441 (10.5%) late. Late group had higher mortality compared to early group (36.9% vs 31.6%, $p < 0.05$), although they were younger (62 vs. 64, $p < 0.05$), with less APACHE (13 vs. 14, $p < 0,05$) and SOFA (3 vs.4, $p < 0,05$) scores and higher PaO2/FiO2 at admission (116 vs. 100, $p < 0,05$). Late intubation was independently associated with mortality (OR = 1.83; 95%CI 1.35–2.47). The use of non invasive ventilation at admission is independently associated with higher risk of death (OR = 1.93, 95%CI 2.3–3.3). No differences were observed in ICU (25 vs. 19, $p = 0.97$) and hospital length of stay (41 vs. 35, $p = 0.7$) nor mechanical ventilation days (15 vs. 15, $p = 0.62$).

Conclusion: Delay intubation beyond the first 24 h of admission in patients with COVID 19 pneumonia increase mortality risk.

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000823

Timing of intubation, ventilatory mechanics and mortality in a cohort of coronavirus disease 2019 patients with severe ARDS. A single center's study

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Intensive Care Medicine Experimental 2022, **10(2)**:000833

Introduction: Increasing time to intubation and mechanical ventilation (MV) may have important effects in patients' outcome.

Objectives: We investigated the ventilatory mechanics and the impact of time of intubation on clinical outcome in patients with COVID-19.

Methods: Prospective, observational, single-center study of patients hospitalised in the Intensive Care Unit (ICU) between February, 2021, and February, 2022. The primary outcome was the impact of intubation timing in patients' survival. The time of intubation was defined as early ($\leq$2 days from hospital admission) or late (>2 days). Secondary outcomes included ventilatory mechanics, MV duration, ICU length of stay (LOS) and ICU mortality.

Results: We included 194 consecutive intubated patients (pts): 66.5% male, median age 65 years old. 136 pts (70,1%) were intubated late and 58 (29,9%) early. ICU mortality was 64% while mortality in early intubated (EI) pts was 44% compared to 72% in late intubated (LI) pts ($p < 0.001$, Figures 1A and 2). Survivals were intubated earlier (3.5 vs 7 days; $p < 0.001$, Fig. 1B). EI pts had similar BMI, admission PaO2/FiO2 ratio, plateau pressure, driving pressure, MV days, ICU LOS and comorbidity number, but were younger, and had lower SOFA score compared to LI pts. EI pts had higher compliance at admission days 1, 6 and 12. Older age, late intubation, lower PaO2/FiO2 ratio, lower compliance, higher SOFA score and higher comorbidity number were independently associated with mortality. After adjusting for age, late intubation continued to be an independent mortality factor.

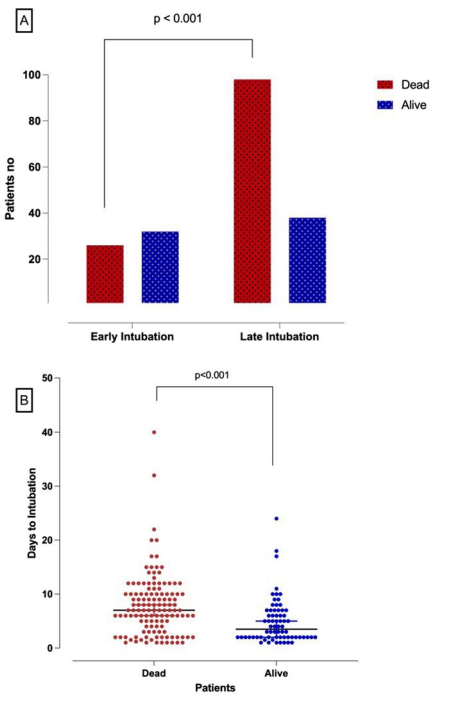

Figure 1: Mortality difference between patients with early and late intubation (A) and difference in days to intubation between patients (dead vs alive) (B)

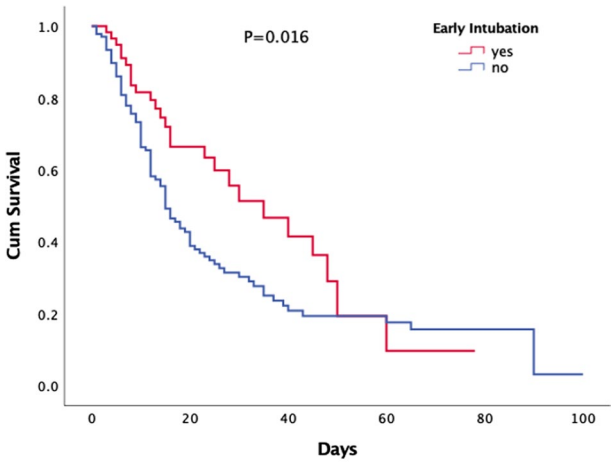

Figure 2: Survival difference in patients with early vs late intubation

Conclusion: In intubated COVID-19 patients, late intubation, older age, lower PaO2/FiO2 ratio, lower compliance, higher SOFA scores and comorbidities associated with increased ICU mortality.

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000838

The experience with high-dose dexamethasone for the management of acute respiratory distress syndrome in patients with moderate and severe COVID 19: A retrospective study

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Intensive Care Medicine Experimental 2022, **10(2)**:000838

Introduction: There is currently no concrete evidence on the ideal dose of corticosteroids for the management of Acute Respiratory Distress Syndrome (ARDS), but the use of low doses of dexamethasone has been shown to reduce mortality in cases of COVID 19 1. After the publication of the Recovery study with the use of dexamethasone at a dose of 6 mg daily for 10 days, the dose began to be questioned in more severe cases and some centers around the world started to adhere to the scheme proposed by the DEXA-ARDS study 2,3.
Objectives: The main objective of this study was to evaluate the safety and efficacy of dexamethasone at the dose recommended by DEXA-ARDS in patients who after at least 10 days from symptom onset presented a worsening of the respiratory function, receiving intravenous high-dose dexamethasone (20 mg daily for 5 days followed by 10 mg daily for 5 more days) in adult patients with moderate or severe ARDS due to confirmed COVID-19, especially with regard to infectious complications and other outcomes such as mortality and impact on respiratory support parameters after 28 days.
Methods: This retrospective observational study was conducted at the Intensive Care Unit of Hospital São Domingos, in São Luís do Maranhão, Brazil. We included 33 patients with COVID-19 pneumonia and moderate or severe ARDS, according to the Berlin definition, between February 2021 and February 2022, who received the referred dose of dexamethasone after excluding active infectious complications at that moment. In addition to the primary outcome of evaluating ventilatory improvement over 10 days, we also analyzed mortality, complications, the curve of inflammatory biomarkers and mechanical ventilation parameters on days 1, 5, 10 and 14 of the beginning of the regimen.
Results: Most patients were male (66%) with a mean age of 52 years. Hypertension and diabetes mellitus were the most prevalent comorbidities. After treatment with dexamethasone, significant improvement in the first 10 days in PaO2/FiO2 (148 [68–291] mmHg vs. 235 [95–485] mmHg, $p < 0.001$) and driving pressure (16 [9–28] cmH2O vs. 15 [8–28] cmH2O, p 0.08) were observed. The 28-day mortality in the group was 18%, and we identified that 90.1% of the patients presented infectious complications during the first 28 days, but without correlation with mortality (p 0.54), even among those who used tocilizumab in association (p 0.82). We also identified that patients who were unable to obtain protective mechanical ventilation with a driving pressure of less than 15 cmH2O on the 5th day of initiation of the regimen had higher mortality (p 0.03).
Conclusion: These data show that the use of high dose dexamethasone can contribute to pulmonary recovery in patients with moderate and severe forms of ARDS due to COVID 19, with a good safety profile, supporting the need for additional randomized clinical trials with higher doses of dexamethasone in patients with ARDS.

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Acknowledgements: The author(s) received no financial support for the research, authorship, and/or publication of this article.

000853

Variance of flow, pressure, tidal volume by non-invasive bilateral electromagnetic phrenic nerve stimulation

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Intensive Care Medicine Experimental 2022, **10(2)**:000853

Introduction: Mechanical ventilation (MV) is the most used short-term life support worldwide and a potentially lifesaving intervention in critically ill patients [1]. Nevertheless, diaphragm atrophy and loss of diaphragm strength are known side-effects of ventilator-induced diaphragm dysfunction (VIDD). VIDD correlates with difficult liberation from MV, longer ICU stay, and increased ICU mortality, and longer MV time [2]. Non-invasive bilateral electromagnetic phrenic nerve stimulation could prevent or counteract VIDD through diaphragm activation and contraction in MV patients [3–4].
Objectives: To investigate the stability of respiratory parameters stimulated by non-invasive bilateral and synchronous electromagnetic phrenic nerve stimulation.
Methods: Subsequently to induction of anaesthesia, intubation, and reversal of the muscle relaxant, five ASA I/II patients scheduled for

elective surgery with general anaesthesia received bilateral non-invasive electromagnetic stimulation of the phrenic nerves with magnetic field intensity of 20%, 30% and 40% consecutively. The frequency and duration of the stimulation signal were set to 25 Hz and 2 s, respectively. Flow, pressure, and tidal volume were directly recorded from the ventilator.
Results: The variance of the stimulated tidal volume generated was 1,13 ml/kg, 6,11 ml/kg and 11,59 ml/kg at 20%, 30% and 40% intensity, respectively. The higher the intensity was set, the more difficult it was to generate a stable tidal volume. Moreover, the variance was in relation to the mean considerably high at all intensities (Figure 1).
The positive peak flow during the stimulated breaths had a rising variance through the first two intensity steps, and decreased slightly afterwards (38,02 vs 78,30 vs 88,38 L/min, respectively). The variance of the negative peak flow at 30% intensity was marginally higher than at 20% (37,63 vs 17,20 L/min, respectively). At 40% intensity the variance dropped to 34,60 L/min.
The variance of the positive peak pressure at 20% and 40% intensity (1,39 mBar; 1,08 mBar) were both higher than at 30% intensity (0,52 mBar) and were high relatively to the mean at all intensities. The variance of the negative peak pressure increased with intensity (0,05 mBar vs 0,17 mbar vs 1,57 mBar, respectively).

Respiratory parameter	Intensity	N	Min.	Max.	Mean	Std. Deviation	Variance (%)
Positive peak flow (L/min)	20%	50	2,75	24,82	13,35	6,17	38,02 (285)
	30%	49	15,12	44,64	27,11	8,85	78,30 (289)
	40%	50	25,27	57,55	42,65	9,40	88,38 (207)
Negative peak flow (L/min)	20%	50	-16,95	-2,49	-9,73	4,15	17,20 (177)
	30%	50	-33,77	-11,95	-20,92	6,13	37,63 (180)
	40%	50	-37,67	-15,68	-26,35	5,88	34,60 (131)
Positive peak pressure (mBar)	20%	50	0,73	4,80	1,90	1,18	1,39 (73)
	30%	50	1,63	4,11	2,59	0,72	0,52 (20)
	40%	50	1,88	6,36	3,25	1,04	1,08 (33)
Negative peak pressure (mBar)	20%	50	-0,92	0,06	-0,50	0,23	0,05 (11)
	30%	50	-2,02	-0,53	-1,24	0,41	0,17 (13)
	40%	50	-6,59	-0,99	-2,71	1,25	1,57 (58)
Tidal volume (mL/kg)	20%	50	0,20	4,05	1,79	1,06	1,13 (63)
	30%	50	1,76	10,21	4,48	2,47	6,11 (136)
	40%	50	0,23	13,72	7,07	3,40	11,59 (164)

Figure 1.. Descriptive statistics of tidal volume (mL/kg), positive and negative peak flow (L/min), positive and negative peak pressure (mbar) during non-invasive bilateral phrenic nerve stimulation at magnetic field intensities of 20%, 30% and 40%

Conclusion: The reproducibility of aimed tidal volumes, positive peak flows and negative peak pressures decreases with magnetic field intensity set in non-invasive bilateral phrenic-nerve electromagnetic stimulations. Negative peak flow and positive peak pressure do not seem be depended on the magnetic field intensity in their reproducibility.

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Acknowledgements: This investigator initiated study was partly funded by STIMIT AG, Biel, Switzerland.

000857

Acid–base disorders in critically unwell patients with COVID-19 prior to initiation of mechanical ventilation

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Intensive Care Medicine Experimental 2022, **10(2)**:000857

Introduction: During the coronavirus disease 2019 (COVID-19) outbreak, multiple studies have investigated laboratory biomarkers in the management and prognostication of COVID-19 patients; however, few have investigated acid–base disturbances (Alfano et al. 2022), and none in the most unwell cohort of patients. This study aims to assess the arterial blood gas (ABG) pattern in a cohort of patients before their imminent invasive mechanical ventilation (IMV), as well as the patterns of acid–base and their association with clinical features, such as pulmonary embolus (PE) or renal dysfunction, and outcomes, including intensive care unit (ICU) length of stay and mortality.
Methods: A single-centre retrospective, observational study in dedicated COVID-19 ICUs at a tertiary teaching hospital in patients with clinical COVID-19 and positive SARS-CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) who received intubation and mechanical ventilation from 1st March 2020 to 1st March 2021. Demographic, ICU length of stay, arterial blood gas (ABG), serum electrolytes, renal function data and the presence of a PE were extracted from an electronic health record. A validated medical software (ABG-a) was used for the automatic and objective interpretation of all ABGs (Rodriguez-Villar et al. 2021, Rodriguez-Villar et al. 2020). Only ABG samples taken before imminent intubation were included (closest to time of induction). One hundred and seventy-eight patients were included in the final analysis. Parametric and non-parametric distributed quantitative variables were compared using the student's t-test and the Mann–Whitney u test, respectively. Logistic regression analysis was used to evaluate the relationship between mortality and the type of acid–base abnormality present. Using the normal acid–base status as a reference category, linear regression analysis assessed the length of ICU stays by acid–base abnormality.
Results: One hundred and fourty-nine patients (83.2%) showed an acid–base disturbance. The most common acid–base disorder was respiratory alkalosis (46 patients; 25.7%), followed by a mixed respiratory alkalosis and metabolic acidosis (40 patients; 22.3%), and combined respiratory and metabolic alkalosis (34 patients; 19%). One hundred and twenty (67%) patients had respiratory alkalosis either as a sole disturbance or as part of the mixed acid–base disorder. Eighty-seven patients (48.6%) had mixed acid–base disorders. Fifty-one patients (28.4%) had an element of metabolic acidosis, but respiratory or metabolic acidosis as single disturbances were rare (3 patients; 1.7% and four patients; 2.2% respectively). Type 2 diabetes ($p = 0.016$), chronic kidney disease (CKD) ($p = 0.006$), acute kidney injury (AKI), or the acute administration of the renal replacement therapy (RRT) ($p = 0.048$) were associated with a mixed respiratory alkalosis and metabolic acidosis. The administration of high concentrations of oxygen by any device was associated with a metabolic and respiratory alkalosis ($p < 0.001$). Hypertension, ischaemic heart disease, significant immunosuppression, asthma, obstructive sleep apnoea, and PE were not correlated with any one pattern of acid–base disorder. Logistic regression analysis did not show any relation between acid–base pattern and ICU length of stay or mortality risk at 28 days.
Conclusion: Most patients admitted to the ICU had acid–base disturbance before IMV, with respiratory alkalosis most prevalent. Regarding the relationship between the type of acid–base disturbance observed and co-existing conditions, none of the patterns of acid–base observed was associated with an increased mortality risk at 28 days.

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000861

Dexamethasone associated to immunomodulatory therapy on survival in COVID-19 at an intensive care unit: an observational cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000861

Introduction: Cytokine storm may lead to an acute respiratory distress syndrome in critically ill patients with COVID-19.
Objectives: We aimed to assess the impact of immunomodulatory therapy on mortality in patients admitted to an ICU.
Methods: This observational study enrolled patients with COVID-19 requiring high-flow nasal oxygen therapy (HFN), non-invasive mechanical ventilation (NIMV) and invasive MV (IMV). Patients were treated with dexamethasone and baricitinib, associated to anakinra if the inflammatory pattern (CRP, ferritin) could be due to interleukin-1 or tocilizumab if it could be ascribed to interleukin-6. Patients were followed until death or discharge from the ICU. The primary endpoint was to evaluate the effects of immunomodulatory therapy on mortality at the ICU. The secondary endpoint was the risk of infections associated with these medications.
Results: Overall mortality was 23,5%. Most patients were under IMV (94,1%). Following the established protocol, many patients received dexamethasone (84,3%) and baricitinb (74,5%) in combination. There was a mortality risk reduction of 95% in patients under dexamethasone (HR -hazard ratio- 0,05, 95% CI 0,01 to 0,22, p < 0,001), 83% with baricitinib (HR 0,17, 95% CI 0,05 to 0,55, p < 0,001) and 72% with anakinra (HR 0,28, 95% CI 0,07 to 1,03, p = 0,04). No significant relationship was found between tocilizumab and mortality risk reduction (HR 0,65, 95% CI 0,21 to 2,04, p = 0,45). Twenty-three (45,1%) patients had infections. Anakinra and tocilizumab treatment were associated with a significant risk for nosocomial infections.
Conclusion: The balance between mortality risk reduction and drug-associated infections suggests that dexamethasone plus baricitinib might be included in the standard care of treatment for COVID-19 ICU in-patients.

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Acknowledgements: No funding was received for this work.

000867

Early, late and very late intubation in COVID 19 patients treated with high flow nasal cannula or continuous positive airway pressure. Is there a difference in patients' prognosis ?

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Intensive Care Medicine Experimental 2022, **10(2)**:000867

Introduction: For COVID 19 patients, timing of intubation and mechanical ventilation are still debated. High flow nasal cannula (HFNC) or continuous positive airway pressure (CPAP) could reduce the need for mechanical ventilation and associated morbidity.
Objectives: We aimed to investigate differences in characteristics and outcome of COVID-19 patients who were treated with HFNC or CPAP and were intubated early, late or very late after the onset of severe respiratory failure.
Methods: Prospective, observational, single-center study. In patients treated with HFNC or CPAP we investigated the impact of intubation timing in patients' prognosis. Intubation timing was defined according to the days of HFNC or CPAP use before intubation as early (≤ 3), late (4–6) and very late (> 6). Secondary outcomes included ventilatory mechanics, MV duration, ICU length of stay (LOS), clinico-laboratory characteristic and ICU mortality.
Results: We included 194 consecutive patients (pts) treated with HFNC or CPAP: 66% were male and median age was 65 years old. From those, 98 pts (50,5%) were intubated early, 62 pts (32%) late and 34 pts (17,5%) very late. Total ICU mortality was 64% while mortality in early intubated pts was 49% compared to 77,4% in late and 82.4% in very late intubated pts (p < 0.001, figures 1 and 2). There was not statistically significant difference in mortality between pts intubated late and very late (p = 0,62). In pts that survived time to intubation was significantly shorter (< 0.001) compared to pts that died. The median time to intubation in early, late and very late intubated patients was 1, 5 and 9 days respectively. Patients had similar BMI (p = 0.52), admission PaO2/FiO2 ratio (p = 0.26), plateau pressure (p = 0.56), driving pressure (p = 0.08), MV days (p = 0.5), ICU LOS (p = 0.07), comorbidity number (p = 0.05) and laboratory characteristics (WBCs, Ferritin, D-Dimer, LDH, CRP). Early intubated pts were younger (64 vs 66 vs 69 years old, p = 0.02), had lower SOFA score (7 vs 7,5 vs 8; p = 0.047) and higher compliance at admission days 6 (p = 0.003) and 12 (p = 0.006) compared to patients intubated late and very late. Older age, intubation timing (late and very late), lower PaO2/FiO2 ratio after intubation, lower compliance at admission days 6 and 12, and higher SOFA score were independently associated with mortality. After adjusting for age, late intubation continued to be an independent mortality factor.

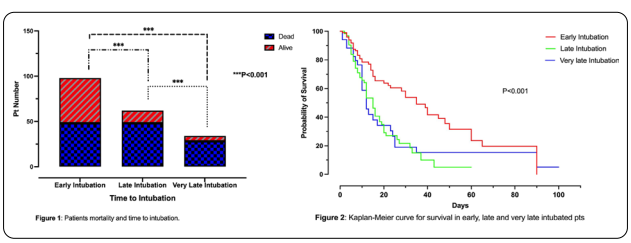

Figure 1: Patients mortality and time to intubation.
Figure 2: Kaplan-Meier curve for survival in early, late and very late intubated pts

Conclusion: In COVID-19 patients treated with HFNC or CPAP, late and very late intubation was associated with increased ICU mortality. More studies are needed to determine the safest intubation time limit, which should probably not exceed 3 days in the absence of pts improvement.

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Acute Respiratory Failure 11

000626

Personalized proning: a machine learning approach to predict responders to prone positioning in intubated patients with COVID-19 ARDS.

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Intensive Care Medicine Experimental 2022, **10(2)**:000626

Introduction: For mechanically ventilated critically ill COVID-19 patients, prone positioning has quickly become an important treatment strategy based on physiological plausibility as well as clinical experience and trials in non-covid-19 ARDS. However, prone positioning in labor intensive and comes with potential adverse effects. Therefore, identifying which critically ill intubated COVID-19 patients will benefit from prone positioning before actually doing so may be of great value.
Methods: From the multi-center Dutch Data Warehouse of COVID-19 ICU patients from 25 hospitals, we selected all episodes of prone positioning in intubated patients. We excluded episodes longer than 24 h. We used supervised machine learning on readily available and clinically relevant features to predict success or failure of prone positioning based on improvements of at least 10% in PaO2/FiO2 ratio, ventilatory ratio, respiratory system compliance, and mechanical power. Separate models were created for each of these outcomes. Re-supination within 4 h after pronation was labeled as failure. We also created models using a 20 mmHg improvement cut-off for PaO2/FiO2 ratio and using a combined outcome parameter. For all models we evaluated feature importance.
Results: Despite extensive modeling using a plethora of machine learning techniques and a large number of potentially clinically relevant features, discrimination between responders and non-responders remained moderate at best. Feature importance was inconsistent between models for different outcomes. Notably, not even being a previous responder to prone positioning provided any meaningful contribution to predicting a successful next proning episode.
Conclusion: In mechanically ventilated covid-19 patients, predicting the success of prone positioning using clinically relevant and readily available parameters from electronic health records is currently not clinically feasible. Given the current evidence base, a liberal approach to proning in all patients with severe COVID-19 ARDS is therefore justified regardless of current patient characteristics or previous results of proning.

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Acknowledgements: T.A. Dam received funding from AmsterdamUMC and the Netherlands Organization for Health Research and Development (project number 10430012010003).

000798

Lateral positioning as a new lung recruitment maneuver - an experimental study

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Intensive Care Medicine Experimental 2022, **10(2)**:000798

Introduction: Recruitment maneuvers are techniques designed to open collapse lungs and keep them opened, based on the application of high pressures during a period of time. However, they expose the patient to hemodynamic instability and their beneficial effects are debatable. Lateral positioning does not require the application of higher airway pressures and could promote alveolar recruitment due to changes in regional transpulmonary pressure.
Methods: Seven pigs were submitted to invasive mechanical ventilation under general anesthesia. A lung injury model was produced by sequentially applying lung lavage followed by injurious ventilation to obtain a PF ratio < 100mmhg. After injury, a recruitment maneuver was performed and open-lung-PEEP (lowest PEEP with collapse < 1%) was chosen during a decremental PEEP titration guided by EIT. After observing massive collapse at PEEP = 5cmH2O, animals were ventilated with VT = 6 mL/Kg, RR 25 bpm and optimal PEEP without recruitment maneuver. All animals were sequentially positioned at (1) supine position, (2) tilted to the left (down), (3) back to supine, (4) tilted to right (down) during 20 min, and finally back to (5) supine. We evaluated the End Expiratory Lung Impedance (ELLZ), arterial blood gases, and respiratory mechanics. Paired T tests were performed to compare the first supine with the last supine position.
Results: all animals presented an increase in respiratory compliance ($P = 0.001$; figure 1A) and PaO2/FIO2 ratio ($P = 0.001$; figure 1C). Increased in EELZ ($P < 0.05$), (figure 1B). The amount of mass of collapsed lung measured by EIT decreased after the lateral positioning ($P = 0.001$; Fig. 1D). Adverse hemodynamics effects were not observed.

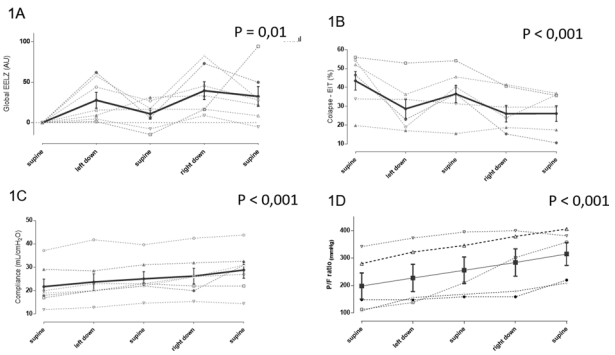

Figure 1. Changes, during sequential lateral position, global End Expiratory lung impedance (EELZ) (1A), respiratory compliance (1C) and mass of collapsed lung (%) estimated by EIT (1B), in PaO2/FIO2 ratio (1D). A significant improvement in PaO2/FIO2 ratio, respiratory compliance and mass of collapsed lung was observed when comparing the first supine position with the final supine position.

Conclusion: Sequential lateral positioning effectively works as a recruitment maneuver, opening collapsed lung areas, improving respiratory mechanics, oxygenation and EELZ, without requiring high airway pressures and presenting no adverse hemodynamics effects.

000831

Bleeding during venovenous extracorporeal membrane oxygenation. Preliminary data from the PROTECMO study

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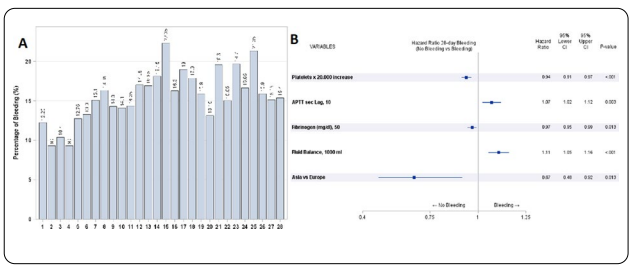
Intensive Care Medicine Experimental 2022, **10(2)**:000831

Introduction: During veno-venous extracorporeal membrane oxygenation (VV ECMO) bleeding is one of the most frequent complications associated with higher morbidity and mortality.
Objectives: Describe the current rate and type of bleeding (in terms of severity and site) in a large cohort of patients under VV ECMO.
Methods: Multicenter prospective observational international cohort study on consecutive V-V ECMO patients enrolled by 41 centers in 19 countries from December 2018 to December 2020. Bleeding episodes were described according to the body site and severity with adjusted categories of the Bleeding Academic Research Consortium score. Type 1: requiring heparin infusion rate reduction or packed red blood cells transfusion (PRBC) transfusion; 2: bleeding requiring heparin infusion rate reduction and PRBC transfusion or non-surgical procedure to stop bleeding; 3: life-threatening bleeding that required PRBC transfusion and surgical intervention for control of bleeding or ECMO discontinuation; Type 4: fatal bleeding.
Results: 652 patients were enrolled with the following baseline characteristics [median, 95% CI or n(%)]: age 52 y (40–60), male gender 463 (71%), BMI 28.4 kg/m2 (24.9–33.7), pre-ECMO hospital stay 5.4 days (1.9–10.9), PaO2/FiO2 ratio 71 (60–95), SAPS-2 40 (30–55), SOFAscore 9 (7–12), Platelets 207 × 103/microL (140–291). Main causes of ARF were COVID-19 (N 218, 32.2%), other viral pneumonia (N 115, 17.6%) and bacterial pneumonia (N 103, 15.8%). 86 patients were within 7 days after a surgical procedure. Longitudinal data include 8482 days on ECMO, and overall days with reported bleeding were 1213 (14.3%). 308 patients did not have any bleeding during the ECMO stay while 344 patients experienced at least one bleeding and in those patients bleeding occurred in median 20% of days. The rate of patients with bleeding was < 15% until day 6 on ECMO and lately ranged from 15 to 22% (Figure 1 A). The main bleeding site was the cannulation (23.7%) followed by airways 23.1%, oronasal (15.4%), intrathoracic (12.1%), intestinal (6%), other abdominal site (5.8%), urinary tract (67%), gastric (5.5%), cerebral (2.8%). The majority of patients had one single site of bleeding (even recurrent) during the ECMO stay while 120 patients had from 2 to 5 sites. No relevant variation in the frequency of the site of bleeding was recognized during the follow-up. Looking at the severity the large majority were low impact episodes: 729 were type 1 (60.7%), 364 (30.3%) type 2, 93 (7.3%) type 3, 16 type 4 (1.3%). Considering the factors associated with increased occurrence of bleeding, in Asia bleeding was significantly less frequent than in Europe and daily, lower platelet and fibrinogen count, more positive fluid balance and higher activated partial thromboplastin time the day before the bleeding were all associated with increased risk of the first bleeding episode (Figure 1B). The occurrence of bleeding was significantly associated with the risk of death in ICU also without considering the fatal episodes: HR 1.67; CI 1.30–2.14, p < 0.01.



Conclusion: Despite improvement, bleeding episodes still occur in more than 50% of patients on VV ECMO and they are associated with increased mortality.

Acknowledgements: PROTECMO study was endorsed by ESICM and funded by 2019 ELSO grant. We acknowledge all the participants of the PROTECMO study group.

000856

Protective effect of Argon against ventilator-induced lung injury – a proof-of-concept study in mice

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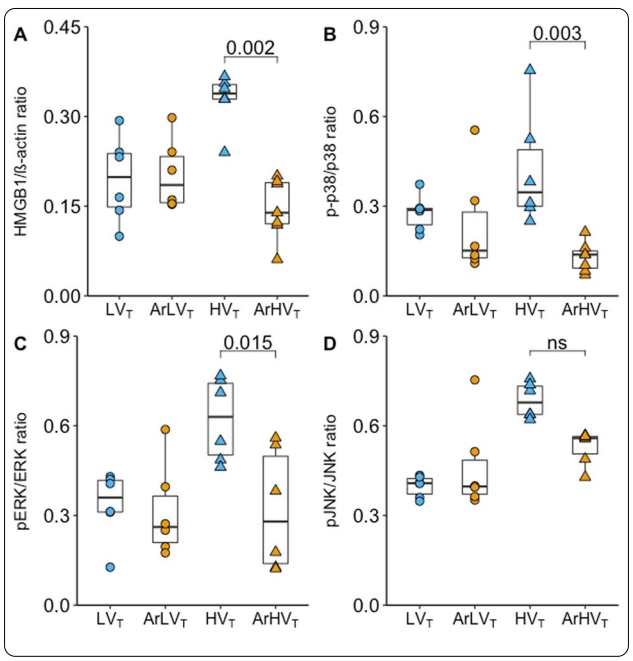
Intensive Care Medicine Experimental 2022, **10(2)**:000856

Introduction: Invasive mechanical ventilation in patients with respiratory failure and ARDS may lead to ventilator-induced lung injury (VILI). This inflammatory driven process of overdistention and mechanical stress of the alveoli further worsens outcome. Argon, an inert noble gas, showed cell protective and immunomodulatory properties in different cell types and forms of acute critical illness models *in vivo*1–3 and may attenuate processes involved in VILI development and progression.
Objectives: To investigate the influence of argon preconditioning on VILI development due to extreme high tidal volume ventilation in a rodent VILI model.
Methods: Anesthetized C57BL/6 mice were invasively ventilated with 30 ml/kg tidal volume (HVT) for four hours to induce VILI. One group received three cycles of inhalative argon/oxygen mixture (50%/50% for 5 min) prior to HVT (n = 11), the other group received no additional treatment (n = 10). Both regimen were also applied to animals ventilated with 6 ml/kg, serving as controls. Bronchoalveolar lavage (BALF) was analyzed for inflammatory markers of VILI (n = 7 per group), as well as wet-to-dry ratio and histological examination (n = 3–4 per group). Mitogen-activated protein kinase pathways were examined for regulatory changes (n = 6 per group). Effects of argon on mRNA expression linked to barrier function proteins were assessed in a pulmonary endothelial cell culture with different degrees of argon exposure. Differences were tested using one-way ANOVA or a Kruskal–Wallis test, as appropriate.
Results: Argon preconditioning slightly reduced IL-6 levels in BALF (557 ± 380 vs. 421 ± 127 pg/mL, NS), whereas no difference occurred for VEGF, MIP-2, and KC between groups. The wet-to-dry ratio was lower in the argon group (4.9 ± 0.4 vs. 5.9 ± 1.0; p = 0.17) with no difference in total protein concentration in BALF and no otherwise histological differences. Alveolar neutrophils after HVT were lower with argon (15.4% vs. 25.4%; p = 0.34). Argon attenuated the overexpression of HMGB1 and activation of p38 and ERK induced by VILI (Fig. 1).



Lung tissue mRNA expression of IL-33 and CSF3 was upregulated, while IL-17 and CSF2 expression was suppressed by argon preconditioning, possibly affecting neutrophil stimulation and regulation. Exposure of lung endothelial cells with argon in vitro for 30 min led to a significant increase in the expression of occludin, claudin, ZO-1, and VE-PTP. Physiological changes were similar in both groups, except for lower peak inspiratory pressures in argon pretreated experiments (25 ± 3 vs. 23 ± 3cmH2O; p = 0.19).
Conclusion: Argon preconditioning had no influence on the inflammatory response to HVT ventilation, however, seems to attenuate the activation of HMGB1, p38 and ERK, potentially reducing inflammatory responses. Further, argon might help to preserve endothelial junctions in VILI thereby reducing edema formation. These promising trends have to be tested in further studies.

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Acknowledgements: None.

000865

Impact of age on the evolution of critical illness due to COVID-19

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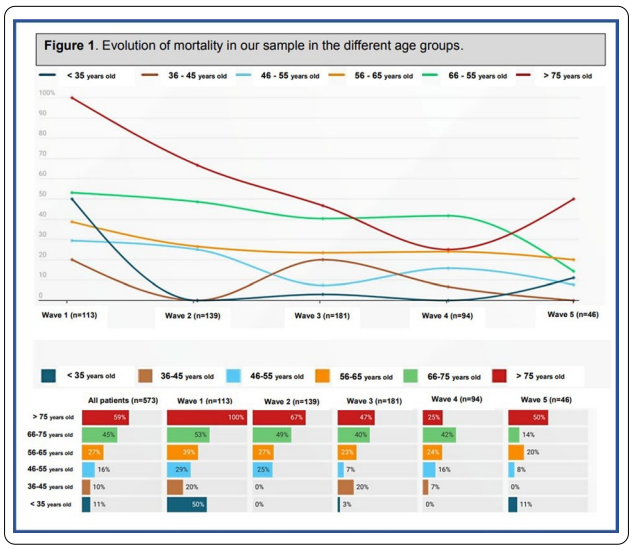
Introduction: COVID-19 had a major impact on society and has posed a challenge for healthcare systems. Since the beginning of the pandemic, emphasis has been placed on identifying the factors that condition a poor prognosis. Age, comorbidity and frailty are the main factors that have been shown to condition a poor outcome and are usually included in these tools.
Objectives: Analyse the impact of increasing age on the evolution of patients with acute respiratory distress syndrome associated with COVID-19 (CARDS).
Methods: Observational and retrospective study of patients admitted to the Intensive Care Unit (ICU) for CARDS between March 2020 and September 2021. Demographic, severity, complications and ventilatory support variables of the cohort were reviewed, categorising patients into age groups (< 35 years, 36–45 years, 46–55 years, 56–65 years, 66–75 years, > 75 years). Categorical variables are expressed as counts and percentages and were compared using a chi-square and Fisher's exact test; continuous variables are expressed as medians and interquartile range [IQR] and were compared with the Kruskall Wallis test. A significance level of 5% (bilateral) was used. Analysis was performed using STATA version 13® (StataCorp LCC).
Results: Of the 573 patients admitted to our ICU, 5% were < 35 years old, 9% 36–45, 16% 46–55, 31% 56–65, 31% 66–75 and 8% > 75. The median [IQR] age decreased as we progressed through the "waves" of the pandemic: 1st wave 65 [55–69] - 5th wave 51 [38–62]. Figure 1 shows the evolution of mortality in our sample in the different age groups. CARDS was more frequent in men in all age groups. Significant differences were found when comparing groups in terms of comorbidity [cardiovascular risk factors—diabetes (p < 0.000), hypertension (p < 0.000), dyslipidaemia (p < 0.000), heart disease

(p < 0.000), obesity (p < 0.000), Charlson (p < 0.000)] and frailty [Clinical Frailty Scale (p < 0.000)]. In terms of severity, all the scales collected (SOFA, APACHE II, PSI, SAPS II) accumulated higher scores as age increased, obtaining statistical significance in all of them. In relation to respiratory support, they required more support with invasive mechanical ventilation (IMV) (p < 0.000) as age increased. Statistically significant results were also obtained for days of IMV (p < 0.000), need of prone position (p < 0.000) and tracheostomy (p = 0.00). They presented higher mortality (p < 0.000) and required more adequacy of the therapeutic effort (p < 0.000) at higher age group. They also required a longer in-ICU length of stay (LOS) (p < 0.000) and in-hospital LOS (p = 0.000).



Conclusion: Increasing age is associated with a higher comorbidity and frailty, which translates into worse outcomes, higher mortality and in-ICU and hospital LOS. The decrease in median age in successive waves of the pandemic may be related to the high vaccination rate and greater compliance with prevention recommendations in older age groups.

000883

Reliability of Respiratory System Compliance Measurement During Assisted Mechanical Ventilation

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Intensive Care Medicine Experimental 2022, **10(2)**:000883

Introduction: A correct plateau pressure (Pplat) value is mandatory to measure respiratory system compliance (Crs). Pplat is always obtained from an inspiratory hold maneuver. This simple maneuver has been classically performed in patients during controlled mechanical ventilation (MV). Conversely, the same maneuver during assisted mechanical ventilation – where the patient is actively breathing – is more difficult and not widespread [1], even though already validated for the measure of inspiratory effort [2]. Literature about this topic is scarce with two interesting studies with small sample [3,4]. For this reason, we conducted an observational study to compare the value of Crs during controlled vs assisted MV in the same patients. Our hypothesis is that Pplat during assisted MV is reliable and thus can lead to a correct measure of Crs.
Objectives: The aim of our study was to demonstrate that a Pplat stable for 2 or more seconds during assisted MV is reliable and it leads to a correct measure of Crs compared to the measure performed during controlled MV.

Methods: Observational, ongoing study. We enrolled 32 patients admitted to our neuro-intensive care unit. Respiratory mechanics (Pplat, intrinsic PEEP, total PEEP, tidal volume, Crs) were calculated in both controlled and assisted MV when the two measurements were performed in a time window of no more than 1 hour and with a same set PEEP and body position (thus, assuming that the respiratory system had same mechanical property). The Pplat obtained during assisted MV was considered reliable if wasstable for 2 or more seconds.

PATIENT CHARACTERISTICS			
Age, years	39.5 [28.2-51.2]		
Male sex, %	65%		
BMI, kg/m²	25.2±3.7		
P_aO_2/F_iO_2, mmHg	370.1±88.6		
F_iO_2, %	35±7%		
P_aCO_2, mmHg	40 [34.5-43.0]		
pH	7,42 [7.38-7.48]		
	VCV	**PSV**	**P VALUE**
Tidal Volume, ml	494.5 [442.5-531.5]	521.5 [430.5-610.0]	0.204
P_{plat}, cmH_2O	13.8 [12.0-16.7]	13.7 [11.8-16.0]	0.777
Driving Pressure, cmH_2O	7.3 [6.8-9.3]	7.7 [5.9-10.0]	0.637
C_{rs}, ml/cmH_2O	62.7±17.5	71.3±22.9	0.09
Pressure muscle index, cmH_2O		-0.75 [-2-2]	

Table 1 BMI Body Mass Index, P_aO_2 partial pressure of oxygen, F_iO_2 fraction of inspired oxygen, P_aCO_2 partial pressure of carbon dioxide, C_{rs} compliance of respiratory system, P_{plat}plateau pressure.
Data are expressed as mean ± standard deviation or median [interquartile range] where appropriate.

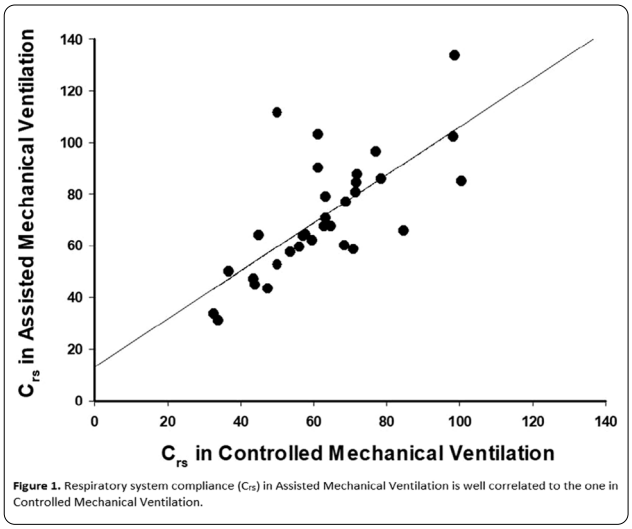

Figure 1. Respiratory system compliance (C_{rs}) in Assisted Mechanical Ventilation is well correlated to the one in Controlled Mechanical Ventilation.

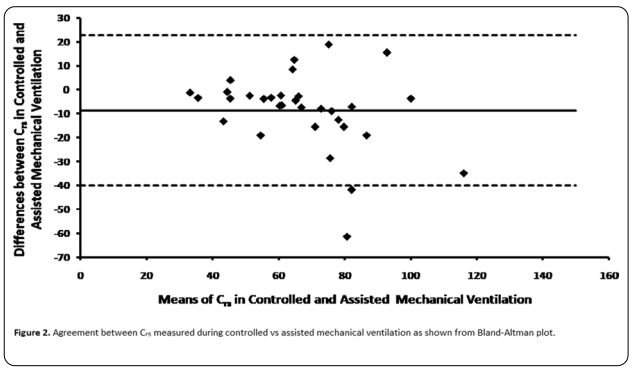

Figure 2. Agreement between C_{rs} measured during controlled vs assisted mechanical ventilation as shown from Bland-Altman plot.

Results: The 32 patients were normal-weight (BMI 25.2 ± 3.7) and with nearly normal oxygenation (PaO2/FiO2 370.1 ± 88.6) and Crs (62.7 ± 17.5). Crs calculated in controlled and assisted MV were not statistically different (62.7 ± 17.5 in controlled and 71.3 ± 22.9 in assisted MV; P = 0.09). The linear regression showed a fairly good relationship

(R = 0.71, P < 0.001) between the Crs values measured during controlled vs assisted MV(Fig. 1). Bland–Altman plot showed good agreement between the two measures (mean -8.8, upper LA 16.01, lower LA -40.2 ml/cmH2O; Fig. 2).
Conclusion: In a population of mechanical ventilated patients without lung injury, a Pplat stable for at least 2 s recorded during an inspiratory hold in assisted MV can give an accurate measure of Crs.

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000907

Pulmonary Artery Pulsatility index is higher in worst vascular and pulmonary conditions in an animal ARDS model. What does this really mean?

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Intensive Care Medicine Experimental 2022, **10(2)**:000907

Introduction: The pulmonary artery pulsatility index (PAPi), the ratio between pulmonary artery pulse pressure (PAPP) and right atrial pressure (RAP), is a marker of right ventricle (RV) dysfunction and also has a prognosis value. The lower the PAPi, the worse the outcomes in RV acute myocardial infarction and cardiogenic shock. However, it has not been studied in ARDS, and no data exists about how pulmonary conditions modify PAPi.
Objectives: To explore the changes in PAPi in an ARDS porcine model with different pulmonary conditions.
Methods: ARDS model combined saline lavage and injurious mechanical ventilation for two hours in 9 pigs. After a lung recruitment maneuver, the optimal PEEP (PEEPopt) was determined at the highest compliance during a decremental PEEP trial. Afterward, three PEEP levels were randomly applied: overdistention (OD), 6 cmH2O above PEEPopt; optimal (OPT), 2 cmH2O above PEEPopt; and collapse (COL), with 6 cmH2O below PEEPopt. Respiratory mechanics, gas exchange, and pulmonary vascular mechanics, including indexed stroke volume (SVi), effective arterial elastance (EAeff, calculated as the difference between mean pulmonary artery pressure (PA) and wedge pressure divided by SVi), reflection magnitude (RM, calculated as the ratio between the amplitude of backward and forward pressure waves), pulmonary arterial compliance (ratio between SVi and PAPP), pulmonary resistance and PAPi were measured at baseline (BL), after ARDS model creation (VILI), and after each PEEP level application.
Results: When compared to BL, PAPi was higher in VILI (1.21 vs 1.99, p < 0.001) which also corresponded to a worse respiratory dynamic compliance (30.4 vs 11.5 ml/cmH2O, p = 0.001) and oxygenation (pO2: 534 vs 125 mmHg, p < 0.001), higher pulmonary vascular resistance (236 vs 462dyn.s.cm-5, p < 0.001), Eaeff (0.30 vs 0.63 mmHg/ml p = 0.001) and PAPP (13 vs 25 mmHg, p = 0.003) and a lower pulmonary arterial compliance (2.71 vs 1.40 ml/mmHg, p = 0.008). When comparing the three pulmonary conditions at three PEEP levels, PAPi was higher in COL vs OPT (1.50 vs 0.95, p = 0.002) and COL vs OD (1.50 vs 1.00; p < 0.001), but no differences were found between OPT and OD. Compared to OPT, COL showed a higher mean PA (31 vs 38 mmHg, p = 0.03), pulmonary vascular resistance (291 vs 444dyn.s.cm-5, p = 0.007), RM (0.32 vs 0.49, p = 0.01), Eaeff (0.36 vs 0.60 mmHg/ml, p = 0.003) and SVi (26 vs 31 ml/m2, p < 0.001) and a worse respiratory dynamic compliance (29 vs 16 ml/cmH2O, p = 0.01) and pO2 (520 vs 185 mmHg, p < 0.001) and a non-significant trend to higher PAPP (15 vs 20 mmHg, p = 0.052). When compared to COL, OD showed a lower RM (0.49 vs 0.32, p = 0.001) and SVi (31 vs 24 ml/m2, p < 0.001) and a higher PaO2 (185 vs 514 mmHg, p < 0.001) but no difference in respiratory dynamic compliance (16 vs 19 ml/cmH2O, p = 0.58). No differences in RAP were found between BL and VILI nor between the three studied pulmonary conditions.
Conclusion: A higher PAPi was observed in the worst pulmonary and vascular conditions (VILI and COL). This could be due to the combined effect of increased SVi and RM. The long-term impact on RV of this should be studied.

Acknowledgements: 2012 ESICM ECCRN Basic Science Award.

000919

Respiratory distress observation scales to predict weaning outcome

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Intensive Care Medicine Experimental 2022, **10(2)**:00091

Introduction: Whether the presence of dyspnea could interfere with the result of a spontaneous breathing trial (SBT) is unknown. Alternatively, to the use dyspnea self-report scales that is challenging in critically ill patients, the five items Mechanical Ventilation – Respiratory Distress Observation Scale (MV-RDOS) has been proposed as a reliable surrogate of dyspnea in non-communicative intubated patients. In the present study, we sought 1) to describe the prevalence of dyspnea in patients clinically deemed ready to undergo a SBT, 2) to assess the evolution of dyspnea during a SBT among patients who success and those who fail and 3) to investigate whether dyspnea can predict the outcome of the SBT.
Methods: Prospective, single-center study in a twenty-two bed ICU in a tertiary center. Patients intubated since more 48 h who had failed a first SBT were eligible if they meet classical readiness to wean criteria. The MV-RDOS was assessed before, at 2-min, 15-min and 30-min (end) of the SBT. The presence of clinically important dyspnea was inferred by a MV-RDOS value $\geq$ 2.6.
Results: Fifty-eight patients (age 63 [51–70], SAPS II 66 [51–76]; med [IQR]) were included and 62 SBTs were analyzed. All patients were deemed ready to be weaned at inclusion (FiO2 30% [30–40]; positive end expiratory pressure 5 cmH2O [5–6]; respiratory rate 22 cycles/min [17–27]),
Conclusion: Despite patients met classical readiness to wean criteria, respiratory distress assessed with the MV-RDOS was frequent at the beginning of SBT. Measuring MV-RDOS before to initiate a SBT could avoid undue procedure and reduce patient's expose to unnecessary suffering.

000931

Time to Diaphragm contraction after non-invasive electromagnetic phrenic nerve stimulation in anesthetized patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000931

Introduction: It is estimated that 16.5 million patients worldwide per year undergo mechanical ventilation (MV) as a life-saving intervention in the intensive care unit (ICU) [1]. Nevertheless, MV leads to complications like ventilator-induced diaphragm dysfunction (VIDD) [2–5]. Techniques preventing or attenuating VIDD through diaphragm stimulation and activation should be further investigated.
Objectives: We hypothesized that time from start of stimulation to onset of diaphragmatic contraction is independent from stimulation intensity using bilateral non-invasive phrenic nerve electromagnetic stimulation. Primary endpoint was time from start of electromagnetic stimulation to effective stimulated inspiration (defined as flow $\geq$ 0.5 L/min) in anesthetized patient.
Methods: To gather the data necessary, we performed bilateral non-invasive electromagnetic phrenic nerve stimulation on five ASA I/II normal weighed patients scheduled for elective surgery with general anaesthesia and planned intubation, shortly after anaesthesia induction. The magnetic field was used with different intensities (20%, 30%, 40%, frequency 25 Hz, 2 s duration).
Results: Based on all patients the mean time from stimulation to inspiration (0.5 L/min flow) was 28.42 $\pm$ 11.02 ms, 22.78 $\pm$ 12.21 ms and 26,88 $\pm$ 18.74 ms at 20%, 30% and 40% intensity, respectively (Figure 1). There was no linear relationship between stimulation intensity and contraction lag; the diaphragm contraction lag was independent of the stimulation intensity ($p = 0.7159$, $r2 = 0.0008979$). The overall contraction lag (all intensities combined) was 26.03 $\pm$ 21.05 ms.

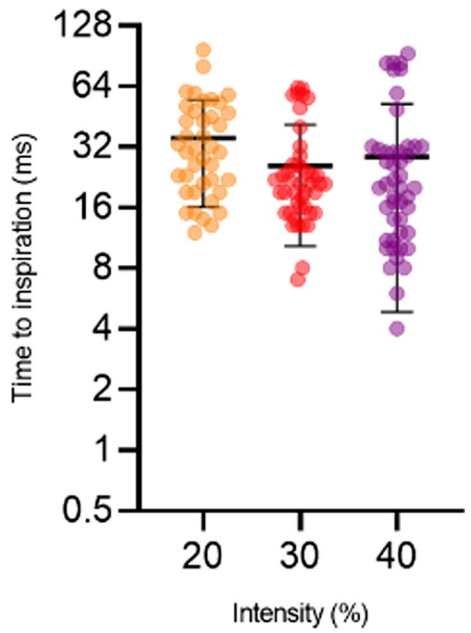

Figure 1. Logarithmic presentation of time (ms) to inspiration (flow $\geq$ 0.5 L/min) after bilateral non-invasive electromagnetic phrenic nerve stimulation with 20% (orange), 30% (red), 40% (violet) intensity. Mean and standard deviation are depicted.

Conclusion: Time to inspiration with a flow above 0.5 L/min after bilateral non-invasive stimulation of the phrenic nerve was independent of the used stimulation intensities (20%, 30%, 40%). Stimulation intensity does not seem to need to be adjusted to ensure adequate conduction time, but can be adjusted according to other necessary parameters (e.g. tidal volume).

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Acknowledgements: This investigator-initiated study was partly funded by STIMIT AG, Biel, Switzerland.

000939

Effect of PEEP and compliance phenotypes on ventilation/perfusion mismatch in COVID-19 ARDS

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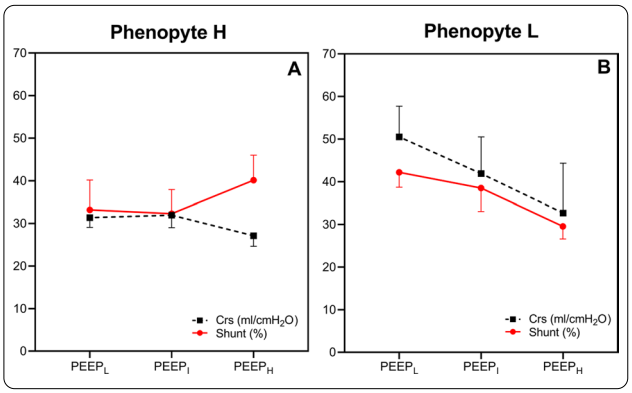
Intensive Care Medicine Experimental 2022, **10(2)**:000939

Introduction: COVID-19 related ARDS (C-ARDS) is characterized by severe hypoxemia [1] with impaired ventilation/perfusion (V/Q) matching but relatively preserved lung compliance. Positive end-expiratory pressure (PEEP) can modify end-expiratory lung volume but can have a not predictable effect on V/Q mismatch in C-ARDS.
Objectives: To assess the effect of PEEP on V/Q mismatch in COVID-19 ARDS patients measured using the Automatic lung parameter estimator (ALPE). Moreover, we evaluated if different compliance phenotypes can be associated to a different effect of PEEP on V/Q mismatch.
Methods: We measured V/Q mismatch in C-ARDS at three PEEP levels (intermediate PEEP (PEEPI), low PEEP (clinical – 50% = PEEPL) and high PEEP (clinical + 50% = PEEPH). Consecutive intubated and mechanically ventilated COVID-19 ARDS patients were enrolled in the study and the ALPE was used to measure V/Q. Alveolar dead space (VDalv) was calculated using the Enghoff modified Bohr's method [2]. Respiratory mechanics measurements, alveolar dead space, shunt and V/Q mismatch (low V/Q and high V/Q) were collected at each PEEP level and a mixed effect model was used to evaluate the impact of PEEP on each component of the V/Q. Furthermore, we classified patients based on the respiratory system compliance measured at

low PEEP in two different respiratory mechanics phenotypes, i.e. high elastance/low compliance (phenotype H) and low elastance/high compliance (phenotype L) [3] and evaluated if these two populations may have a different behavior in terms of V/Q mismatch at different levels of PEEP.

Results: Seventeen C-ARDS patients aged 66 [60–71] years with a PaO2/FiO2 of 141 ± 74 mmHg were studied at PEEPL = 5.6 ± 2.2 cmH2O, PEEPI = 10.6 ± 3.8 cmH2O and PEEPH = 15 ± 5 cmH2O. Shunt (p = 0.91), low V/Q (p = 0.8), high V/Q (p = 0.67) and alveolar dead space (p = 0.08) were not significantly influenced, on average, by PEEP. In all our patients, the respiratory system compliance decreased significantly when increasing PEEP, without significant improvement of PaO2/FiO2 (p = 0.26). Finally, in the two phenotypes, PEEP had opposite effects on shunt, with a decrease in the phenotype L and an increase in phenotype H (p = 0.048).



Conclusion: PEEP has a heterogeneous effect on shunt in COVID-19 ARDS with an overall limited effect on V/Q mismatch. A different and opposite effect could be seen in compliance phenotypes, with an increase of shunt in the phenotype H and a decrease in phenotype L. In COVID-19 patients whit no PEEP-related improvement of lung mechanics, high PEEP may reduce lung protection without improving V/Q mismatch. Compliance phenotypes could influence the effect of PEEP on V/Q mismatch.

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Acute Respiratory Failure 12

000915

Non-Invasive Ventilatory Support with Pharmacological Respiratory Overdrive Management versus Invasive Mechanical Ventilation as Initial Strategy in COVID-19 Patients – Differences in Mortality

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Intensive Care Medicine Experimental 2022, **10(2)**:000915

Introduction: High-Flow Nasal Cannula (HFNC) and conventional Non-Invasive Ventilation (NIV) are two modalities of Non-Invasive Ventilatory Support (NIVS) that have proven safe and effective for the initial management of acute respiratory failure in critically ill COVID-19 patients [1]. Increased respiratory effort and patient self-inflicted lung injury (P-SILI) have emerged as concerns in this particular subset of patients [2, 3]. Little is known regarding mortality compared with patients primarily supported with Invasive Mechanical Ventilation (IMV).

Objectives: To assess differences in Intensive Care Unit (ICU) and in-hospital mortality between two groups of patients selected according to initial respiratory failure management strategy: IMV versus NIVS with pharmacological overdrive management.

Methods: Single-center retrospective study including adults admitted in a portuguese ICU with severe acute respiratory failure due to critical COVID-19 disease upon admission, 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) NIVS with HFNC and/or conventional NIV (CPAP, BiPAP or Helmet CPAP) combined with pharmacological management of respiratory overdrive, targeting a respiratory rate inferior to 20–22 cpm, with one or a combination of the following: remifentil perfusion, dexmedetomidine perfusion, boluses of morphine (2–4 mg up to a maximum of 4/4 h) and short-acting oral benzodiazepines (eg. alprazolam 0,25–0,5 mg 8/8 h). The chosen type of NIVS and drugs prescribed depended upon clinical judgement of the intensivists' team in charge. Patients with ICU lengh of stay (LOS) inferior to 24 h and those who required rescue with a modality of extracorporeal membrane oxygenation were excluded. Data regarding demographics, worst PaO2/FiO2 ratio and SOFA score on day 1 (both during the first 24 h of ICU admission), length of IMV and NIVS, type and duration of overdrive-control drugs were collected by electronic process revision.

Results: 149 patients were included, 68,4% of which primarily allocated to a NIVS strategy (Table 1). Worst PaO2/FiO2 were similar between the two subgroups and worst day 1 SOFA score was significantly higher in the IMV group. Total duration of ventilatory support, ICU and in-hospital LOS were significantly lower in the NIVS group (analysis took into account failure of initial ventilatory support). We observed a tendency towards lower mortality in the NIVS group, reaching statistical significance concerning in-hospital mortality.

	NIVS group (n = 102)	IMV group (n = 47)	*p* value
Age (median; IQR), years	65,0; 15	70,0; 15	0,360
Male gender, no. (%)	74 (72,5%)	30 (63,8%)	0,281
Worst day 1 PaO2/FiO2 ratio (median; IQR)	99; 52	104; 66	0,662
Day 1 SOFA score (median; IQR)	4; 2	7; 3	< 0,001
Duration of ventilatory support (median; IQR), days	7; 8	26; 30	< 0,001
Failure of initial ventilatory support, no. (%)	21 (20,6%)	2 (2,5%)	
ICU LOS (median; IQR), days	7; 8	26; 30	< 0,001
Hospital LOS (median; IQR), days	15; 15	32; 43	< 0,001
ICU mortality, no. (%)	23 (22,5)	12 (25,5)	0,482
In-hospital mortality, no. (%)	25 (23,4%)	13 (27,7%)	0,003

Conclusion: When comparing COVID-19 patients requiring ICU admission due to severely acute respiratory failure initially supported with NIVS versus IMV, the NIVS group showed significantly lower duration of ventilatory support, ICU and hospital LOS, as well as lower mortality rates. Significantly higher day 1 SOFA scores were observed in the IMV group, attesting the adequate clinical allocation of each strategy

despite similar degrees of hypoxemia and gas exchange impairment (reflected in similar worst day 1 PaO2/FiO2 ratio) in both groups.

000765

Association between development of pneumothorax and use of airway pressure release ventilation(APRV) in Covid-19 patients: a small case control series

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Intensive Care Medicine Experimental 2022, **10(2)**:000765

Introduction: COVID-19 is understood to be a cause of acute respiratory distress syndrome (ARDS) [1], which is a common cause of refractory hypoxemia [2]. It is known that APRV increases mean airway pressure and may be associated with increased risk of barotrauma and pneumothorax [3]. APRV has been increasingly deployed as a rescue mode of ventilation in patients with severe hypoxaemia due to COVID-19 [4]. There is limited evidence documenting the risk of pneumothorax in patients with COVID-19 undergoing different modes of mechanical ventilation [5].
Methods: A single centre retrospective observational study was conducted in a UK critical care unit between 1st January 2021 to 31st December 2021. A total of 122 patients were admitted for mechanical ventilation for COVID-19 and, using deidentified data, ten of these patients were identified as developing pneumothoraces. We evaluated the mode of ventilation in these 10 patients (case group), comparing them with 10 COVID-19 patients of similar characteristics, also receiving mechanical ventilation (control group) who did not develop pneumothoraces. Our aim was to assess if an association existed between APRV and the incidence of pneumothorax. Categorical data was examined using a Fisher's Exact test with an alpha level of 0.05. Statistical analysis was performed using R (version 4.1.3, Vienna, Austria).
Results: In the case group, six patients (60%) were on APRV, two patients (20%) on DuoPAP, and two patients (20%) on P-SIMV. In the control group, we observed 4 patients (40%) on DuoPAP, three patients (30%) on APRV, and two patients (20%) on P-SIMV (see Table 1). There was no statistically significant association between the incidence of pneumothorax and APRV ($p = 0.37$). The average (SD) age of patients in the case and control group were 64.3 (9.5) years and 60.8 (7.8) years respectively. The number of male patients in the case and control group were 7 (70%) and 8 (80%) respectively. In the case group, four patients (40%) had pre-existing lung disease (i.e., asthma, COPD, ILD) as compared to three patients (30%) in the control group.
Table 1.

	Pneumothorax	
	Yes	**No**
APRV	6	3
Other mode of ventilation	4	7

Conclusion: To the best of our knowledge, there is only one prior retrospective observational study which shows an increased risk of pneumothorax in COVID-19 with APRV [3]. Our small retrospective study suggests that there may be an increased incidence of pneumothorax in patients with COVID-19 undergoing APRV as compared with those receiving other modes of ventilation. However, since APRV is usually used as a rescue technique, it may be that those patients selected for APRV had more severe disease. Since this data did not reach statistical significance, larger prospective data is required to assess whether there is increased risk associated with the use of APRV in patients with COVID-19 pneumonia.

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Acknowledgements: Not applicable.

000874

Patient-ventilator asynchrony detection by surface electromyography (sEMG) in ARDS patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000874

Introduction: In ARDS treatment, a temporal mismatch of patient effort and ventilator support is difficult to detect and manage and has deleterious consequences for patients [1, 2].
Objectives: This study aims to determine whether non-invasive surface electromyography (sEMG) can detect patient-ventilator asynchrony as reliable as esophageal pressure measurement.
Methods: We included adult patients with severe ARDS. Intercostal and costal margin sEMG were recorded over ≥ 10 min during three phases of treatment. Two independent experts segmented 100 inspiration cycles per patient and treatment phase. Onset of inspiration based on flow and airway pressure was marked, as was onset of patient effort in Pes and sEMG, respectively. Only the sEMG channel with better signal-to-noise ratio was used in further analysis. We investigated the inter-rater disagreement in the three domains by estimating the absolute onset disagreement of both experts. The triggering of the ventilator was compared to patient activity in Pes and sEMG, the difference is considered as trigger delay. All breaths were classified as follows: ineffective effort, passive, synchronous trigger, delayed trigger, reverse trigger, double trigger and asynchrony index was calculated [1, 3, 4].
Results: We present preliminary data for 12 patients; 3120 breaths were segmented (see Table 1). Within these cycles, 1626 inspiratory efforts in Pes and 1586 efforts in sEMG were annotated. Regarding the timing of the breaths, we found the following inter-rater disagreements: $|\Delta t \text{ flow}| = 23 \text{ ms} \pm 74 \text{ ms}$, $|\Delta t \text{ Pes}| = 59 \text{ ms} \pm 138 \text{ ms}$ and $|\Delta t \text{ sEMG}| = 77 \text{ ms} \pm 103 \text{ ms}$. The disagreement in Pes and sEMG is higher than in flow segmentation, but comparable between methods. The derived trigger delay was significantly correlated between both experts (Pearson's $r = 0.83$ and $r = 0.91$ for trigger delay Pes and sEMG respectively; $p < 0.001$ each). When using an average of both experts to compare the sEMG to Pes trigger delay, we can show a significant correlation (Pearson's $r = 0.90$; $p < 0.001$). A minor systematic deviation between Pes and sEMG of 81 ms could be observed, indicating that sEMG is annotated after Pes. This deviation in trigger delay could not be attributed to either method. Efforts could not be properly detected for 9.25% (297/3210) breaths in sEMG signal and 8% (257/3210) of breaths in Pes. A good agreement between methods could be shown for double and reverse trigger classification. sEMG detected more ineffective efforts than Pes measurement (Pes ineffective effort count = 3, sEMG ineffective effort count = 33). In Pes, more breaths

were classified as delayed trigger than in sEMG based measurement (see Table 1), this could be either due to the aforementioned systematic deviation or the deviation between both experts. The asynchrony index calculated from sEMG showed a significant correlation to the asynchrony index calculated from Pes (Pearson's r = 0.53; p = 0.0012).

Table 1: Classification of breaths by sEMG and Pes measurement

		sEMG classification							
		ineff. effort	double trigger	reverse trigger	delayed trigger	synchr. trigger	passive	missing	total
Pes classification	ineff. effort	2	0	0	0	0	0	1	**3**
	double	0	78	0	0	0	0	4	**82**
	reverse	0	0	30	0	0	0	0	**30**
	delayed	0	0	0	166	30	0	71	**267**
	synchr.	0	0	1	141	881	0	221	**1244**
	passive	0	0	0	0	0	1327	0	**1327**
	missing	31	4	1	48	173	0	0	**257**
	total	**33**	**82**	**32**	**355**	**1084**	**1327**	**297**	**3210**

Conclusion: The preliminary data suggest that sEMG has the potential to substitute Pes in the detection of patient respiratory activity. Advances in sEMG processing could further improve reliability and accessibility of the method. Further development of the method may lead to a routine use for this non-invasive approach to monitoring of respiratory activity.

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Acknowledgements: Funding was received by Dräger (Drägerwerk AG & Co., Lübeck, Germany). Dräger took no influence on study design, data processing or interpretation of data.

000938

Experience with extracorporeal membrane oxygenation support during COVID-19 pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000938

Introduction: When mechanical ventilation is not enough, extracorporeal membrane oxygenation could play a role as a form of rescue therapy and may provide beneficial results in the hands of skilled clinicians in centers with experience in using ECMO properly in selected patients.
Objectives: To describe the characteristics of patients admitted to a critical care unit in a third level hospital during COVID-19 pandemic who required the use of extracorporeal membrane oxygenation support (ECMO).
Methods: Observational, prospective study in patients on ECMO support during Covid-19 pandemic in H.G.U Gregorio Marañón ICU, between May and September 2021. Demographic data, comorbidities, clinical status before support, organic support, ICU stay complications, severity scores, RESP score (Respiratory ECMO Survival Prediction), outcome and a-year old functional classification through mMRC scale (modified Medical Research Council scale), were collected. Descriptive analysis was expressed as means (standard deviation) for normally distributed quantitative variables, medians (interquartile range) for non-normally distributed variables, and as percentages for categorical data.
Results: One hundred fifty five patients were admitted for severe COVID 19, needing ECMO support 17% (26 patients) of them. 92% (24 patients) required VV-ECMO support, 62% due to refractory hipoxemya, 38% to hypoxemia/severe respiratory acidosis and two patients VA-ECMO to severe ARDS with severe left ventricular systolic dysfunction, whom were converted after resolution to VV-ECMO. The age was 54 ± 9 years, 73% were men, APCHE II at admission was 13 ± 4. Comorbidities: Obesity 50%, arterial hypertension 38%, lung disease 31%, diabetes 19%, cardiovascular disease 15%, immunosupression 7.7%. **Data prior to ECMO support**: APACHE II 17.5 ± 3.7, SOFA 7.3 ± 2.5, pO2/FiO2 73 ± 20, pCO2 70.5 ± 19.7 mmHg, mechanical ventilation days 12.4 ± 12 (50% of patients more than seven days). 65% of patients had aggressive ventilation (plateau pressure > 30 cmH2O, driving pressure > 15 cmH2O) during 1.38 ± 1.8 days. Inhaled nitric oxide 61.5%, prone position 100% with a number of maneuvers of 3 (1–5), neuromuscular blockers 100%, vasoactive support 69% and acute renal failure needing extrarenal depuration 19%. ICU stay complications were: ventilator-associated pneumonia 15%, catheter-associated bacteraemia 8%, arrhythmia 8% and pneumothorax 8%. The duration of ECMO support was 23 ± 11 days, with 44 ± 20 total days of mechanical ventilation, 61% requiring tracheostomy. The **mortality on ECMO was 50%** (44% limitation of therapeutic effort, 31% multiorgan failure, 12% cardiovascular event). ICU stay was 53 ± 27 days and hospital stay 73 ± 58 days. **ICU and hospital survival was 39%.** Considering RESPscore groups, the survival was: Group II 83.3%, Group III 23.5%, Group IV 33.3%. The majority of patients who survived presented a **poor functional classification (mMRC) at one year after hospital discharge:** 30% Class II; 70% Class III.
Conclusion: In our experience, we obtained a long hospital stay, a high number of complications and mortality in COVID 19 critically ill patients who needed ECMO support, as well as, a severe functional impairment in survivors after a year.

000943

ROX index as a predictor of High-Flow Nasal Cannula failure in critical COVID-19 patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000943

Introduction: The optimal time for iniciation of mechanical ventilation in COVID-19 patients is uncertain. ROX index could help to identify patients at high risk of needing mechanical ventilation.
Objectives: The purpose of this study was to identify if ROX index in the first 24 h ICU-admission is a good predictor of High Flow Nasal Cannula (HFNC) support failure and need of mechanical ventilation in critical ill patients with severe COVID-19.
Methods: Observational, prospective study in COVID-19 patients admitted in Gregorio Marañón Hospital ICU (Madrid, Spain), between July–September 2021. Demographic and clinical data, vaccination status, comorbidities, severity scores, organic support and outcomes were collected. The ROX index refers to a combination of the ratio of oxygen saturation (measured by pulse oximetry) to fraction of inspired oxygen and respiratory rate (SpO2/FiO2/RR). It was calculated in the first 24 h of ICU-admission in all patients. Descriptive statistics were expressed as mean ± SD or median with interquartile range for continuous variables and percentages for categorical data. By means of a simple logistic regression analysis the ROX index was associated to HFNC support failure, and the effect was estimated by its corresponding Odds Ratio (OR).The ability of the ROX index to discriminate HFNC support failure was assessed using the area under the receiver operating characteristic curve (AUROC). Estimation of their calibration was established through the Hosmer–Lemeshow goodness of fit test. To evaluate the extent to which the ROX index was valid for prediction of HFNC failure, sensitivity (S), specificity (E), overall validity of

prediction, positive and negative predictive values (PPV, NPV) were all determined.
Results: Eighty-eight patients were included, 58% were male. Age 53 ± 14 years, Charlson Comorbidity Index 0 (0–1), 23% complete vaccination with at least one dose 17%. Admission severity scores: APACHE II 14 (11–16), SOFA 2 (2–3), PO2/FiO2 84 (70–109). At the moment of admission, 80% needed HFNC with ROX index 3.3 (2.7–4.1), requiring mechanical ventilation 85% (27 ± 25 days) and prone position 77% (2; 1–4 sessions). 58% needed vasopressor therapy, 22% had acute renal failure and 40% had others complications during admission. The ICU stay was 35 ± 28 days and the median hospital stay was 48 ± 32 days. The prognosis was unfavourable in 15% of patients. In the **univariate analysis**, those patients with HFCN support failure presented a lower ROX index (3.3 ± 0.8 vs 4.7 ± 0.8, p < 0.00). We confirmed that **ROX index in the first 24 h of ICU admission** was predictive of HFNC failure and need for mechanical ventilation **OR 0.23; CI 95% 0.11–0.51. Using the AUROC curves**, the **ROX index in the first 24 h of ICU admission** demonstrated a good discriminative power of High Flow Nasal Cannula failure (AUC 0.85; CI 95% 0.72–0.98), with a good calibration ability (Chi-squared test 10.26, p = 0.25) and with better performance indicators (S 95%, E 81%, PPV 96% and NPV 75%).
Conclusion: Our data show that the ROX index in the first 24 h of ICU admission demonstrated a good discriminative power of High Flow Nasal Cannula failure in critical patient with severe COVID-19.

000960

A burden of fluid, sodium, and chloride due to intravenous fluid therapy in mechanically ventilated patients: a post-hoc analysis of multicenter cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000960

Introduction: Fluid creep is a major source of fluid volume, sodium, and chloride in critically ill patients.
Objectives: This study aimed to address the absolute and relative proportions of volume, sodium, and chloride in intravenous-fluid sources among mechanically ventilated patients according to oxygenation status.
Methods: This study was a post-hoc analysis of the prospective multicenter cohort study conducted in 23 intensive care units (ICUs) in Japan from January 1, 2018, to March 31, 2018. Consecutive adult patients who underwent mechanical or noninvasive ventilation upon ICU admission and stayed ICU more than 24 h were included. We evaluated fluid therapy until 7 days after ICU admission according to oxygenation status. Fluid creep was defined as fluids administered as drug diluents and for the maintenance of catheter patency when administered at ≤ 20 mL/h. The patients were followed-up until hospital discharge.
Results: Among the 588 included patients, a mean intravenous-fluid volume of 2,662 mL was administered within 24 h of ICU admission, and it gradually decreased and yet remained > 1,000 mL per 24 h. Crystalloid solution was the main intravenous fluid within 24 h of ICU admission. After 24 h, the amount of glucose-containing fluid and fluid creep increased, and was the major source of intravenous intake. The median fluid creep within 24 h of ICU admission was 661 mL (25.0% of the total intravenous-fluid volume), and the proportion of fluid creep gradually increased throughout the ICU stay. After adjusting for the prespecified confounding factors, septic shock and a higher severity score were associated with a larger amount of total intravenous fluid and fluid creep. In addition, hypoxemic respiratory failure was associated with a reduction in the total amount of intravenous fluid but not with fluid creep.
Conclusion: Reducing fluid creep potentially contributes to further fluid restriction, although a conservative fluid strategy has been widely accepted for managing patients with respiratory failure. Our findings provide a rationale for further research that assesses the feasibility of conservative fluid management in patients with respiratory failure.

000975

Ventilatory management of COVID-19 ARDS: a case series

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Introduction: COVID-19 is mainly characterized by a respiratory illness of varying severity, ranging from asymptomatic or mildly symptomatic to severe respiratory failure, acute respiratory distress syndrome and multi-organ failure. There is still an urgent need to better understand ventilatory strategies and outcomes of severe COVID-19 patients.
Methods: Retrospective case series of 227 consecutive patients with laboratory-confirmed COVID-19 admitted to ICU between March 2020 and December 2021. Demographic and clinical data were collected.
Results: Several ventilatory support modalities were used. Most patients were managed non-invasively for at least part of their ICU stay, the majority before progression of hypoxemia and being intubated for invasive mechanical ventilation. Exclusive non-invasive ventilatory support, either High Flow Nasal Oxygenation, Non-Invasive Ventilation or both was used in 65 patients (28.6%). 28-day mortality rate in the group of patients whose hypoxemia was managed entirely non-invasively was 12.3% (8 patients). 164 patients were invasively ventilated. Most intubations (65%) occurred in the first 24 h after ICU admission, and mechanical ventilation mean duration was 14 days. About 19% (31 patients) were intubated relatively later, after 5 days in the ICU. This happened mainly in immunosuppressed patients, in whom attempts were made to delay intubation and its infectious complications. Proportion of time under invasive mechanical ventilation was on average 52.8% of the total length of ICU stay. Reintubation rate was 10% (22 patients), occurring on average 2 to 3 days after planned extubation. Patients often remained under invasive ventilation for difficult and prolonged weaning, thus requiring tracheostomy. In total, 32 tracheostomies were performed, 16 were performed in the operating room, for initial concerns related to aerosol generation. The procedure occurred on average at day 26. We recorded 2 deaths due to complications from tracheostomy. Median ICU and hospital stay was 15 and 25 days, respectively, and 28-day-mortality rate was 38%. Death occurred in half of the subgroup of patients that underwent invasive mechanical ventilation (81 patients, 50%), regardless of whether they had received non-invasive ventilation prior to intubation. Invasive ventilation exposure was significantly more common in the deceased group (61 versus 91%, p = 0.005).
Conclusion: A large proportion of critically ill COVID-19 patients required prolonged mechanical ventilation. There was a striking difference in 28-day mortality between patients managed solely non-invasively and the ones subjected to invasive mechanical ventilation. Tracheostomy was often used to manage difficult weaning but was performed relatively later due to need of prolonged aggressive ventilation and proning.

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000998

Impact of the Different Waves of the COVID-19 Pandemic on the Tracheostomy Rate

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Intensive Care Medicine Experimental 2022, **10(2)**:000998

Introduction: The COVID-19 pandemic changed the dynamics of hospitals and healthcare. Regarding the increase of respiratory patients, some treatments or procedures inherently associated with this pathology gained more presence in ICUs.
Objectives: To evaluate the impact of the different waves of the pandemic on the performance rate of tracheostomy in critically ill COVID-19 patients.
Methods: Observational, single-center, retrospective study. Adult critically ill PCR-confirmed COVID-19 patients admitted to ICU (Mar 2020-Oct 2021) were included. Demographics, respiratory support, day of intubation/extubation/tracheostomy and method of tracheostomy were recorded. A multidisciplinary tracheostomy team was formed in the first wave, including: General Surgery, Maxillofacial Surgery, Otorhinolaryngology, Anesthesiology and Intensive Care Medicine. Starting and ending dates of each wave were defined based on reported nationwide follow-up data (1st-Mar 2020, 2nd-Oct 2020, 3rd-Dec 2020, 4th-Feb 2021, 5th-Jun 2021). Follow-up ended at death or discharge from ICU. Data are expressed as absolute numbers or percentages, as appropriate. Differences were assessed by Chi-square. $p < 0.05$ was considered statistically significant.
Results: A total of 618 patients were included during all the waves, 67% were male, mean age 59 years (±12). Out of the total, 279 (45%) required invasive mechanical ventilation (IMV), showing a significant decrease in the need for IMV when analyzing the different waves individually (72.5%-51.3%-38%-26.9%-37%), $p < 0.001$. Total percentage of tracheostomy in IMV treated patients was 13% (n = 85), a significant decrease was observed in the different waves (38%-27.5%-26%-24%-22%), $p < 0.001$. Mean time of IMV until tracheostomy was 17 days. Out of the total, 61% (n = 52) of tracheostomies were surgically performed; in the first wave the percentage was 83%, showing a progressive decrease in the following waves.
Conclusion: The need for invasive mechanical ventilation was higher in the first wave, as well as the indication for tracheostomy. The remaining waves showed a progressive decrease in both parameters.

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Acknowledgements: no financial or technical support was received to conduct this study.

001004

Duration of mechanical ventilation prior to extracorporeal membrane oxygenation in COVID-19 patients: a retrospective analysis

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Introduction: The use of Extracorporeal Membrane Oxygenation (ECMO) in patients with COVID-19-associated Acute Respiratory Distress Syndrome (ARDS) may be a promising strategy if maximal conventional treatment fails to assure adequate oxygenation and ventilation.1 ELSO guidelines for Veno-Venous ECMO (VV-ECMO) consider a duration of mechanical ventilation exceeding 7 days as a relative major contraindication for VV-ECMO in patients with COVID associated with ARDS. 1. In contrast, other reports indicate that prolonged time of invasive mechanical ventilation (IMV) prior to ECMO indication was not associated with an increased mortality. 2. Therefore, the purpose of this study was to investigate the clinical course and outcome of patients supported with VV-ECMO for COVID-19-induced-ARDS and compare mortality rates between different durations of MV.
Methods: We conducted a retrospective analysis of all consecutives COVID-19 patients submitted to VV-ECMO between 2020 and 2021 in a tertiary referral hospital in Southern Brazil. Demographic data, diagnosis on admission, comorbidities, mechanical ventilation, length of stay and mortality in 90 days were recorded. Kaplan–Meier curves were used to calculate the time-dependent occurrence of death between short duration (< 7 days) of IMV prior to ECMO versus long duration IMV (≥ 7 days). We considered a p value < 0.05 statistically significant.
Results: During the study period, 14 patients (median age 48.5 [IRQ 44.2–58.0]; 6 [42.9%] men) were treated with ECMO for COVID-19. All 14 patients had ARDS, 2 (14%) of them complicated with tracheal laceration and 3 (21%) with bronchopleural fistula. Ten patients (71.4%) survived at day 90 after ECMO implantation. Median ECMO duration was 18 (IRQ 15.5–34.3) days, and median time from intubation to ECMO start was 4 (IRQ 1.0–9.5) days. Of 6 patients with a pre-ECMO IMV duration ≥ 7 days (42,9%), 4 subjects (66%) survived at 90 days. Kaplan Meier curve showed no difference between patients with IMV course longer than 7 days (p-value 0.139).

Conclusion: In conclusion, no difference on survival was demonstrated between short and prolonged time of IMV prior to ECMO in our cohort study.

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000841

RecruitmEnt Assessed by eleCtRical Impedance Tomography (RECRUIT study). A Multicentre study

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Intensive Care Medicine Experimental 2022, **10(2)**:000841

Introduction: Defining the potential for lung recruitment is a crucial aspect of safe PEEP selection in mechanically ventilated patients, but no valid method exists to define the best PEEP. By using electrical impedance tomography (EIT), we aim to quantify recruitability and determine the potential beneficial and harmful physiological effects of PEEP in patients with COVID-19 related acute respiratory distress syndrome (ARDS).

Methods: In this observational international study from the PLUG group (NCT04460859) COVID-19 patients with moderate and severe ARDS were enrolled within the first week of ARDS diagnosis. EIT recordings, ventilator data, hemodynamics and arterial blood gases were obtained during lung (de)recruitment maneuvers. PEEP was set to 6, 16 and 24 cmH2O for 5-min per step, after which a decremental PEEP titration from 24 to 6 cmH2O (in steps of 2 cmH2O) was performed. Recruitment-to-inflation (R/I) ratio was assessed with a single-breath maneuver during a 16 to 6 cmH2O PEEP drop, and an EIT-based R/I ratio was calculated for these same breaths. Lung collapse, overdistension and respiratory system compliance were calculated for each step, and we determined the PEEP level at the intercept of the relative overdistention and collapse curves during a decremental PEEP trial (Costa et al. [1] approach). To facilitate the presentation, recruiters were defined as patients with a > 25% decrease in collapse from PEEP 6 (at start protocol) to PEEP 24 cmH2O. Differences in parameters between groups were assessed with the Wilcoxon rank sum test.

Results: Of the 90 patients analyzed till date (of the 107 enrolled) (61% male; age: 58.5 ± 11.8y; BMI: 30.8 ± 6.2 kg/m2; P/F at admission: 122 ± 36 mmHg), 72% were categorized as recruiters, with a significantly higher R/I ratio as compared to non-recruiters (Tab.1). R/I ratio correlated with the % decrease in collapse ($r = 0.52$, $p = 0.001$). In contrast to non-recruiters, recruiters improved respiratory mechanics and gas exchange (higher PaO2/FiO2) (Tab.1), without compromising hemodynamics. The optimal PEEP as per Costa approach was 14.2 vs. 10.6 cmH2O for recruiters vs. non-recruiters. Costa individual PEEP level varied between 6 and 19 cmH2O, but at this PEEP, respiratory mechanics were similar for recruiters and non-recruiters, with medians for collapse and overdistention below 5% and 10%, respectively (Tab.1).

Conclusion: Recruitability varies widely among COVID-19 patients; most are recruitable without requiring very high PEEP levels. In recruiters, PEEP results in improved mechanics and gas exchange, without compromising hemodynamics. EIT seems useful to identify recruitability and to support selecting a personalized PEEP.

Table 1. Characteristics of recruiters and non-recruiters, and their response to increases in PEEP

	Recruiters (n=65)	Non-recruiters (n=25)	p-value
Recruitability			
Decrease in collapse PEEP 6 to PEEP 24, %	39.0 [32.3; 45.7]	16.9 [10.2; 20.5]	-
Ventilator-based R/I ratio	0.81 [0.54; 0.95] (n=53)	0.60 [0.46; 0.77] (n=24)	0.020
EIT-based R/I ratio	0.94 [0.86; 1.09] (n=31)	0.65 [0.53; 0.93] (n=12)	0.009
Baseline characteristics			
PaO_2/FiO_2 at ICU admission, mmHg	120 [100; 142]	125 [98; 136]	0.992
Age, years	58.5 [49; 65]	64 [60; 70]	0.012
Body mass index, kg/m²	30.7 [26.6; 34.4]	28.4 [25.2; 31.9]	0.067
Crs at different PEEP steps, ml/cmH_2O			<0.001[1]
PEEP 6	27.9 [22.3; 33.6]	27.8 [22; 33.8]	
PEEP 16	29.1 [22.8; 37.9]	25.7 [18.6; 32.5]	
PEEP 24	23.9 [18.4; 30.4]	15.6 [11.3; 19.5]	
PaO_2/FiO_2 at different PEEP steps, mmHg			<0.001[1]
PEEP 6	93 [62; 124]	116 [91; 148]	
PEEP 16	125 [100; 179]	120 [96; 154]	
PEEP 24	249 [170; 336]	154 [107; 253]	
Mechanics at Costa PEEP level			
PEEP according to Costa approach, cmH_2O	14 [12; 16]	10 [8; 13]	<0.001
Crs, ml/cmH_2O	36.0 [30.5; 44.2]	31.9 [24.4; 40.7]	0.100
ΔPaw, cmH_2O	8.0 [7.0; 9.9]	8.4 [7.5; 9.7]	0.658
Collapse, %	4.8 [3.3; 7.3]	4.0 [1.9; 5.6]	0.121
Overdistention, %	7.2 [6.0; 10.3]	9.3 [6.1; 13.4]	0.116

Values are presented as median with interquartile range [IQR]. [1] p-value for the interaction effect of PEEP level x group, as assessed per a linear mixed effects model. Abbreviations: Crs, respiratory system compliance; EIT, electrical impedance tomography; FiO_2, fraction of inspirated oxygen; ICU, intensive care unit; PaO_2, partial arterial oxygen pressure; ΔPaw, airway driving pressure (calculated from Crs and the set tidal volume); PEEP, positive end-expiratory pressure; R/I ratio, recruitment-to-inflation ratio

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Acknowledgements: The study received financial support from Draeger and Timpel.

Acute Respiratory Failure 13

000815

Management and outcomes of pregnant women admitted to intensive care unit for severe pneumonia related to SARS-CoV-2 infection: the multicenter and international COVIDPREG study.

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Intensive Care Medicine Experimental 2022, **10(2)**:000815

Introduction: Management and outcomes of pregnant women admitted to ICU for COVID-19 remain to be investigated.

Methods: This observational multicenter study was conducted in 32 ICUs in France, Belgium and Switzerland. Maternal management and maternal and neonatal outcomes were analyzed and compared with those of pregnant women hospitalized for influenza infection.
Results: Among the 187 women with COVID-19 (33 ± 6 years old and 28 ± 7 weeks' gestation), 76(41%) were obese, 12(6%) had diabetes mellitus and 66(35%) had pregnancy-related complications. Standard oxygenation, high-flow nasal oxygen therapy (HFNO) and non-invasive ventilation (NIV) were used in 21%, 64% and 22% of patients, 73(39%) were intubated and 15(8%) required venovenous extracorporeal membrane oxygenation (VV-ECMO) during hospitalization. Awake prone positioning and prone positioning before fetal extraction were performed in 4% and 9% of patients. In multivariate analysis, risk factors for intubation were obesity (CSH = 2.00, 95%CI(1.05–3.80), p = 0.03), term (CSH = 1.07, 95%CI(1.02–1.10), per + 1 week gestation, p = 0.01), extent of CT-Scan abnormalities > 50% (CSH = 2.69, 95%CI(1.30–5.60), p < 0.01) and NIV use (CSH = 2.06, 95%CI(1.09–3.90), p = 0.03). Fetal extraction was required during ICU stay in 35% of patients, mainly for maternal respiratory worsening. The rate of maternal and/or neonatal complications increased with the invasiveness of maternal respiratory support. Compared to influenza infection, HFNO was more frequently used in patients with COVID-19 and VV-ECMO in patients with influenza, while obstetric management and maternal and neonatal outcomes were similar.
Conclusion: In ICU, a third of pregnant women with COVID-19 were intubated and required fetal extraction. Management of these patients requires close collaboration between intensivists, obstetricians and pediatricians.

000898

The pharmacology of airway management in critically-ill COVID-19 patients in an Intensive Care Unit (Medical ICU) in a secondary-level university Hospital: insights from the first to the sixth wave of the pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000898

Introduction: Airway management and endotracheal intubation (ETI) in critically-ill patients is a procedure with some risks and posible life-threatening complications. Besides, there is an associated risk due to severe hypoxemia in critically-ill COVID-19 patients that involves working in a safe and protective environment, which can lead to an increase in the difficulty of airway management.
Objectives: To describe the pharmacology of airway management in critically-ill COVID-19 patients admitted to our Unit with severe acute hypoxemia requiring ETI and invasive mechanical ventilation.
Methods: Retrospective and descriptive study from the first (March 2020) to the sixth (December 2021) wave of the pandemic. 201 patients were admitted (18 were excluded: 13 transferred to anaesthetic department and 5 transferred to other hospital). The remaining 183 patients were included: 79 needed non-invasive respiratory support: non-invasive ventilation (nIV) 31, High Flow Nasal Cannula (HFNC): 9 and mixed (nIMV + HFNC): 39 patients. 104 patients required ETI (10 were excluded: ETI in A&E Department: 3, ETI in other hospital: 2 and data non available: 5). The following parameters were analyzed in the remaining 94 patients: gender, group age, APACHE II score, SOFA, comorbidities, drugs used in airway management: hypnotics, neuromuscular blockers, others. First-attempt intubation device used: direct laryngoscopy (DL), video laryngoscope (VL) (Airtraq type), laryngoscopic view according to Cormack-Lehane classification (CL): good (CL grade 1/2), poor (CL grade 3/4), devices used: Frova introducer, bougie, maneuver for improving laryngoscopic view (BURP, Sellick), and complications: hypoxia (SpO2 < 80 mmHg), hypotension (systolic blood pressure < 90 mmHg), bradycardia (HR < 40 bpm) and cardiac arrest.
Results: 94 patients (68 male/26 female), group age: < 60 years old: 24, 60–70: 52, > 70 years old: 18 patients. APACHE II score: 26 ± 7.4, SOFA: 7.4 ± 2.8, comorbidities: BMI > 30 kg/m^2: 18, COPD/asthma: 15 immunocompromised: 8. Drugs used for ETI: hypnotics: etomidate(ETO) 51, propofol (PF) 11, midazolam (MDZ) 26, ketamine (KET) 6, neurmoscular blockers: succinylcholine (SC) 24, rocuronium(RC) 63, cisatracurium (CS) 7 and others: fentanyl (FNT) 15, lignocaine (LC) 3, atropine (ATP) 5. Direct laryngoscopy was performed in 77 patients, with good view in 65 of them (CL grade 1: 55 patients, grade 2: 10 patients) and poor in 12 (CL grade 3: 9 patients, grade 4: 3 patients). Video laryngoscope was used in 17 patients: good view in 13 of them (CL grade 1: 11 patients, grade 2:2 patients), and poor in 4 (CL grade 3: 2 patients, grade 4: 2 patients). In the 12 patients with poor laryngeal view during DL, the rescue technique used was: bougie + BURP: 4 patients, frova introducer: 3, frova + BURP: 3 and VL: 2. In the 4 patients with poor laryngeal view during VL, the rescue technique was: DL + frova: 1, DL + frova + BURP: 2 and percutaneous tracheostomy in 1 patient. Complications: SpO2 < 80 mmHg: 19 patients, systolic blood pressure < 90 mmHg: 14, bradycardia: 6 and cardiac arrest in 2 patients.
Conclusion: In our series, the most commonly drugs used in critically-ill COVID-19 patients for airway management were etomidate (54%) and rocuronium (67%). Laryngoscopic view (first attempt) was good (CL grade 1/2) in 84% (DL) and 76.5% (VL) of the patients. The most common complications were: SpO2 < 80 mmHg: 19%, and SBP < 90 mmHg: 15%.

000941

Prognostic factors prior to extracorporeal membrane oxygenation support in COVID-19 critical ill patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000941

Introduction: Limited data are available about venovenous extracorporeal membrane oxygenation in patients with severe hypoxemic respiratory failure due to coronavirus disease 2019 (COVID-19).
Objectives: The aim of this study was to identify the risk factors for unfavourable prognosis in COVID-19 critical ill patients with severe respiratory failure who required extracorporeal membrane oxygenation support (ECMO).
Methods: Prospective, observational study, carried out on a cohort of critical ill patients with severe Covid-19 who required ECMO support in H.G.U Gregorio Marañón ICU, between March and August 2021. Epidemiological and clinical data, severity scores, as well as variables related to mechanical ventilation support (MV) parameters used before their inclusion in ECMO were included. All patients were managed according to the recommendations of the Extracorporeal Life Support Organization (ELSO). Descriptive data were expressed as means (SD) for normally distributed continuous variables, medians (IQR) for non-normally distributed variables, and percentages for categorical data. Continuous variables were compared using a simple logistic regression analysis (OR), and categorical data by the Chi-square test (RR). Risk factors related to an unfavourable prognosis were obtained by a multiple logistic regression model that included those variables that were significant from the univariate analysis and those considered clinically relevant.
Results: Twenty-six patients were included in the study. Age 55 (55–60) years, 73% male, previous chronic pathology 69%, APACHE II admission 13 ± 4. **Prior to ECMO support**, the patients had: PO2/FiO2 73 ± 20, SOFA 7 ± 3, RESP score 2 (0–2 0.25), mechanical ventilation days 8 (2–20), 65% of them aggressively ventilated (plateau pressure > 30 cmH2O and driving pressure > 15 cmH2O) for 1 (0–1.25) days. 100% of patients required prone position (3; 1–5 maneuvers), 61% received Nitric oxide, 69% vasopressor therapy and 19% renal replacement therapy. The duration of ECMO support was 23 ± 11 days,

the ICU stay 53 ± 27 days and **61% of patients had an unfavorable prognosis.** In the **univariate analysis**, the variables related to mortality were: **Age > 55 years** (RR 27; 95% CI 2.6–284.7), **chronic pathology** (RR 1.1; 95% CI 0.2–5.9), **APACHE II admission** (OR 0.7; 95% CI 0.5–1), **SOFA pre-ECMO** (OR 0.9; 95% CI 0.6–1.2), **RESPscore** (OR 0.8; 95% CI 0.5- 1.2), **aggressive mechanical ventilation days** (OR 1.2; 95% CI 0.7–2). In the **multivariate analysis**, including the variables prior to ECMO support, the only independent prognostic factor for mortality was: **Age > 55 years OR 27; 95% CI 2.6–284.7.**
Conclusion: In our series we had a high mortality and a long ICU stay in severe covid-19 patients who required ECMO support, being the age the only independent factor for unfavourable prognosis.

000963

Influence of high-flow nasal oxygen and non-invasive ventilation on mechanical ventilation outcomes in COVID-19 patients with acute respiratory failure

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Intensive Care Medicine Experimental 2022, **10(2)**:000963

Introduction: High-flow nasal oxygen (HFNC) and non-invasive ventilation (NIV) are frequently used during acute respiratory failure in coronavirus disease 2019 (COVID-19) patients. However, their efficacy and safety remain uncertain. Randomized trials comparing HFNC with NIV suggested that HFNC may increase rate of intubation or death, but it remains unclear whether HFNC compared with NIV affects mortality (1).
Objectives: To compare hospital mortality and length of hospital stay (LOS) between COVID-19 patients with acute respiratory failure that used NIV alone and patients that used NIV in association with HFNC according to the use of invasive mechanical ventilation (MV).
Methods: Retrospective single-center cohort study conducted in a private hospital in Brazil. We compared COVID-19 acute respiratory failure patients that used NIV alone or in association to HFNC stratified according to the use of MV. Mortality was assessed by unadjusted and adjusted logistic regression analysis using group VNI alone as a reference level and presented as odds ratio (OR) along with 95% confidence interval (95%CI).
Results: We analyzed 1,725 patients who used NIV alone [36.3% (626/1,725)] or the association of NIV with HFNC [63.7% (1,099/1,725)]. Among patients that did not receive MV [59.8% (1,032/1,725)], 38.7% (399/1,032) used only NIV and 61.3% (633/1,032) received the association of NIV with HFNC. Compared with patients that received the association of NIV with HFNC, patients that used only NIV were more frequently women (37.1% vs. 27.8%; $p = 0.002$) and had a higher SAPS 3 [45 (39–51) vs. 43 (39–49); $p = 0.05$]. Unadjusted mortality [3.8% (15/399 patients) vs. 5.2% (33/633 patients); OR 1.41 95%IC: 0.76–2.63; $p = 0.28$) did not differ between patients that used only NIV and patients that used NIV with HFNC (OR 1.41; 95%IC: 0.76–2.63; $p = 0.28$). When mortality was adjusted for SAPS 3 score, patients that used the association of NIV with HFNC had increased odds for mortality (aOR 2.54; 95%IC 1.22–5.31; $p = 0.013$) compared with patients that used only NIV alone. Median (IQR) hospital LOS [13 (10–18) vs. 10 (7–13) days; $p < 0.001$) was higher in the group that used the association of NIV with HFNC. Among patients that received MV [40.2% (693/1,725)], 32.8% (227/693) of patients used NIV alone and 67.3 (466/693) received the association of NIV with HFNC. SAPS 3 score was higher [49 (43–55) vs. 46 (41–52); $p < 0.01$] in patients that used only NIV than in patients that used NIV with HFNC. Hospital mortality [29.4% (137/466) vs. 20.7% (47/227); OR 1.60; IC95% 1.09–2.33, $p = 0.015$) (aOR1.11; IC95% 1.08–1.40, $p < 0.001$)] and hospital LOS [27 (18–41) vs. 25 (15–40); $p = 0.009$)] were higher in the group that used the association of NIV with HFNC.
Conclusion: The association of NIV with HFNC in patients that required and did not require invasive mechanical ventilation may be associated with increased mortality. Further studies are needed to better understand this association.

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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.

001001

Superinfection in COVID-19 patients treated with corticosteroids and immunomodulators

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Intensive Care Medicine Experimental 2022, **10(2)**:001001

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.

001018

Clinical impact of the oximeters' inaccuracy (bias and errors) – secondary analysis of the OXYGAP study

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Intensive Care Medicine Experimental 2022, **10(2)**:001018

Introduction: Pulse oximetry is daily used worldwide to measure SpO2 in order to monitor and titrate oxygen support. We previously showed that four among the most frequently used oximeters have significant bias (systematic errors from -3% to + 1%) and inaccuracy (random error) in comparison with the gold standard SaO2. The main objective of this study was to highlight the impact of the oximeters' variability on monitoring and clinical decisions in acutely ill patients.
Methods: We prospectively included 210 stable ICU patients with an arterial catheter in place. For all included patients, we compared SpO2 values for each of the four evaluated oximeters (Nonin, Nellcor, Massimo and Philips) and concomitant PaO2 and SaO2 values from the arterial blood gases. When the patients met the criteria for hypoxemia (SaO2 < 90% or PaO2 < 60 mmHg), we evaluated which oximeter could detect hypoxemia (SpO2 < 90%). For each measurement, we evaluated for each oximeter when the oxygen support should be maintained even, increased or decreased to maintain a SpO2 value between 92 and 96%.
Results: Mean age of the patients was 66.3 year, 73% were men, skin pigmentation was light (Fitzpatrick 1 or 2 in 96.2% of the patients). The SpO2-SaO2 bias went from -3.1% (Nonin), to + 0.9% (Philips) ($P < 0.001$). With Nellcor and Masimo, bias were -0.3 ($P < 0.03$) and -0.2% ($P = 0.17$) respectively. Nonin oximeter underestimated arterial oxygenation in 91% of the cases but detected 100% of hypoxemia defined by PaO2 < 60 mmHg. Philips overestimated oxygenation in 55% of the cases but detected 11% of episodes of hypoxemia. Based on the oximeter used, the management of oxygen support to maintain the patients within a SpO2 target of 92–96% differed a lot. To keep the patients within this SpO2 target, in the cohort of 210 patients, it would be required to increase oxygen in 60.6% vs. 19.1% vs. 18.7% vs. 10.4% and to decrease oxygen in 1.0% vs. 6.2% vs. 9.1% vs. 20.9% of the cases ($p < 0.0001$) when using Nonin, Nellcor, Masimo or Philips oximeter respectively.
Conclusion: The variability of SpO2 measurements between oximeters has a significant impact for the monitoring and management of oxygen support. The bias of each oximeters should be known by clinicians and SpO2 targets should be adapted to the oximeter brand used by clinicians.

001020

Effect of decreasing respiratory rate on lung injury biomarkers in mechanically ventilated patients with Covid-19 associated Acute Respiratory Distress Syndrome

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Intensive Care Medicine Experimental 2022, **10(2)**:001020

Introduction: Protective ventilation strategies which limit tidal volume (Vt) and airway pressures, are strongly recommended in patients with acute respiratory distress syndrome (ARDS) to prevent ventilator-induced lung injury (VILI). High respiratory rate (RR), an essential parameter related to the energy applied to the lungs has shown to increase lung injury biomarkers in preclinical studies. However, the clinical role of RR remains uncertain.
Objectives: To evaluate the effect of decreasing RR on systemic lung injury biomarkers, in patients with Covid-19-associated ARDS (CARDS).
Methods: Prospective, randomized crossover study in patients with CARDS within the first 48 h of mechanical ventilation, PaO2:FIO2 ratio less than 200, and requiring deep sedation and neuromuscular blockade. All patients were ventilated with Vt 6 ml/kg PBW, and PEEP and FiO2 according to the ARDSNet table. Patients with PaO2:FIO2 ratio below 150 mmHg were treated with prone positioning.
The 24-h protocol consisted of 12 h at low, and 12 h at high RR, with patients, allocated randomly to sequence low–high or high-low. RR was adjusted according to a nomogram directed to obtain an 8–10 breaths/min difference between periods while maintaining pH and PaCO2 within safety limits (pH 7.20–7.45 and PaCO2 35–60 mmHg). Hemodynamic and respiratory mechanics were registered, and arterial blood samples were drawn for gas exchange and quantification of lung injury biomarkers at baseline, 12, and 24 h.
Results: Thirty-two patients with CARDS (26 male (81%), 52 [44–56] years, PaO2:FIO2 104 [74–125]) were enrolled. Twenty-five patients (78%) had severe ARDS and 25 (78%) were in prone positioning. All patients completed the protocol and the median RR at high and low RR periods was 30 [26–32] and 20 [16–22] breaths/min ($p < 0.001$), respectively. As compared with high RR, during low RR, minute ventilation decreased by 27% (11.2 [9.4–12.8] vs 8.2 [6.7–9.9] L/min, $p < 0.001$) and mechanical power by 29% (24 [18–31] vs 17 [13–20] J/min, $p < 0.001$). PaCO2 and pH remained within safety limits: pH 7.44 (7.38–7.47) vs 7.34 (7.30–7.40), $p < 0.001$; PaCO2 38 (35–46) vs 53 (44–58) mmHg, $p < 0.001$, for high and low RR, respectively). Respiratory system mechanics did not differ between periods. No difference between periods was observed in any inflammatory marker (IL-6, IL-8, TNF-R1), nor in the markers of epithelial or endothelial damage (s-RAGE; SP-D, and Angiopoietin-2), nor the marker of profibrotic activity (TGF-ß) (Table).
Table. Plasma levels biomarkers of inflammation and injury at baseline, and low and high respiratory rate.

Biomarker(pg/mL)	Baseline	Low RR	High RR	p-value*
Interleukin-6	13 [7-38]	12 [6-22]	12 [8-20]	0.633
Interleukin-8	41 [22-61]	33 [23-43]	39 [19-51]	0.426
TNF-R1	2,529 [1,947-3,485]	2,384 [1,988-2,802]	2,778 [2,066-3,199]	0.211
SP-D	14,440 [6,287-29,134]	14,408 [7,607-27,540]	14,370 [8,131-29,471]	0.984
RAGE	4,845 [2,080-7,435]	2,782 [1,411-5,244]	2,932 [1,558-5,858]	0.723
Angiopoietin-2	2,775 [1,637-5,623]	2,618 [1,802-5,739]	2,507 [1,654-5,610]	0.821
TGF-ß	3,185 [1,121-5,503]	3,482 [1,029-5,712]	3,338 [1,469-32,759]	0.682

Results are presented as median [interquartile range]. Abbreviations: SP-D, surfactant protein D; RAGE, Receptor for advanced glycation end products; TGF-ß, transforming growth factor-ß. * Comparison between high and low RR using Wilcoxon signed-rank test.
Conclusion: Decreasing respiratory rate -and thus minute ventilation and the power of ventilation- does not induce changes in lung injury biomarkers when a protective ventilation strategy is maintained in patients with CARDS.

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Acknowledgements: Fondecyt 1191315-2019.

001049

Lateral Body Positioning with Appropriate PEEP Improves Lung Homogeneity in an Experimental Model of Acute Respiratory Distress Syndrome

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Intensive Care Medicine Experimental 2022, **10(2)**:001049

Introduction: When compared with supine position, a lateral position strategy [1] changes the pleural pressures gradient, so that the transpulmonary pressure becomes larger in the nondependent units and smaller in the dependent ones. With an appropriate PEEP, that may yield simultaneous regional/selective lung recruitment and relief of lung overdistension and, consequently, result in a more homogeneous ventilation distribution. Other potential effects of a lateral positioning strategy are changes in ventilation/perfusion matching due to effects like attenuation of regional overdistension within the lung units suffering excessive stretch and, consequently, less diversion of pulmonary blood flow away from these units. Pulmonary blood flow distribution can be also changed by a diminution of regional collapse within the less ventilated lung units and, as a result, regional changes in hypoxic pulmonary vasoconstriction efficiency.
Objectives: We aimed to study the effects on ventilation and perfusion distributions of a sequential lateral positioning strategy using electrical impedance tomography (EIT) [2] imaging in a porcine experimental model of early acute respiratory distress syndrome (ARDS).
Methods: We performed a two-hit injury ARDS model [3] in seven pigs. All animals were studied in five body positions in a sequential order, 15 min each: Supine 1; Lateral Left (left up); Supine 2; Lateral Right (right up); Supine 3. During each lateral positioning, PEEP level was adjusted upwards whenever necessary to prevent collapse of the dependent lung units. Lateral positioning (30°) was performed with a platform-based rotation bed. At the end of each step, physiological and EIT measurements were acquired. EIT-based lung perfusion was obtained by injecting a 10-mL bolus of 10% hypertonic saline solution into a central venous catheter during an expiratory pause. For both regional ventilation and perfusion EIT analyzes, the lungs were subsegmented into two ways: A) four quadrants; and B) ventral and dorsal halves.
Results: Ratio of arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen (FIO2) [PaO2/FIO2 Ratio] in all protocol (*steps*), *mean ± SD*: *448 ± 69* (*baseline*), *51 ± 8* (*after establishment of experimental ARDS model*), *80 ± 26* (*Supine 1*); *131 ± 48* (*Lateral Left*); *138 ± 58* (*Supine 2*); *180 ± 89* (*Lateral Right*); *219 ± 124* (*Supine 3*). Ventilation distribution, ventral vs. dorsal half, in %, in the following protocol (*steps*): *73:27* (*Supine 1*); *68:32* (*Lateral Left*); *64:36* (*Supine 2*); *63:37* (*Lateral Right*); *59:41* (*Supine 3*). Also the ventilation distribution in quadrants became significantly more homogenous along the lateral positioning strategy, markedly when comparing Supine 1 and Supine 3 steps. The perfusion distribution, (supine vs. lateral) presented an antigravitational effect, i.e. increased perfusion in the lung positioned upwards.
Conclusion: Our sequential lateral positioning strategy provided a meaningfully more homogeneous ventilation distribution and oxygenation benefit in a porcine experimental model of early ARDS. Our findings also suggest that the lateralization engendered an antigravitational effect on the perfusion distribution, likely related to a diminution of hypoxic pulmonary vasoconstriction.

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Acknowledgements: Grant Agency of the Czech Republic: projekt GA ČR 22-34020S.

001071

Impact of the oximeters' bias on automated oxygen titration – secondary analysis of the OXYGAP study

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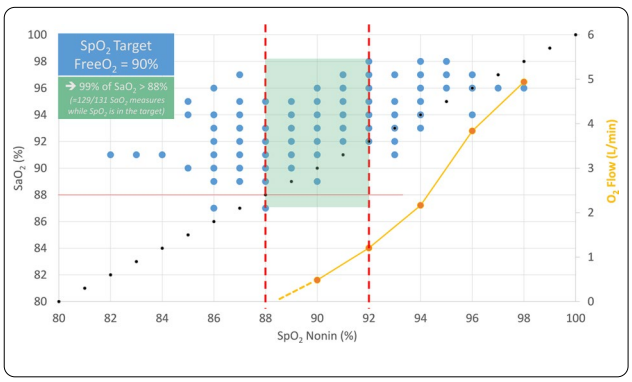
Intensive Care Medicine Experimental 2022, **10(2)**:001071

Introduction: We previously showed in the OXYGAP study that the NONIN oximeter had a significant bias of -3% in patients with light pigmentation in comparison with the gold standard SaO2. The main objectives of this study was to evaluate the safety of different SpO2 targets with FreeO2 (automated oxygen titration and weaning device) and the impact on oxygen utilization in regards to these results.
Methods: We prospectively included 211 stable ICU patients with an arterial catheter in place. For all included patients, we compared SpO2 values for each of the four evaluated oximeters (Nonin, Nellcor, Massimo and Philips) and concomitant PaO2 and SaO2 values from the arterial blood gases. We evaluated the impact of utilization of SpO2 targets of 90 and 88% with FreeO2 (using the NONIN oximeter) on arterial oxygenation and oxygen utilization.
Results: The mean age of the patients was 66.3 years, 73% were men, and skin pigmentation was light (Fitzpatrick 1 or 2 in 96.2% of the patients). The SpO2-SaO2 bias was -3.1% (Nonin). Nonin oximeter underestimated arterial oxygenation in 91% of the cases but detected 100% of hypoxemia defined by PaO2 < 60 mmHg. In this database, with SpO2 targets set at 90 and 88%, the SpO2 target ± 2% would provide arterial oxygen saturation above 88% in 129/131 patients (99%) (Figure) and 91/93 patients (98%) respectively. Based on previous data, the utilization of SpO2 targets of 90% would reduce a lot of oxygen consumption (1).



Conclusion: Oximeter embedded in the FreeO2 is Nonin which has a bias of -3% in comparison with SaO2 in the studied population. SpO2 targets of 90 and 88% ensure sufficient oxygenation and should be used first to avoid high oxygen flows.

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Acknowledgements: COI: FL and ELH are co-founder of Oxynav that develo and commercialize the FreeO2.

001041

Lung necropsy of covid-19 patients: presence of thrombus in lung parenchyma

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Introduction: One of the main factors that marked the prognosis of COVID-19 patients during the pandemic waves was the presence of thrombosis, which in turn determined the need for anticoagulation and complications.
Objectives: Evaluate the presence of thrombi in the lung parenchyma and check its correlation associated with the previous diagnosis of pulmonary thromboembolism or deep vein thrombosis.
Methods: Forty-three lung parenchyma fine-needle punctures were performed on deceased patients with confirmed COVID-19 disease, collecting which of them had been previously diagnosed with thrombosis, D-dimer levels, activated partial thromboplastin time and INR at admission and at the time of exitus. In addition, multiple variables in terms of demographics and personal background.
Results: 27% did not have a pre-exitus diagnosis of pulmonary thromboembolism or deep vein thrombosis. Only 16% have confirmed intraparenchymal thrombosis (or fibrin debris) in the lung autopsy study. The DD at admission was only normal in 4 patients, presumably those who were infected with COVID19 nosocomially. At the time of Exitus there is no DD in range.The INR was normal in more than half of the patients upon admission to the ICU, as well as at the time of exitus. More than half of the patients had normal aPTT at admission, higher than 40%. The values at death are artifacted by the presence of shock, multi-organ dysfunction and heparinization.
Conclusion: More studies are needed to determine the role of anticoagulation in COVID19 patients,Among our patients, we have found intraparenchymal thrombi at lung autopsy in patients with APTT and INR elevated. Thrombosis has not been the main cause of death in any of our patients.

Acute Respiratory Failure 14

001124

Mortality analysis of Sars Cov2 in critically ill patients

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Introduction: During the last two years after the beggining of the worldwide pandemic caused by Sars Cov2, we have developed more knowlegde about the pneumonia and acute distress respiratory syndrome (ARDS) caused by virus infection. The improvement in treatments, management of the disease and vaccination has changed the course of the pandemic and disease's severity.
Objectives: Our aim is to establish the main risk factors associated with mortality increase in Sars cov2 patients, and the main causes of mortality in patients admitted in the ICU; also, to compare mortality between the admissions in the ICU in different pandemic waves.
Methods: We performed a retrospective, observational and analytical study with 750 patients admitted to the ICU with the diagnose of coronavirus disease between March 2020 and March 2022. A database was created in SPSS with baseline features (comorbidities, age); APACHE score, mortality, cause of death, and the need of mechanical ventilation.
Results: 750 patients were included in the study with a mean age of 58.96 ± 13.35, mean APACHE score was 10.81 ± 5.23, mean days of mechanical ventilation were 11.74 ± 15.84 and overall mortality was 27.2%. 65.1% of patients were male and 34.9% were female, 28.5% had diabetes, 8.7% renal insufficiency, 5.7% had chronic obstructive pulmonary disease and 7.6% had inmmunosuppression. Male sex, older age, inmmunosuppression, diabetes, renal insufficiency, prolongued mechanical ventilation and high APACHE score were associated with an increased in mortality ($p < 0.05$). Main causes of death were refractory hypoxemia (43.1%), refractory septic shock (39.7%), brain death (4.4%) and pulmonary embolism (2.5%). There was a decrease in mortality between first and fifth wave (from 39 to 12%), although it increased in last wave (26%). Statistical test shows there was no statistically significant difference in mortality between pandemic waves. Statistical test of sixth wave shows an increased number of patients with renal insufficiency and inmmunosuppressed patients ($p < 0.05$) in comparison with other waves.
Conclusion: Mortality has decreased between the first and fitht wave, albeit mortality raised in the sixth and last wave. It can be explain by the fact that there was a larger proportion of patients without inmmunosuppression and renal failure admitted in our ICU during the last wave and the fact that these clinical features are associated with a higher mortality. Main causes of death in our population infected with sars cov2 that were admitted in ICU were refractory hypoxemia and refractory septic shock.

000859

Inflammatory phenotype and respiratory failure severty in patients under mechanical ventilation support due to Covid-19

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Introduction: Risk factors related with inflammation has been described in Covid-19 patients. Lymphocytes count, ferritin, lactic dehydrogenase and D dimer has been associate whit disease progression, complications and mortality in critical care patients with Covid-19. Including a combination of this risk factor, the Inflammation Phenotype was graded in Mild, Moderate, and severe according to the outcome associated to each factor risk reported in the literature. We analyzed the Inflammatory Phenotype in patients management under mechanical ventilation and their association with lung failure severity and its outcome during critical care.
Objectives: Determine the asociation betewn inflamatory response and lung failure severity.
Methods: Observational analytical retrospective study. We included ARDS patients due to COVID-19 with need of invasive mechanical ventilation support, that were admitted in the intensive care units between March 2020 and 2021. We describe the Lymphocytes count, ferritin, lactic dehydrogenase and D dimer level together and their relation the ARDS severity, respond to mechanical ventilation, duration of mechanical ventilation and mortality.
Results: 49 patients meeting the inclusion criteria were analyzed, we classified 31 patients whit no severe inflammation (11 patients in mild level, 20 patients in moderated) and 18 patients in severe inflammation level. no significant difference was found in hospital mortality. The PAFI level was lower in patients with severe inflammation (111,7 vs 142,2). No different was found in compliance and driving pressure (33,1 vs 33,14 and 14,1 vs 13,8 respectively). The mechanical power was similar in the first day of mechanical ventilation, however the mechanical power enhances in patient with severe inflammation at 4th day (5,38 vs 1,44 j/min). The length in the critical care unit and the

days of mechanical ventilation were greater in patients with severe inflammation compared with patients with no severe inflammation (24,6 vs 18,6 and 22,4 vs 14,32 respectively).
Conclusion: The inflammatory compromise in patients under mechanical ventilation due to covid-19 disease is associated with the severity of ARDS: a lower oxygenation index, an increment in mechanical power during the first four, longer days of mechanical ventilatory support and intensive care stay. No difference in mortality was found.

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000944

Complement activation in COVID-19 and targeted therapeutic options: a scoping review

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Introduction: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to the first pandemic caused by a coronavirus [1]. Mortality rates in severe Coronavirus disease 2019 (COVID-19) remain high due to multi-organ failure inflicted by uncontrolled inflammation [2], even with SARS-CoV-2 vaccinations [3, 4]. The complement system plays an important role in the innate immune response by marking pathogens, mediating lysis and attracting inflammatory cells to the infection site [5]. Increasing evidence suggests a key role for complement activation in the pathogenesis and disease severity of COVID-19 [6, 7].
Objectives: In this scoping review, we aim to create an overview of complement activation and targeting in COVID-19.
Methods: PubMed/Medline, Embase (Ovid) and Cochrane Library were accessed for articles until January 13, 2022. Search terms include COVID-19, SARS-CoV-2 and complement. Eligible articles were divided into histopathological studies, preclinical studies, omics, observational and clinical interventional studies. The inclusion criteria for human studies were an age of $\geq$ 16 years, presumed or diagnosed SARS-CoV-2 infection, available complement measurements or studies targeting the complement system. Language was restricted to English articles. Exclusion criteria were case reports, case studies with <4 patients, abstracts or articles of which the full-text was not available. Three independent reviewers screened the articles by title and abstract.
Results: A total of 1528 articles were screened of which 129 articles were included. In total, 14 histological and/or autopsy studies, 14 preclinical studies, 31 multi-omics studies, 65 observational studies and 13 clinical interventional studies were identified. Eight studies were included in multiple categories. Histopathological, preclinical, multi-omics and observational studies showed apparent complement activation through all three complement pathways after SARS-CoV-2 infection and a correlation with disease severity and mortality. The complement system was targeted at MASP-2, C1-esterase, C3, C5 and C5a, mostly in severe COVID-19 patients. Two non-randomized controlled trials inhibiting C5 with eculizumab in severe COVID-19 patients showed a significant improvement in PaO2/FiO2 (P/F) ratio in the treatment group [8, 9], however one trial combined eculizumab with JAK1/2 inhibitor ruxolitinib [8]. The other trial observed a significant improvement in estimated survival at day 15 in patient treated with eculizumab solely [9]. Only one study reported the inhibition of C5a using a randomized controlled trial (RCT) [10]. The primary endpoint of mean P/F ratio five days after randomization showed no significant difference, however preliminary secondary outcomes seemed to be in favor of patients treated with C5a inhibitor vilobelimab.
Conclusion: Histopathological, preclinical, multi-omics and observational studies showed apparent complement activation through all three complement pathways and a correlation with disease severity and mortality. Different drugs targeting the complement system have been studied in COVID-19, of which those blocking the final common pathway seem most promising. Adequately powered, double blind RCTs are necessary in order to further investigate the effect of targeting the complement system in COVID-19.

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001011

The PROMIZING trial enrolment algorithm to early identify patients ready for unassisted breathing

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Introduction: The process of liberating patients from mechanical ventilation (MV) accounts for a significant proportion of the ventilation time. Finding strategies to minimize this duration is desirable. As part of a clinical trial, we developed a simple algorithm to identify patients who tolerate assisted ventilation but still require ongoing MV to be randomized.
Objectives: This is an ancillary analysis of the Proportional Assist Ventilation for Minimizing the Duration of MV (PROMIZING, NCT02447692) study. The PROMIZING study is an ongoing multi-centre randomized controlled trial comparing pressure support ventilation (PSV) and proportional assist ventilation with load-adjustable gain factors (PAV+) to facilitate weaning from MV. After enrolment, a step-by-step algorithm identified patients eligible to be randomly assigned to receive either PSV or PAV+. We focus here on patients who passed all steps, and despite being previously unsuspected, were ready for separation.
Methods: The algorithm for enrolment of patients included five steps: [1] enrolment criteria for ensuring that patients were able to trigger ventilator breaths with a reasonable level of assistance, [2] PSV tolerance trial consisting in a pressure of 5–20 cmH2O for at least 30 min, [3] general weaning criteria, [4] Zero continuous positive airway pressure tolerance trial (using a pressure level of 0 cmH2O during 2 min), and [5] spontaneous breathing trial (T-piece or no assistance on the ventilator using CPAP and a pressure level of 0 cmH2O during 30–120 min, with FiO2 40%).
Results: Among the 374 ineligible patients, 93 (25%) patients passed all the five steps of the enrolment algorithm. Fifty-nine (65%) were male and the mean ± SD age was 65 ± 13 years. The mean duration from intubation to enrolment was 4.5 ± 4.1 days. At time of enrolment, most patients were on PSV (87%) with a mean fraction of inspired oxygen of 34 ± 6%, pressure support of 8.7 ± 2.9 cmH2O, and positive end-expiratory pressure of 6.1 ± 1.6 cmH2O. Minute ventilation was 9.0 ± 3.1 L/min with a respiratory rate of 17.4 ± 4.4 breaths/min. All patients were liberated from MV with a median [IQR] delay between enrolment and extubation of 5 [1–49] hours. Only 7 (8%) patients required reintubation.
Conclusion: The stepwise algorithm developed for screening and randomizing patients in the PROMIZING study turned out to be a useful tool to aid in early identification of patients ready to separate from the ventilator. The algorithm permitted the identification of a large proportion of patients who passed the weaning process and have been safely removed from the ventilator, while their clinicians predicted a duration of ventilation higher than 24 h**.**

Acknowledgements: This study is funded by a Canadian Institutes of Health Research (CIHR) Operating Grant: Industry-partnered Collaborative Research Grant, with Covidien LP, a Medtronic company as the industry partner, and by a CIHR Project Grant. Funding from Covidien LP, a Medtronic company, is provided through the Covidien Investigator Sponsored Research (ISR) Program and subsequently the Medtronic External Research Program (ERP).

001022

A Phase 1/2A Study of Decidual Stromal Cells for the Treatment of COVID-19 ARDS

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Intensive Care Medicine Experimental 2022, **10(2)**:001022

Introduction: Acute respiratory distress syndrome (ARDS) in COVID-19 is associated with high mortality. Decidual stromal cells (DSCs) are placentally-derived stroma cells that are known to exert immunomodulatory and anti-inflammatory effects and could be beneficial in the treatment of COVID-19 associated ARDS. Here we provide a preliminary report on a phase 1/2A single arm trial of DSCs in the treatment of mechanically-ventilated patients with COVID-19, conducted between December 2020 and June 2021.
Objectives: To determine safety and explore efficacy of DSC in the treatment of COVID-19 ARDS.
Methods: Nineteen subjects were enrolled at 2 hospitals in Toronto, Canada and received 1 million DSCs/kg intravenously within 72 h of initiation of mechanical ventilation, along with best standard of care. An optional second dose was given 5–8 days later for patients who were still eligible. Primary endpoint was safety (adverse events (AEs)). Secondary endpoints included survival at Day 28 and Day 90, ventilator-free days at Day 28, length of ICU stay, duration of hospitalization and hospital survival. To compare outcomes of the treated patients with those of untreated patients, a 2:1 propensity matching was performed with patients who were admitted to the same intensive care units during the same time period and met the eligibility criteria for the study but were not enrolled due to lack of DSC availability.
Results: Nineteen mechanically-ventilated patients were enrolled between December 2020 and June 2021. Median age was 54y (25–70) and 11/19 (57%) were male. Comorbidities included obesity (n = 8), asthma (n = 7), diabetes mellitus (n = 5), and hypertension (n = 4). Median P/F ratio at the time of first DSC infusion was 118 (68–200). One patient experienced a transient hypoxic event that was judged as probably related to the DSC infusion. Possibly related grade 3–4 SAEs included ARDS (n = 1), pulmonary embolism (n = 1), hypoxemia (n = 1) and bacteremia (n = 1). SAEs that were deemed unrelated included bacteremia (n = 3) and ventilator associated pneumonia (n = 3). Seven of nineteen patients met criteria for a second DSC infusion. Overall, DSC infusions were found to be safe. Survival at 28 and 90 days in the DSC study group was 16/19 (84%). Propensity score matching generated a group of 38 mechanically-ventilated patients who were matched with respect to hospital site, age, sex, number of comorbidities, treatment with tocilizumab and steroids, and baseline P/F ratio. Hospital survival in the matched cohort was 21/38 (55%). Survival in the DSC group was significantly greater than in the propensity-matched control group ($p < 0.05$).
Conclusion: DSC infusion was shown to be safe in mechanically-ventilated patients with COVID-19 ARDS and may be beneficial in treating severe disease.

001084

Clinical outcomes and pulmonary function test of critically ill COVID-19 patients: Which firstly as rescue therapy?

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Intensive Care Medicine Experimental 2022, **10(2)**:001084

Introduction: A nationwide critically ill coronavirus disease 2019 (COVID-19) cases still occur in South Korea. We hypothesized that the

long duration of respiratory support for these patients affects their lung function after survival.
Methods: Patients with laboratory-confirmed COVID-19 pneumonia for admission to ICU in a tertiary, academic hospital in South Korea from January 2020 to August 2021 were reviewed retrospectively, then we collected demographic and clinical data of them categorized by hypoxic respiratory failure who required at least a high flow nasal cannula (HFNC) or higher respiratory support such as mechanical ventilation (MV), inhaled nitric oxide, prone position, or extracorporeal membrane oxygenation (ECMO) during hospitalization. We analyzed outcomes of the patients according to methods and order of rescue treatment, and elucidated which factors influenced on pulmonary function of survivors. Association was analyzed between the duration of HFNC before MV and results of pulmonary function test after discharge was done using Spearman's rank order correlation. A chi-square test was performed to compare the mortality of ECMO vs. inhaled nitric oxide with or without prone position.
Results: Of the total 134 patients, the mean age was 65 (28–94) years old and 87 (64.9%) were male. 109 (81.3%) had at least one comorbidity including hypertension, diabetes mellitus, or malignancy. 79 (59.0%) patients eventually failed in HFNC and received respiratory support more than and including MV. Among them, 49 cases required rescue therapy including inhaled nitric oxide, prone position, or ECMO. ECMO was first applied as an emergent procedure due to a sudden deterioration in six cases, and inhaled nitric oxide with or without a prone position was applied before ECMO in 43 patients. In these 43 cases, 17 patients were eventually applied with ECMO, and 26 haven't been applied ECMO. The mortality rate of all patients was 23.9%, that of patients who have applied MV 29.1%, and that of patients who have applied rescue therapy 36.7%. There was no statistically significant difference between ECMO treatment and inhaled nitric oxide with or without prone position (40.9 vs. 29.6%, $p = 0.409$). Followings are the result of pulmonary function test of survivors: FEV1/FVC [median = 0.83 (0.57–0.99)], FEV1 [median = 87% (28%-153%)], FVC [median = 81% (21%-122%)], DLCO [median = 69% (10%-119%)]. Trends of negative correlation between the duration of HFNC before MV and FVC (rho = -0.435; $p = 0.055$) were shown.
Conclusion: Inhaled nitric oxide and/or prone position as rescue therapies could be an acceptable alternative first treatment option before applying ECMO in critically ill COVID-19. Delayed intubation under HFNC before MV might be associated with poor lung function after their recovery.

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001096

Diaphragmatic atrophy in adult with Covid 19 Pneumonia under mechanical ventilation in our Intensive Care Unit

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Intensive Care Medicine Experimental 2022, **10(2)**:001096

Introduction: Beside ultrasound in the intensive care units have become an essential tool, in our case, measuring the kinetics and diaphragmatic atrophy is important as it is associated with delayed weaning from mechanical ventilation (MV) and increased mortality and morbidity in critically ill patients.
Objectives: To measure diaphragmatic atrophy using bedside ultrasound in patients admitted to our intensive care unit (ICU) with Acute Respiratory Failure (ARF) due to Covid-19 Pneumonia.
Methods: Prospective study of adults from 18 to 80 years admitted to our ICU who underwent MV due to ARF and Covid 19 Pneumonia from November 2020 to May 2021. We excluded patients with high dose chronic corticosteroids, neuromuscular disease, diaphragmatic paralysis, obesity with BMI > 40 and more than 2 weeks of MV. We measured with high-frequency linear probe diaphragm thickness (Tdi) in the mid-axillary line (zone of apposition) of the right diaphragm during inspiration (Tdi insp) and expiration (Tdi exp) in the first 24 h of ventilation and 24 h prior to extubation. Change of Tdi exp during MV: Tdi exp prior to extubation – Tdi exp initially / Tdi exp initially × 100. Percentage of atrophy was calculated as changes in Tdi exp/total days of MV.
Results: 27 patients were enrolled. Median age 62 y (21–77). Median days of MV 7.2 (4.1–13.7). All patients received 8 mg ev of dexamethasone for 10 days and protective ventilation with Vt of 4–6 mg/kg ideal weight. At intubation: median Tdi exp 2.5 mm (1.8–2.9), median Tdi insp 2.8 mm (2.3–3.4). 24 h prior to extubation: median Tdi exp 1.7 mm (1.4–2.3). Median change in Tdi exp during MV was -28% (-38% to -17.2% with $p < 0.015$). Daily atrophy rate of 8.7%.
Conclusion: The daily rate of diaphragmatic atrophy in patients under MV with ARF due to covid pneumonia in our series was 8.7%, higher than bibliography with around 6% with other causes of ARF, although our series is small and further studies need to be performed.

001119

A Retrospective propensity score–matched cohort study on effectiveness of Convalescent plasma in COVID19 pneumonia: A single centre study and experience

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Introduction: Convalescent plasma is considered to treat COVID19 infection as it offers passive immunity by therapeutic antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Its efficacy is preliminary but it has been compassionately used in hospitalized patients. However, the published data from multiple randomized control trials or matched treatment–control studies are inconclusive. (1–5) Hence, whether the convalescent plasma therapy is a viable treatment option for COVID-19 is still not fully understood. Convalescent plasma has been known to suppress viraemia and improve clinical symptoms in different viral infections.
Objectives: This study was aimed at analysing administration of Convalescent COVID-19 plasma (CCP) in COVID19 pneumonia on clinical symptoms, severity markers and outcomes compared to the matched cohort during the same time interval.
Methods: Study design and patients: We retrospectively analysed data of 106 critically ill COVID-19 patients over a span of 5 months from November 2020 to March 2021.Data was collected from the patient files/Computerized Patient Record System (CPRS) after obtaining approval from the local ethics committee. Patients admitted in the COVID intensive care units (COVID-ICU) with a confirmed diagnosis of acute COVID-19 infection (by SARS-CoV-2 polymerase chain reaction testing or cartridge based nucleic acid amplification test) were included. In our ICU, on a compassionate basis, we administer ABO-compatible convalescent plasma to a select few patients when they have moderate to severe COVID within 10 days of illness and have an increased oxygen requirement and radiologically, deterioration in COVID 19 features on chest roentgenogram(CXR), computed tomography Chest(CT) or both. Those who fit these criteria and yet refused to give informed consent for convalescent plasma treatment have been included as controls. The following groups have been excluded for the purposes of the study:those who were pregnant or lactating, those with immunoglobulin allergy or IgA deficiency. All patients included in this cohort received standard therapy irrespective of whether they received CCP or not. As per institutional protocol, for those who consented, we administered one dose of 200 mL of CCP after blood cross matching. This CCP was derived from recently recovered donors with the neutralizing antibody titers above 1:640.
Results: The 7-day mortality rate following the day of CCP administration was 13.3% in the CCP group and 12.1% in the control group (OR 1.12, 95% CI 0.18–6.88, p-value 0.906; Fisher's Exact test, p-value 1.00). The proportion of patients with the composite outcome of worsening in oxygenation or mortality at 7 days was 26.7% in the CCP group and 60.6% in the control group (OR 0.24, 95% CI 0.062–0.09, p-value 0.035; $\chi 2$ test, p-value of 0.029). The overall mortality rate was 26.7% in the CCP group against 57.6% in the control group (OR 0.27, p-value 0.053; $\chi 2$ test, p-value of 0.047) and the discharge rates were 73.3% and 42.4% respectively (OR 3.73, 95% CI 0.98–014.20, p-value of 0.053; $\chi 2$ test, p-value of 0.047). In the control group, 48.5% were on invasive ventilation before the median 8 days and in the CCP group, this proportion was 13.3% before the day of plasma administration ($\chi 2$ test, p-value of 0.044). Duration of hospital stay was lower in the CCP group (median 12 days, IQR 8.5–14.27, range 5–38) compared to the control group (median 17 days, IQR 13–27, range 5–51) with a p-value of 0.049 on the independent samples Mann–Whitney U test.
Conclusion: COVID-19 Convalescent Plasma (CCP) does not significantly improve mortality in our study population. However, in some cases especially if the patient is already on invasive ventilation, it may increase the hazard for mortality, which in our study also did not assume statistical significance. CCP shortened the duration of hospital stay and increased the rates of discharge statistically significantly.

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001128

Influence of the prone position in the bronchoalveolar lavage: efficiency in the retrieval of the volume instilled and pulmonary mechanics

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Introduction: Being the bronchoalveolar lavage a common technique within the ICU to achieve a certain diagnostic in ventilator associated pneumonia we should ascertain its effects on the pulmonary compliance in patients that, sometimes, require a prone position as part of point of care treatment, such as ARDS.
Objectives: The main objective is to compare the changes in the pulmonary compliance after performing a bronchoalveolar lavage in patients in prone and supine position.
Methods: Prospective observational study from the April 1st to December 1st of 2021, in which we included all patients who were diagnosed of ARDS and required a bronchoalveolar lavage as a diagnostic procedure. The technique was protocolized, using single use bronchoscopy (Ambu aScope 4 Broncho) and instilling 150 cc, regardless of the position in which they were (being prone or supine position). We compiled data before, 5 min and 90 min after the procedure: Compliance, volume instilled and recuperated. We calculated the delta compliance 5–90 min. Data was analyzed with SPSS v22. The cuantitative variables are represented as media $\pm$ SD and the cualitative ones as percentage $\pm$ SD.
Results: We included a total of 48 patients. The percentage of the recuperated saline was 34.95% $\pm$ 7.69; finding no statistical difference ($p = 0.53$) between prone and supine position (respectively, 33.70% $\pm$ 5.99 and 35.82% $\pm$ 8.80). The basal media compliance was 38.22 $\pm$ 12.29 ml/cmH2O: 38.72 $\pm$ in supine and 36.68 $\pm$ in prone

position. The patients in which the technique was practiced in supine position experimented a decrease in the compliance in the next 90 min of -4.49 ml/cmH2O while the patients in prone position experimented a slight increase of + 1.02 ml/cmH2O (p = 0.022).
Conclusion: In our series we found no statistical differences in respect of the recuperation of the volume instilled in the lavage, whether it was done in prone or supine. We have found a slight increase in the compliance in the patients in prone position 90 min after the lavage, concluding that it can be safely done in either position by experimented operators.

Acute Respiratory Failure 15

000920

Interventions relieving dyspnea in noncommunicative mechanically ventilated patients show responsiveness of the Mechanical Ventilation - Respiratory Distress Observation Scale (MV-RDOS)

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Introduction: Dyspnea is one of the main stressful experiences in critically ill patients, with deleterious consequences. Because dyspnea is a self-reported symptom, it cannot be directly assessed in intubated noncommunicative patients. Here, we investigated the performance and responsiveness of the mechanical ventilation - respiratory distress observation scale (MV-RDOS), a newly described dyspnea observation scale, designed to infer the presence of dyspnea in intubated patients.
Methods: Between February 2016 and February 2017, communicative and noncommunicative dyspneic patients were prospectively included. Noncommunicative patients were considered as dyspneic at screening based on a MV-RDOS score ≥ 2.6 and either a respiratory rate > 25 breaths/min or visible inspiratory contractions of neck muscles were observed. The dyspnea visual analog scale (D-VAS, only in communicative patients), the MV-RDOS and the electromyographic (EMG) activity of two inspiratory muscles, the parasternal intercostal and alae nasi muscles, were measured before (baseline) and after two interventions designed to reduce dyspnea: adjustment of ventilator settings, followed, in the presence of persistent dyspnea, by morphine administration. A therapeutic intervention was considered to have effectively relieved dyspnea when dyspnea in communicative patient was no longer present or when the MV-RDOS of non-communicative patients was < 2,6.
Results: Fifty patients (age: 67 [61–76] years, SAPS II: 52 [35–62]) were included, 25 of these patients were noncommunicative. Dyspnea was relieved in 25 (50%) patients after ventilator adjustments and in 21 (42%) of the remaining 25 patients after morphine administration. Changes in ventilator settings comprised an increase of pressure support level for 50 (100%) patients (from 7 [6–8] cmH2O at baseline to 15 [14–16] cmH2O after adjustments, p < 0.001). The maximum dose of 10 mg was reached in 19 (76%) of the 25 patients remaining dyspneic after ventilator settings adjustments. In noncommunicative patients, the MV-RDOS decreased from 5.5 [4.2–6.6] at baseline to 4.2 [2.1–4.7] (p < 0.001) after ventilator adjustments and to 2.5 [2.1–4.2] (p = 0.024) after morphine administration. MV-RDOS and alae nasi/parasternal EMG activities were positively correlated (conditional correlation coefficient RC = 0.84 and RC = 0.92, respectively). Similar results were observed in communicative patients and MV-RDOS was also positively correlated with D-VAS (RC = 0.86).
Conclusion: MV-RDOS seems efficient to detect and monitor dyspnea in noncommunicative intubated patients and may help to improve dyspnea management in mechanically ventilated patients.

Acknowledgements: Fond de Recherche en Santé Respiratoire - Fondation du Souffle 2015.

001019

Utilization of Temporary Diaphragm Pacing Electrodes to Decrease Mechanical Ventilation and Improve Diaphragm Function d

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Intensive Care Medicine Experimental 2022, **10(2)**:001019

Introduction: Studies have shown diaphragm pacing (DP) prevents ventilator induced diaphragm dysfunction (VIDD) secondary to mechanical ventilation (MV) improving extubation and facilitates injured phrenic nerves recovery. The FDA recognized the need to decrease MV burden during the COVID-19 pandemic and authorized a temporary DP system.
Objectives: Report the largest experience of temporary DP data; reviewing indications and results.
Methods: This is a retrospective analysis of prospective IRB approved databases of non-randomized interventional experience at a single institution. Subgroup analysis was then limited to patients implanted with the temporary DP system (TransAeris, Synapse Biomedical) at an index surgical procedure or laparoscopically.
Results: Database included 197 patients with DP from 1/2020 to 1/2022 for all indications. From FDA authorization in 4/2020 until 12/31/21, 53 patients were implanted with the temporary electrodes. Age ranged from 2 months to 81 years with 19 females and 34 males. There were no adverse events related to electrode implantation, stimulation or subsequent removal. Seven patients were implanted laparoscopically with post-operative diaphragm stimulation for acute respiratory failure from unilateral diaphragm dysfunction (3); central sleep apnea from ROHHAD syndrome(1); VIDD post cardiac procedure; and chronic respiratory failure from COVID-19(2). The other 46 patients were implanted at the time of operations associated with high risk of post-operative MV and included cardiac(16); complex open vascular(14); lung transplant(10); liver transplant(3); heart transplant(2) and emergency colectomy in patient with ALS(1). In 6 of these patients there was rapid weaning and no diaphragm stimulation was necessary. The remainder underwent diaphragm stimulation to facilitate weaning and maintain diaphragm strength. Analysis of lung transplant patients showed the electrodes identified phrenic and diaphragm dysfunction early in the post-operative period allowing electrical stimulation therapy. Analysis of the thoracoabdominal approach for complex vascular cases showed DP use improved diaphragm muscle strength. In cardiac procedures with pre-existing unilateral dysfunction, DP prevented paradoxical diaphragm movement and associated sleep dysfunction.
Conclusion: Prolonged MV leads to significant morbidity, mortality and cost. The pandemic highlighted the shortage of ICU beds and the need to improve ventilator weaning. DP was safely used in this report to wean from MV, prevent VIDD and the electrodes can identify and improve recovery of phrenic nerve injuries,

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001076

Extracorporeal membrane oxygenation (ECMO) use in COVID-19: Hospitalar mortality and associated factors

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Intensive Care Medicine Experimental 2022, **10(2)**:001076

Introduction: The minority of COVID-19 patients develops severe respiratory failure that require mechanical ventilation (MV) (1). Despite the high mortality rate, the majority of patients can be treated with conventional strategies as protective ventilation, neuromuscular blockade and prone position (1). However, standard treatment is not enough to treat some patients and ECMO has been used as a salvage treatment. Studies with use of ECMO during the covid-19 pandemic are scarce in mid and low income countries with heterogeneous results (2,3).
Objectives: The aim of the present study was to describe the clinical characteristics, outcomes and factors associated with increased mortality in COVID-19 patients who had ECMO support.
Methods: This is a retrospective analysis of a cohort with prospectively collected data from patients admitted to 4 tertiary private hospitals in Rio de Janeiro – Brazil from March 2020 to June 2021. All patients with confirmed diagnosis of COVID-19, ICU admission and use of ECMO. Clinical data and outcomes collected from EPIMED system(4) and medical records.
Results: Data from 64 consecutive patients diagnosed with COVID-19 and using ECMO were used in the analysis. Median age was 51 (IQR 41–65) years, 80% male, 80% arterial hypertension, 25% diabetes mellitus and body mass index (BMI) 30 (IQR 27–37). On ECMO start day: SOFA 11(IQR 8–12) points, PaO2/FiO2 91(IQR 74–124), PaCO2 71 (IQR 58–87) mmHg and length of mechanical ventilation days 4 (IQR 2–10) days 0.44% of patients were diagnosed with ventilator associated pneumonia and 61% required renal replacement therapy (RRT). The most frequent complications were: thrombocytopenia 58%, hemolysis 25%, gastrointestinal bleeding 23%, neurological complications 23% and ECMO system coagulation in 9%. Age, RRT use and neurological complications were higher in non-survivors. In the multivariate analysis RRT (OR 5.32[1.34–21.0]) and age (OR 1.05[1.00–1.11]) were independent factors associated to increased mortality.
Conclusion: The mortality of patients with COVID-19 and ECMO use is high in the studied population mainly in older patients and those using RRT.

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Acknowledgements: No grants.

001098

Diaphragmatic thickness measured by bedside ultrasound to evaluate atrophy in Intensive Care Units during mechanical ventilation

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Intensive Care Medicine Experimental 2022, **10(2)**:001098

Introduction: Beside ultrasound in the intensive care units have become an essential tool, in our case, measuring the kinetics and diaphragmatic atrophy is important as it is associated with delayed weaning from mechanical ventilation (MV) and increased mortality and morbidity in critically ill patients.
Objectives: To measure diaphragmatic thickness of patients admitted to our intensive care unit under MV due to ARF and Covid 19 Pneumonia using bedside ultrasound performed by two intensive care physicians. To evaluate the inter-rater reliability correlation coefficient for this technic.
Methods: Prospective study of adults from 18 to 80 years admitted to our ICU who underwent MV due to ARF and Covid 19 Pneumonia from November 2020 to May 2021. Two different and blinded intensive care physicians measured, with a high-frequency linear probe, the diaphragm thickness (Tdi) in the mid-axillary line (zone of apposition) of the right diaphragm during inspiration (Tdi insp) and expiration (Tdi exp) in the first 24 h of ventilation and 24 h prior to extubation. The median of 3 measures for each value was selected.
Results: 27 patients were enrolled. For all measurements the inter-rater reliability correlation coefficient of these two physicians was 0.96 ($p < 0.002$).
Conclusion: The use of bedside ultrasound by intensive care physicians to measure diaphragmatic thickness and thus atrophy of our patients is a feasible and reproducible technic in our daily practice.

001150

Characteristics and outcome of COVID-19 ARDS patients on VV ECMO – single center experience

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Intensive Care Medicine Experimental 2022, **10(2)**:001150

Introduction: The corona virus disease 2019 (COVID-19) pandemic, due to the novel severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), has caused a worldwide surge in hospitalizations for pneumonia with acute respiratory distress syndrome (ARDS) (1). A subset of patients with hypoxemia refractory to conventional management required use of extracorporeal membrane oxygenation (ECMO), as a bridge to recovery (2).
Objectives: The aim of this study was to review the characteristics and outcome of patients with severe Covid-19 ARDS treated with VV ECMO.
Methods: Observational, retrospective study included patients who were admitted to the Intensive Care Unit (ICU) of Institute for Pulmonary Diseases of Vojvodina from December 2020 until March 2022 due to SARS CoV-2 confirmed by positive polymerase chain reaction analysis of nasopharyngeal swab. All the patients fullified 2012 Berlin ARDS criteria. VV ECMO was initiated due to refractory hypoxemia despite optimal ventilatory management. Baseline demographic data, Acute Physiology and Chronic Health Evaluation score (APACHE II), Sequential Organ Failure Assessment score (SOFA score), Charlson comorbidity index, ARDS severity using PaO2/FiO2 ratio, ECMO days and ECMO weaning were recorded as well as ICU outcome.
Results: Between December 1st, 2020 and March 31th, 2021 VV ECMO was initiated in 30 Covid-19 ARDS patients with refractory hypoxemia despite optimal ventilatory management. Out of the total number, 20 patients were cannulated in another hospital by mobile ECMO team

and successfully transferred to our ICU. In one patient two ECMO procedures were required. The average age was 44 years (IQR 35–49), with the observed group consisting of 17 men (56%). Arterial hypertension and obesity stood out as the most common comorbidities. Among 13 women treated with VV ECMO, 4 were pregnant and two were immediately postpartum. One patient was fully vaccinated. All the patients met Berlin criteria from 2012 for severe ARDS with median PaO2/FiO2 ratio of 89,5 (IQR 73,7–100,7). The median APACHE II score was 15 (IQR 14–19,2), median SOFA score 7 (IQR 6–8) and median Charlson comorbidity index was 0 (IQR 0–1). None of the patients were mechanically ventilated for more than 48 h before starting the VV ECMO procedure. Median number of days on ECMO was 12 (IQR 6–25,2). Fifteen patients (50%) were successfully weaned from ECMO and 12 (80%) were transferred from the ICU to the step-down unit. ICU mortality as well as hospital mortality was 60%. Significant thrombotic complications were observed in 11 patients (36%) and oxygenator replacement was necessary in 4 cases.
Conclusion: VV ECMO was successfully applied as a bridge to recovery in severe Covid-19 ARDS patients. Primary interhospital ECMO transport can be safely performed and should be considered in selected patients.

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Acknowledgements: This review received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

001155

Physiological parameters of pulmonary function in ICU-patients with COVID-19, an observational study

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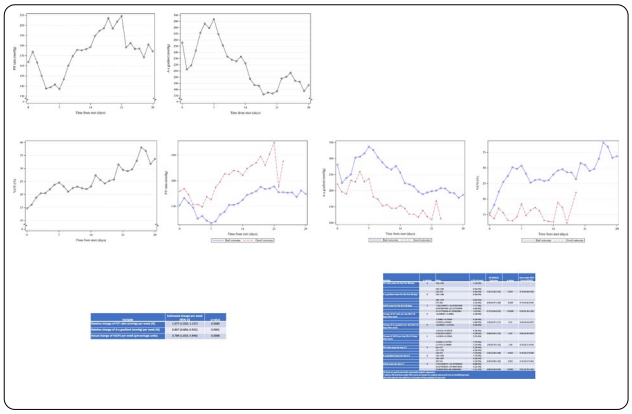
Introduction: During the first wave of the COVID-19 pandemic, the respiratory components of critical COVID-19 were not fully understood. To better understand the progression of disease in patients requiring intensive unit care (ICU) care, we collected data allowing us to assess changes over time of selected respiratory physiological parameters (P/F ratio, A-a gradient and fraction of physiological dead space (Vd/Vt).
Objectives: To map and evaluate the trajectory respiratory function in ICU-patients with critical COVID-19, enabling us to understand the clinical course of this novel disease and to explore if respiratory parameters is usable as outcome predictors.
Methods: This single-centre observational study at Sahlgrenska University Hospital, Mölndal prospectively included patients with critical COVID-19 requiring ICU-treatment including mechanical ventilation. We collected data to calculate and map the development of P/F ratio, A-a gradient and Vd/Vt. The patient-cohort was divided into two subgroups: good outcome (survival and ICU length of stay < 21 days) and bad outcome (death and/or ICU length of stay > 21 days). The predictive value for outcome of P/F ratio, A-a gradient and Vd/Vt were assessed using logistic regression analysis.
Results: Totally, 31 patients were included. The overall trends of P/F ratio, A-a gradient and Vd/Vt showed an initial period of deterioration over the first 7–10 ICU-days, after which P/F ratio and A-a gradient began to improve (Figure 1.1–3). The estimated relative change per week was statistically significant (p-value < 0.05) for all three parameters (Table 1). Figures 2.1–3 showed the development of P/F ratio, A-a gradient and Vd/Vt over time, respectively, for the two subgroups. As noted, the P/F ratio and A-a gradient in the subgroup of patients with bad outcome showed a more pronounced period of deterioration around ICU-day 7. Mean values for Vd/Vt in these patients (bad outcome) continuously increased over the first 28 ICU-days, from 15% to a peak value of almost 40%. Logistic regression analysis showed that the mean values of P/F ratio, A-a gradient and Vd/Vt during ICU-days 5–7 were predictive of good patient outcome, with significant p-values (Table 2).



Conclusion: Observing the trends of P/F ratio, A-a gradient and Vd/Vt in ICU-patients with critical COVID-19 improves the comprehension of this disease. The continuous increase in Vd/Vt in patients with a worse outcome emphasizes the impact of a vascular component in severe COVID-19. Further, we could demonstrate that values of the investigated three respiratory parameters on ICU-days 5–7 could be used to predict outcome in patients with critical COVID-19.

001159

Lung function in post-ICU, COVID-19 patients, an observational follow-up study

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Intensive Care Medicine Experimental 2022, **10(2)**:001159

Introduction: The clinical manifestation of COVID-19 ranges from asymptomatic to severe acute respiratory failure and death. Due to the large number of cases with respiratory failure and need for mechanical ventilation, there is a reason to consider the potential post-COVID effects regarding pulmonary function.
Objectives: To explore the post-COVID effects and the extent on lung abnormalities, using chest CT images, spirometry and DLCO, 4–6 months after the discharge from ICU. Furthermore, to evaluate the correlation between CT and spirometry/DLCO findings at follow-up.
Methods: This was a single-centre observational study conducted at the Department of Anaesthesiology and ICU at Sahlgrenska University Hospital, Mölndal. Forty patients ^{3}18 years old were included. All patients were admitted and mechanically ventilated in the ICU due to COVID-19, between 24th of March and 11th of August 2020, and then followed up with chest CT and spirometry/DLCO, 4–6 months after the discharge from the ICU. The radiological protocol was performed on the 256-slice multidetector computed tomography of the thorax without contrast. All parenchymal lesions were recorded. Their distribution was assessed according to lung anatomy which included 5 lobes. The grade of lobe involvement was assessed using a visual scale generating points: grade 1–1 point (1–5% involvement), grade 2–5 points (6–25%), grade 3–10 points (26–50%), grade 4–15 points (51–75%), and grade 5–20 points (more than 76%).Spirometry and diffusing-capacity for carbon monoxide (DLCO) was also performed.Diffusing-capacity of the lung was assessed using a single-breath DLCO technique. Lung function outcomes were also expressed in absolute values and in z-scores calculated

as (measured value-predicted value)/standard deviation (SD) obtained in the reference population.
Results: All 40 patients were examined with a chest-CT at the time of follow up, but only 30 underwent a spirometry/DLCO. The majority of patients were men (80%). The mean length of stay in ICU for all 40 patients was 23 ± 17.5 days.Radiological lesions were common and only 5 of 40 patients did not have any radiological changes. The three most common radiological findings were fibrous stripes n = 33 (83%), traction bronchiectasis n = 20 (50%) and ground glass n = 11 (28%) (Table 1). These radiological findings were located, in 60% of patients in the upper lobes (Table 1). Furthermore, the total number of lung points for all patients was 217.Spirometry and DLCO findings in 30 patients were expressed in absolute values and in z-scores (z). As it is shown in Table 2 30% of patients had DLCO < -1.96 z and 23% VA < -1.96 z. The Spearman's correlation between total lung point and spirometry variables was significant for FEV1z, FVCz, SVCz and VAz.
Conclusion: The vast majority of post- ICU, COVID-19 patients have a lot of radiological changes at 4–6 months after the ICU discharge. This finding is not associated with the same extent of functional impairment measured with spirometry/DLCO. Further studies are needed to explore this discrepancy.

Table 1. Spearman`s correlation coefficient with respective p-values

	FEV1 z	FVCz	FEV1/FVCz	SVCz	DLCOz	VAz	DLCO/VAz
CSS	-0.259 (0.037)	-0.374 (0.002	0.380 (0.002)	-0.556 (0.001)	0.440 (0.001)	-0.45(0.001)	-0.004 (0.975)

001166

Preoxygenation in SARS-COV-2 hypoxemic pneumonia

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Intensive Care Medicine Experimental 2022, **10(2)**:001166

Introduction: Patients with SARS-CoV-2 hypoxaemic lung disease were at risk of severe desaturation during intubation.
Objectives: We decided to compare 2 preoxygenation process: non invasive ventilation (NIV) alone vs NIV associated to high-flow nasal cannula oygen (HFNC) to assess safety and effectiveness of each modality.
Methods: It was a prospective bi-center randomized study. Were enrolled confirmed COVID-19 patients admitted to the intensive care unit and requiring orotracheal intubation from 1St April to 30th September, 2021. Patients were randomised to receive preoxygenation using NIV (pressure support = 10 cmH2O, positive end-expiratory pressure = 5 cmH2O, FiO2 = 100%) (G1), the face mask is removed during direct laryngoscopy vs NIV combined with HFNC (flow = 60 L/min, fraction of inspired oxygen (FiO2) = 100%) (G2), nasal goggles are kept in place during laryngoscopy. Were compared: The lowest oxygen saturation (SpO2) recorded during different stages of intubation (preoxygenation, apnoea and in post intubation). Intubation-related complications were reported as secondary outcomes.
Results: During the study period, 107 patients were included (G2 = 29 patients, G1 = 42 patients). Mean age of the study population was 58 ± 11 years. In both groups the main reasons for respiratory failure were hypoxemic SARS-CoV-2 pneumonia. The two groups were comparable in terms of comorbidities and initial clinical presentation, including time to ICU admission and clinical severity (assessed by IGSII, APPACHEII and Charlson scores). The PaO2/FiO2 ratio before pre-oxygenation was 59.5 ± 18.6 mmHin G2 vs 65 ± 23 mmHg in G1 (p = 0.27), with a mean lowest SpO2 of 80% ± 12.5 and 84% ± 9.5 respectively (p = 0.6). The minimal pulse oximetry value during pre-oxygenation procedure was significatly higher in G2 (85.5% ± 8.5 vs 78.4% ± 14 in G1 (p = 0.013)). The lowest SpO2 at apnoea and 5 min after the end of the intubation procedure were comparable in the two groups. It were 61.5% ± 21.5 vs 68.5% ± 18 (p = 0.14) and 77.6% ± 17.4 vs 77.2% ± 17(p = 0.9) respectively. We recorded no significant differences in intubation-related complications between the 2 groups: it occures in 26 patients in G2 and 31 patients in G1 (p = 0.09). It were essentially: severe hypoxemia with desaturation below 80% during the procedure (24 patients in G2 vs 20 patients in G1; p = 0.31); cardiac arrest occurded (4 patients in G2 and 3 patients in G1 p = 0.35) and severe collapse (12 patients in G2 and 11 patients in G1, p = 0.18). Moderate complications were comparable between 2 groups: barotrauma [3 vs 0], cardiac arrhythmia [3 vs 1] and difficult intubation 3 vs 0. We did'nt note any case of oesophageal intubation or dental injury.
Conclusion: This study shows that HFNC combined to NIV in comparison to NIV alone was more efficient in increasing SpO2 during pre-oxygenation but not during apnea and after intubation of severe hypoxemic patient with SARS-CoV-2 pneumonia.

Acknowledgements:
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000828

Monitoring of heated wire humidifier hygrometric performances with heater plate temperature

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Intensive Care Medicine Experimental 2022, **10(2)**:000828

Introduction: Under-humidification and associated complications may occur with heated humidifiers (HH) (1, 2). Hygrometric performances of heated wire humidifiers are reduced by high ambient and high outlet ventilator temperatures. We recently demonstrated that HH performances with MR850 could be evaluated at the bedside by the heater plate temperature (1, 3). With new HH, it is unclear if such a relationship exists and if the monitoring is required.
Objectives: To evaluate the relation between humidity delivered by heated wire HH and heater plate temperature in another prospective serie of measurements and with another HH.
Methods: On a bench test, we measured heater plate temperature, inlet chamber temperature and delivered humidity with MR850 system and FP950 (Fisher & Paykel). The measurements were performed at different ambient temperatures (from 20 to 30 °C), with constant minute ventilation (10 l/min). In each condition, hygrometric measurements with the psychrometric method were performed at a steady state.
Results: We performed 69 measurements with the FP950 and 147 with the MR850 including all conditions. We found a good correlation between heater plate temperature and absolute humidity delivered with MR850 (R2 = 0.92) (Figure) and with FP950 (R2 = 0.83). Heater plate temperature above 62 °C (73/147 measurements) with the MR850 was a very good predictor of absolute humidity delivered above 30 mgH2O/L (100% of the cases when HP temperature was above 62 °C) (Figure). Below 62 °C, 18/74 (24%) were above 30 mgH2O/L. With the MR850, 53% of the measurements of humidity were below 30 mgH2O/L with usual settings (37/40), while with the FP950, whatever the tested conditions, even with high ambient temperature (AT), absolute humidity (AH) delivered was above 30 mgH2O/L (Table).

	FP950	MR850 All	MR850 (37/40)	MR850 (40/40)	MR850 Auto
n	69	147	53	39	55
Mean ± SD AH (mgH2O/L)	35.4 ± 1.8	31.9 ± 5.6	28.7 ± 5.9	37.7 ± 2.7	31.0 ± 3.4
AH < 30 mgH2O/L	0 (0%)	56 (38%)	28 (53%)	1 (3%)	28 (51%)
Mean ± SD AT (°C)	24.4 ± 3.9	26.3 ± 3.1	26.5 ± 3.5	26.1 ± 3.1	26.1 ± 2.8
AT > 25 °C	29 (42%)	88 (60%)	34 (64%)	22 (56%)	31 (56%)

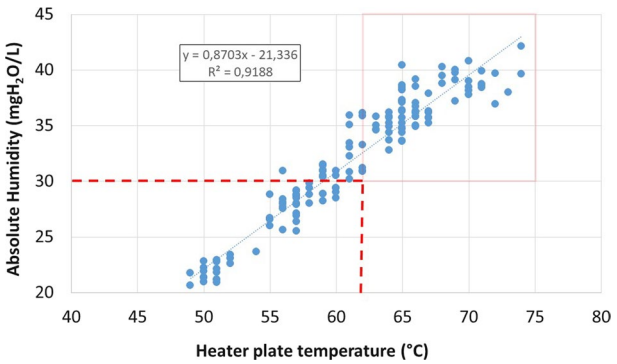

Figure. Relationship between heater plate temperature and absolute humidity delivered by the MR850. When heater plate temperature was above 62 °C, absolute humidity delivered was above 30 mgH2O/L in 100% of the cases.

Conclusion: In this bench study, we found a good correlation between heater plate temperature and humidity delivered with heated wire humidifiers MR850 and FP950. With previous generation HH (MR850), humidity delivered is low when ambient temperature is high, as previously shown and heater plate monitoring allows for detection of under humidification. As previously found, with MR850, heater plate temperature > 62 °C is an excellent predictor of adequate humidity delivered. With the new generation HH, there is no need to monitor the heater plate temperature, as it never under-humidified whatever the tested conditions.

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001125

Role of therapeutic effort limitation during Sars Cov2 pandemic in ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:001125

Introduction: Therapeutic effort limitation has experienced significant importance in last years. The increasing growth in technological field in Intensive Care Unit (ICU) has led to a longer dying process, with further suffering for patients and families. Limitation of therapeutic effort allows us to try to prevent futility. During Sars cov2 virus pandemic, intensivists had been making this decision more frequently due to overcrowding of the ICU, based on patient's prognosis and clinical features.
Objectives: Our study aims to define the main causes of death in patients with limitation of therapeutic effort and to look for the clinical features and patient's characteristics that are associated with limitation of therapeutic effort.
Methods: We performed a retrospective observational study that includes 750 patients admitted to the ICU with a diagnosis of Sars cov2 infection between March 2020 to March 2022. We gathered information about baseline features of patients, therapeutic effort limitation decision and causes of death.
Results: The study included 750 patients diagnosed with Sars Cov2 infection; among them, 94 patients underwent therapeutic effort limitation. The main cause of death in patients that underwent limitation of therapeutic effort was refractory hipoxemia (70.2%) and the second cause of death was refractory septic shock (14.9%) as in patients that did not underwent therapeutic effort limitation. There was a statistically significant association between chronic obstructive pulmonary disease, age above 65 years, inmunosupression and obesity (defined as body mass index above 30) and therapeutical effort limitation ($p < 0.05$). Renal insufficiency was also associated with the decision of limitation of therapeutic effort but there wasn't stattistically significant difference ($p = 0.05$). Elder age (age above 65 years), inmunosupression and renal insufficiency were also associated with poor prognosis and death in patients who didn't underwent limitation of therapeutic effort ($p < 0.05$).
Conclusion: During Sars cov2 virus pandemic, ICU's overflow caused intensivists to focus on the need of patient selection. Our study shows that the causes of death of patients who underwent limitation of therapeutic effort were the same as those who were not and that clinical features associated with limitation of therapeutic effort decision were also the same associated with poor prognosis and death in patients who didn't suffered limitation of therapeutic effort.

Acute Respiratory Failure 16

000997

Inspiratory effort and Elastance in Covid-19 patients mechanically ventilated. Evaluation through different ventilatory strategies

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Intensive Care Medicine Experimental 2022, **10(2)**:000997

Introduction: In Covid 19 patients with respiratory failure, an increase in the respiratory drive has been described, which could lead to the development of P-SILI due to uncontrolled transpulmonary and transvascular pressures (1,2). On the other hand, two patterns of elastance have been described in these patients, high and low elastance (3). Based on the P-SILI hypothesis and elastance, different authors advocate radical changes to ventilator management (4). However, the respiratory mechanics just before switching to spontaneous breathing or at the time of estimation of the respiratory drive and the relationship between both have not been sufficiently studied.
Objectives: To compare the respiratory response to different spontaneous ventilatory strategies based on the drive, effort, and power of breathing, to evaluate the possible reduction of muscular effort; as well as its relationship with the elastance of the respiratory system (Ers) and prognosis.
Methods: *Design.* Prospective physiological study, involving 11 mechanically ventilated patients with pneumonia COVID-19; over 2 months (April–May 2020). All patients were ventilated with an Evita 2D or XL ventilator (Dräger®). We included patients on assisted mechanical ventilation with Pressure Support Ventilation (PSV) or suitable for PSV as per clinical decision. Sedation RASS Scale of -2 to -3. *Data Acquisition:* Respiratory signals of Airway Pressure (Paw), Flow (V'), and volume (V) were recorded via the MEDIBUS® interface, at a sampling rate of 125 Hz, using personal software. After clinical stabilization under assist-volume control mode (ACV), three spontaneous breathing were performed in random order in all patients: PSV with three assistant levels 10 (5–15) cmH2O with PEEP 10 cmH2O; Airway pressure release ventilation (APRV), high pressure 20 cmH2O with expiratory time for 75% peak flow expiratory; and CPAP double 20/10

cmH2O (CPAPd). The recording time was 60 min., in each ventilatory strategy. *Measurements:* Elastance of the respiratory system (Ers), total Resistances (Rrs), and total PEEP (PEEPt) were obtained in the passive mode using multiple linear regression. In spontaneous modes, by occlusion maneuvers and time constant (t). Muscle Pressure (Pmus) by Equation of Motion. Parameters related to the respiratory drive (P0.1), effort (ΔPmus, PTP/min), and Work J/min, were calculated. The clinical and demographic characteristics were collected. *Statistical analysis:* Continuous variables are expressed as median (IQR). Data were compared by ANOVA on the ranks sum test. Pearson correlation was used for assessing the relationship between the variables.

Results: Patients N 11, 7. Sex 7 Male (63,33%). Age 61 (51–69) year. APACHE II score 19 (18–21). Body mass index 30 (27–32) Kg/cm2. Tª 37 (36–37.5) ºC. Comorbidities (N): Hypertension (5), Abdominal surgery (2), Diabetes (1), Kidney transplantation (1), Lymphoma (1), COPD (1). Days on ventilator 14 (6–2). pH 7.33 (7.25–7.43). PaO2/FiO2 193 (164–248) mmHg. FiO2 0.4 (0.4–0.5). PCO2 54 (40–62) mmHg. Lactic 1.1 (0.7–1.4) mmol/L. Tª 36 (36–37.2)ºC. ECMO (1). Survival 6 (54.54%), survivors vs non-survivors according to Ers 23.64 (17.71–30.16) vs 25.59 (16.34–36.39) cmH2O/L, respectively (p = 0.791). Pearson correlation: Driver and Work of breathing vs Ers: R 0.041 P 0.005 and R 0.37 P 0.011, respectively.

Table 2. Comparison of respiratory parameters between the applied ventilation modes.

Table. Comparison of respiratory parameters between the applied ventilation modes

	ACV	PSV 10 (5-15cmH2O)	APRV	CPAPd (20/10cmH2O)	P
Respiratory frequency (breaths/min)	25 (24.5-26)	18.83 (16.64-21.38)	16.06 (11.63-25.6)	18.59 (13.22-25.45)	0.993
Tidal volume (ml)	425 (390-450)	583 (394-850)	514 (321-635)	438.09 (380-636)	0.279
pH (units)	7.33 (7.25-7.43)	7.34 (7.27-7.47)	7.31 (7.23-7.41)	7.32 (7.24-7.38)	0.998
PCO2 (mmHg)	54 (40-62)	42 (24-54.75)	56 (42-64)	53 (43-66)	0.891
PO2 (mmHg)	82 (77-100)	83 (63.5-113)	70.5 (64.25-103)	80 (69-107)	0.887
Total PEEP (cmH2O)	11 (10.45-11.2)	10.05 (8.4-10.5)	10 (5.8-11.2)	10	N/A
Ers (cmH2O/L)	21.96 (18.11-37.45)	22.5 (20.12-28.93)	24.97 (18.53-30)	23 (19.37-29-86)	0.990
Rrs (cmH2O/L/s)	11.87 (10.47-14.29)	15.7 (11.51-18.56)	14.76 (11.99-20.85)	11.85 (10.05-12.67)	0.083
P0.1 (cmH2O)	N/A	6.01 (3.72-8.19)	6.77 (4.76-9.22)	6.65 (4.32-12.62)	0.854
Delta Muscle Pressure (cmH2O)	N/A	12.77 (10.14-16.90)	15.77 (10.84-23.37)	16.16 (6.93-17.76)	0.521
PTPpmus (cmH2O.s/min)	N/A	141.42 (97.13-184.84)	148.75 (102.05-255.53)	156.95 (84.18-335.11)	0.963
WOB (Joule/min)	N/A	10.19 (5.33-16.56)	10.53 (4.88-24.75)	14.38 (4.12-23.76)	0.969
Mean distending pressure (cmH2O)	N/A	14.73 (13.75-16.02)*	20.67 (19.68-22.13)	19.28 (17.63-22.82)	<0.001

Conclusion: We found in the patient's studies: High respiratory driver, inspiratory efforts, and work; in any of the ventilatory modes tested, regardless of elastance. These are factors potentially favoring P-SILI. In these cases, we propose returning to sedation, and partial paralysis if required.

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001091

Respiratory effort and respiratory drive signs during spontaneous breathing in mechanical ventilated patients with COVID-19

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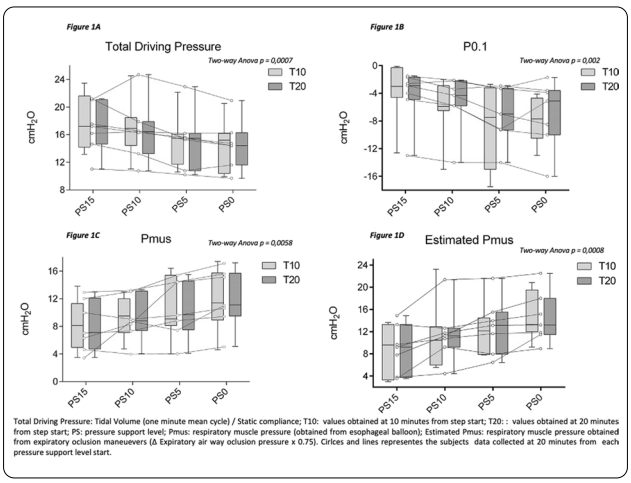
Intensive Care Medicine Experimental 2022, **10(2)**:001091

Introduction: In mechanical ventilated patients, a vigorous respiratory effort can cause deleterious effects1. Different reasons explain why it's elevated, such as pain, anxiety, delirium, inadequate ventilatory assistance, etc2. This scenario might be even more complicated in COVID 19 patients, considering these subjects present an exacerbation in respiratory effort with decreased levels of pressure support, inducing self inflicted lung injury1,3. Nonetheless, other consequences can become the weaning phase challenging and longer in this situation, due to high sedative doses in order to control the respiratory effort, resulting in longer mechanical ventilation duration and more days in Intensive Care Unit5. Moreover, patients with high muscle pressure can also present elevated driving pressure, which is remarkably associated with mortality4.

Objectives: Measure the respiratory effort and total driving pressure during pressure support variation in COVID 19 patients.

Methods: This transversal study was approved by the institutional ethics committee. Seven patients with ARDS due to COVID 19 during the mechanical ventilation weaning phase. The group was submitted to four levels of pressure support (15-10-5-0cmH2O). Esophageal balloon was used to assess the respiratory muscular pressure. Baydur maneuvers were considered to obtain the relation Esophageal Pressure (Pes)/Air way occlusion pressure (Paw) and the slope range: 0,8–1,2 was aceptable 6,7. Estimated Pmus was obtained from expiratory occlusion maneuvers (Δ Expiratory air way occlusion pressure × 0.75)8. The values were obtained at 10 and 20 min from the start of each level of Pressure Support (4 steps). The software LabVIEW was used to analyze the traces. The measures of Pes were obtained from one minute mean cycle at 10 min from start of pressure support step and in the end of each pressure step. Two-way ANOVA test for repeated measures was performed using GraphPad Prism version 6.00 for windows. P values < 0,05 was considered statistically significant.

Results: Seven patients were included. Total driving pressure behavior is presented on Figure 1A, which was proportional to PS decreasing, the median value at 20 min with PS15 was 17.18; PS10 16.4; PS5 15.4 and PS0 14.4 cmH2O. The same is observed in P0.1 values, suggesting a respiratory drive activation (Figure 1B); median in PS 15 was -2.9; PS10 -4.3; PS5 -7 and PS0 -5.1 cmH2O. Meanwhile, Pmus increased when the PS reduced (Figure 1C); median in PS15 was 7.1; PS10 8.8; PS5 9.6 and PS0 11.1 cmH2O. The same tendency was found in Estimated Pmus values (Figure 1D); PS15 median was 9.22; PS10 11,25; PS5 13.12 and PS0 13.2cmH2O.



Total Driving Pressure: Tidal Volume (one minute mean cycle) / Static compliance; T10: values obtained at 10 minutes from step start; T20: : values obtained at 20 minutes from step start; PS: pressure support level; Pmus: respiratory muscle pressure (obtained from esophageal balloon); Estimated Pmus: respiratory muscle pressure obtained from expiratory occlusion maneuevers (Δ Expiratory air way oclusion pressure x 0.75). Cirlces and lines representes the subjects data collected at 20 minutes from each pressure support level start.

Conclusion: Although both total driving pressure and respiratory effort should be controlled, it can be challenging to satisfy both aspects during the weaning phase. Further investigation is required on this subject.

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001153

Role of vaccination in Sars Cov2 virus pandemic: association between mortality and vaccination status in critically ill patients admitted in ICU

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Introduction: Vaccination has been a milestone in the fight against Sars Cov2 infection by decreasing the need of hospital and Intensive Care Unit (ICU) admission and the risk of death in hospitalized patients. Nevertheless, there are still patients who suffered severe respiratory failure that require ICU admission even after vaccination beginning.
Objectives: Our study aim to show the effect of vaccination on critically ill patients in ICU and its effect on mortality.
Methods: We performed a retrospective observational study that included patients admitted to the ICU with a diagnosis of Sars cov2 infection between March 2020 to March 2022. We collected information about vaccination status, mortality and patient's baseline features. Vaccination pattern was considered fullfilled when patients had received two vaccine doses or a third dose if the last dose was six months before confirmed infection by Sars cov2.
Results: Our study gathered 750 patients diagnosed with Sars Cov2 infection. There was 90 patients (12%) who had begun vaccination and only 43 of them had completed vaccination pattern representing only 5.7%. There weren't any statistical significant diferences regarding mortality between vaccinated and non-vaccinated even with those with a completed pattern ($p > 0.05$). There was no relation with vaccine type. There wasn't a decrease in mortality associated with vaccination status in the last wave, having a 39% of completed vaccination patients.
Conclusion: Our study shows that vaccination doesn't decrease the risk of mortality in patients that are already admitted in ICU because of illness severity. However the proportion of patients that had fulfilled their vaccination pattern at the time of their ICU admission was very low in comparison with unvaccinated patients. Vaccination decrease hospital admission and risk of death, albeit it didn't decrease mortality in critically ill patients that were already in ICU. These fact could explain the small proportion of patients with complete vaccination pattern that required admission in ICU.

001132

Evaluation of proning triggers in patients with ARDS secondary to COVID-19 in a Critical Care setting

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Intensive Care Medicine Experimental 2022, **10(2)**:001132

Introduction: Acute respiratory distress syndrome (ARDS) is a serious complication of COVID-19. The PROSEVA trial concluded that the early proning of patients with (ARDS) improved mortality.[1]
Objectives: The primary objective of this study was to determine what our Critical Care unit used as a trigger to prone intubated patients with ARDS secondary to COVID-19 and compare this with the current evidence base.[1]
Methods: This was an observational study with retrospective review of medical notes and charts of intubated and proned patients with ARDS secondary to COVID-19 over a two-year period. It took place in a Critical Care setting of a tertiary hospital in Scotland. Sixty-two patients were identified as having been intubated and proned. Nine of these patients were excluded due to extracorporeal membrane oxygenation (ECMO). The time between intubation and proning was measured. The PaO2/FiO2 (P/F) ratio at the documented decision to prone was compared with the P/F ratio most recent to the time the patient was proned. The proning FiO2 was also recorded. Lastly, it was noted whether the patient was proned during a day or a night shift. This data was then reviewed to determine the differences in unit practices between the "first wave" of COVID-19 and subsequent waves.
Results: During the first wave, the median FiO2 at proning was 0.76 and the median P/F ratio was 13.5. During the subsequent waves the median FiO2 at proning was 0.85 and the median P/F ratio 11.7. The overall median FiO2 was 0.83 with a median P/F ratio of 12. In fact, 81% of patients were proned with an $FiO2 \geq 0.7$. During the first wave, the median time between intubation and proning was three days, with 22% of patients being proned within 24 h of intubation. During subsequent waves the median time was one day, with 74% of patients being proned within 24 h of intubation. The day shift appeared a more common time to prone patients in wave 1 with 69% of proning taking place. This had dropped to 47.5% during subsequent waves. Although, 15% of the 52.5% proned during nightshift occurred during the first hour.
Conclusion: In most cases, the trigger for proning in our Critical Care unit was an escalating FiO2 requirement, rather than using a P/F ratio of < 20 kPa. After the first wave, patients were more likely to be proned at an earlier stage in their illness, this along with an increase in proning during night shift appears to be reflective of increased confidence in using proning as a therapy in these patients due to increased familiarity with the technique. It is proposed that the implementation of a proning guideline using a FiO2 trigger to achieve oxygen saturation of 88–92% would encourage earlier proning in this patient group.

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001165

Severe COVID-19 pneumonia in pregnant women: clinical characteristics and prognosis

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Introduction: The COVID-19 pandemic has led to an unprecedented global health crisis. The exact nature of the impact of the disease on maternal and neonatal health has raised several questions. Indeed, the data in the literature on this subject remain limited. Pregnancy-induced immunological and hemodynamic changes may increase the risk of developing a severe form of COVID-19 compared to non-pregnant women of the same age.
Objectives: Our study aims to describe the epidemiological, clinical and therapeutic characteristics and to determine the predictive factors of a poor prognosis of parturients women with severe COVID 19 pneumopathy admitted to an intensive care unit.
Methods: This is a retrospective descriptive study, over a period of 11 months (April 2021 to February 2022). We included all peripartum patients admitted to the ICU for SARS COV2 pneumonia. Data entry and statistical study were performed with SPSS 22 software. A value of $p < 0.05$ is considered significant.
Results: During the study period we collected 20 parturients with a median age of 34 years. The main comorbidities found were: obesity (35%), gestational diabetes (10%), gravid hypertension (15%), asthma (10%), hypothyroidism (10%). None of the patients was vaccinated against SARS COV2. The average gestational age was 34 weeks (25–37). The average hospital stay was less than or equal to 5 days in 75% of the cases. The decision to perform an emergency fetal extraction for maternal rescue was made in 50% of the patients. 20% of cesarean sections were performed under general anesthesia. An initial CT scan was performed in 50% of the patients; 40% had between 50 and 75% involvement. Biological data showed elevated procalcitonin and CRP in 35% of women. D-dimer levels were elevated to 10 times normal in 15% of patients. The most prescribed initial oxygen therapy modes: MHC for 3 patients, OHD for 4 patients and alternating with NIV for 10 patients. 3 patients required continuous NIV. All parturients received treatment with corticosteroids, effective anticoagulation and antibiotic therapy. Tocilizumab was prescribed in all parturients immediately postpartum. During the stay in the intensive care unit, one patient developed acute functional renal failure requiring hemofiltration. Two patients had liver cytolysis between 2 and 4 times normal. In our series, eight deaths were reported. The causes of this outcome were massive pulmonary embolism with intra VD thrombus in 2 cases, septic shock with pulmonary onset in 3 cases and severe refractory ARDS under ECMO in 3 patients. 12 patients progressed well with a decrease in oxygen requirements and transfer to a medical service.

predictive factors of mortality
obesity $p = 0.034$
severe ARDS $p = 0.028$
bacterial nosocomial infection $p = 0.006$
use of mechanical ventilation $p < 0.001$
septic shock $p = 0.004$

Conclusion: COVID 19 pneumonitis occurring in the perinatal period can be severe and maternal–fetal life-threatening. Altered maternal respiratory physiology and increased abdominal pressure complicate the management of mechanical ventilation. Fetal extraction by cesarean section may optimize ventilatory management. Therefore COVID-19 may be associated with an increased risk of preterm birth and other adverse pregnancy outcomes.

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001199

An observational multicentre cohort study of 498 critically ill adult Covid-19 patients and follow-up at three months

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Introduction: Predictive factors for the development of severe COVID-19 disease and the consequences of increased health care burden in the ICU are inadequately studied.
Objectives: To describe demographics, patient characteristics, risk factors and outcomes in critically ill COVID-19 patients.
Methods: In this prospective multicentre cohort study, we enrolled laboratory-confirmed, critically ill COVID-19 patients in six intensive care units (ICUs) in the Skåne Region, Sweden. Demographics and clinical data were collected in a quality registry. Health care burden in the ICU was defined as the total number of ICU-treated Covid-19 patients in the Region on the day of admission. Surviving patients had a follow-up at three months for assessment of neurological function using the Glasgow Outcome Scale Extended (GOSE), an eight-grade scale (1–8) with higher numbers representing better outcomes. The primary outcome was 90-day mortality, the secondary outcome was GOSE at 90 days.
Results: Among 498 included patients between May 11, 2020, and May 10, 2021, 74% were male with a median age of 66 years and a median body mass index (BMI) of 30 kg/m2. Invasive mechanical ventilation was employed in 72%. Mortality in the ICU, in-hospital and at 90 days was 30%, 38% and 39% respectively. Mortality increased rapidly from 14% at age 60 to 91% at age 80 or older. Increasing health care burden in the ICU was independently associated with a two-fold increase in mortality. A BMI of 30–45 kg/m2 compared to 25–30 kg/m2 was not associated with higher mortality. Apart from age and ICU burden, smoking status, angiotensin converting enzyme inhibitor (ACEi) medication, cortisone use, arterial oxygen partial pressure to fractional inspired oxygen (pO2/FiO2), $pCO2 > 7{,}3$ kPa and inflammatory markers on admission, were all independent determinants of 90-day survival. Ongoing ACEi treatment conferred a 3/4 reduction in 90-day mortality compared with angiotensin receptor blockers. GOSE at 90 days, showed that good recovery was independently associated with inflammatory markers on admission but not with age, BMI, or comorbidities.
Conclusion: In critically ill COVID-19 patients, the 90-day mortality was 39% and increased sharply at age 60 or older. History of smoking and burden in the ICU were strongly associated with mortality while high BMI was not. Ongoing ACEi treatment was positive for survival. A good recovery (GOSE) was independently associated with levels of inflammatory markers on ICU admission.

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Acknowledgements: Swedish Heart and Lung Foundation, Region Skåne Regional Funding.

001261

Tracheostomy Outcomes in Critically Ill COVID-19 Patients: A Systematic Review and Meta-Analysis

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Introduction: The effects of optimal tracheostomy timing and technique on outcomes in patients with COVID-19 remain unclear. We performed an extensive systematic review and meta-analysis of mortality in COVID-19 mechanically ventilated patients who received tracheostomy. We sought to determine the effect of tracheostomy time and type (surgical vs. percutaneous tracheostomy) on mortality. Secondary outcomes included study timeframe, Intensive Care Unit (ICU) and hospital length of stay (LOS), decannulation from tracheostomy, duration of mechanical ventilation (MV), and tracheostomy complications.
Methods: Four databases were screened between January 1st 2020 and January 10th 2022 (PubMed, EMBASE, Scopus, and Cochrane) and papers were selected according to the PRISMA and PICO guidelines. Meta-analysis and meta-regression for main outcomes were performed. Tracheostomy timing was analysed as a continuous variable (mean time to tracheostomy, days) as well as categorically i.e., early vs. late (<14 vs ≥ 14 days).
Results: Our search yielded 9,024 potentially relevant studies, of which, 48 (N = 5,320 patients) were included. Overall mortality for tracheostomized COVID-19 patients was 21.6% (95%CI = 18.1–25.1, I2 = 90.5%) with no significant difference between early vs. late [26.0% (95%CI = 17.7–34.3, I2 = 84.6%) vs. 17.8% (95%CI = 13.6–22.0, I2 = 91.6%), p = 0.08] and percutaneous vs. surgical groups [22.8% (95%CI = 17.2–28.3, I2 = 80.9%) vs. 14.7% (95%CI = 8.5–20.8, I2 = 87.9%), p = 0.06]. Also, mean time to tracheostomy was not significantly related to mortality (gradient = -0.75, p = 0.08). Study follow up time (> 30 days vs. ≤ 30 days) had no significantly effect on mortality [28.4%, (95%CI = 19.5–39.3) vs. 17.2%, (95%CI = 11.4–25.3) respectively]. Studies with earlier start date had greater overall mortality (gradient = -0.28, p = 0.11) and study start date accounted for 15% of the between study variance (heterogeneity) observed in mortality. Overall, ICU-and hospital LOS were 29.6 (95%CI = 23.8–35.5, I2 = 98.6%) and 38.7 (95%CI = 33.0–44.4, I2 = 93.8%) days respectively, with no significant difference between early and late groups. Time to decannulation [23.8 days (95%CI = 19.7–27.8, I2 = 98.7%)] was not significantly different between early vs. late and surgical vs. percutaneous groups. Overall duration of MV was 15.35 days (95%CI = 15.0–15.6, I2 = 99.3%). Those with late tracheostomy (compared to early tracheostomy) had decreased duration of MV [13.70 (95%CI = 13.4–14.0) vs. 20.80 (95%CI = 20.3–21.5), p = 0.00]. The most common complications were stoma infection/ breakdown/ulcers/necrosis (7.6%, 95% CI = 3.5–11.8) followed by bleeding (7.0%, 95% CI = 7.4–8.7). Bleeding was more common in the early (vs. late) [6.4% (95%CI 3.8–8.9 vs. 5.0% (95%CI 2.8–7.3), p = 0.44] and surgical (vs. percutaneous) [5.6 (95%CI 2.0–9.1, I2 = 0.0%) vs. 6.9 (95%CI -1.6–15.4), p = 0.83] groups.
Conclusion: In COVID-19 mechanically ventilated patients, the timing and type of tracheostomy were not associated with mortality and have unclear impact on patient outcome.

001296

Time between weaning eligibility criteria and the first separation attempt in patients receiving mechanical ventilation: Insights from the WEAN SAFE Study.

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Intensive Care Medicine Experimental 2022, **10(2)**:001296

Introduction: Duration of invasive mechanical ventilation (MV) is associated with short term and long term outcomes, including mortality and quality of life. Initiating weaning according to pre-defined criteria could minimize potential delays in weaning ventilation.
Objectives: To describe the time from pre-defined weaning eligibility criteria to the first separation attempt and identify the factors associated with delay superior to one day for patients enrolled in the WEAN SAFE study (WorldwidE AssessmeNt of Separation of pAtients From ventilatory assistancE; NCT03255109).
Methods: WEAN SAFE is an international prospective observational study that enrolled patients receiving mechanical ventilation for at least 2 days. We defined weaning eligibility criteria (WEC) as the following (modified from [1]): FiO2 < 0.5, positive end-expiratory pressure (PEEP) < 10 cmH2O, receiving no or low doses of, and not receiving paralyzing agents. A separation attempt as previously defined [2] as one of the following: a spontaneous breathing trial or an extubation in intubated patients; a session of spontaneous ventilation without support in tracheostomized patients. We performed a multilevel logistic regression to identify factors associated with time from meeting WEC to the first SA longer than one day. We included patients level variables and centre level parameters.
Results: Of the 5,869 patients enrolled in 476 centres from the 5 continents, 4,523 (77%) had at least 1 separation attempt (and 4,225 had no missing variables for the multivariable model) occurring at a median [IQR] of 5 [4–8] days after intubation. Weaning eligibility criteria were met at 3 [3–4] days after intubation and delay from this event to the first separation attempt was superior to one day in 2136 patients (47%). Admission for trauma and higher initial (non-neuro) SOFA score were associated with higher risk of a delay (Table 1). Conversely, admission for planned surgery and male sex were associated

with less delay. Being treated in centers from high income European countries was associated with higher risk of a delay from WEC to the first SA as compared to middle income countries and non-European high income countries. The use of weaning protocol did not seem to reduce these delays.

Factors associated with longer delay from weaning eligibility criteria to the first separation attempt

Variable	Odds ratio	95% CI	p-value
Age (for 10 years)	1.01	0.97–1.05	0.689
Admission for monitoring	1.06	0.57–1.95	0.858
Admission for planned surgery	0.77	0.59–0.99	0.045
Admission for trauma	2.10	1.63–2.7	< 0.001
Admission for urgent surgery	0.88	0.73–1.06	0.182
Frailty	1.17	0.99–1.38	0.072
Initial non-neuro SOFA score	1.07	1.05–1.09	< 0.001
Male sex	0.84	0.73–0.96	0.011
Immunocompromised status	0.96	0.73–1.26	0.757
Obesity	1.01	0.86–1.18	0.928
COPD (Gold 3–4)	0.98	0.7–1.37	0.902
Number of beds in the ICU	1.00	0.99–1	0.130
ICU with waning protocol	0.92	0.75–1.12	0.392
Middle income country	0.76	0.6–0.96	0.023
Non-European high income country	0.79	0.63–0.99	0.044

Conclusion: The variables found associated with longer delay from meeting weaning eligibility criteria to the first separation attempt depends on the patient's characteristics and type of admission. Being a woman and being treated in Europe (high income countries) were also associated with longer delay.

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Acknowledgements

1. * On behalf of the WEAN SAFE investigators
2. This study was endorsed by the European Society of Intensive Care Medicine (ESICM) and the European Respiratory Society (ERS)

001307

Raised ferritin levels are associated with increased mortality in critically unwell patients with COVID-19

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Intensive Care Medicine Experimental 2022, **10(2)**:001307

Introduction: An estimated 3–5% of patients hospitalised with coronavirus disease 2019 (COVID-19) require mechanical ventilation and critical care unit admission [1]. Despite significant treatment advances, mortality in COVID ARDS patients remains above 30% and it is prudent to identify those patients at most risk. Ferritin levels have been routinely measured in COVID-19 patients' blood as a surrogate marker of hyperinflammation but it remains unclear whether hyperferritinaemia is associated with worse outcomes in COVID-19 [2].

Objectives: 1) To assess whether ferritin in COVID patients, measured in blood within the first 24 h after tracheal intubation, was associated with intensive care unit (ICU) mortality; and 2) to correlate ferritin with serum cytokine concentrations.

Methods: Patients were recruited to the study 'Multi-organ failure in SARS-CoV-2: identifying mechanisms and potential therapeutic targets' (REC: 20/NE/0153) from July 2020 to January 2022 from four ICUs (Hammersmith, Charing Cross, St Mary's and Chelsea & Westminster Hospitals). Demographical, biochemical and ventilatory data were prospectively collected, within 24 h of tracheal intubation, in COVID ARDS (n = 141) and non-COVID ARDS (n = 12) patients, in addition to intubated patients with concurrent sepsis (n = 13). Corresponding serum cytokines were also measured using Luminex multiplex cytokine kits.

Results: Our COVID patient cohort had an ICU mortality of 38%. Median ferritin in COVID ARDS was 1443 ng/mL compared to 519 ng/mL in non-COVID-ARDS and 419 ng/mL in intubated patients with sepsis. In COVID ARDS patients, ferritin was substantially higher in those ICU patients that subsequently died (died: 2368 ng/mL vs alive: 1055 ng/mL $p = 0.001$). This relationship with mortality was also observed with CRP ($p = 0.018$) suggesting that these patients were inflamed but not with other commonly measured biomarkers such as white cell count ($p = 0.178$), d-dimer ($p = 0.074$) or troponin ($p = 0.156$). In COVID-ARDS, ferritin levels were higher in those patients with worse PaO2/FiO2 ratio, although not statistically significance ($p = 0.07$). Ferritin levels did not correlate with serum pro-inflammatory cytokines measured including IL-1α ($p = 0.161$), IL-1β ($p = 0.429$), IL-6 ($p = 0.160$), IL-8 ($p = 0.923$), IL-10 ($p = 0.544$), TNFα ($p = 0.971$), IFNγ ($p = 0.676$).

Conclusion: Our data demonstrate ferritin levels measured within 24 h of intubation are dramatically elevated in COVID-ARDS patients and significantly increased in those patients with the highest mortality and severest disease. In contrast to previous reports [3], ferritin levels did not correlate with serum pro-inflammatory cytokines, suggesting that whilst ferritin was associated with increased acute inflammation in COVID-19, it is not necessarily a surrogate marker of circulating cytokines. Our observations would support the routine testing of ferritin in critically unwell COVID-19 and highlight its value as a biomarker of disease severity and ICU outcome.

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Acknowledgements: P89938 – National Institute of Academic Anaesthesia.

001328

The Role of Dissolved Oxygen in VV ECMO Treatment

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Intensive Care Medicine Experimental 2022, **10(2)**:001328

Introduction: The dissolved oxygen fraction is, in comparison to the hemoglobin bound oxygen fraction, quite often considered clinically irrelevant in ECMO therapy. Previous work of our group showed for the first time, that dissolved oxygen can account for up to one third of the total oxygen delivered by the membrane lung (ML). Ref(1).
Objectives: To describe the role of dissolved oxygen on oxygenation during VV ECMO support, measurement of oxygen transfer of the native lung (V NL O_2) and membrane lung (V ML O_2) was performed in patients with acute respiratory distress syndrome (ARDS).
Methods: We performed a systematic analysis of data obtained in the MEEP trial (Measuring Energy Expenditure in ECMO Patients; Charité ethics EA/1/293/13 Ref(3)). Oxygen uptake via the membrane lung (V ML O_2) was calculated using blood gas analysis and physiological equations, published as the MEEP approach. Ref(2,3) Further, fractions of hemoglobin bound (V ML O_2 HB) and dissolved oxygen (V ML O_2 DISS) were calculated separately. Oxygen exchange via the native (V NL O_2) lung was measured using indirect calorimetry (Quark RMR and Q-NRG+; Cosmed Srl, Rome, Italy). The total oxygen uptake of the patients was calculated as follows: V TOTAL O_2 = V NL O_2 + V ML O_2.

Results: We included 23 mechanically ventilated ARDS patients (> 18 years) undergoing VV ECMO support and acquired 101 valid datasets. Baseline characteristics are displayed in Table 1.

Table 1: Baseline characteristics

number of patients	23
female, n (%)	6 (26.1)
male, n (%)	17 (73,9)
age, years, median (IQR)	52 (44/63)
BMI, median (IQR)	25.9 (22.8/30.6)
SOFA, median (IQR)	9 (8/13)
ICU admission diagnosis, n (%)	
bacterial pneumonia	9 (39.1)
viral pneumonia	5 (21.7)
PJP	2 (8.7)
exacerbation of COPD	2 (8.7)
lung fibrosis	2 (8.7)
ARDS without pathogen detection	3 (13)
Hb, mg/dl, median (IQR)	8.3 (7.8/9.3)
ECMO BF, liter/min, median (IQR)	3.3 (2.7/4.2)
ECMO sweep gas flow, liter/min (IQR)	3.5 (2.0/5.2)
FiO2, %, median (IQR)	45 (35/60)
PEEP, cmH2O, median (IQR)	15 (13/18)

In this patient collective oxygen uptake was mostly realized by ECMO (V TOTAL O_2, ml/min, median 271 (IQR 221/316), V NL O_2, ml/min, median 96 (IQR 45/160), V ML O_2, ml/min, median 160 (IQR 131/197)). Calculations of fractions of extracorporeal oxygen uptake show that a median of 126 ml/min (IQR 98/150) were transferred bound to hemoglobin and 36 ml/min (IQR 30/41) as physically dissolved oxygen. Further, we found that dissolved oxygen accounts for a median of 22.8% (IQR 19.6%/26.8%) of extracorporeal and 13.4% (IQR 10.4%/16.8%) of overall oxygen uptake. Figure 1.

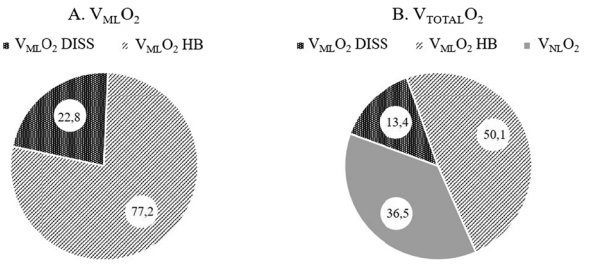

Figure 1. **A**: Percent of oxygen uptake as dissoved oxygen ($V_{ML}O_{2\ DISS}$) and hemoglobin bound oxygen ($V_{ML}O_{2\ HB}$) of extracorporeal oxygen uptake ($V_{ML}O_2$). **B**: Percent of oxygen uptake of the native lung ($V_{NL}O2$), as dissoved oxygen ($V_{ML}O_{2\ DISS}$) and hemoglobin bound oxygen ($V_{ML}O_{2\ HB}$) of overall oxygen uptake ($V_{TOTAL}O_2$).

Conclusion: Our study reveals that a clinically significant amount of the extracorporeal oxygen uptake is provided as physically dissolved oxygen.

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Acute Respiratory Failure 17

001043

Power as an indicator of risk for ventilator-induced lung injury. Which power is more relevant?

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Intensive Care Medicine Experimental 2022, **10(2)**:001043

Introduction: To damage a physical structure takes work that is lost in the process. Resistive work does not cause damage in peripheral lung, vide infra. During the breath, it is unclear if total elastic work (Wel,tot) correlates with the potentially damaging elastic work lost in the lung (Wel,lost).
Objectives: To retrospectively analyse the relation between Wel,lost and Wel,tot in ARDS patients under volume-controlled ventilation.
Methods: The Ethics Committee of Henri Mondor University Hospital approved the study of 14 ARDS patients ventilated for 3 days.1 Sinusoidal flow modulation during tidal breaths allowed analysis of elastic pressure, Pel. separated from resistive pressure. Mean age was 59 ± 13, SAPSII 62 ± 21, Vt 6 ± 1 ml/kg of predicted body weight and respiratory rate 25 ± 4 breath/min. PEEP was 8 and 15 cm H2O.

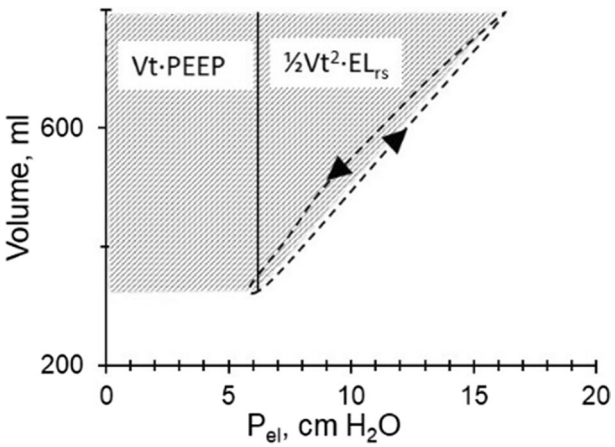

Figure 1. The loop, interrupted line, represents inspiratory and expiratory Pel during a breath. The loop area represents the elastic work lost in the lung during the breath, Wel,lost. The total inspiratory elastic work, Wel,tot, hatched area, covers the components Vt·PEEP, the rectangle and ½Vt2·ELrs, the triangle. ELrs is elastance of the respiratory system.

Results: Results: At low and high PEEP Wel,lost was 15 ± 5% and 13 ± 7 of Wel,lost, respectively (p = 0.50). Wel,tot showed no correlation to Wel,lost (R2 = 0.0031).
Discussion: Ventilation induced lung injury (VILI) occurs in peripheral lung. As airway resistance is overwhelmingly located in y-piece, tracheal tube and major airways, resistive work does not cause VILI. Work absorbed by an elastic structure under deformation but returned after withdrawal of the deforming force does not cause damage. Accordingly, only Wel,lost, 14% of Wel,tot, may cause VILI. As Wel,tot lacks correlation to Wel,lost, Wel,tot does not allow estimation of risk for VILI. Power, that is work times respiratory rate (RR), shares this limitation. Power transmitted from the ventilator to the respiratory system (Powerrs) can be calculated from flow and pressure signals. Notably, Wel,lost includes work associated with barotrauma and atelectrauma but includes components which may be unrelated to VILI, potentially limiting its usefulness as risk indicator for VILI.
Conclusion: The concept that mechanical power delivered by a ventilator defined by its resistive and elastic components indicates risk for lung injury has limitations. The elastic energy lost at each tidal breath may be a better indicator of the risk of VILI than total elastic work or Powerrs, and merits to be studied prospectively.

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001145

Unintentional Fluid Overload in Patients with ARDS due to COVID–19

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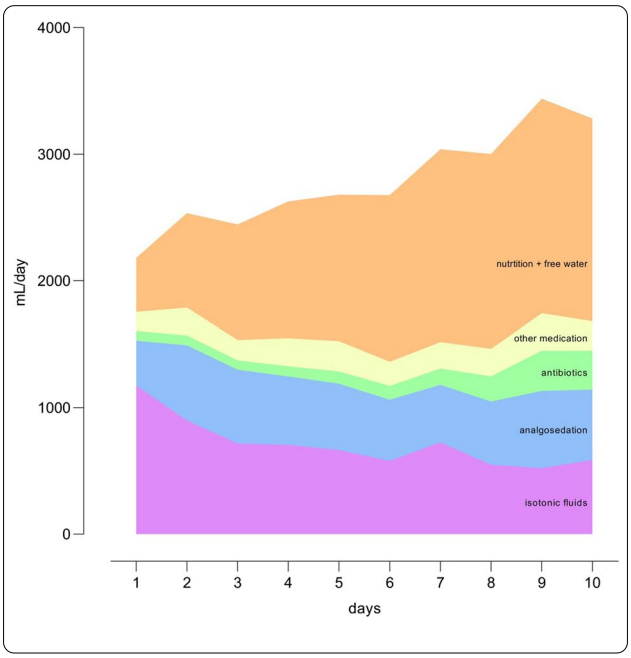
Intensive Care Medicine Experimental 2022, **10(2)**:001145

Introduction: Fluid overload has an association with poor outcome in ARDS patients (1). Fluid overload could be prevented by reducing 'unintentional' fluid loading.
Objectives: To determine unintentional fluid loading in patients with ARDS due to COVID–19.
Methods: Observational single center study during the first wave of the national outbreak in the Netherlands. The amounts of all fluids were collected up to 10 days after start of invasive ventilation from the electronic patient records. Five fluid categories were created, namely isotonic infusion fluids, fluids used for parenteral antibiotics, fluids used for analgosedation, fluids used for other medication, and (par) enteral nutrition and free water.
Results: We collected data in 32 patients: 21 males and 11 females. The amounts of fluids administered per day are presented in the figure. The total amount of administered fluids declined over the first days. Potential 'unintentional' administered fluids accounted for a one-third of the mean daily total fluid volume. Isotonic infusion fluids (25%) and (par)enteral nutrition and free water (43%) were the greatest contributors to the total administered fluid volume. Fluids used for analgosedation (19%) was the major source of potential unintentional fluids. From the second day of invasive ventilation until the last, the quantity of this group remained about the same.
Conclusion: This retrospective observational study suggests that potential 'unintentional' administered fluids accounted for 32% of the fluid intake among critically ill COVID–19 patients. Awareness of these sources of fluids allow the health care professional to manage fluid intake appropriately.
Figure 1. Graphical representation of the course in amounts of fluid (in mL/day) of the different fluid groups over 10 days of invasive ventilation.



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Acknowledgements: None.

001170

Prognosis of severe SARS-Cov-2 pneumonia treated with Tocilizumab

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Introduction: The SARS-CoV-2 virus is responsible for hypoxemic pneumonitis that can lead to acute respiratory distress syndrome (ARDS). Establishing a therapeutic strategy that decreases the severity of SARS-CoV-2 infection is a global public health emergency. Several molecules have been tested, including tocilizumab (TCZ), an inhibitor of the interleukin-6 receptor signaling pathway.
Objectives: The aim of this study was to assess the prognosis of severe Covid-19 pneumonia treated with TCZ.
Methods: This was a descriptive retrospective study including patients with severe to critical forms of COVID-19 infection presenting with respiratory distress and hospitalized in the Covid resuscitation unit of our hospital over a period of 4 months from July to October 2021. All patients were treated with TCZ in addition to standard care according to the criteria defined by the WHO. We collected the demographic, clinical, biological and radiological parameters as well as patients' evolution. The data collected was analyzed using the SPSS 20.0 statistical software.
Results: 32 out of 140 patients (22.85%) were treated with TCZ (18H/14F). The median age of the patients was 63.4 years. Twelve patients (37.5%) had a double dose of TCZ. 69.45% of the patients received the TCZ between the 8th and the 10th day of the hospitalization. During the administration of the treatment, 18 patients (56.25%) were on non-invasive ventilation alternating with optiflow, 10 patients (31.25%) were on non-rebreather mask and 4 patients (12.5%) only were on mechanical ventilation. Thrombocytopenia was noted in 3 patients (9.37%) while neutropenia occurred in 8 patients (25%). 7 patients (21.87%) had hepatic cytolysis. The occurrence of septic shock was reported in 14 patients (43.75%). No cases of allergy were noted. An increase in oxygen requirements was noted in 28 patients (87.5%) including 26 patients requiring recourse to mechanical ventilation (92%). The mortality rate was 81.25%.
Conclusion: TCZ is a therapeutic alternative recommended by the WHO in severe forms of SARS-Cov-2 pneumonia. However, our series showed a very high mortality rate. These results could be explained either by the delay in administration of the treatment or by the absence of dose adjustment according to the dosage of inflammatory cytokines. However, an increase in the sample size is necessary in order to obtain statistically more valid results.

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001262

Impact on the Ability of Health Care Professionals to Correctly Identify Patient-ventilator Asynchronies of the Simultaneous Visualization of Estimated Muscle Pressure Curves on the Ventilator Display - a Randomized Cluster Study (Pmus Study)

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Intensive Care Medicine Experimental 2022, **10(2)**:001262

Introduction: Patient-ventilator asynchronies occur because of a mismatch between neural (patient) and ventilator inspiratory and expiratory phases. Typically, asynchronies are detected by visual inspection of ventilator waveforms with low sensitivity, even when performed by experts in the field. Recently, estimation of the inspiratory muscle pressure (Pmus) from airway pressure and flow waveforms was made possible by using an artificial intelligence algorithm proposed by Magnamed® (São Paulo, Brazil).
Methods: We conducted a prospective cluster-randomized study with parallel assignment to compare the sensitivity to detect patient-ventilator asynchrony between a conventional group using visual inspection of the ventilator waveforms (flow and pressure tracings) with the Pmus group who had in addition the estimated muscle pressure (Fig. 1). Participants were exposed to 49 different scenarios including synchronous and asynchronous ventilatory cycles obtained using the ASL-5000 lung simulator comprising different combinations of respiratory system mechanics, patient effort, and ventilatory modalities.

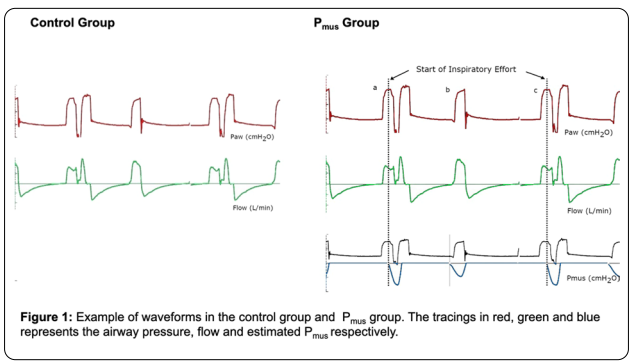

Figure 1: Example of waveforms in the control group and P_{mus} group. The tracings in red, green and blue represents the airway pressure, flow and estimated P_{mus} respectively.

The sample size was estimated in 98 participants based on the expectation of a ten percentage-point difference in the sensitivity between

groups. The primary outcome was the mean asynchrony detection rate (sensitivity). Statistical significance was set at 0.05.
Results: The sensitivity per participant in identifying asynchronies was higher in the Pmus group (65.8 ± 16.2 vs. 52.9 ± 8.4, p < 0.001) even when considering asynchronies by type (Fig. 2).

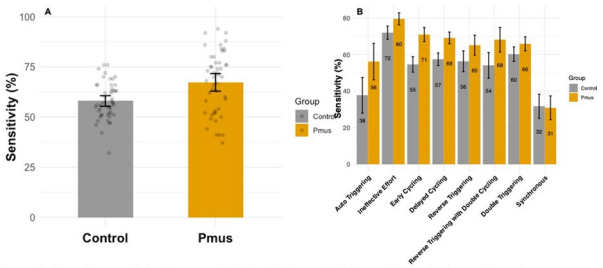

Figure 2: Asynchrony detection sensitivity. **A** -Overall. **B** -Asynchrony by type. Error bars represent the standard error of the mean and dots the individual sensitivity per participant.

Conclusion: The display of the Pmus waveform improved the ability of healthcare professionals to recognize patient-ventilator asynchronies by visual inspection of ventilator tracings.

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Acknowledgements: We would like to thank Toru Miyagi Kinjo and Julio Akira Ueda from Magnamed®, for assistance in the development of the scenarios.

001325

Accuracy of low-cost versus high-cost oximeters – A secondary analysis of the OXYGAP study

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Intensive Care Medicine Experimental 2022, **10(2)**:001325
Introduction: Pulse oximetry is a noninvasive technology used regularly to monitor oxygen saturation and titrate oxygen needs (1). However, these machines are expensive, limiting access in universal health care especially in low-income countries (2). In recent years, low-cost oximeters have become more available, but there is little validation on their accuracy (3,4). Few manufacturers evaluated the accuracy of their product and studies done to evaluate them were mostly made on healthy subjects, in controlled parameters (2,3).
Objectives: The main goal of this study was to compare the accuracy between four high-cost (HC) and two low-cost (LC) oximeters in clinical parameters.
Methods: This prospective study included 211 stable ICU patients with an arterial catheter. Six oximeters were evaluated including four HC (Nonin (Plymouth, MN), Massimo (Irvine, CA), Philips (Eindhoven, Netherlands), and Nellcor (Pleasanton, CA)), as well as two LC oximeters (Contec CMS50DL and Beijing Choice C20). The LC ones were chosen based on a previous study on the accuracy of LC oximeters where only the Contec CMS50DL and Beijing Choice C20 met the International Organization for Standardization (ISO) criteria for accuracy (3). Accuracy was defined by the bias and precision (standard deviation) of each oximeter. The bias was obtained by the mean difference between pulse oximeter readings (SpO2) and arterial saturation (SaO2) (SpO2-SaO2) (5). Each oximeter was evaluated on the number of times it would over and underestimate and its ability to detect hypoxemia defined by a SaO2 < 90% (5).
Results: Mean arterial saturation was 93.6 ± 2.2%. All the tested oximeters had poor precision (high random error, see figure) and correlations with SaO2 were poor. HC oximeters had a mean bias between -3.1 ± 2.1% with Nonin and 0.9 ± 1.9% with Philips. In comparison, LC oximeters had a bias of -2.7 ± 2.4% for Contec CMS50DL and -0.8 ± 2.3% for Beijing Choice C20. While the majority of HC oximeters (Nellcor, Massimo, Philips) had a bias of less than ± 1.0%, only Beijing Choice C20 had a similar result. Contect CMS50DL underestimated 84% of the time and could detect 100% of hypoxemia. Beijing Choice C20 underestimated 51% of the time and detected 50% of hypoxemias. In HC oximeters, Nonin underestimated the most at 91.3% of the time being able to detect 100% of hypoxemias.

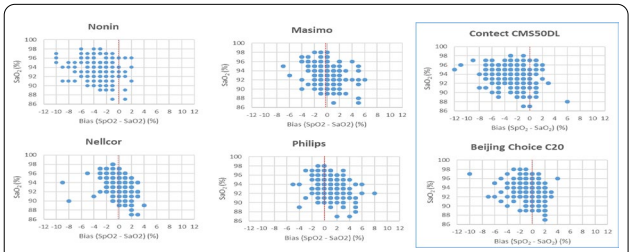

Figure: SpO2 gap from SaO2 at different SaO2 values for high-cost Nonin, Nellcor, Masimo, Philips oximeters and low-cost oximeters Contect CMS50DL and Beijing Choice C20.

Conclusion: We found that the LC oximeters Contect CMS50DL and Beijing Choice C20 have similar accuracies compared with HC oximeters in clinical settings. Knowing the characteristics of these oximeters could help give more access to universal health care, especially in low-income countries or in situations where resources are exhausted.

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001332

The ZEEP-PEEP test in patients with helmet CPAP: a prospective physiologic study

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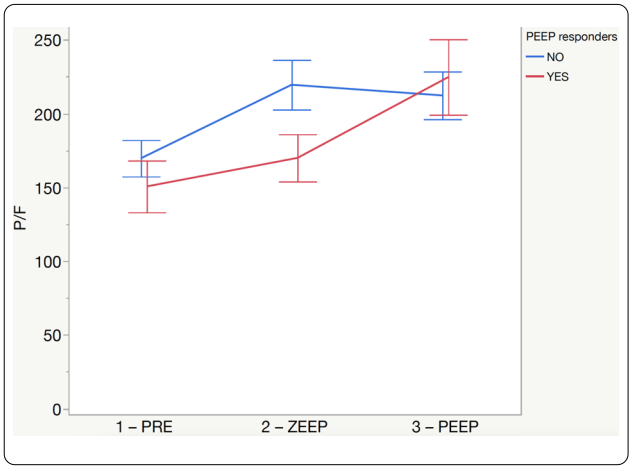
Intensive Care Medicine Experimental 2022, **10(2)**:001332

Introduction: The helmet is a well tolerated interface to deliver continuous positive airway pressure (CPAP) in hypoxemic patients. The improvement in oxygenation after helmet application may be explained by the recruitment obtained by positive end expiratory pressure (PEEP) or by the administration of a more accurate inspiratory fraction of oxygen (FiO2). When oxygen is administered with other devices (e.g. venturi masks, nasal cannulas) the patient may inhale a not predictable fraction of room air, thus decreasing the actual FiO2. At our institution, we have designed a ZEEP (zero end-expiratory pressure)-PEEP test to define if a patient benefits from the PEEP effect or from a the increased actual FiO2. The test consists in applying the helmet and comparing oxygenation parameters before and after the application of a PEEP valve.
Objectives: We aim to describe the use of ZEEP-PEEP test during helmet CPAP, performed to assess the relative oxygenation improvement attributable to the PEEP application.
Methods: We conducted a prospective physiological single-center study enrolling adult patients admitted to the ICU with clinical indication for treatment with helmet CPAP. Arterial blood gas data and vital parameters were recorded at three different time points: before the application of the helmet (1-PRE), after the application of the helmet without PEEP (2-ZEEP) and finally after the application of PEEP (3-PEEP). The FiO2 was maintained constant during the three steps. We defined a patient "PEEP responder" when we observed an improvement in the ratio of arterial oxygen tension to FiO2 (pO2/FiO2) of more than 10% after the application of PEEP. A sample size of 100 patients was calculated. Parameters from the three steps were compared by Wilcoxon Signed Rank test, the Bonferroni correction was applied for multiple comparison.
Results: To date, 24 patients have been enrolled. Helmet CPAP was used in 20 patients after extubation and in 4 cases in the acute non-intubated patient. Before helmet CPAP, oxygen was mainly delivered by Venturi mask (67%), 21% of patients were treated with high-flow nasal cannula and the remaining with reservoir mask. COVID-19 related ARDS was the most frequent diagnosis among enrolled patients (48%). Compared to step 1—PRE, pO2/FiO2 ratio was significantly improved during helmet CPAP both at the ZEEP and the PEEP step ($p < 0,01$). The percentage of "PEEP responders" was 38%. Figure 1 shows the improvement in pO2/FiO2 ratio in PEEP responders and non responders.



Conclusion: In a population mainly characterized by patients with COVID-19 pneumonia ARDS in the post-extubation setting, oxygenation was significantly improved with helmet CPAP. Performing the ZEEP-PEEP test allowed to assess the impact of PEEP on the improvement of oxygenation during helmet CPAP. Our findings suggest that the improvement in oxygenation secondary to helmet application may also be due to the increase of the effective effective oxygen fraction inspired from the patient and, only in a minor proportion of our population, an additional increase in the pO2/FiO2 ratio might be obtained by applying PEEP.

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Acknowledgements: None.

001374

Our COVID-19 pandemic proning experience

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Intensive Care Medicine Experimental 2022, **10(2)**:001374

Introduction: Since March 2020, over 40,000 patients have been admitted to Intensive Care Units in the UK with COVID-19 as the primary diagnosis (1). These patient numbers placed a huge burden on the National Health Service (NHS), particularly Intensive Care Units (ICUs). The management of patients with COVID-19 is primarily supportive, with many patients needing respiratory support via non-invasive Continuous Positive Airway Pressure (CPAP) or Invasive Positive Pressure Ventilation (IPPV) (2). Early in the pandemic, studies from China, stated that in hospitalised patients with COVID-19, 42% developed an acute respiratory distress syndrome (ARDS) type illness with a subsequent mortality rate of 52% (3). In the UK, mortality in those patients requiring admission to the ICU was 42.4% (4). As a result of the severe hypoxia and ARDS-type illness suffered by COVID-19 patients, the Surviving Sepsis Campaign's COVID-19 subgroup recommended the use of Prone positioning in patients with COVID-19 pneumonitis (5). Prone positioning is the action of changing a patient from a supine position to lying face down. Randomised controlled trials have demonstrated that oxygenation and mortality can be significantly improved in patients requiring IPPV for ARDS. As a result, prone positioning has been used for the management of ARDS for over 40 years (4,6).
Objectives: To describe our experience of how we adopted prone positioning during the COVID-19 pandemic and how we improved efficiency and patient safety in our practice with experience using a multidisciplinary approach.
Methods: Patients admitted to our ICU with COVID-19 pneumonitis requiring IPPV were proned if their P/F ratio was < 20 kPa post intubation. We developed a proning standard operating procedure and educated staff to facilitate the prone positioning of all eligible patients. Prospective and retrospective data collection techniques were used. Datix reporting was used to identify any complications of proning.
Results: During the COVID-19 pandemic between March 2020 and February 2022, 367 patients were admitted to our ICU. Of these patients, 214 required IPPV. The median age of those proned was

60 years (47,73) with a median BMI of 33 (27,36). The length of stay for patients that required IPPV was 11.9 (6.6,21.3) days. 56.1% of patients survived to discharge from ICU. 174 of these patients underwent early prone positioning. The median number of days proned was 3 (2,5) with a median of 2 (1,4) consecutive days of proning. 89 (51%) patients developed pressure injuries, 10 (5.7%) patients with facial oedema, there were no cases of visual loss reported. There was 1 (0.6%) central line dislodgement. 2 (1.1%) patients had reported shoulder dislocations, 7 (4%) of which developed a long-term nerve injury as a consequence. There were no accidental extubations or cardiac arrests reported in the prone position.

Conclusion: We adopted prone positioning as our mainstay of treatment for intubated COVID-19 patients with refractory hypoxaemia. As we gained more experience we were able to adapt our technique to ensure better patient as well as staff safety. Prior to the pandemic, prone positioning has been used infrequently on our ICU. We developed an approach to education and the safety of proning that enabled us to include over 100 clinical and non-clinical members of hospital staff that were new to the ICU environment within our ICU MDT. This allowed Critical Care trained staff to provide the specialist care required to patients without the additional time burden associated with being part of the proning team. This enabled us to provide safe and effective patient care whilst proning multiple patients who met our unit criteria despite the enormous number of staff required.

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Acknowledgements: Nothing to declare.

001396

Treatment of mechanically ventilated patients with hypoxemic respiratory failure and acute respiratory distress syndrome using a multidisciplinary care pathway: A pilot implementation study

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Intensive Care Medicine Experimental 2022, **10(2)**:001396

Introduction: A significant gap exists between ideal evidence-based practice and real-world application of evidence-informed therapies for patients with hypoxemic respiratory failure (HRF) and Acute Respiratory Distress Syndrome (ARDS). Pathways can help integrate and organize the use of evidence-based care and help overcome potential barriers.

Objectives: To assess the feasibility and acceptability of a multidisciplinary, stakeholder derived, evidence informed care pathway for the management of HRF and ARDS.

Methods: This study protocol was registered at Clinicaltrials.gov: NCT04070053. One twelve bed medical-surgical ICU was used to prospectively pilot this pathway using a quasi-experimental before and after study design. All mechanically ventilated patients admitted to the ICU were included in the study and received the pathway intervention. There were no exclusion criteria for entry into the pathway; however not all steps are be applicable to all patients. A pre-implementation period of 52 weeks (September 2018 to August 2019) was defined as the baseline period. Pilot implementation occurred over a four-week implementation period (August 2019 to September 2019). A 52-week post-implementation period (September 2019 to August 2020) was used to assess feasibility and acceptability. To maximize adherence an implementation science-based based on identified barriers was used and included audit and feedback, education, training, clinical decision support, site champions, reminders, implementation support, and empowerment. The primary feasibility outcome was a composite fidelity score that measured adherence to 5 key steps of the pathway. Results were analyzed using segmented linear regression model based on patient level data and adjusted for age and median PF ratio within first 24 h of ventilation start. The primary acceptability outcome was the proportion of theoretical framework of acceptability constructs graded with a median score of 5 or above from a 7-point Likert scale, indicating agreement.

Results: A total of 429 patients were included in the preintervention period and 491 patients in the post-intervention period. The median age (interquartile range [IQR]) in the pre and post intervention periods were 60(45–70) and 57(45–67) respectively. The median SOFA (interquartile range [IQR]) in the pre and post intervention periods were 8(5–11) and 8(5–11) respectively. The frequency and proportion of patients with HRF in the pre and post intervention group was 294 (68.5%) and 309 (62.9%) respectively. The frequency and proportion of patients with ARDS in the pre and post intervention group was 136 (31.7%) and 142 (28.9%) respectively. The median composite fidelity score, as a measure of adherence to the pathway, increased in the post intervention period in comparison to the preintervention period in all mechanically ventilated patients (pre: 80[57–100] vs post: 100[67–100], $p < 0.001$), as well as patients with HRF (pre: 67[43–92] vs post: 80[60–100], $p < 0.001$) and ARDS (pre: 67[53–82] vs post: 76[60–94], $p < 0.002$). Driving pressure was lower in the post intervention period (pre: 13.0 [11.0–15.0] vs post: 11.0 [9.5–14.0], $p < 0.001$) as well as the mechanical power were lower in the post intervention period (pre: 23 [18–30] vs post: 20 [15–25], $p < 0.001$). Exploratory analysis suggested that achieving a composite fidelity score of > 90% was associated with a lower median ICU length of stay (adjusted odds ratio 0.49 (0.41–0.57) $p < 0.001$, as well as an increase in 28 day ventilator free days (adjusted odds ratio 1.15 (1.11–1.20), $p < 0.001$. 77 clinicians rated the pathway as acceptable in 7 out of 7 domains of acceptability.

Conclusion: A comprehensive care pathway for patients with HRF and ARDS is feasible and acceptable to clinicians. Adherence to the pathway may be associated with improved physiological and clinical outcomes. This study will inform a future cluster randomized stepped wedge implementation study to test the clinical effectiveness of this pathway.

Acknowledgements: MSI foundation and Critical Care Strategic Clinical Network Seed Grant.

001400

Inhaled nitric oxide (iNO) in the management of COVID-19 associated ARDS: A "NO-GO"?

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Intensive Care Medicine Experimental 2022, **10(2)**:001400

Introduction: Severe coronavirus disease 2019 (COVID-19) can lead to COVID 19-associated acute respiratory failure (CARDS). CARDS fulfills

the Berlin definition of acute respiratory distress syndrome (ARDS) but differs from other forms of ARDS. Inhaled nitric oxide (iNO) is a selective vasodilator of pulmonary arteries and may improve oxygenation by reducing pulmonary shunt fraction in severe ARDS.[1] Furthermore, iNO seems to inhibit coronavirus replication.[2] So far, little is known about the role of iNO in CARDS [3].

Objectives: The aim of this study was to assess, whether the use of iNO in CARDS could improve arterial oxygenation by pulmonary shunt reduction, decrease length of mechanical ventilation (MV), lower length of hospital/Intensive Care Unit (ICU)-stay and reduce 30-day mortality.

Methods: This retrospective, observational, monocentric cohort study was cleared by the local ethics authority and focused on adult COVID-19 positive patients, admitted to an ICU of a quaternary care hospital in Germany for respiratory failure between 03/2020–10/2021. All patients included were suffering from CARDS and were managed with lung protective MV as per ARDSnet recommendations[4], with dexamethasone as per Recovery trial[5] and proning[6] (if PaO2/FiO2 $\leq$ 150 mmHg). iNO with 15 parts per million was initiated in case of PaO2/FIO2 < 200 mmHg according to the treating physician´s decision. Patients receiving iNO for right heart failure/pulmonary hypertension were excluded from this study. The direct effect of iNO was assessed by comparing cumulative results of the last three consecutive arterial blood gas (ABG) results (1–2 h apart) each before iNO and after iNO. Furthermore, demographic data, ABG results, length of MV, length of hospital/ICU-stay and 30-day mortality were compared in the iNO vs the non-iNO group.

Results: 56 CARDS patients were included in the study: 19/56 (33.93%) patients received iNO. In the iNO group vs non-iNO group 68.42% vs 70.27% were male (p = 0.56), mean age was 60.18 ± 15.37 vs 64.32 ± 13.33 years (p = 0.1), mean body mass index was 32.31 ± 7.06 vs 29.66 ± 7.97 kg/m2 (p = 0.23) and mean APACHE Score was 24.53 ± 13.06 vs 21.95 ± 8.83 (p = 0.39). In the iNO group PaO2/FiO2 ratio (151.37 ± 47.49 mmHg vs 138.80 ± 32.50 mmHg; p = 0.35) and shunt-fraction (23.02 ± 5.44 vs 23.74 ± 4.52, p = 0.66) did not differ significantly before and after application of iNO and furthermore, did not differ in the iNO vs the non-iNO group. In contrast, length of MV (589.98 ± 652.25 vs 255.35 ± 232.81; p = 0.01), length of ICU-stay (548.75 ± 396.92 vs 371.67 ± 264.30; p = 0–05) and 30-day mortality (84.21% vs 40.24%; p = 0.002) were increased in the iNO vs the non-iNO group.

Conclusion: In this retrospective study, iNO did not improve oxygenation or ventilation/perfusion mismatch in CARDS. In contrast, the use of iNO was associated with an increased length of MV/ICU-stay and increased 30-day mortality, most likely due to a more severe course of CARDS. Larger, randomized multicenter studies are required to prove this association.

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Acknowledgements: This Study and its authors received no financial support.

001408

Impact of intubation on the evolution of fractions of inspired oxygen in patients treated with high flow oxygen therapy for COVID-19 associated pneumonia

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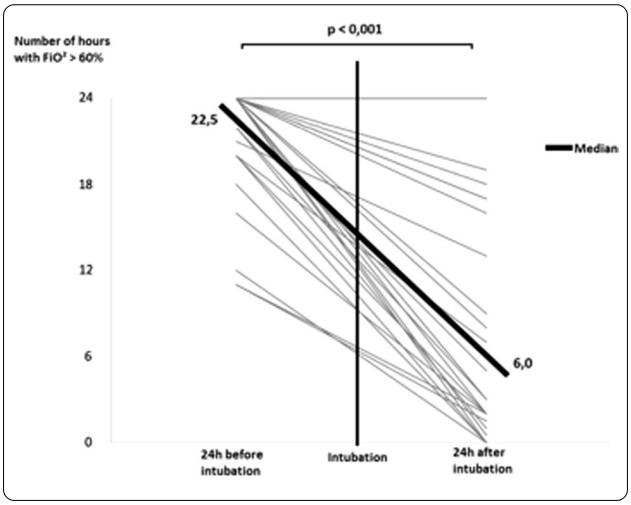
Introduction: Since second wave, High Flow Oxygen Therapy (HFOT) is a first line treatment for COVID-19 associated respiratory failure. However, patients treated with HFOT may be exposed for a long time to high Fractions of Inspired Oxygen (FiO2), potentially leading to hyperoxic alveolar injuries.

Objectives: We aimed to determine whether intubating patients after HFOT failure was associated with a decrease in high FiO2 exposure within the 24 first hours following intubation.

Methods: Among 218 patients admitted for COVID-19 associated pneumonia in Medical Intensive Care Unit (ICU) at Besançon teaching hospital between October 2020 and October 2021, 27 treated with HFOT for more than 24 h before intubation were retrospectively included. The number of hours exposed to FiO2 > 60% and > 90% during the 24 h preceding intubation and the 24 h following intubation were calculated and compared.

Results: Most of the 27 patients were men, with a median age of 71 years-old. Twenty-one patients performed awake prone positioning (PP) under HFOT. The median PaO2/FiO2 ratio was 79 mmHg before intubation, and 193 mmHg 24 h after protective ventilation using a median Positive EndExpiratory Pressure (PEEP) of 12 cmH2O. The median dynamic compliance of the respiratory system was 40 cmH2O. All ventilated patients benefited from neuromuscular blockade and PP. Seven (26%) died in ICU. The median number of hours with FiO2 > 60% decreased from 22,5 (Interquartile range – IQR – [20,0; 24,0]) within the 24 h under HFOT preceding intubation to 6,0 [4,0; 9,8] within the 24 h following intubation, corresponding to a median difference of -15,0 [-18,0; -8,8], statistically significant (p < 0,001).



The median number of hours with FiO2 > 90% decreased from 3,0 [1,3; 15,5] to 2,0 [1,3; 3,0], corresponding to a median difference of -2,0 [-10,0; 0,], statistically significant (p = 0,005).

Conclusion: Intubation itself likely doesn't explain the decrease in FiO2. High PEEP, neuromuscular blockade, and prone positioning are confounding factors. FiO2 is also dependant from the target of oxygenation set as a goal. To the best of our knowledge, this study is nevertheless the first caring about this pragmatic issue. Its main

limitations are a retrospective and monocentric design, and a small sample size. To conclude, in COVID-19 patients treated with high flow oxygen therapy > 24 h, intubation is associated with a statistically significant decrease in high FiO2 exposure. Whether intubation could decrease hyperoxic alveolar injury need to be investigated.

Acute Respiratory Failure 18 + Health Services Research & Outcome 15

001305

Lung Recruitment Potential in Patients with Severe Acute Respiratory Syndrome due to SARS CoV 2

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Introduction: Recent evidence suggests that in patients infected with COVID-19, lung severity should be quantified by segments prior to bedside evaluations of the patient's respiratory mechanics and alveolar recruitment capacity, knowing what their characteristics are and relationship after an alveolar recruitment maneuver with PEEP titration in a world population is insufficient.
Objectives: To compare the characteristics of the alveolar recruitment potential based on ventilatory mechanics and segmental pulmonary severity by chest tomography after a pulmonary recruitment maneuver with PEEP titration, in patients with SARS Cov-2 on admission to the ICU.
Methods: The study corresponds to a descriptive cross-sectional cohort design. A total of 42 patients (69% men, with 38% presenting more than 2 chronic diseases, age 51.4 [42.3 -63.0] years), were assigned into two groups prior to evaluating the inspiratory recruitability index (R/I index), high recruitment potential group (HRPG) (n = 21) and low recruitment potential group (LRPG) (n = 21), was compared with the assessment of severity index by chest tomography (CT- SS) and ventilatory mechanics after a pulmonary recruitment maneuver with PEEP titration. The sample was expressed as median /interquartile range/ or frequency (percentage) as appropriate. For continuous variables with normal and non-normal distribution, we used the Student's t-test and the Mann–Whitney test. For comparisons of categorical variables we used a chi-square test or Fisher's exact test. respectively. Spearman's correlation coefficient (rho) was calculated to compare the relationship of the variables. All data analyzes were performed with R software. Statistical significance was considered when $p < 0.05$.
Results: Patients with HRP have lower airway opening pressure ($p = 0.029$), higher PEEP ($p = 0.027$), lower driving pressure ($p = 0.037$) and lower mean pressure ($p = 0.016$), when evaluating CT – SS show significantly less severity in anterior ($p = 0.003$) and apical ($p = < 0.001$) segments of the right lung and anterior ($p = 0.029$), apical ($p = 0.043$), superior ($p = 0.009$) and anterior basal segments ($p = 0.006$) left lung compared with LRP. When correlating ventilatory mechanics (LRP (rho = -0.116), HRP (rho = 0.431) and pulmonary severity (LRP (rho = 0.093), LRP (rho = 0.113) as a function of recruitment potential, we found no significant relationship.
Conclusion: Patients who have HPRG present better ventilatory mechanics and less pulmonary severity in relation to patients with LPRG, after a pulmonary recruitment maneuver with PEEP titration, allowing to know the characteristics and ranges of the Chilean population for the R/I index, with safe method that can be used at the patient's bedside.

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001343

Remdesivir, peripheral microcirculatory alterations, and ICU-mortality in COVID-19 patients with ARDS. Data from the HEMOCOVID-19 multicenter study

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Intensive Care Medicine Experimental 2022, **10(2)**:001343

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 COVID-19 treatments, ICU-mortality and 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 due to hypoxemia, and with a clinical diagnosis of ARDS were included. Treatments for COVID-19 disease, active or already administered, were computed. Respiratory, hemodynamic, and microcirculatory parameters were simultaneously evaluated within the first week of admission. Local tissue oxygen saturation (StO2), 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 StO2 parameters: deoxygenation rate (DeO2), reoxgenation rate (ReO2), and hyperemic response (AUCH). Patients were followed-up until ICU-discharge or death.
Results: One hundred-and-thirty COVID-19 patients were studied. Administered treatments: corticosteroids (88.5%), low molecular weight heparin (65.4%), tocilizumab (22.3%), remdesivir (14%), hydroxychloroquine (3.8%), and convalescent plasma (3%). Only remdesivir distribution differed between ICU survivors and non-survivors (21% vs 0%, *p* 0.05). Patients with previous administration of remdesivir showed less pronounced microcirculatory alterations (Table).

	No-Remdesivir (n = 112)	Remdesivir (n = 18)
Age (years)	57 ± 12	56 ± 13
Gender (male) (%)	64	88*
BMI	30 ± 5	32 ± 7
Days from hospital admission	8 ± 15	8 ± 8
Days from ICU admission	4 ± 4	4 ± 3
Invasive MV at inclusion (%)	71	65
PF ratio (%) (n = 57)	183 ± 89	178 ± 70
SF ratio (%)	206 ± 84	209 ± 65
D-dimer (ng/mL)	5981 ± 13,358	5418 ± 13,163
Ferritin (ng/mL)	1478 ± 997	1052 ± 972
C-reactive protein (mg/dL)	13.8 ± 18.1	5 ± 7.1*
StO2 (%)	68 ± 6	64 ± 4*
THC (U)	42 ± 15	50 ± 17*
DeO2 (%/min)	-5.3 ± 2.1	-5 ± 2
ReO2 (%/min)	75 ± 39	82 ± 33
Hyperemia AUC (U)	7.8 ± 4.5	10.4 ± 5.4*

Conclusion: In our population, remdesivir treatment was associated with improved survival. Patients previously treated with remdesivir showed less pronounced microcirculatory alterations, although we cannot infer causality. Whether remdesivir improves the microcirculation of severe COVID-19 patients deserves to be further explored.

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001399

Comparison between the first and second wave of patients with COVID-19 who required mechanical ventilation in an Argentine ICU

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Intensive Care Medicine Experimental 2022, **10(2)**:001399

Introduction: The information regarding characteristics and ventilatory results comparing the first(W1) and the second wave (W2) in Argentina are limited. The main objective of this study was.
Objectives: to describe general characteristics and ventilatory variables in covid 19 patients who required invasive mechanical ventilation (IMV) and compare differences between waves. Secondarly, factors associated with mortality in intensive care unit (ICU) were studied.
Methods: We conducted a prospective observational cohort study that included patients older than 18 years infected with SARS- CoV2 consecutively admitted to ICU with IMV between August 1, 2020, and Junes 30, 2021. We included 412 patients.
Results: We found statistically significant differences in age [W1 64(55–72) versus w2 59 (50–66) years], presence of COPD [W1 n = 42 (19.8%) versus W2 n = 13(6.3%)], plateau pressure [W1 27(25–30) cmH2O versus O2 n = 24 (22–27) cmH2O], driving pressure (ΔP) [w1 15 (13–17) cmH2O versus W2 12 (11–14) cm H2O] compliance [w1 40 mLcmH2O (32–46) versus O2 = 33 mL/cm H 2 O (27–40)]; reintubation [O1 30.4% (n = 63/207) versus O2 13.7% (n = 28/205)]. We identified as independent factors associated with mortality the following variables: age [OR 1.07(95% CI 1.05–1.09)], the ΔP in the first 24 h [OR 1.19(95% CI 1.10–1.28)] and W2 [OR 1.81 (95% IC1.12–2.93); p = 0.015.
Conclusion: During W2 the patients were younger. It was possible to achieve ventilatory mechanics more adjusted to a protective ventilation strategy. In conclusion, in the patients studied, age and ΔP were independent predictors of mortality.

001425

PaO2/FiO2 ratio changes are poor predictors of proning success in COVID-19 ARDS

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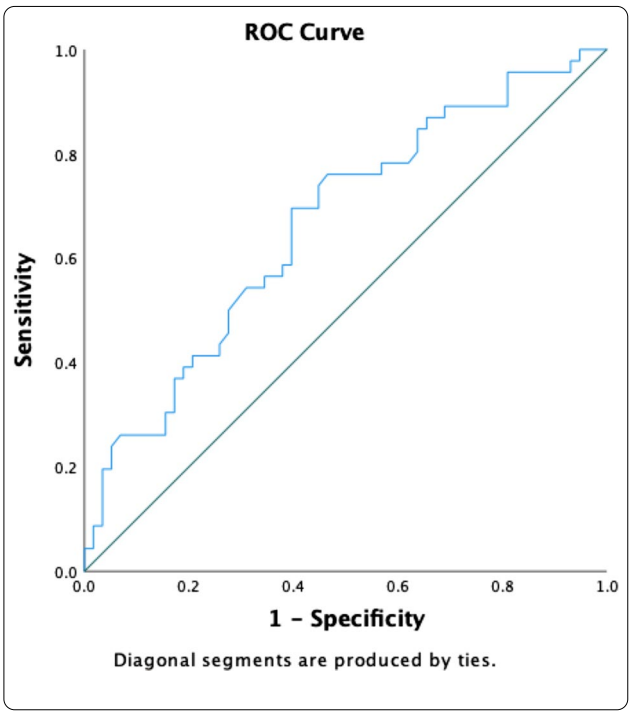
Introduction: Improvement in PaO2/FiO2 ratio (ΔP/F) is commonly viewed as marker of success and predictor of good outcome in proned patients with ARDS. Recently it has been suggested that this parameter has poor discriminatory power for mortality (1). There is conflicting data if this simple index could be used to predict outcome in COVID-19.
Objectives: To examine the clinical utility of PaO2/FiO2 improvement to discriminate between survivors and non-survivors.
Methods: Single centre, retrospective observational study involving all mechanically ventilated patients with COVID-19 induced ARDS between March 2020-April 2021, who had at least one session of prone positioning. Basic demographic data and ventilatory parameters prior to proning (PP), 1 h, 6 h, 12 h into the proning session then prior to supination (PS) were collected. Survivors were comapred to non-survivors using Mann–Whitney U test and ANOVA with Welch modification for non-parametric data. ROC was plotted and AUC calculated for ΔP/F.
Results: 105 patients had at least one session of prone positioning, 75% of these sessions were within 24 h of ICU admission. Male/female ratio was 85/19, median [IQR] age was 60 [14]. 97% of patients were ventilated in pressure regulated volume control mode. Overall ICU mortality was 56%. There was no significant difference between survivors and non-survivors in PEEP, FiO2 or PIP. P/F ratios were similar between the groups PP and during t proning, with significant within

group improvement. P/F (median [IQR]) was significantly higher before supination in the survivors (Table 1).
Table 1. P/F ratio of survivors and non-survivors

P/F ratio	Survivors n = 46	Non-survivors n = 59	p-value
PP	14.5 [5.3]	14.3 [4.3]	0.703
1 h	19.5 [9.4]	17.1 [7.9]	0.574
6 h	22.4 [11.0]	19.0 [10.5]	0.117
12 h	22.3 [9.5]	20.0 [9.3]	0.053
PS	23.2 [12.5]	20.2 [9.6]	0.002

ΔP/F only showed poor to moderate discriminatory power AUC 0.648 (95%CI 0.542–0.754).



Conclusion: Based on our data, P/F ratios improved significantly in both survivors and non-survivors with significantly better P/F in the former group with otherwise identical ventilatory parameters. However, ΔP/F was not able to discriminate between the groups and should not be used as the main marker to evaluate the success and outcome of proning in COVID-19 ARDS.

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001438

Interstitial Lung Disease in COVID - critical care patients

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Introduction: Interstitial lung disease (ILD) secondary to COVID -19 has increasingly been described in ARDS COVID -19 critical care patients. The underlying pathology is not fully understood but might be associated with abnormal cytokine pattern and cell repair. Some authors report a positive response to high dose steroid treatment in critical care patients with COVID-19 ILD, yet evidence is lacking regarding ICU outcomes.
Methods: One year (2021) retrospective study describing critical care patients admitted in two ICU's of a portuguese hospital centre with COVID -19 ARDS who developed ILD with persistent and severe respiratory failure. The authors describe which respiratory support they had, steroid treatment (weigh-based or pulses), infectious complications and ICU outcome.
Results: During a one year period, 30 cases of ILD were diagnosed based on chest CT scan, persistent respiratory failure and exclusion of infectious cause. Every patient had severe respiratory failure requiring invasive mechanical ventilation with or without Extracorporeal Membrane Oxygenation (ECMO). All patients received high dose steroid therapy with weight based or pulses. Infectious complications after steroid initiation included six cases of ventilator associated pneumonia. Retrospective blind reporting of chest CT scan pattern classified patients into organizing pneumonia (OP) and other patterns. There were 8 (26,7%) with OP and 22 (73,4%) with other patterns. No deaths were observed in the OP group and 2 died with other patterns. Chi square analysis of data showed no statistical difference (p = 0.388).
Conclusion: COVID-19 associated ILD is a rare diagnosis in ARDS critical care patients and management remains a matter of debate. Larger studies are needed as well as prospective studies on the benefits of steroids in these patient's outcome.

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001447

The conclusion of two years' experience with COVID-19: features, outcomes

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Introduction: The COVID-19 pandemic is a global health crisis. It has preoccupied the world for the last two years because of its contagiousness and its important morbi-mortality. It causes pneumonia with acute respiratory distress syndromes requiring hospitalization in intensive care.
Objectives: Our study aims to evaluate the epidemiological, therapeutic and evolutionary characteristics of patients with SARS-CoV-2 pneumonia hospitalized in an intensive care unit.
Methods: This was a retrospective, descriptive study conducted in an intensive care unit. We included all patients hospitalized in an intensive care unit with confirmed SARS-CoV-2 pneumonia during the period from march 2021 to September 2021. The clinic-demographic, biological, therapeutic and evolutionary data of the patients were recorded.
Results: 323 patients were enrolled. The mean age was 58 ± 12 years with a gender ratio of 1.15. The main history was hypertension and diabetes in 37,3% and 33,1% of cases. Obesity was found in 81 cases. A COVID-19 vaccination was received by 6 patients, 3 of whom had received a full course. The main signs were dyspnea (n = 207), cough (n = 169) and fever (n = 167). Median IGSII and SOFA scores were 30

[24–38] and 4 [3–5], respectively. Chest CT scans were performed in 294 cases. The extent of involvement was between 50 and 75% in 112 cases and between 25 and 50% in 84 cases. Pulmonary embolism was found in 81 cases (25%). The median PaO2/FiO2 ratio on admission was 105 [41–250]. High-flow oxygen therapy was required in 110 cases and non-invasive ventilation in 75 cases. Invasive mechanical ventilation (IMV) was required in 26 cases on first day of admission. The invasive mechanical ventilation was required during hospitalisation in 116 cases. The median duration of IMV was 10 [1–40] days. Pneumothorax was diagnosed in diagnosed in 43 cases. Weaning from IMV was noted in 30 cases, 8 of which were reintubated. The occurrence of nosocomial infections was noted in 135 cases. The use of vasoactive drugs was necessary in 43% of cases. Acute renal failure was noted in 50 cases. The length of stay was 10 [2–42] days. The rate of mortality in the ICU was 45%. Multivariate analysis showed that independent predictor factors of mortality were age > 65 year, nosocomial infection, acute renal failure,thrombo-embolic events and invasive mechanical ventilation.
Conclusion: The use of invasive mechanical ventilation in COVID-19 patients in the ICU was frequent. The mortality rate remains high.

001289

The Incidence of Delirium in Covid-19 critically ill patients and its effect on muscle strength

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Introduction: A large proportion of ICU patients develop delirium, which has been identified as a serious complication of ICU stay. It has been associated with important outcomes, such as increased days on mechanical ventilation and length of ICU stay.
Objectives: The study aims to assess the incidence of delirium in Covid-19 ICU patients and its consequence in muscle strength. Secondary outcomes are days of mechanical ventilation (MV) and ICU length of stay in patients with delirium.
Methods: All patients admitted in the Covid-19 ICU of General Hospital of Chalkida that were mechanically ventilated for > 48 h were included in the study. Exclusion criteria were: history of mental disease, brain injury, hearing problems and end of life patients. Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) was used to assess the presence of delirium. Manual Muscle Strength Test (MMST) was used to evaluate muscle strength and MRC scale for the clinical diagnosis of ICU acquired weakness. All were assessed at weaning period.
Results: Ninety-six Covid-19 critically ill patients (F:40/M:56, 58.3 ± 14.3 years) were included from 11/2020 till 2/2022.The presence of delirium during weaning time reached 51%. Patients had Sofa score: 5 (5–7) [median (IQR)] and significant reduced muscle strength 38 ± 12. Patients diagnosed with delirium had significantly reduced muscle strength (35.8 ± 12 vs 44.4 ± 6, $p < 0.01$), increased days under MV (9.7 ± 1.2 vs 2.7 ± 0.5, $p < 0.01$) and ICU stay (16.7 ± 3.5 vs 4.5 ± 0.8, $p < 0.01$).
Conclusion: These descriptive data underline the increased incidence of delirium and its serious effects in Covid-19 critically ill patients. Further studies are needed to fully investigate the risk factors of these patients and the long-term effects.

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001350

Exercise intolerance in COVID-19 ICU survivors compared to patients complaining of long COVID after mild disease: a metabolic perspective

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Introduction: Exercise limitation reported in COVID-19 patients who survived a stay in intensive care unit (ICU) and in long COVID patients has been poorly explained.
Objectives: The aims of this retrospective study were to assess exercise capacity using cardiopulmonary exercise testing (CPET) coupled to an oxidative stress assessment in COVID-19 ICU survivors, and to compare their CPET profile to patients complaining of long COVID after mild disease.
Methods: Adults surviving an ICU stay ≥ 7 days for a severe COVID-19 pneumonia and attending our follow-up clinic 3 months after discharge (ICU group), and previously healthy patients complaining of persistent exercise intolerance after a mild COVID-19 that did not require hospitalization (LC group) were included. Parameters of CPET on a cycle ergometer were collected at rest, at anaerobic threshold (AT), at peak exercise and during recovery. In addition, blood biomarkers of systemic inflammation (C-reactive protein (CRP), myeloperoxidase (MPO)) and oxidative stress status (OSS, including vitamin C, thiol proteins (PSH), glutathione peroxidase (GPx), copper/zinc ratio, total hydroperoxides (ROOH)) were determined simultaneously in some patients of ICU group. Data are expressed as median and quartiles.
Results: A total of 54 patients were included: 31 in ICU group (21 males, 61 [54–67]y, BMI 32.9 [30.1–34.8] kg/m2, ICU stay 15.4 [9.7–25.6]d) and 23 in LC group (7 males, 44 [37–50]y, BMI 25.8 [22.3–30] kg/m2). In ICU group, at rest, oxygen uptake (VO2) was elevated (8 [5.6–9.7] ml/min/kg). AT was reached early, at 81 [72.5–87.2]% of peak VO2. Maximum effort was reached at low values of workload and VO2 (66 [40.9–79.2]% and 74.5 [62.6–102.8]% of respective predicted maximum values). Ventilatory equivalent for carbon dioxide remained within normal ranges. Cardiac response was appropriate with a normal oxygen pulse profile and an appropriate chronotropic adaptation. Metabolic efficiency was low: 15.2 [12.9–17.8]%. The 50% decrease in VO2 after maximum effort was delayed, at 130 [120–170] sec, with still high respiratory exchange ratio (1.13 [1–1.2]). Three months after ICU discharge, CRP was into normal ranges (1.95 [0.95–2.69]mg/L), while MPO was elevated (92 [75.5–106.5]ng/mL). OSS was altered with low PSH concentration (296 [260–360] µM), increased GPx concentration and copper/zinc ratio (respectively 64.5 [61.7–90]UI/g and 1.18 [0.95–1.24]). ROOH was abnormally high in 50% (5/10) of the tested patients. LC patients were tested 12 [5–14] months after infection. They benefited from a complete clinical assessment before CPET, and none of them presented cardiopulmonary sequelae of COVID-19 infection. At CPET, they reached peak workload and VO2 predicted values. However, their metabolic profile was similar to ICU group at a lesser extent: high resting VO2 (6.1 [4.4–7.6] ml/min/kg), early cardiopulmonary adaptation to effort (AT at 85 [75–91]% of predicted maximum VO2), low metabolic efficiency (22 [21.5–23.5] %) and delayed and incomplete recovery.
Conclusion: Exercise capacity was reduced 3 months after a critical COVID-19, due to an altered metabolic profile, in a context of persistent inflammation and oxidative stress. To a lesser extent, similar exercise and metabolic abnormalities were observed in LC group, suggesting a common inflammatory pathogenesis.

Acknowledgements: We would like to thank the Province of Liège authorities and collaborators for their help during the pandemic.

001364

Subcostal vs trans-hepatic approach for inferior vena cava evaluation in healthy volunteers: agreement of M-mode and artificial intelligence

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Introduction: Changes in inferior vena cava (IVC) diameters according to the respiratory cycle are clinically used to estimate the value of central venous pressure and to anticipate the probability of fluid-responsiveness in critically ill patients. In spontaneously breathing patients, an IVC collapsibility index (CI) higher than 40%-48% (according to various studies) has been used as cut-off for fluid responsiveness. Imaging of the IVC is usually performed via sub-costal (SC) approach with a sagittal view of the vessel. However, the SC imaging may not be feasible under several conditions (laparotomy, mediastinal drains, obesity); in such cases, the coronal trans-hepatic (TH) visualization of the IVC may represent an alternative for the evaluation of fluid-responsiveness. Whether this ultrasound approach for IVC visualization is interchangeable remains debated. Moreover, artificial intelligence (AI) software have 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 compared results obtained with both standard M-mode calculation and AI assessment in a population of 60 healthy young adults, after obtaining their informed consent. 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 60 volunteers, two patients did not have both SC and TH windows (3.3%), and for further three (5%) it was not possible to obtain the TH visualization. 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	13.9%	-18.1	45.8
			IVC Max diameter	-1.7 mm	-9.6	6.1
			IVC Min diameter	-4.4 mm	-14.5	5.6
AI SC	AI TH	Repeated measures	Collapsibility index	6.9%	-22.8	36.7
			IVC Max diameter	-2.0 mm	-9.3	5.4
			IVC Min diameter	-2.3 mm	-13.3	8.7

Conclusion: Comparing two different sites of measurement of the IVC, we found clinically significant differences between the estimation of the vessel size and variation over the respiratory cycle in spontaneously breathing volunteers. These differences 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 the AI, the LoA remained very large. As per previous smaller studies, our study does not support the interchangeability of SC and TH approach for IVC visualization.

Acute Respiratory Failure 19

001120

Non-invasive ventilatory support in the Management of SARS-CoV-2 Patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001120

Introduction: In the context of the pandemic, treatment for respiratory failure in COVID-19 included the therapeutic possibilities of non-invasive ventilation (NIV), in the modalities of continuous positive airway pressure (CPAP) and bilevel positive pressure (BiPAP), as well as, the use of high-flow nasal oxygen therapy (HFNO). It is currently believed that both NIV and HFNO can avoid the need for intubation or invasive ventilation by providing additional inspiratory support and being indicated mainly when hypoxaemia is associated with a modest worsening of ventilation needs and the need to increase alveolar ventilation or reduce the workload of the respiratory muscles.
Objectives: The purpose of this paper is to analyse the use of non-invasive ventilation (HFNO and NIV) in the management of patients with SARS-CoV-2 pneumonia admitted to the intensive care unit (ICU).
Methods: Retrospective analysis referring to all patients with SARS-CoV-2 Pneumonia submitted to non-invasive ventilatory support admitted to the ICU between March 1, 2020 and March 1, 2021.
Results: 74 patients were admitted who underwent non-invasive ventilatory support (HFNO and NIV). At the time of starting HFNO and/or NIV all patients had PaO2/FiO2 ratio > 150. Median age was 67 years and 81% were male. All patients had at least one comorbidity to be highlighted: Hypertension 78.4%, Obesity 50%, Diabetes Mellitus 40.5%, Obstructive Sleep Apnoea Syndrome 13.5% and Cardiovascular Disease 12.2%. HFNO was used in 36.5% of patients and 77% in NIV, and 10 patients alternated between HFNO and NIV. The mean duration of HFNO and NIV was 1.39 and 4.77 days respectively and 78.4% of the patients needed to escalate ventilatory support to invasive mechanical ventilation (IMV). The mean PaO2/FiO2 ratio at the time of orotracheal intubation was 92 and the mean time between starting NIV and IMV was 2.91 days. The mean length of stay was 14 days and the mean APACHE and SAPS scores were 20.7% and 46.4%, respectively. The mortality rate was 37.8%.
Conclusion: The use of non-invasive ventilation, especially in situations of high critical patient care needs, as happened during the second wave of the COVID-19 pandemic in Portugal, helped to avoid intubation and invasive mechanical ventilation in some patients. However, in the absence of clinical and blood gas improvement, monitoring should be very strict and IMV should be considered more promptly.

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Acknowledgements: None.

001157

Non-invasive assessment of work of breathing and extubation outcome in critically ill patients

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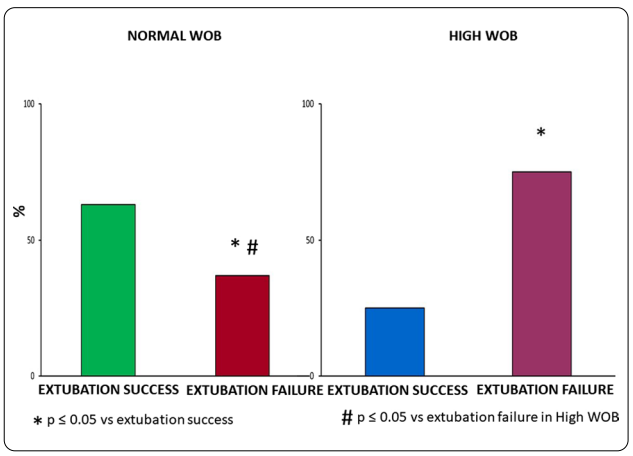
Introduction: After intubation and mechanical ventilation, the primary treatment goal is to restore patient's ability to breath independently. Defining suitable candidates for weaning is of critical importance in clinical practice. Commonly, blood gas analysis parameters (P/F $\geq$ 150 with FiO2 $\leq$ 0.4), ventilatory parameters (Tidal Volume between 5 and 8 ml/predicted body weight, PEEP $\leq$ 8, respiratory rate between 15–30 breaths/min) and calculated parameters such as Rapid Shallow Breathing Index, are used to identify patients who may be eligible for weaning.
Objectives: To evaluate if adding Work of Breathing (WOB) to the common clinical parameters should have helped the clinicians to easily identify patients at high risk of weaning failure.
Methods: A brief trial of proportional assist ventilation plus (PAV+) (30 min) with 15% of assistance was performed in patients already judged eligible for weaning according to clinical parameters. WOB was recorded every 5 min during the trial. According to the manufacturer's indications, WOB was defined LOW (< 0.3 Joule/liter), NORMAL (0.3–0.7 Joule/liter), HIGH (> 0.7 Joule/liter).
Results: Weaning was performed in 102 patients. A preliminary data analysis was conducted in 63 patients. In this cohort of patients WOB was normal in 71.4%, low in 3.2% and high in 25.4%. The percentage of weaning failure and success in the normal and high WOB class are shown in Figure 1.



Conclusion: In patients with high WOB, the weaning failure rate was significantly higher as compared with patients with normal WOB. Clinical parameters may not be sufficient to identify patients at high risk of weaning failure. Further studies are needed to evaluate if respiratory mechanics measurements and other parameters may have a role in predicting weaning failure.

001233

Extracorporeal respiratory support of severe hypoxemic respiratory failure in COVID-19 pneumonitis

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Introduction: Veno-venous extracorporeal membrane oxygenation (V-V ECMO) is a recommended option for the support of patients with severe acute respiratory failure associated with COVID-19 pneumonitis. During the pandemic, we started V-V ECMO support of these patients from March 2021 at our centre.
Objectives: The aim of this study was to determine the intensive care unit (ICU) and in-hospital survival, duration of extracorporeal support, ICU and hospital length of stay and rates of complications.
Methods: A retrospective analysis of the pre-ECMO demographics, respiratory parameters and the outcome variables of all COVID-19 positive patients who received V-V ECMO support from March 2021 to April 2022 was performed.
Results: Eighteen patients were included in the analysis (5 women, age 44 $\pm$ 10 years, Apache II score 14 $\pm$ 6). Three women were in the immediate postpartum period, five patients were retrieved and transported to our department on mobile ECMO, two patients were decannulated but still in the ICU at the time of this report. The patients had their first positive SARS-CoV-2 PCR test 12 $\pm$ 8 days before admission, and were already hospitalised for 9 $\pm$ 7 days. Fifteen patients received non-invasive ventilation for 6 $\pm$ 6 days, two high-flow nasal oxygen therapy, each for one day. They were intubated and received invasive mechanical ventilation for 4 $\pm$ 4 (0–18) days prior to ECMO initiation. Prone position was applied in 15 cases. The Lung Injury Score was 3,2 $\pm$ 0,3, the PaO2/FiO2 ratio was 71 $\pm$ 19 mmHg. A femoro-jugular configuration was applied in 17 cases and femoro-femoral configuration in 3 cases, 2 patients had 2 ECMO runs. During the 20 ECMO runs, 31 oxygenators were used. The duration of V-V ECMO support was 26 $\pm$ 20 days, and the longest run lasted 70 days. The patients were mechanically ventilated for 29 $\pm$ 21 days. ICU and hospital length of stay was 38 $\pm$ 27 (1–94) days and 42 $\pm$ 29 (1–97) days, respectively. 11 patients were successfully weaned from ECMO and decannulated. ICU survival was 56% (9/16), in-hospital survival was 50% (8/16) at the moment of the report. The most common complications were major bleeding (11 patients) and super-infections. All patients discharged from the hospital are in good physical and neurological condition.
Conclusion: At our department, during the last three waves of the COVID-19 pandemic similar results to that reported by the Extracorporeal Life Support Organisation COVID-19 Registry were achieved.

001330

Efficacy of thoracic fluid content by cardiometry in predicting weaning failure in icu- a prospective observational study

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Introduction: Weaning is an art of gradual liberalization from the ventilatory support after the resolution of primary illness. Thoracic fluid content measured by cardiometry has a promising role and can be used as an adjuvant non-invasive tool in predicting weaning failure.
Objectives: Primary objective: To evaluate the role of thoracic fluid content (TFC) during spontaneous breathing trial for prediction of weaning outcome.

Secondary objective: To analyse the correlation between TFC and extravascular lung water index (EVLWI). To analyse if the lung ultrasound score, echocardiographic parameters and NT Pro BNP measured before SBT either alone or in combination can predict weaning failure.
Methods: Study Design: A prospective observational study. Study Setting: Intensive Care Unit of All India Institute of Medical sciences, New Delhi. Study Population: Adult patients who were eligible for a spontaneous breathing trial after 48 h of mechanical ventilation.
Inclusion criteria
1. Patients on mechanical ventilator for more than 48 h.
2. All patients considered eligible for a SBT by the attending physician as per standard ICU protocol: FiO2 < 0.5, PEEP ≤ 5 cm H2O, PaO2 /FiO2 > 200, respiratory rate < 30 breaths per minute, alert and cooperative and hemodynamic stability in the absence of high doses of vasopressor therapy.

Exclusion criteria
1. Patients on short term mechanical ventilation for less than 48 h in the immediate postoperative period.
2. Patients aged < 18 years
3. Patients with spinal cord injury above T8 level
4. Presence of significant cardiac arrhythmia
5. Patients with diaphragmatic paralysis
6. Patients planned for prophylactic noninvasive ventilation after extubation.
7. Patients in whom a suitable ultrasonographic image could not be obtained for lung, diaphragm and cardiac measurements.

Results: Thoracic fluid content with a Cut off > 33 kohms-1 has an ability to predict weaning outcome with a sensitivity and specificity of 52.94% and 86.05% withAUROC:0.692(0.560 – 0.805).TFC has a high negative predictive value of 82.2% and a positive predictive value of 60%.There was a significant positive correlation between Pre SBT thoracic fluid content and Pre SBT EVLWI with correlation coefficient of 0.286.Similarly there was a statistically significant positive correlation between post SBT TFC and post SBT EVLWI, Post SBT TFC and post SBT PVPI with correlation coefficient of 0.567, 0.483 respectively.
Conclusion: Thoracic fluid content with a Cut off > 33 kohms -1has an ability to predict weaning failure. Higher TFC is strongly associated with weaning failure. TFC has a high negative predictive value therefore it can be used as screening tool for ruling out weaning induced pulmonary edema. There was a good correlation between TFC and EVLWI and hence it can be used as a surrogate for assessment of extravascular lung water.

001375

Contribution of SpO2 /FiO2 and PaO2 /FiO2 Ratios in Patients with COVID-19 Acute Respiratory Distress Syndrome

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Intensive Care Medicine Experimental 2022, **10(2)**:001375

Introduction: The diagnostic criteria for Acute Respiratory Distress Syndrome (ARDS) utilize the arterial partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FIO2) (P/F) ratio measured by arterial blood gas analysis to assess the degree of hypoxemia. the pulse oximetric saturation (SpO2)/FIO2 (S/F) ratio can be an effective, noninvasive surrogate for the P/F ratio in monitoring ARDS gravity.
Objectives: We aim to assess eventual correlation between S/F and P/F ratios to determine severity predictive abilities, among ARDS COVID-19 patients.
Methods: We conducted a retrospective descriptive study, including all critically ill COVID 19 patients meeting ARDS criteria, from September 2020 to December 2021. Were recorded P/F and S/F ratios, 1 h after implementation of mechanical ventilation. A scatterplot of S/F vs P/F ratios was utilized to determine the linear relationship between the two measurements. The equation for this regression line was employed to determine threshold values for S/F ratios correlating with several P/F ratios (300,200 and 100 defining mild, moderate and severe ARDS). This equation was: $S/F = 44.21 + 0.76*P/F$ ($p < 0.001$. S/F values were examined as a substitute of P/F ratio to assess the ARDS severity.
Results: Were included 172 patients. Gender ratio was 1.64. Mean SAPS II, APACH II and ISARIC 4C scores were, respectively, 24.6 ± 8.8, 7.9 ± 4.5 and 9.16 ± 3.3. The most frequent comorbidities were: obesity (50%) with a mean body mass index of 30.6 ± 8.2, diabetes (40.1%), hypertension (38.4%) and respiratory diseases (22.7%). Means of both S/F and P/F ratios were, respectively, 103.12 ± 64.4 and 123.85 ± 65. Ninety-six patients (55.8%) had needed orotracheal intubation. Mean length of hospital stay was 10 ± 6.6 days [1–40]. Global mortality was 59.3%. the P/F severity classifying ratios of 300, 200 and 100 corresponded respectively to S/F ratios of 272.21, 196.21 and 120.21. Concordance equation was able to identify severe ARDS (90% sensitivity and 75.9% specificity); moderate ARDS (49.2% sensitivity and 84% specificity) and mild ARDS (45% sensitivity and 90% specificity).
Conclusion: SF ratio is a reliable noninvasive surrogate for P/F ratio to identify patients with ARDS with the advantage of replacing invasive sampling by non-invasive pulse oximetry.

001406

Volume Support Ventilation Mode Versus Pressure Support Ventilation mode in Spontaneous Breathing Trial

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Intensive Care Medicine Experimental 2022, **10(2)**:001406

Introduction: Till date, the benefit of using dual control ventilation modes in spontaneous breathing trials has been conflictin(1), many trials were done to evaluate different modes for weaning yet most of them showed no benefit over traditional PSV mode(1) volume support Ventilation (VSV) is a pressure-limited mode that uses a target tidal volume and minute ventilation for feedback control. Thus, the level of pressure support is continuously adjusted to deliver the preset tidal volume.
Objectives: the purpose of this study was to compare the efficacy of pressure support ventilation mode(PSV) and volume support ventilation(VSV) mode as strategies for discontinuation of mechanical ventilation and extubation.
Methods: We performed a randomized trial and enrolled 50 patients in a general intensive care unit having readiness and eligibility criteria of SBT., all eligible patients were allocated into one of two groups in the SBT: conventional pressure support ventilation (PSV, 10 cmH2O) (25 patients), or VSV with target volume 6 ml /kg IBW(25 patients) for 2 h. Tolerance of the breathing trial served as a basis for the decision to wean the mechanical ventilation and remove the endotracheal tube. Extubation failure was considered if reintubation was necessary or if the patient required non-invasive ventilatory assistance (both within 48 h). Oxyegenation index and dyssynchrony index were also measured before, during and after the SBT trial in both groups.
Results: There were no differences between both groups in the baseline characteristics. There were also no differences in the pre SBT trial hemodynamic and respiratory measures between both groups. We did not observe any difference between both groups regarding the tolerance of the breathing trial and the success of weaning(17 in the PSV vs 16 in the VSV group p 0.76), the extubation failure(4 in the PSV group vs 2 in the VSV group P 0.66), and oxygenation index after the trial yet the patient ventialtor dyssyncrony index was lower in the VSV group compared to the PSV group.
Conclusion: Using VSV mode in SBT compared to PSV mode did not reduce the extubation failure nor improved the tolerability of the trial yet it improved the dyssynchrony index during the trial.

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001421

Timing of Prone Positioning during venovenous Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome

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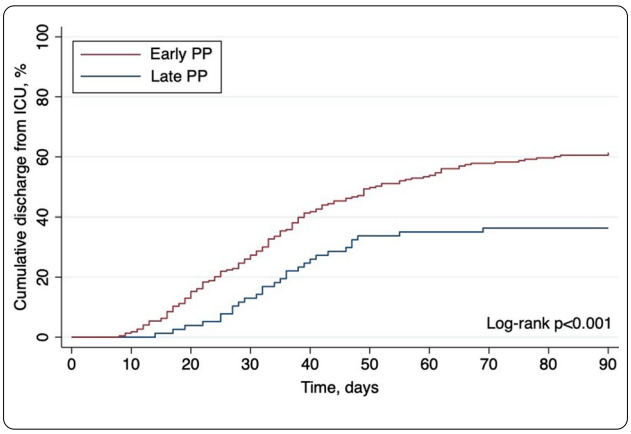
Introduction: Prone position reduces mortality in severe Acute Respiratory Distress Syndrome (ARDS) patients [1]. Previous studies showed that the use of prone positioning (PP) in patients with ARDS on venovenous extracorporeal membrane oxygenation (vv ECMO) improve respiratory mechanics and gas exchange [2] and might be associated with lower mortality [3,4]. The benefit of PP might reduce over time, as the lung may develop progressive organization and fibrosis [5]. We hypothesized that Early PP during extracorporeal support may be associated with a a greater improvement of the respiratory system compliance (Cpl,rs) and better outcomes compared with late PP.
Objectives: The aim of this study was to assess the association of timing to PP during vv ECMO and the probability of being discharged alive from the intensive care unit (ICU) at 90 days.
Methods: We analyzed individual data from five original studies which included patients who underwent prone positioning during ECMO. Patients who underwent PP $\geq$ 6 days after the ECMO start were included in the Late PP group. Adjusted COX-proportional models by using pre-defined covariates selected a priori [3] were used to explore the independent association of the time to PP with the probability of being discharged alive from the ICU at 90 days.
Results: 300 patients were included, 77 in the Late PP and 223 in the Early PP group. When time to PP was analyzed as a continuous variable, the longer the time to PP during vv ECMO, the lower the probability of being discharged alive from the ICU (adjusted HR 0.90 for each day increase—95% CI 0.87–0.93). PP was associated with improvement of Cpl,rs over time only in the Early PP group (4 $\pm$ 9 vs 0 $\pm$ 12 ml/cmH2O in the Late PP group, group-by-time interaction p = 0.04). The unadjusted cumulative 90-day probability of being discharged alive from the ICU was 60 vs 37% in the Early vs Late PP group (log-rank test, p < 0.001). The adjusted hazard ratio for being discharged alive from the ICU in the Early vs Late PP group was 2.60 (95% CI, 1.95–3.48, p-value < 0.001).



Conclusion: In a large cohort of ARDS patients receiving veno-venous extracorporeal support, Early PP during ECMO led to a greater improvement of the Cpl,rs over time whereas Late PP group did not. Furthermore, Early PP group was independently associated with a higher probability of being discharged alive from the ICU at 90 days.

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001432

Pseudo-Reverse triggering, a new asynchrony, associated with forced expiration during spontaneous breathing in Pressure support ventilation

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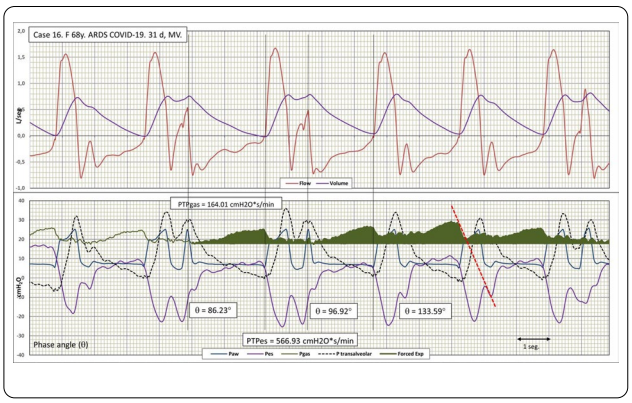
Introduction: Reverse triggering (RT) is a patient-ventilator asynchrony in which the respiratory center is activated in response to passive lung inflation, and attributed to reflex phenomena (1). We have observed a similar phenomenon during effort initiated by the patient associated with forced expiration, for which we adopted the term

"Pseudo-Reverse Triggering", which can be accompanied by double cycling (2). This interaction patient-ventilator can have consequences such as the development of P-SILI. To our knowledge, this case series represents the first description of this new form of patient-ventilator asynchrony.
Objectives: To describe the features of this asinchorony associated with forced expiration during spontaneous breathing modes.
Methods: Prospective observational study of all patients admitted at ICU (January to May 2020) mechanically ventilated more 72H, during spontaneous Pressure support mode. Apparent RT was inspected visually on monitoring of flow, airway pressure (Paw), esophageal (Pes) with available gastric or intra-vesical pressure (Pgas, iVP), and the physical examination evidenced forced expiration. The ethics committees approved the original clinical study, including in RT-PSV 2017. Demographic, and data clinical, were collected. Apparent RT was defined as a pattern in which an inspiratory effort of the patient occurred over a specific and repetitive phase of each ventilator cycle initiated by the patient. The characteristic of this patient-ventilator relationship was identified. Data Acquisition: Flow was measured with a Fleisch pneumotachograph, Paw, Pes, and Pgas (probe, Nutrivent Sidam®) were connected to differential pressure transducers (range ± 50 kPa). iVP by Edwards® TruWaveTM transducer. Sampling at 1045 Hz. The time of recording was 60 min. Physiological measurement: Phase angle, the effort of forced expiration (PTPgas), and effort in regular cycles (PTPes). The phase angle of delay of sequential effort. Data were analyzed by descriptive statistical methods.
Results: Of the 27 pts with force expiration, 8 cases (29%) showed apparent RT (Pseudo-RT); of which 5 (62.5%) were male, age 61 (57.75–61). Diagnosis: Lung transplantation 4 (50%), ARDS pneumonia 2 (25%), Abdominal surgery 1 (12.5%), Meningitis 1 (12.5%). Days on ventilator 7 (5–8). Phase angle 86.5º (77.75–100.89). Breath-Staking 66.66% of the cases. PTPgas 187.5 cmH2O*s/min (134.75–217.75). Sedation level: RASS -2–3. Figure 1: Representative case of Pseudo-Reverse triggering due to forced expiration.



Conclusion: Pseudo-reverse triggering is an asynchrony that can be generated by the release of forced expiration during modes of spontaneous ventilation. This phenomenon may be responsible for uncontrolled trans-alveolar pressure, especially in cycles with double cycling, with overdistention and stretching that favor P-SILI.

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001441

Obesity and its impact on COVID-19

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Introduction: Many observational studies have suggested that obesity confers an increased risk of morbidity–mortality in the general population and may compromise prognosis in critically ill patients.
Objectives: The aim of our study was to determine whether obesity is a risk factor for poor outcome in patients afected by COVID-19 admitted to ICU.
Methods: This study was performed at the hospital ICU, a 22-bed secondary ICU in Tunisia. It was a retrospective study enrolled between 1st March 2021 and 31st September 2021 in patients with confrmed RT-PCR Covid19. Body mass index (BMI) was used as indicator for obesity status. Simplifed Acute Physiology Score (SAPS II), Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, comorbidities, invasive mechanical ventilation requirement, ICU length of stay and mortality were evaluated. Patients were divided into two groups: G1: obese, BMI ≥ 30 kg/m2 and G2: non-obese, BMI < 30 kg/m2.
Results: During the study period, 323 patients with COVID-19 pneumonia were admitted. A total of 197 patients (61%) with BMI-defined obesity were included in G1, and 126 (39%) were assigned to G2. Median age was 59 [34–90] years in G1, and 53 [25–85] in G2.Demographic data and comorbidities (sex ratio, SAPS II, APACHE II, hypertension, diabetes, chronic respiratory failure) were similar between the 2 groups. There was significant difference between PaO2/FiO2 ratio at admission between group 1: 107 ± 36,6 mmHg and group 2: 102 ± 25 mmHg, p < 0.001. At admission, non-invasive mechanical ventilation was prescribed in 170 patients (86.2%) in group 1, and in 73 (59,3%) in G2 with p = 0.14. Obesity does not represent limiting factor for awake prone position: instead the obese patients were more adherent to the prone position in spontaneous ventilation (67,5 vs 65,4%; p = 0,426). No adverse efects as pressure ulcer were observed. Length of ICU stay was similar in two groups (11,2 ± 8.4 day [2–30] vs 10.3 ± 6.9 day [2–28]). No signifcant diferences were observed in need to invasive mechanical ventilation (58,5% vs 54,1%; p = 0.39) and mortality (58,3% vs 51.4%; p = 0.11).
Conclusion: Obesity conferred an increased risk for intensive care unit admission, but it did not seem to be associated with increased risk for need for invasive mechanical ventilation, or infuence ICU length of stay and/or mortality.

001449

Dramatic clinical worsening in Covid-19 patients before entering public health system. Comparison of vaccinated and not vaccinated patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001449

Introduction: In these Covid years beyond the shock of the initial months(1) we have improved progressively the management of covid pneumonia and our knowledge of the Sars Cov2 is totally different than the beginning of the pandemic (2). Now we know that covid infection is a systemic pathology and we can identify it only during the hospitalization such as thrombotic microangiopathy (3,4), but also after the hospital discharge from hospital(5) and postmortem with autopsy which had shown cerebral, hepatic, heart and kidney damage (6).
Objectives: We would describe the difference among vaccinated and not vaccinated(7) patients in pre-covid setting, during hospital and ICU admission and the mortality rate and we would evaluate if a longer stay at home could provoke not only a respiratory worsening but also a systemic failing.

Methods: This is a monocentric retrospective descriptive study. We admitted critically ill patients in emergency ward then in ICU with confirmed SARS-CoV-2 pneumonia. Patients were divided in two groups: not vaccinated (no vax) and vaccinated (vax). Who received at least two doses of the SARS-CoV-2 vaccine were included in the vax group. We analyzed for every patient: the time between the beginning of covid-19 symptoms and the admission in Hospital; the Charlson Comorbidity Index (CCI)(8); the CT severity score (CT-SS) (9) for the first CT during the admission in hospital and the Saps II in ICU (10). The time of study was from 1 November to 15 of January 2022. Categorical variables are presented as numbers and proportions and were compared using Pearson's $\chi 2$.
Results: 54 consecutive patients admitted in ICU during the time of study, 36 were not vaccinated (66,6) while 18 (33.3%) were vaccinated. Vax patients were older with 76 of median age, versus 60 for no vax (p0,004); went in Hospital after 4 days of symptoms, instead the no vaccinated after 7 days (p0,020); and they had a CCI of 5 versus 2 for no vax. The CT-SS was 10 for vax and 13 no vax group (p0,07). Saps II in ICU was 35 for no vax and 39,5 for vax group (p0,051); the mortality was 27,7% for vax and 38,8% for no vax patients (p 0,4).
Conclusion: Patients no vax during their "stay at home and wait" had a fast worsening such that when they were admitted in emergency department and the ICU, they had the severity scores and mortality like vax patients although older and with higher CCI. Patient no vax who died had a higher BUN compared survived. It could be an early marker of systemic worsening and it could help clinicians to start with intensive treatment instead to manage early only the respiratory system.

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Acknowledgements: I don't have any grant.

Cardiovascular Dynamics 1

000052

Fibrinolysis-Contraindicated Patients in the All-Comer FLASH Registry: Acute and Long-Term Outcomes of Mechanical Thrombectomy for Pulmonary Embolism

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Intensive Care Medicine Experimental 2022, **10(2)**:000052

Introduction: Fibrinolysis is contraindicated in patients with pulmonary embolism (PE) who present with risk factors for severe or potentially life-threatening bleeding events. Catheter-guided mechanical thrombectomy does not require the use of fibrinolytic agents and represents a promising interventional treatment option in this patient group. However, clinical data on its safety and effectiveness are lacking.
Objectives: This sub-analysis of the FLASH registry (NCT03761173) aimed to evaluate the safety and effectiveness of the FlowTriever System (Inari Medical, Irvine, CA) in PE patients with contraindications to fibrinolysis.
Methods: Up to 1,000 all-comer PE patients are being enrolled in FLASH and followed through 6 months post-treatment with the FlowTriever System. Baseline characteristics are collected, including relative and absolute contraindications to fibrinolysis as reported by the treating physicians according to ACCP guidelines. Patients are risk-stratified according to current ESC guidelines, and predefined acute and long-term outcomes are evaluated.
Results: The first 500 patients enrolled in FLASH included 205 (41.1%) with contraindications to fibrinolysis (absolute: 11.7%; relative: 88.3%). The most common relative contraindications were recent bleeding, surgery, or invasive procedure (33.7%) and age > 75 years (28.2%). In the lytic-contraindicated cohort, the median age was 67 [56–78] years, and 106 (51.7%) were women. Thirteen (6.3%) patients had high-risk PE and 192 (93.7%) had intermediate-risk PE, with 167 (81.5%) being intermediate-high-risk. Pre-thrombectomy hemodynamic measurements showed that 55 (26.8%) patients had a cardiac index (CI) < 2 L/min/m^2, indicating cardiogenic shock. Immediately after thrombectomy, mean PA pressure decreased from 32.0 ± 8.6 to 24.7 ± 8.4 mmHg (-22.5% for paired values, $P < 0.0001$), heart rate decreased from 100.9 ± 14.8 to 90.5 ± 15.7 bpm (-9.4% for paired values, $P < 0.0001$), and CI increased from 1.6 ± 0.3 to 2.0 ± 0.6 L/min/m^2 (20.4% for paired values, $P < 0.0001$) in those patients who had low CI at baseline. Post procedure, 115 (58.7%) patients did not require ICU admission overnight. There were no mortalities or device-related major adverse events (MAEs) at 48 h and no access site complications. Four (2.0%) episodes of major bleeding were recorded; one occurred in a patient who received adjunctive catheter-directed thrombolysis. Among patients with outcomes available, all-cause mortality was 1.6% at 30d and 6.7% at 6 m. The RV/LV ratio measured by echo decreased from 1.27 ± 0.51 at baseline to 0.76 ± 0.19 at 6 m. Improvements in median mMRC dyspnea (baseline: 3 [1–4], 48 h: 1 [0–2], 6 m: 0 [0–1]) and PEmb-QoL Frequency of Complaints (48: 13 [0–25], 6 m: 0 [0–9]) scores were observed.
Conclusion: Mechanical thrombectomy appears to improve acute hemodynamics and long-term functional outcomes in PE patients with contraindications to fibrinolysis. The low mortality and MAE rates suggest that thrombectomy is characterized by a good safety profile in this patient population.

Acknowledgements: The FLASH registry is funded by Inari Medical.

000065

Comparison of early postoperative outcomes after mitral valve surgery with and without concomitant tricuspid valve repair

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Introduction: Functional tricuspid valve (FTV) regurgitation secondary to mitral valve (MV) disease is a frequently occurring pathology and has been shown to have negative impact on survival and quality of life. Novel surgical practices in mitral valve replacement/repair include an option for concomitant tricuspid repair in specific cases. The aim of our study is to investigate early postoperative morbidity and mortality of the above practice in our Cardiothoracic Department.
Methods: From June 2012 to September 2021, a total of 187 elective cardiothoracic surgery patients underwent mitral valve replacement/repair due to MV regurgitation. A concomitant TV repair performed in 19 of them. Group B consists of those 19 patients, age 63.2 ± 10.9, Euro score II 3.6 ± 1.5, median CPB Time 114 s. Group A consists of patients undergoing isolated MV repair, age 68.3 ± 7.4, Euro score II 2.05 ± 4.1, median CPB Time 134 s. The following factors were compared between group A and group B: New onset atrial fibrillation (AF), Acute Kidney Injury(AKI- KDIGO criteria), Renal replacement therapy (RRT), prolonged ventilation (> 24 h), post op use of Intra-Aortic Balloon Pump (IABP), prolonged ICU stay (> 3 days) and mortality. Chi square test was used for statistical analysis.
Results: Results are shown in Table 1.
Table 1: Comparison of post-surgical outcomes for patients in Group A compared to those in Group B.

	Group A N = 158	Group B N = 19	P value
AF	37 (23.4%)	9 (47.4%)	**< 0.01**
AKI	37 (23.4%)	8 (42.1%)	**< 0.01**
RRT	4(2.5%)	1(5.3%)	0.4
Reintubation	5(3.2%)	0	0.4
Prolonged vent	11(7%)	2(10.5%)	0.5
IABP	4(2.5%)	2(10.5%)	0.07
Prolonged ICU stay	11(7%)	1(5.3%)	0.7
Mortality	7(4.4%)	3(15.8)	**0.04**

Conclusion: Concomitant TV repair in mitral valve surgery when compared with mitral valve replacement/repair alone, was associated with higher mortality, higher incidence of atrial fibrillation and high incidence of AKI, in our cohort of elective cardiothoracic surgery patients.

000078

Fingolimod does not prevent endothelial glycocalyx damage in injured cultured human umbilical vein endothelial cells

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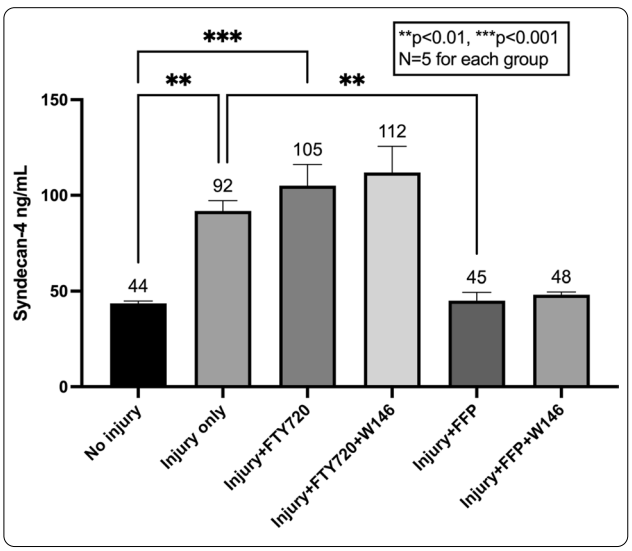
Intensive Care Medicine Experimental 2022, **10(2)**:000078

Introduction: Endothelial glycocalyx (EG) damage is associated with poor outcomes in critical illness. There are no EG specific therapies in clinical use. Fresh frozen plasma (FFP) restores the EG [1], but the mechanism is unknown, and it has multiple components, some of which appear to be detrimental [2]. Fingolimod (FTY720) is a sphingosine-1-phosphate receptor (S1PR) agonist used for the treatment of multiple sclerosis. It attenuates vascular hyperpermeability and organ dysfunction in animal models of critical illness [3]. While sphingosine-1-phosphate restores the EG in cell culture [4], the effect of FTY720 on the EG is unknown.
Objectives: The aim of this study was to test the hypothesis that FTY720 prevents EG damage in injured cultured human umbilical vein endothelial cells with similar efficacy to FFP.
Methods: Human umbilical vein endothelial cells were grown to confluence then maintained in media (uninjured) or media containing 1.0 nM adrenaline, 10 ng/mL TNF-α and 100 μM H2O2, for 4 h (injured). Cells were assigned to one of six groups: uninjured without treatment, injury without treatment, injury and 50 ng/mL FTY720 with and without 10 μM of the S1PR1 inhibitor W146, and injury and 25% FFP with and without 10 μM W146. The EG component syndecan-4 was measured in cell supernatants using enzyme-linked immunosorbent assay, and mRNA expression of syndecan-4 and thrombomodulin were quantitated in cell lysates using qPCR.
Results: Syndecan-4 concentration in the supernatant increased 2.1-fold with the injury protocol, consistent with EG damage (Figure). This was attenuated to baseline levels by FFP, but there was no treatment effect from FTY720. S1PR1 inhibition by W146 did not reverse the protective effect of FFP. Cell injury increased syndecan-4 mRNA and decreased thrombomodulin mRNA expression, and this was unaffected by treatment with FFP or FTY720.



Conclusion: The cell injury protocol stimulated EG shedding into the cell culture supernatant, and this was prevented by FFP via a mechanism that was independent of the sphingosine-1 phosphate receptor, S1PR1. FFP did not upregulate the expression of SDC-4 mRNA in the context of an injured EG, suggesting its beneficial effect on the EG is due to prevention of damage rather than repair. FTY720 did not prevent EG shedding, suggesting that S1PR is not a target for prevention of EG damage in this cell type. Further work is required to investigate the influence of timing of exposure, dose, injury stimulus, culture conditions, effect on different EG components, cell type, and different S1PR agonists.

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Acknowledgements: This study was funded by the Australian National Health and Medical Research Council Centre of Research Excellence Grant for Patient Blood Management in Critical Illness and Trauma.

000111

Comparison of door-to-balloon time between ST-elevation myocardial infarction and its equivalents

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Intensive Care Medicine Experimental 2022, **10(2)**:000111

Introduction: In patients with ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary interventions (pPCI), shorter door-to-balloon (D2B) time is considered to be a crucial factor for clinical outcomes. However, a number of patients with coronary occlusion present to the emergency department (ED) with atypical electrocardiographic (ECG) findings, known as STEMI-equivalents. These ECG findings may be more difficult to interpret, possibly causing a delay in cardiac catheterization laboratory activation and pPCI. We investigated whether patients presenting with STEMI-equivalent findings are associated with a longer D2B time compared to STEMI patients.
Methods: This is a retrospective chart study of patients who arrived at a regional emergency department of a teaching hospital in South Korea between January 2019 and October 2019. Patients who underwent emergent coronary angiography and pPCI by activating cardiac catheterization laboratory were enrolled. According to electrocardiographic findings, we divided patients into STEMI and STEMI-equivalent groups. We compared door-to-ECG (D2E) time, ECG-to-activation (E2A) time, activation-to-laboratory (A2L) time, laboratory-to-balloon (L2B) time and D2B time between the groups. Then, we analyzed whether STEMI-equivalent ECG is an independent predictor of delayed D2B time > 90 min.
Results: A total of 149 patients were included in the study. 18 (12.1%) patients presented with STEMI-equivalent ECG, which included 3 isolated posterior myocardial infarctions, 7 aVR ST-elevations with diffuse ST-depressions, 3 LBBBs with positive Sgarbossa criteria, and 5 new or presumably new onset RBBBs. Compared to the STEMI group, A2L time (58.0 [47.0–86.0] min vs. 49.0 [40.0–55.0] min, $p = 0.009$) and D2B time (88.0 [76.0–121.0] min vs. 79.0 [70.0–88.0] min, $p = 0.010$) were significantly delayed in the STEMI-equivalent group. After controlling possible confounding factors, STEMI-equivalent ECG was an independent predictor of D2B time > 90 min (Odds ratio 3.845, 95% confidence interval 1.094–13.518, $p = 0.036$).
Conclusion: A2L time, and therefore D2B time, were significantly delayed in patients presenting with STEMI-equivalent ECG. STEMI-equivalent ECG was an independent predictor of delayed D2B time > 90 min. Prompt recognition of STEMI-equivalent ECGs may help shorten the time between patient arrival and pPCI.

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000114

The impact of the COVID-19 pandemic on patients with cardio/cerebrovascular disease visiting the emergency department

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Intensive Care Medicine Experimental 2022, **10(2)**:000114

Introduction: The coronavirus (COVID-19) pandemic situation is a state that has a great impact on the medical system and society. In order to respond to a pandemic situation, various methods such as a pre-triage system are being operated in the emergency medical field. However, there are insufficient studies on the effects of this pandemic situation on patients visiting the emergency department (ED), especially those with cardio/cerebrovascular disease (CVD) classified as a time-dependent emergency.
Methods: We performed a retrospective analysis using a parallel comparison cohort from 2019 on patients from April 2020 to December 2020 after the pre-triage system was established. The primary outcome was in-hospital mortality. CVD was defined by final diagnosis.
Results: During the same period, the number of ED visitors decreased to 79.1% before COVID-19. Overall patient mortality increased and that of patients with cardiovascular disease also increased, while mortality from cerebrovascular disease did not increase. Meanwhile, the ED length of stay increased in all patients but did not increase in patients with cardiovascular disease.
Conclusion: As with prior studies conducted in other regions, in our study, the total number of ED visits decreased compared to before COVID-19. Overall mortality increased, particularly in cardiovascular disease.

000265

A Retrospective Single-centre Observational Study Looking At The Extent Of Liver Dysfunction Post-Cardiac Surgery

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Introduction: Liver dysfunction and injury is a relatively rare but recognised complication after cardiac surgery [1]. This study aimed to investigate the incidence of liver dysfunction in patients undergoing cardiac surgery, using pre-existing scoring systems.
Methods: This was a single-centre observational retrospective study. All adult patients (above 18 years old) undergoing all types of cardiac surgery between April 2017 and December 2019 were included. To grade liver dysfunction the pre-existing risk scores Child-Turcotte-Pugh (CTP) and Modified End-Stage Liver Dysfunction (MELD) scores were calculated from routine blood tests taken. From analysis, a MELD > 10 was used as a definition of significant liver dysfunction. From there a number of analyses were conducted including univariate and multivariate regression analyses. A backward stepwise Likelihood Ratio Logistic Regression analysis was used to identify the most

significant variables associated with Meld Scores > 10. In-hospital mortality was studied as an outcome, as was Kaplan–Meier Survival curves. The area under the Receiver Operating Characteristic curve was generated in all models as predictors of in-hospital mortality.
Results: 2275 patients were identified within the study period. 215 patients had to be removed due to insufficient investigations to calculate either a pre- or post-operative MELD score, leaving a total study group of 2060. 1644 patients (79.8%) had a MELD score > 10, with 416 patients (20.2%) having a MELD score of > 10. The median age of patients with a MELD score < 10 was 67 vs 69 for patients with a MELD score > 10, p < 0.001. 1226 patients (74.6%) in the MELD < 10 group were male, with 330 patients (79.3%) being male in the group with a MELD > 10 (OR = 1.31, p = 0.044). 57 patients (2.8%) died during the study period, 48 of these patients had a MELD score > 10 (OR = 23.7, p < 0.001). A MELD score > 10 was associated with a greater median stay in intensive care (2.78 vs 1.08, p < 0.001), and a longer post-operative stay (10 days vs 6 days, p < 0.001). Coronary artery bypass grafting (CABG) was the most common surgery (1441, 70.0%), followed by valve surgery (776, 37.7%) and aortic surgery (194, 9.4%). Valve surgery was most associated with a MELD > 10 (OR = 2.31, p < 0.001) especially multiple valve surgeries (OR = 4.37, p < 0.001), higher than both aortic surgery (OR = 2.29, p < 0.01) and CABG surgery (OR = 0.45, p < 0.001). Surgeries that required cardiopulmonary bypass (C PB) were associated with MELD > 10 (OR = 1.52, p < 0.051). There was also a greater median bypass time (123 vs 98 min, p < 0.001) and median cross-clamp time (89 vs 70 min, p < 0.001) in the group with a MELD > 10. MELD scores and ICNARC scores were the best at predicting mortality (AUC 0.88 and 0.92 respectively, p < 0.001). From the multivariate regression analysis Endocarditis (OR = 4.37, p < 0.013), emergency surgery (OR = 4.27, p < 0.001) and use of an intra-aortic balloon pump (OR = 3.55, p < 0.024), were most associated with a post-operative MELD score > 10. Kaplan–Meier survival curve analysis demonstrated a MELD score > 10 is associated with reduced survival over time.
Conclusion: MELD is a useful score for grading liver dysfunction in patients after cardiac surgery. A MELD score > 10 is predictive of significant liver dysfunction in patients undergoing cardiac surgery and is associated with increased length of stay and increased mortality post-cardiac surgery. MELD has the potential to be used to risk stratify patients pre- and post-cardiac surgery.

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Acknowledgements: Not applicable.

000276

Mechanical complications after central venous catheterisation in the ultrasound-guided era: a prospective cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:000276

Introduction: To the best of our knowledge, no large prospective systematic multicentre studies on risk factors for mechanical complications after central venous catheterization have been published after the widespread introduction of US guidance.
Objectives: To determine the incidence of mechanical complications and to identify associated independent risk factors in a healthcare system where real-time ultrasound guidance is clinical practice for central venous access.
Methods: All central venous catheter insertions in patients ≥ 16 years at four emergency care hospitals between 2 March 2019 and 31 Dec 2020 were eligible for inclusion. During the study period, dedicated collaborators at each study site continuously reviewed the insertion records and chest X-rays. The primary outcome measures were mechanical complications that occurred within 24 h after catheterisation. Multivariable logistic regression analysis was used to determine associations between independent variables and major mechanical complications defined as pneumothorax, arterial catheterisation, major bleeding, serious cardiac arrhythmia and persisting nerve injury. The study was registered at clinicaltrials.gov (NCT03782324) and the study protocol was published in September 2019.[1].
Results: In total, 12 667 central venous catheter insertions were prospectively included. The incidence of mechanical complications was 7.7% (95% exact binomial confidence interval [CI] 7.3 – 8.2), out of which 0.4% (95% CI 0.3 – 0.5) were major mechanical complications. Patient BMI < 20 kg/m2 (OR 2.63 [95% CI 1.20 – 5.32]), male operator sex (OR 2.65 [95% CI 1.36 – 5.57]), limited operator experience (OR 3.12 [95% CI 1.71 – 5.60]) and number of skin punctures (OR 2.11 [95% CI 1.58 – 2.72]) were associated with a higher risk for major mechanical complications (Table 1).
Table 1. Multivariable logistic regression analysis for major mechanical complication

	Major mechanical complication1		
Independent variables	***Odds Ratios***	***95% CI***	***p***
Patient BMI < 202	2.63	1.20–5.32	**0.010**
Patient BMI [3]302	0.77	0.34–1.57	0.488
Positive pressure ventilation	0.75	0.41–1.35	0.330
Male operator sex	2.65	1.36–5.57	**0.007**
Limited operator experience [< 100]3	3.12	1.71–5.60	**< 0.001**
No. of skin punctures	2.11	1.58–2.72	**< 0.001**
Observations	10 634		

1 Pneumothorax, arterial catheterisation, bleeding requiring blood transfusion, invasive intervention or with life-threatening consequences, cardiac arrhythmia requiring urgent medical intervention, or nerve injury with clinical symptoms persisting > 72 h.
2 Compared to patients with BMI 20–30 kg/m2.
3 Compared to operators that had performed [3]100 CVC insertions at the beginning of the study period.
Conclusion: In a healthcare system where ultrasound guidance is clinical practice for central venous access, the incidence of major mechanical complications was found to be low. Patient BMI < 20 kg/m2, male operator sex, limited operator experience, and more than one skin puncture were identified as independent risk factors of major mechanical complications.

000307

Feasibility of continuous non-invasive finger blood pressure monitoring in adult patients admitted to the intensive care unit: a PHYSIC substudy

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Intensive Care Medicine Experimental 2022, **10(2)**:000307

Introduction: Hypotension in intensive care unit (ICU) admitted patients is common and associated with adverse events [1–5]. Continuous blood pressure (BP) monitoring is therefore applied in most ICUs to ensure timely treatment of hypotensive events. Non-invasive continuous blood pressure (cNIBP) methods using finger cuffs are

precise and reliable [6–9], but failure to obtain an adequate cNIBP signal is described in up to 12% of ICU patients [6]. Clinical predictors of an inadequate cNIBP signal are scarce, leaving the clinician with limited tools to identify patients suitable for cNIBP monitoring in the ICU.
Objectives: Our primary objective was to identify the percentage of patients admitted to the ICU with an inadequate cNIBP signal. In addition, we aimed to identify patient characteristics available at admission associated with a decreased cNIBP signal quality.
Methods: Data from a single center prospective observational study of 499 adult ICU patients were used for the analysis (PHYSIC study, Trial NL7150). Reasons for failure to obtain cNIBP data were annotated by a researcher if applicable. When available, the signal quality of the first hour of cNIBP measurement was determined using an open source BP waveform signal quality index (SQI) [10]. Patients with failed cNIBP monitoring due to an inadequate cNIBP signal were assigned the lowest possible SQI score. The explanatory power of individual patient characteristics expressed in R-Squared (R^2) was determined through univariate linear regression. Multivariable linear regression was used to determine the adjusted multiple R^2 in SQI score based on a combination of patient characteristics.
Results: Among the 499 eligible patients, at least one hour of cNIBP data was available in 392 (79%) patients and an inadequate cNIBP signal was observed in 26 (5%) patients. The remaining 81 (16%) patients were excluded from analysis due to missing cNIBP data unrelated to signal quality (e.g. patient refusal). The five characteristics with largest R^2 for signal quality were ICU admission diagnosis (4.8%), lactate (4.6%), history of diabetes mellitus (DM) (2.4%), norepinephrine dosage (1.9%), and heart rate (1.8%). Multivariable linear regression of SQI score using age, mean arterial pressure, heart rate, patient temperature, hemoglobin, lactate, history of chronic kidney disease, DM, and myocardial injury had an adjusted R^2 value of 0.11, meaning 11% of the variance in SQI was explained by the linear relation between SQI and included variables.
Conclusion: Overall cNIBP monitoring is feasible in the majority of adult patients admitted to the general ICU. Although several patient characteristics were associated with a decreased cNIBP signal quality, most of the variation in cNIBP signal quality remained unexplained. Identifying ICU patients suitable for cNIBP monitoring therefore remains challenging. Variables associated with a decreased finger perfusion, such as finger skin temperature, might be of interest for future research.

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Acknowledgements: Unrestricted grant by Edwards Lifesciences LLC, One Edwards Way, Irvine, CA 92,614 USA.

000324

Low mixed venous oxygen saturations during the first hours after ICU admission are associated with 1-year mortality after cardiac surgery – a single-center retrospective study

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Intensive Care Medicine Experimental 2022, **10(2)**:000324

Introduction: Goal directed therapy with mixed venous oxygen saturation (SvO2) values has been shown to improve outcome after cardiac surgery (1). SvO2 sampling requires the insertion of a pulmonary artery catheter (PAC). Although the use of PAC has been linked with rare but serious complications, a Cochrane review suggested that the use of PAC is not associated with increased mortality (2). Recent evidence even suggests that patients in cardiogenic shock have lower short-term mortality when monitored with PAC (3). It is not clear, however, which level of SvO2 should be targeted postoperatively after cardiac surgery (1,4,5).
Objectives: To assess whether postoperative SvO2 values obtained with PAC at ICU admission and 4 h after admission are associated with 1-year mortality in cardiac surgical patients.
Methods: 6282 patients underwent cardiac surgery in Oulu University Hospital, Finland, during the years 2007–20. All patients were monitored with a PAC. SvO2 values were obtained at ICU admission and 4 h after admission. The patients were divided into four groups: *Group A:* SvO2 > 60% at ICU admission and 4 h after admission; *Group B:* SvO2 > 60% at ICU admission but < 60% 4 h after admission; *Group C:* SvO2 < 60% at ICU admission but > 60% 4 h after admission; *Group D:* SvO2 < 60% at ICU admission and 4 h after admission. Cox regression model and Kaplan–Meier survival curves were used to assess 1-year mortality between the groups. Cox regression model was adjusted with gender and APACHE II and SOFA scores at ICU admission. We give hazard ratios with 95% CIs with the Cox model. Data are presented as % and medians with 25th-75th percentiles.
Results: 74.4% of the 6282 patients were male. The median age was 68 years (60–74). 1-year crude mortality of the whole cohort was 4.3%. 52.9% underwent coronary artery bypass grafting (CABG), 29.1% valvular surgery, 12.1% combined CABG and valvular procedures, 3.5% surgery of the ascending aorta and 2.4% other cardiac surgery. 7.2% of the procedures were classified as emergency or salvage. Apache II score was 14 (11–17) and SOFA score was 6 (5–7) at ICU admission. Cox regression hazard ratios for 1-year mortality are shown in Table 1 and Kaplan–Meier analysis in Figure 1. The highest hazard ratio was observed in patients with SvO2 < 60% at ICU admission and 4 h after admission.
Table 1. Hazard ratios for 1-year mortality. Both crude and adjusted values are shown.

	Hazard ratio, crude	P-value	Hazard ratio, adjusted	P-value
Group A	1	< 0.001	1	< 0.001
Group B	1.69 [1.17–2.42]	0.005	1.46 [1.01–2.1]	0.043
Group C	2.66 [1.8–3.93]	< 0.001	2.05 [1.38–3.04]	< 0.001
Group D	4.18 [3.1–5.65]	< 0.001	2.98 [2.18–4.06]	< 0.001

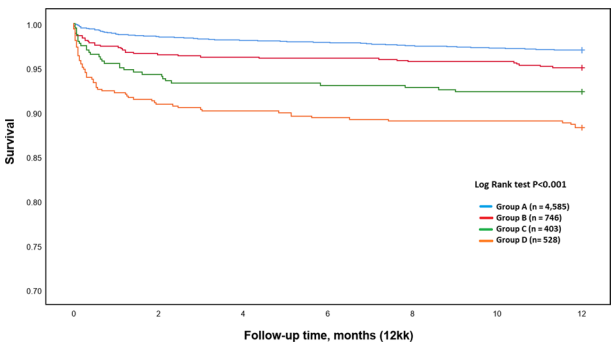

Figure 1. Kaplan–Meier survival curves.

Conclusion: Lower SvO2 values at ICU admission or 4 h after admission are associated with increased 1-year mortality after cardiac surgery. Goal-directed therapy protocols targeting SvO2 > 60% may be beneficial. Prospective studies are needed to confirm these findings.

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000371

Effect of dexmedetomidine on new onset atrial fibrillation in critically ill patients

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Introduction: New-onset atrial fibrillation (NOAF) is the most frequent arrythmia reported in intensive care units. Dexmedetomidine (DEX) is widely used sedatives which has unique mechanisms that might reduce NOAF occurrence. In this study, we tested hypotheses that the incidence of NOAF is lower in critically ill patients given DEX.

Methods: This is a retrospective observational study using Medical Information Mart for Intensive Care (MIMIC) IV database. Patients were divided into two groups according to DEX usage (DEX vs non-DEX). Propensity score matching was conducted to adjust confounders between the groups. The primary outcome was NOAF, defined as newly developed atrial fibrillation within 7 days of ICU admission. Results were externally retrospectively validated with 5,025 cases from Seoul National University Bundang Hospital dataset.
Results: Of the 17,992 patients in the MIMIC IV dataset (3,057 for DEX and 14,935 for non-DEX), a total of 8,881 patients (propensity-score matches 3,050 for DEX and 5,831 for non-DEX) were included after propensity score matching (mean age 60.4 ± 16.8 years, 64.4% male). Compared to non-DEX, the incidence of NOAF was significantly lower in DEX (14.0% vs 19.5%, p < 0.001, Figure 1). Ventilator duration, ICU and hospital length of stay were significantly longer in DEX (3.0 ± 2.2 days vs 2.6 ± 2.2 days, p < 0.001; 7.2 ± 5.3 vs 5.6 ± 4.6 days, p < 0.001; 15.3 ± 12.2 days vs 12.8 ± 13.6 days, p < 0.001, respectively, Table 1). However, in-hospital mortality was significantly lower in DEX compared to non-DEX (8.6% vs 15.7%, p < 0.001, Figure 2). Significant additive interaction between DEX and NOAF on in-hospital mortality was detected. The estimates of the relative excess risk due to interaction was 0.76 (95% confidence interval, 0.21–1.30). We also observed a lower incidence of NOAF in DEX compared to non-DEX in our external validation cohort (11.4% vs 25.5%, p < 0.001).

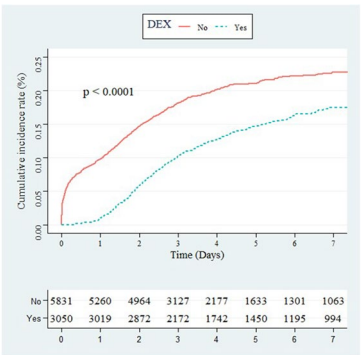

Figure 1. Kaplan-Meier curves for new onset atrial fibrillation occurrence according to dexmedetomidine usage

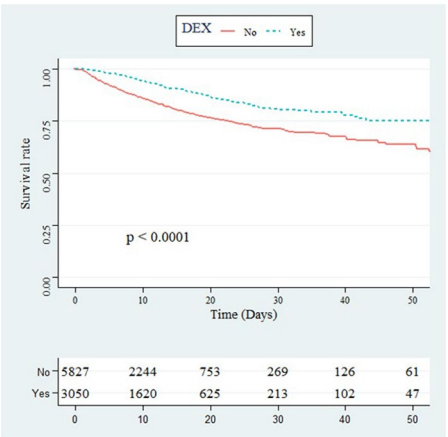

Figure 2. Kaplan-Meier curves for in-hospital mortality according to dexmedetomidine usage

Table 1. Clinical outcomes according to dexmedetomidine usage

Variable	Overall (n=8,881)	Non-DEX (n=5,831)	DEX (n=3,050)	*P* value[2]	*HR (95% CI)*
New onset Atrial Fibrillation, (%)	1,536 (17.6)	1,136 (19.5)	427 (14.0)	<0.001	0.62 (0.55-0.69)
Time to development of a trial fibrillation, days	1.6 ± 1.5	1.3 ± 1.3	2.6 ± 1.5	<0.001	
Ventilator duration, days	2.7 ± 2.2	3.0 ± 2.2	2.6 ± 2.2	<0.001	
Length of Stay, days					
ICU LOS	6.2 ± 4.9	7.2 ± 5.3	5.6 ± 4.6	<0.001	
Hospital LOS	13.7 ± 13.2	15.3 ± 12.2	12.8 ± 13.6	<0.001	
Mortality, (%)					
In-hospital mortality	1,183 (13.2)	922 (15.7)	261 (8.6)	<0.001	0.47 (0.41-0.53)
90 days mortality	1,268 (14.2)	981 (16.7)	287 (9.4)	<0.001	

Conclusion: In critically ill patients, dexmedetomidine was associated with a significant reduced risk of NOAF.

Cardiovascular Dynamics 2

000383

Cardiogenic Shock: Incidence, Aetiology, Management & Outcomes in a Tertiary Intensive Care Unit

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Introduction: Cardiogenic shock (CS) is a syndrome of primary cardiac dysfunction resulting in inadequate cardiac output, and a life-threatening state of tissue hypoperfusion, which can often lead to multiorgan failure and death if not treated in a timely and adequate fashion(1). Mortality remains high at more than 40%(2), but despite this CS has not received the same medical attention as other shock states such as sepsis. Beyond the acute myocardial infarction (AMI) subgroup, a limited evidence base has resulted in heterogenous approaches to management, including the timing, choice and institution of mechanical circulatory support (MCS), with variable impact.
Objectives: To describe the incidence, aetiology, management, and outcomes of patients with CS in a large tertiary ICU, to better guide resources, and advise and improve future management strategies.
Methods: We conducted a single centre retrospective review and service evaluation of consecutive ICU patients admitted with, or who subsequently developed, CS from February 2019 to October 2021. All patients were evaluated using the electronic health records. CS was defined using the IABP Shock II Trial(3) criteria. Demographics, aetiology, management, modes of MCS, and outcomes were analysed.
Results: Of the 8345 ICU admissions during this time, 315 (3.8%) patients diagnosed with CS were identified. Following application of the IABP Shock II Trial(3) definition of CS, and exclusion of duplicate entries, 249 records were included for final analysis. Incidence of CS in ICU was 3%. Median age was 65 years (IQR 54–74), 172 (69%) were male, and median ICU admission SOFA score was 15 (IQR 13–17). Overall ICU mortality was 44%. Of all patients presenting with CS 119 (48%) had suffered a cardiac arrest (CA) either prior to or during their admission; 45 (38%) were in hospital (IHCA) and 74 (62%) were out of hospital (OOHCA). AMI was the leading cause of CS, accounting for 129/249 (52%) of the cases. Other causes of CS included 20 cases of cardiomyopathy (8%), 20 post cardiotomy (8%), 18 cases of arrhythmias (7%), 8 cases of myocarditis (3.2%), 6 pulmonary embolism (2.4%), 5 valvular causes (2%) and 29 other causes (12%).
CS developed as a result of acute left ventricular failure in 141 (57%), acute right heart failure in 18 (7%), and acute biventricular failure (BVF) in 90 (36%) cases respectively. Mechanical circulatory support was used in 97 (39%) patients (60 IABP, 12 Impella and 25 V-A ECMO). All 8 patients with myocarditis survived to ICU discharge. Cardiac tamponade, cardiomyopathy, post cardiotomy and arrhythmias had an ICU mortality of 29%, 30%, 30%, 33% respectively. Other causes of CS were associated with higher ICU mortality including valvular causes (40%), AMI (47%), PE (50%) and other causes (72%). ICU mortality was 42% in those managed with MCS compared to 41% with medical management alone.
Conclusion: Cardiogenic shock is an important cause of morbidity and mortality in ICU. Overall mortality was high at 44% in keeping with international outcomes. AMI was responsible for the majority of cases. Myocarditis was associated with the best outcomes with 100% survival in this cohort. Mortality rates were similar in patients managed with MCS compared to medical therapy alone. More research is still required into developing optimal management strategies in order to improve outcomes in cardiogenic shock.

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000470

Phenotypic Heterogeneity of Fulminant COVID-19-Related Myocarditis in Adults

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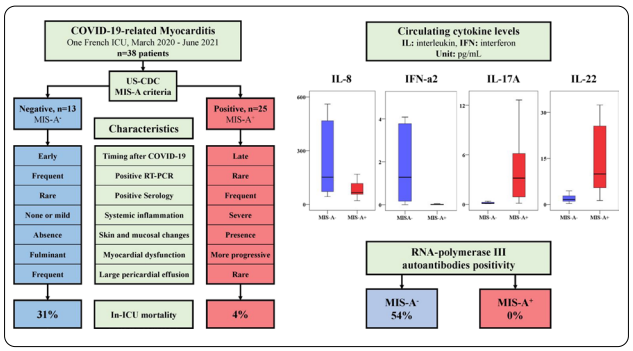
Introduction: Adults who have been infected with SARS-CoV-2 can develop a multisystem inflammatory syndrome (MIS-A), including fulminant myocarditis(1–3). Yet, several patients fail to meet MIS-A criteria, suggesting the existence of distinct phenotypes in fulminant COVID-19-related myocarditis.
Objectives: To compare the characteristics and clinical outcome between patients with fulminant COVID-19-related myocarditis fulfilling MIS-A criteria (MIS-A+) or not (MIS-A−).
Methods: A monocentric retrospective analysis of consecutive fulminant COVID-19-related myocarditis in a 26-bed ICU.
Results: Between March 2020 and June 2021, 38 patients required ICU admission (male: 66%; mean age: 32 ± 15 years) for suspected fulminant COVID-19-related myocarditis. In-ICU treatment for organ failures included dobutamine 79%, norepinephrine 60%, mechanical ventilation 50%, VA-ECMO 42% and renal replacement therapy 29%. In-hospital mortality was 13%. Twenty-five (66%) patients met the MIS-A criteria. MIS-A- compared to MIS-A + patients were characterized by a shorter delay between COVID-19 symptoms onset and myocarditis, a lower left ventricle ejection fraction, a higher rate of in-ICU organ failure, and were more likely to require mechanical circulatory support with VA-ECMO (92% versus 16%, $p < 0.0001$). In-hospital mortality was higher in MIS-A- patients (31% vs. 4%). Cytokine profiling

highlighted the presence of two distinct cytokine production profiles (**Central illustration**): MIS-A + had higher IL-22 (9.93 vs. 1.5 pg/mL, p < 0.0001), IL-17 (3.2 vs. 0.15 pg/mL, p < 0.0001) and TNF-a (21.1 vs. 8.0 pg/mL, p = 0.05) levels, as compared to MIS-A- patients, while the latter had higher IFN- a2 (2.4 vs. 0.013 pg/mL, p = 0.001) and IL-8 (158.7 vs. 65.7 pg/mL, p = 0.02), respectively. Moreover, RNA-polymerase III autoantibodies were found in seven (54%) MIS-A- patients, five of them being female. Finally, to elucidate the relative importance of the various bio-clinical parameters listed above with the clinical profile of MIS-A + or MIS-A- patients, we performed non-supervised PCA using study parameters contributing, in a statistically significant manner, to inter-patient variation. The results from PCA underlined important overall differences between MIS-A + and MIS-A- patients. The data also further highlight parameters most contributing to either clinical status *i.e.*: fibrinogen (p < 0.0001), CRP (p < 0.0001), IL-17 (p < 0.0001), IL-22 (p < 0.0001), IFN-a2 (p = 0.001) levels, SARS-CoV-2 serology (p < 0.0001) and SARS-CoV-2 RT-PCR (p < 0.0001), LVEF (p = 0.01) values on admission and the presence of RNA polymerase III autoantibodies (p = 0.001).



Conclusion: MIS-A+ and MIS-A− fulminant COVID-19-related myocarditis patients have 2 distinct phenotypes with different clinical presentations, prognosis and immunological profiles. Differentiating these 2 phenotypes is relevant for patients' management and further understanding of their pathophysiology.

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Acknowledgements: This study was supported by the Fondation de France, "Tous unis contre le virus" framework Alliance (Fondation de France, AP-HP, Institut Pasteur) in collaboration with Agence Nationale de la Recherche (ANR Flash COVID19 program), by the SARS-CoV-2 Program of the Faculty of Medicine from Sorbonne University ICOViD programs, by the Programme Hospitalier de Recherche Clinique PHRC-20-0375 COVID-19 (PI: G.G.). MPdC was supported for this study by a grant from: la Société Française Nationale de Médecine Interne (SNFMI-2021).

000551

Portal pulsatility index and renal venous impedance index predict congestion and its response to diuretic volume depletion

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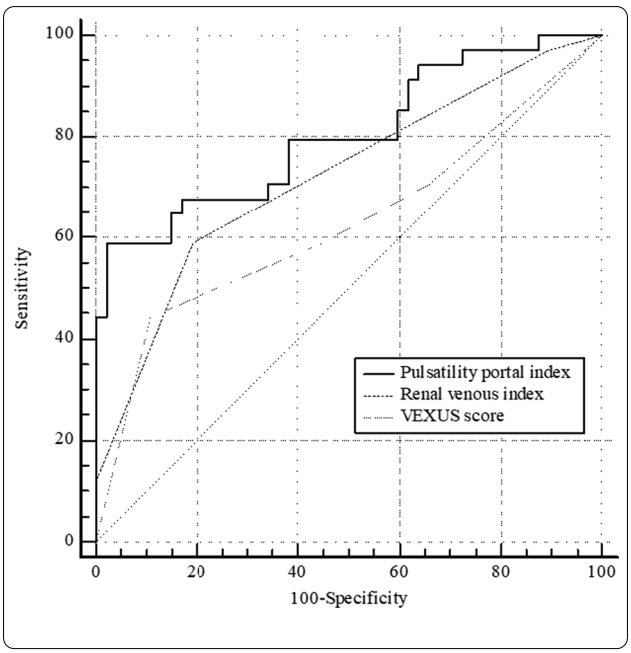
Intensive Care Medicine Experimental 2022, **10(2)**:000551

Introduction: Fluid overload and venous congestion are associated with morbi-mortality in the intensive care unit (ICU). The administration of diuretics to correct the fluid balance is common, although there is no strong relationship between the consequent fluid loss and clinical improvement. The use of natriuretic response to diuretic dose test to predict an appropriate decongestion was suggested, but this approach is limited by the patients' variability. There is a need for the validation of reproducible parameters of venous congestion in ICU. The promising portal pulsatility index (PI), the renal venous impedance index (VII), and the VEXUS score are some potential tools.
Objectives: The study aimed to evaluate the ability of portal PI and renal VII to predict congestion and diuretic response in ICU.
Methods: Prospective, observational, single-centre study. University-affiliated medico-surgical cardiovascular intensive care unit. Eighty-one adult patients for whom the clinician decided to introduce loop diuretic treatment. Hemodynamic and ultrasound measurements were performed at inclusion and two hours after the initiation of the diuretics. The patients' characteristics were noted at inclusion, 24 h later, and at ICU discharge. Venous congestion diagnosis was based on a clinical score > 3. The primary endpoint was a positive response to volume depletion defined by the normalization of the congestion score at ICU discharge.
Results: 43/81(53%) patients had clinically significant congestion at inclusion with a median congestion score of 4 (4–5). Clinically congestive patients with clinical congestion had a higher baseline portal PI (37% (26–58) vs 27% (20 vs 37), p = 0.004) and renal VII (0.29 (0.05–0.41) vs -0.3 (-0.33–0.33), p = 0.001). The baseline portal PI was the best predictor of two-hour clinical congestion improvement (AUC = 0.80, CI95%:0.70 to 0.92, p = 0.001), followed by renal VII (AUC = 0.72, CI95%:0.61 to 0.84, p = 0.001). Both parameters were able to predict further congestion improvement.



Conclusion: The portal PI and renal VII were predictive for appropriate response to volume depletion in congestive patients. The portal PI should be considered in future studies.

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Acknowledgements
1. Suzanne Rankin for proofreading and reviewing the English manuscript
2. Departement of anaesthesiology and critical care (Dijon university hospital)

000561

Hemodynamic monitoring and partial pressure of venous to arterial carbon dioxide gradient in early resuscitation of severe burn patients

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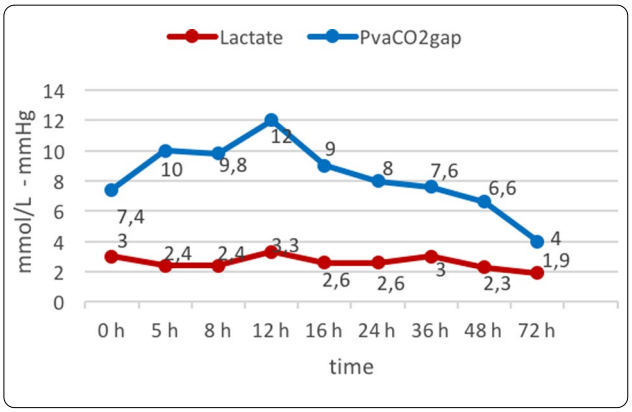
Intensive Care Medicine Experimental 2022, **10(2)**:000561

Introduction: Partial pressure of venous to arterial carbon dioxide gradient (Pv-aCO2 gap) and lactate levels have been considered as markers of tissue hypoperfusion, helpful to guide resuscitation in the treatment of shock. A relation between hemodynamic and these parameters has been stablished in different groups of patients with hemodynamic shock but severe burn patients.
Objectives: The aim of this study is to analyse the relation between hemodynamic parameters and analytic indicators of hypoperfusion such as Pv-aCO2 gap and lactate levels during early resuscitation in severely burn patients.
Methods: We did a prospective observational in patients admitted to Burn Intensive Care Unit from june 2018 to may 2021 with more than 30% of total body surface area (TBSA) burned. Pv-aCO2, lactate levels and hemodynamic measurements were performed during the period of admission and at least for 72 h during the initial resuscitation. We considered statistical significance with $p < 0.05$ and used Spearman's test, simple regression and ROC curves.
Results: In the study period a number of 27 patients were recruited, 23 of whom (83.2%) were men and 4 (14.8%) women. Mean age was 51 ± 16 years and TBSA $41.81 \pm 18\%$. Main burning mechanism was flame (85%). Pv-aCO2 gap correlated scarcely with lactate levels ($r = 0.203$, $p = 0.001$), maintaining high levels during the observation period and reaching its maximum at hour 12 ± 10 mmHg, same time of highest lactate (3.3 ± 3 mmol/l). In addition, at hour 12 we observe the worst hemodynamic situation with the lowest cardiac index (2.2 ± 0.8 l/min/m2). ROC curve analysis, in order to predict low cardiac index (< 2.2 l/min/m2) from Pv-aCO2 gap, determined an AUC = 0.7 with S = 0.7 and E = 0.73 in levels of Pv-aCO2 gap above 8.5 mmol/l. In curve ROC analysis using lactate levels to determine low cardiac index (< 2.2 l/min/m2), we had an AUC = 0.76 with S = 0.66 and E = 0.72 with lactate levels higher than 2.5 mmol/l.



Conclusion: Tissue hypoperfusion of severely burn patients may be evaluated indistinctly with lactate levels or Pv-aCO2 gap higher than 2.5 mmol/l and 8.5 mmHg respectively, being both good indicators of hemodynamic situation because of its relation to low cardiac index (< 2.2 l/min/m2) in early resuscitation.

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Acknowledgements: To all the health team that work daily at the Burn Intensive Care Unit in Hospital La Paz and made possible this study.

000570

Sedation using remimazolam does not reduce the duration of mechanical ventilation after elective cardiovascular surgery

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Intensive Care Medicine Experimental 2022, **10(2)**:000570

Introduction: Remimazolam has no metabolite activity [1], can be antagonized by flumazenil, and is less likely than propofol to cause hypotension [2]. At our institution, remimazolam or propofol is the primary sedative used during ventilation after cardiac surgery. It has not been known whether or not use of remimazolam for sedation after cardiovascular surgery affects the time to extubation or the need for vasoactive agents.
Objectives: Aim of this study is to clarify whether there is a difference in the duration of mechanical ventilation after elective cardiovascular surgery according to whether or not remimazolam is used for postoperative sedation.
Methods: This single-center study was approved by our institutional clinical research ethics committee. The need for written informed consent was waived in view of the retrospective observational nature of the research. All patients who received mechanical ventilation after elective cardiovascular surgery at our institution between August 2020 and February 2022 were enrolled. All patients received continuous sedation from the end of surgery until extubation. The timing of extubation was at the discretion of the intensivist without any specific protocol. The patients were divided into two groups according to whether remimazolam was administered (REM group) or not administered (non-REM group) in the intensive care unit (ICU). The primary study outcome was the duration of mechanical ventilation. Secondary outcomes were the extubation success rate, length of stay in the ICU, use of vasoactive agents, and the in-hospital mortality rate. A p-value < 0.05 was considered statistically significant.
Results: In total, 221 patients were included in the study. Remimazolam had been administered in 53 patients (at a mean [$\pm$standard deviation] initial dose of 0.27 ± 0.14 mg/kg/h) and not in the remaining 168 patients. The mean duration of mechanical ventilation was 8.3 ± 9.9 h in the REM group and 7.6 ± 12.7 h in the non-REM group ($p = 0.64$). All patients were successfully extubated. The duration of ICU stay was 56 ± 25 h in the REM group and 54 ± 31 h in the non-REM group ($p = 0.66$). There was no significant between-group difference in the frequency of use of vasoactive agents (i.e., dopamine, dobutamine, and noradrenaline). All patients were transferred from the ICU to a general ward. There were two in-hospital deaths in the non-REM group.
Conclusion: There is no significant difference in the duration of ventilation, length of ICU stay, frequency of use of vasoactive agents, or in-hospital mortality according to whether or not remimazolam is used for sedation after elective cardiovascular surgery.

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Acknowledgements: This work was supported by JSPS KAKENHI Grant Number 22K09116.

000602

Low postoperative perfused vessel density is associated with increased soluble vascular cell adhesion molecule-1 after cardiovascular surgery with cardiopulmonary bypass

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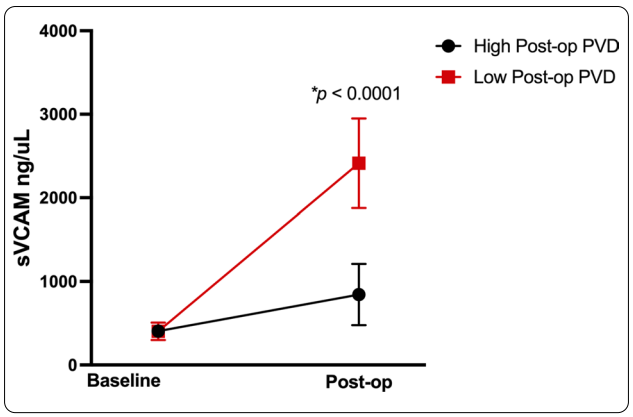
Introduction: Poor microcirculatory function after cardiovascular surgery with cardiopulmonary bypass (CPB) is associated with significant morbidity and worse clinical outcomes [1]. A number of mechanisms have been proposed for reduced microcirculatory blood flow during critical illness including inflammatory-mediated vascular endothelial injury, microthrombosis, and an inadequate balance between vasoconstrictive and vasodilating molecules. During periods of shock, increased oxidative stress and low endogenous nitric oxide bioavailability can cause an upregulation of endothelial cell adhesion molecules (CAMs) which bind activated monocytes and T lymphocytes, causing increased vascular wall inflammation and injury [2].
Objectives: To compare plasma levels of inflammatory markers and soluble VCAM-1 (sVCAM-1) in patients with high and low postoperative functional capillary density after cardiovascular surgery with CPB.
Methods: These are preliminary results from the MicroRESUS study, an ongoing prospective, single-center, observational study of the microcirculation during resuscitation after elective CABG or valvular surgery patients. Sublingual microcirculation imaging (CytoCam, Braedius Medical BG, the Netherlands) was obtained within 2 h of ICU admission after surgery. Perfused vessel density (PVD) was manually calculated from video sequences using the ESICM 2nd consensus standards and AVA 3.1 software (Microvision Medical, the Netherlands) to estimate functional capillary density [3]. Patients were divided into 2 groups based on their postoperative PVD. High PVD was defined as ≥ 22 mm/mm2 and low PVD < 22 mm/mm2. Soluble VCAM-1, IL-6, IL-8, and IL-10 levels were measured in duplicate with a commercially available enzyme-linked immunoassay (Thermo Fisher Scientific, Waltham, MA USA; Quansys Biosciences, Logan, UT, USA) using plasma taken from patient blood samples drawn at the time of microcirculation measurement.
Results: We enrolled 40 patients, who were 64 (± 9) years old, 80% male, and had a EuroSCORE II of 2.1 (± 2.3). Postoperative PVD was 27.8 (± 2.9) vs. 16.7 (± 2.4) mm/mm2 in the high vs. low PVD group, respectively. There were no differences in subject demographics, CPB times, cross clamp times, hemodynamics, or catecholamine infusion doses between groups. Overall, postoperative IL-6 (4.0 ± 16 vs. 535 ± 608 pg/mL; $p < 0.0001$), IL-8 (5.8 ± 9.0 vs. 35 ± 41 pg/mL; $p < 0.0001$), and IL-10 (16 ± 46 vs. 671 ± 1148 pg/mL; $p < 0.0001$) increased from baseline. There was no difference between baseline or postoperative levels of IL-6, IL-8, or IL-10 between groups with high and low postoperative PVD. Overall, sVCAM-1 also increased after surgery (405 ± 195 vs. $1{,}829 \pm 1752$ ng/mL; $p < 0.0001$). Patients with high postoperative PVD had similar sVCAM-1 levels before and after surgery (406 ± 167 vs. 844 ± 786 ng/mL; $p = 0.64$). Patients with a low postoperative PVD had an increase in sVCAM-1 compared to baseline (403 ± 225 vs. 2413 ± 1144 ng/mL; $p < 0.0001$) and a higher sVCAM-1 concentration compared to patients with a high postoperative PVD **(Figure 1)**.



Conclusion: Low postoperative microcirculatory perfused vessel density is associated with a high plasma sVCAM-1 level, indicating increased endothelial injury and activation compared to patients with a high postoperative PVD.

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Acknowledgements

1. Penn Abramson Critical Care & Resuscitation Research Fund
2. National Center for Advancing Translational Sciences of the NIH KL2TR001879

000610

Diastolic dysfunction and mortality in COVID-19 patients admitted to ICU: a single-center study

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Introduction: SARS-CoV-2 is responsible of the Coronavirus disease 19 (COVID-19) and triggers a multi-systemic infection involving different organs. The lungs are the most affected, but a significant cardiovascular involvement has been repeatedly demonstrated. Left ventricular diastolic dysfunction (LVDD) is associated with mortality and weaning failure in intensive care unit (ICU) patients.
Methods: We participated to the international COVID-ECHO study (collaboration between experts in critical care echocardiography) which aimed at characterizing cardiovascular dysfunction by means of advanced echocardiography in COVID-19 patients admitted to ICU. Hereby we present single center data on LVDD assessment (as per latest guidelines), and its association with patient's outcome.

Results: Between 06.10.2020 and 18.02.2021, advanced echocardiography was performed in 35 patients, full data on LVDD were available for 26 patients (74%) but 3 were excluded as they had severely depressed ejection fraction (<35%). Of the remaining 23 patients (median age 66 years, BMI 29, 70% males; hypertension 61%, chronic obstructive pulmonary disease 22%, smoking history 22%, chronic kidney disease 17%, diabetes 4%), 16 were mechanically ventilated (70%) and 8 had diagnosis of LVDD (35%). Nine patients survived (39%) and we found no differences in ICU mortality regarding LVDD nor in the single parameters used to diagnose and grade LVDD. However, non-survivors had a trend towards greater incidence of LVDD (50%, vs survivors 11%; p = 0.06) and higher E/e' ratio (11.4 ± 3.1, vs survivors 9.3 ± 2.4; p = 0.11).
Table 1. Evaluation of Left Ventricular (LV) diastolic dysfunction in patients with coronavirus disease receiving advanced echocardiography

	Overall n = 23	Survivors n = 9	Non-survivors n = 14	p-value
Tricuspid regurgitation jet (m/sec)	1.7 ± 0.9	1.5 ± 0.9	1.9 ± 0.9	0.47
E wave (cm/sec)	56.3 ± 18.8	64 ± 14.2	69.8 ± 21.4	0.48
E/e' ratio	10.6 ± 2.9	9.3 ± 2.3	11.4 ± 3.1	0.11
e' wave (cm/sec)	7.0 ± 2.3	7.2 ± 2.2	6.8 ± 2.4	0.67
E/A ratio	0.92 ± 0.33	0.94 ± 0.33	0.91 ± 0.35	0.87
Left Atrial volume A-L (ml/m2)	77 ± 45	70.4 ± 32.4	81.3 ± 52.9	0.48
Left Atrial volume MODs (ml/m2)	68 ± 40.4	62.6 ± 29.4	71.5 ± 46.9	0.52
LV Diastolic Dysfunction	34.7%	11.1%	50%	0.06
grade I	26%	35.7%	11.1%	
grade II	8.6%	0%	14.2%	
grade III	0%	0%	0%	
indeterminate	13%	22.2%	0%	

Conclusion: In this single center sub-study on COVID-19 patients, assessment of LVDD according to latest guidelines was feasible in two-thirds of the overall cohort. Our results suggest that ICU mortality could be possibly associated with LVDD and higher values E/e' values. The small sample size of patients recruited warrants larger investigations.

000652

Should I Swan or should I not

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Intensive Care Medicine Experimental 2022, **10(2)**:000652

Introduction: The Swan-Ganz flotation catheter was introduced in critical ill patients in 1970 (1) (2) with the aim of a bedside hemodynamic monitoring that lead to a more physiology-based treatments. Since then, the use of Swan-Ganz catheter has become widespread to

clinical practice of non-critical and critical care patients without strong evidence of its benefit (3) (4). The randomized controlled trials demonstrated that pulmonary artery catheterization was associated with an increased mortality (3) (5) (6), except for patients in cardiogenic shock (7), leading to a decline in its use (8). However, Swan-Ganz has still a place in intensive care unit (ICU) for properly selected patients and the need of trained doctors with expertise to interpret its hemodynamic data is still required (9).

Objectives: The purpose of this study is to review the use of Swan-Ganz catheter in the intensive care unit of a tertiary care hospital regarding patients' demographic characteristics, indications, safety, mortality and trends in pulmonary artery catheter use from 2011 to 2021.

Methods: A retrospective chart review was conducted on all adult patients who had a Swan-Ganz placed in our multidisciplinary intensive care unit from 2011 to 2021.

Results: In a ten-year period, a total of 69 patients had Swan-Ganz catheter placed (from a total of 8205 patients), of whom 8 were excluded (missing data on Swan Ganz related complications). Of the 61 patients included in our analysis, 67% were male, the mean age was 63 years, the average length of ICU stay was 18.7 days, the mean SOFA score 8.67, the mean APACHE-II was 25.85, the mean SAPS-II was 55.26, the overall mortality was 32% (24.06% in patients without Swan-Ganz). The 3 most frequent diagnosis at the admission were post cardiorespiratory arrest shock (26.23%), septic shock (22.95%) and cardiogenic shock (14.75%). The mean duration of Swan-Ganz placement was 4.5 days and the main goal of the placement was hemodynamic monitoring 88.5%, followed by characterization of shock 11.5%. The only complication registered was pneumothorax in one patient (1.64%).

Conclusion: Our study shows that the use of the Swan-Ganz catheter in selected patients was associated with fewer complications compared with previous studies and with benefit in hemodynamic management (6) (10). Regarding our ICU we identified some areas of improvement in what concerns a standardized registration of the Swan-Ganz catheter of early complications and the response to treatment guided by Swan-Ganz interpretation.

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000655

The normalization of arterial lactate and venous-to-arterial CO2 difference as a new prognostic tool for cardiogenic shock resuscitation

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Intensive Care Medicine Experimental 2022, **10(2)**:000655

Introduction: Cardiogenic shock (CS) is a life-threatening condition responsible for unacceptable mortality of > 40% by two weeks (1,2,3). Assessing CS patients' severity is crucial to prompt therapeutic escalation in due time (4). Whereas cardiac output and systolic blood pressure are of insufficient accuracy, arterial lactate might improve mortality prediction (5,6), but with essential drawbacks (7). Venous to arterial CO2 partial pressures gradient (P(V-A)CO2) is a validated tool to guide septic shock resuscitation (8) but not yet widely investigated in CS.

Objectives: We aimed to investigate how the normalization of arterial lactate and P(V-A)CO2 together could confirm the quality of CS patients' resuscitation and predict their survival at day 14.

Methods: We retrospectively screened all the patients admitted with CS to the general Intensive Care Unit (ICU) of the Erasme University Hospital (Brussels, Belgium), irrespectively of its aetiology, from January 2011 to October 2020. CS was determined according to the ICU discharge final diagnosis. Exclusion criteria were age < 18 years old; heterogeneous hemodynamic profile where CS represented a minor mechanism; refractory cardiac arrest; ICU early discharge of alive patients in < 48 h (i.e., not a severe CS); and patients who died from post-anoxic encephalopathy. In our local database (Critical Care Manager®, PICIS, USA), we gathered clinical data and blood gas analyses (BGA) during the first four "8-h" intervals after CS diagnosis inside the ICU. If available, venous BGA values from mixed venous blood samples via a pulmonary artery catheter were preferred to central venous line BGA. After setting arbitrary pathological thresholds for arterial lactate at > 2,5 mmol/L and P(V-A)CO2 at > 7 mmHg, we analysed their normalization's predictive value—separately and in combination—to assess survival at day 14.

Results: We retrieved 911 patients with a diagnosis of CS, from which 425 patients were included after applying the exclusion criteria. Overall, 264 patients died during the first two weeks (62%). Table 1 provides the main clinical characteristics. The most frequent aetiologies of CS were acute myocardial infarction (AMI-CS) (33%) and post-cardiotomy CS (22%). As shown in Table 2 and Figure 1, the best predictive value of survival at day 14 was reached at the third time-interval (17–24 h), where arterial lactate normalization alone showed a sensitivity of 91% with a specificity of 50%, and P(V-A)CO2 normalization alone showed a sensitivity of 48% with a specificity of 62%. Once coupled, both arterial lactate and P(V-A)CO2 normalizations outperformed the previous results with a sensitivity of 84% and a specificity of 71%.

	Parameter	Global cohort (n=425)	Survivors at D14 (n=161)	Non survivors at D14 (n=264)	P value
Characteristics	Age (mean ± SD)	66,5 ± 14,8	63,5 ± 15,1	68 ± 14,4	ns
	Female n(%)	157 (37)	55 (34)	102 (39)	ns
	BMI (mean ± SD)	26,9 ± 5,9	26,5 ± 5,7	27,3 ± 6	<0,0001
Medical history, n(%)	Arterial hypertension	244 (57)	98 (61)	146 (55)	ns
	Ischemic heart disease	229 (54)	83 (52)	146 (55)	ns
	Diabetes	121 (29)	49 (30)	72 (27)	ns
	Chronic heart failure	118 (28)	62 (39)	56 (21)	0,0001
	Tabagism	109 (26)	45 (28)	64 (24)	ns
	Chronic kidney disease	97 (23)	32 (20)	65 (25)	0,05
	Asthma / COPD	67 (16)	23 (14)	42 (16)	ns
	Pulmonary hypertension	36 (9)	16 (10)	20 (8)	ns
	Stroke	23 (5)	13 (8)	10 (4)	ns
	Cirrhosis	15 (4)	5 (3)	10 (4)	ns
CS Etiology, n(%)	AMI-CS	138 (33)	36 (22)	102 (39)	0,0006
	Post-cardiotomy	94 (22)	63 (39)	31 (12)	<0,0001
	Septic cardiomyopathy	66 (16)	17 (11)	49 (19)	0,03
	Acheff-CS	40 (9)	13 (8)	27 (10)	ns
	Miscellaneous	27 (6)	15 (9)	12 (5)	ns
	Tako-tsubo	16 (4)	6 (4)	10 (4)	ns
	Post heart transplant	14 (3)	1 (0)	13 (5)	0,02
	Myocarditis	8 (2)	2 (1)	6 (2)	ns
	Post LVAD implant	6 (1)	5 (3)	1 (0)	0,03
Associated diagnosis, n(%)	Cardiac arrest	104 (25)	15 (9)	89 (34)	<0,0001
	Tamponade	19 (5)	6 (4)	13 (5)	ns
Therapeutic support, n(%)	Pulmonary artery catheter	147 (35)	77 (48)	70 (27)	<0,0001
	Noradrenaline	329 (77)	130 (81)	199 (75)	ns
	Dobutamine and/or Levosimendan	309 (73)	137 (85)	172 (65)	<0,0001
	Mechanical ventilation	291 (68)	102 (63)	189 (72)	ns
	Veno-arterial ECMO	88 (21)	19 (12)	69 (26)	0,0003
	Renal replacement therapy	76 (18)	24 (15)	52 (20)	ns
	Intra-aortic balloon pump	26 (6)	10 (6)	16 (6)	ns

Table 1. *Characteristics of the population. The categorical variables are expressed as proportions and percentages, the continuous variables are expressed as mean and standard deviation (SD); Statistical analysis performed by Fisher's exact test; AdvHF-CS: advanced heart failure related cardiogenic shock; AMI-CS acute myocardial infarction related cardiogenic shock; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; CS: Cardiogenic shock; ECMO: Extracorporeal membrane oxygenation; LVAD: Left ventricle assistance device.*

Time interval	Parameter normalization	Sensitivity (%)	Negative predictive value (%)	Specificity (%)	Positive predictive value (%)
0-8h	Arterial lactate	66	74	66	57
	$P_{(V-A)}CO_2$	28	51	65	42
	Arterial lactate and $P_{(V-A)}CO_2$ coupled	35	63	82	60
9-16h	Arterial lactate	75	69	59	66
	$P_{(V-A)}CO_2$	56	51	49	54
	Arterial lactate and $P_{(V-A)}$ CO_2 coupled	77	67	59	71
17-24h	Arterial lactate	91	81	50	70
	$P_{(V-A)}CO_2$	48	44	62	65
	Arterial lactate and $P_{(V-A)}CO_2$ coupled	84	71	71	84
25-32h	Arterial lactate	93	86	41	61
	$P_{(V-A)}CO_2$	57	54	49	52
	Arterial lactate and $P_{(V-A)}CO_2$ coupled	94	85	39	65

Table 2. *Accuracy of arterial lactate normalization (≤ 2,5 mmol/L) alone, $P_{(V-A)}CO_2$ normalization (≤ 7 mmHg) alone, or in combination, to predict survival at day 14; $P_{(V-A)}CO_2$: venous-arterial CO_2 pressure gap.*

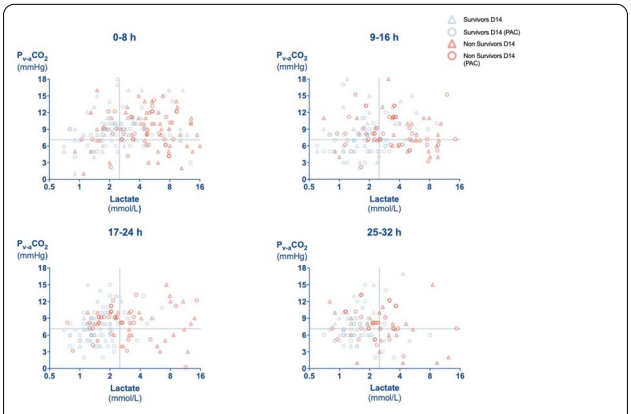

Figure 1. *Correlation between arterial lactate and $P_{(V-A)}CO_2$ measurements during the first 32 hours after cardiogenic shock diagnosis; D14: day 14; PAC: Pulmonary artery catheter; $P_{(V-A)}CO_2$: venous-arterial CO_2 pressure gap.*

Conclusion: Our retrospective study suggests that, during the early stages of CS patients' resuscitation, arterial lactate and P(V-A)CO2 normalization, in combination more than taken individually, could be a valuable tool to confirm survival within the first two weeks.

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Acknowledgements: None.

000659

Association between ventricular-arterial coupling and extravascular lung water index in critical ill patients

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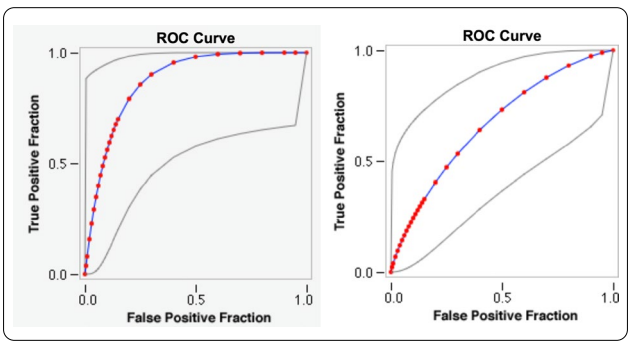
Introduction: For many patients in the intensive care unit, questions related to hemodynamic management can´t be answered with a simple clinical exam and require minimally invasive hemodynamic monitorization to determinate and improve their hemodynamic state. Transpulmonary thermodilution is a method that provides a complete hemodynamic assessment that takes in consideration the value of extravascular lung water index (ELWi) and other parameters to quantify ventricular- arterial coupling (VAC).
Objectives: Describe the association between ventricular arterial coupling and ELWi.
Methods: We reviewed the medical records of patients admitted in the intensive care unit of Hospital Juárez de México in the months of july to december 2018 that met inclusion criteria. We used the Mann-Whitney U test for nonparametric test and Pearson´s correlation between continuous quantitative variables for data distribution; the statistical significance was established with a p value of < 0.05.
Results: We found information of 20 patients admitted to the ICU, no correlation was found between ELWi and VAC with r2 of -0.0514 ($p = 0.9913$) and ELWi and AE with r2 -0.2311 ($p = 0.3271$); correlation on day 2 of arterial elastance (AE) and day 2 of VAC with a $r2 = 0.96$ by Pearson´s correlation. ELWi and VAC had AUC-ROC of 0.875 (Fig 1) and 0.667 (Fig 2) respectively to predict 30-day mortality.



Conclusion: Hemodynamic evaluation through the assessment of cardiovascular function with transpulmonary thermodilution in critically ill patients includes the ELWi and also VAC, we are still looking to determine if the enhancement of these variables has an impact in mortality, however in this small sample there was no association found between both; patients with ventricular arterial decoupling had higher mortality.
Among the patients in this study, there was no association found between ELWi and VAC; ELWi is a good predictor of mortality in this population.

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Cardiovascular Dynamics 3

000714

Agreement of capillary refill time measurements performed at finger and earlobe in healthy volunteers: a pilot study

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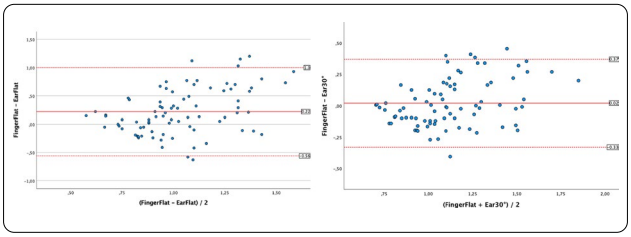
Introduction: Capillary Refill Time (CRT) is a well-known parameter reflecting peripheral tissue perfusion. It is widely used as part of a simple and structured assessment of perfusion in critically ill patients. Measurement involves the visual inspection of blood returning to distal capillaries after they have been emptied by pressure applied on the distal phalanx of a finger. However, for critically ill patients undergoing surgery the assessment of their CRT at the finger level is precluded in most cases by presence of surgical drapes. Nonetheless, CRT can be assessed in other sites (i.e. earlobe) that could be accessible during surgery. Whether the values measured at finger level and at the earlobe are interchangeable remains an open question.
Methods: We performed a prospective observational study comparing values of CRT measured in healthy adult volunteers with no pre-existing medical conditions at three different sites and/or position. A single operator performed these measurements by applying firm pressure with a glass microscope-slide in the following sites/positions: 1) ventral surface of the index finger at distal phalanx level (semi-recumbent position, finger at the height of the hip or "finger-flat"); 2) earlobe with the volunteer in semi-recumbent position with a torso elevation of 30° ("earlobe-30°"), and 3) earlobe with volunteers supine ("earlobe-0°). The pressure was increased until the skin was blank and then maintained for 15 s. The time for return of the normal skin color was registered with a chronometer and was video recorded for evaluation of inter- and intra- rater variability and for external validation. Vital parameters as well as non-invasive hemodynamic monitoring were performed using the Clearsight® device (Edwards lifescince, CA, USA). The non-parametric Friedman pairwise-test was used to assess between group differences; the Bland–Altman analysis was performed to evaluate the mean bias between measurements and to calculate the limits of agreement (LoA). Correlation between measurements was performed with the Spearman test.
Results: We collected data from 82 volunteers, with a median age of 30 years (interquartile range [IQR] 27–35). As compared with CRT measured at finger level [median 1.04 s (IQR 0.8–1.39)], CRT measured at "earlobe-0°" was significantly smaller [0.88 s (IQR 0.75–1.06); $p < 0.001$], whilst CRT assessed at "earlobe-30°" was similar [1.10 s (IQR 0.90–1.26); $p = 0.52$]. As shown in the Bland–Altman diagram (Figure 1a), when comparing the CRT at "finger-flat" position and at "earlobe-0°", the Bias was 0.22 s (standard deviation 0.40) and the LoA were -0.56 (lower) and 1.00 (upper). The same plot analyzing CRT at "finger-flat" position and at "earlobe-30°" showed a smaller Bias (0.02 ± 0.18 s) and the LoA were -0.33 and 0.37 respectively (Figure 1b).



Conclusion: In healthy volunteers, CRT measured at the earlobe with the head at 30° seems producing similar results to the assessment performed at the finger level, with good accuracy and good precision. Conversely, the CRT measured at the earlobe with the patient in supine position (0°) produces different results as compared to the finger CRT, with lower accuracy and precision. These preliminary results do not entirely support the interchangeability of CRT assessment at different sites (finger and earlobe), especially when considering the CRT assessed at earlobe with the patient supine (0°), which would be of interest for its possible use in the operating room. Studies on critically ill patients may be useful to confirm these preliminary results.

000669

Myocardial Work: operator reliability with novel advanced echocardiography techniques in the ICU

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Introduction: There is a growing body of evidence supporting the use of speckle-tracking echocardiography (STE) in critical illness.1 Originally described by Russell et al., 2 myocardial work (MW) is a novel non-invasive STE-based technique that estimates myocardial performance based upon pressure-strain loops. MW is capable of quantifying constructive and wasted work and already has many identified clinical applications.3 However, the clinical benefit of using MW in critically unwell patients with sepsis has yet to be evaluated. The CRiSIS study (ISRCTN 23,174,569) aims to determine if any association exists between MW and mortality in sepsis.
Objectives: To evaluate inter- and intra-operator reliability using this novel technique and whether operator reliability can be improved by focused training.
Methods: Deidentified data from the CRiSIS study for 14 patients were examined by two independent echocardiographers competent in myocardial strain imaging.4 Operator 1 was new to the tool, whilst operator 2 was competent in MW measurements. STE and MW were analysed using GE EchoPAC (version 2.0.4) with their proprietary Myocardial Work package. Following standard measurements for strain using an 18-segment model, myocardial work is then estimated following identification of aortic and mitral valve events within the cardiac cycle. Images were collected using a GE S70 R2 echocardiographic device and a M5Sc cardiac probe. The first set of measurements were

made with no extra-training. The second set of measurements were made following training via the GE Vivid Club platform. Inter- and intra-rater interclass correlation coefficients (ICC) for global longitudinal strain (GLS) and global work efficiency (GWE) were determined using R (version 4.1.3, Austria, Vienna).
Results: For GLS, the inter-rater ICC (95% CI) for the first and second round of measurements were 0.94 (0.84–0.98) and 0.99 (0.96–1.00) respectively, indicating excellent inter-reliability. For operator 1, the intra-rater ICC (95% CI) was 0.96 (0.87–0.99) and for operator 2 was 0.98 (0.94–0.99), both indicating excellent intra-reliability. For GWE, the inter-rater ICC (95% CI) for the first and second round of measurements were 0.52 (0.00–0.82) and 0.94 (0.81–0.98) respectively, indicating an increase from moderate to excellent inter-reliability. For operator 1, the intra-rater ICC (95% CI) was 0.49 (0.00–0.80), indirectly suggesting a marked improvement in operator 1's performance, and for operator 2 was 0.93 (0.79–0.98).
Conclusion: This study shows that even for the echocardiographer competent in GLS measurements, further training is required to gain competency in MW assessment in order to achieve excellent inter- and intra-rater reliability. This is an important consideration if use of the tool is to become more routine in critical care settings. Following focused training, excellent inter-operator reliability can be achieved making the potential benefits of MW achievable for echocardiographers.

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000689

Right ventricular systolic pressure and mortality in patients admitted to ICU due to COVID-19 infection

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Intensive Care Medicine Experimental 2022, **10(2)**:000689

Introduction: The mechanisms of cardiovascular injury in patients with COVID-19 and ARDS are related to lung parenchymal damage and altered pulmonary vasculature hemodynamics (1), resulting in higher afterload for the right ventricle (RV) followed ultimately by RV dysfunction (2). Right ventricular systolic pressure (RVSP) is a useful tool to measure afterload for the RV.
Objectives: The aim of this study is to describe the clinical characteristics and echocardiographic findings of patients admitted to ICU due to COVID-19 infection. Furthermore, we aimed to determine the effect of RVSP and ARDS on mortality in this population.
Methods: This is a single-center retrospective study from March 2020 to August 2021. The study included hospitalized adult patients with confirmed COVID-19 infection by RT-PCR, who had an echocardiogram performed during admission. A total of 223 patients were included. Demographics, clinical factors, and findings in 2D echocardiogram before and during hospital admission were obtained. Right ventricular dilation and dysfunction were obtained by qualitative assessment, and RVSP was calculated with the Bernoulli equation. Statistical analyses were performed using SAS 9.4. We evaluated the differences between ICU admission groups by one-way ANOVA, Wilcoxon rank-sum or Fisher exact test, as appropriate to test differences between ICU admission groups.
Results: The overall mean age was 64 ± 16 years, 60% were male, 21% AA, and 68% Hispanics. ICU admission was required for 122 (55%) of patients, of which 98 (80%) were diagnosed with shock (80 distributive, 25 cardiogenic), 86 (70%) required CRRT, and 105 (86%) developed ARDS. Mortality was 28% in the overall cohort and 55% vs. 7% in patients who required vs. who did not require ICU admission, respectively. Table 1 shows demographic, clinical and echocardiographic characteristics by ICU admission group. Logistic regression models showed a significant effect of ARDS (OR 27.9, $p < 0.001$) and RVSP (OR 1.16 for every 5 unit increase (CI 1.04–1.29), p 0.008) on mortality. ARDS was associated with higher RVSP on mixed linear regression analysis (B coefficient of 7.88, $p < 0.001$). Higher RVSP during admission as compared to pre-admission echocardiogram and higher mortality was seen in patients with ARDS (Figure 1).
Conclusion: In our study, higher mortality was observed in patients with COVID-19 infection who required ICU admission. Measures of RV dysfunction such as RVSP was associated with ARDS and higher mortality supporting the theory of deleterious effect of ARDS on RV dysfunction in patients with COVID-19. Further studies including advanced imaging might be useful to understand the association of RV dysfunction and long term outcomes.

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000733

The Automation of Sub-Aortic Velocity Time Integral Measurements: Clinical Evaluation of an Artificial Intelligence-Enabled Tool in Critically Ill Patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000733

Introduction: The assessment of the sub-aortic velocity time integral (VTI) is part of the echocardiographic evaluation of critically ill patients. It is operator-dependent and time-consuming. An artificial intelligence (AI) tool has recently been developed for the automatic assessment of VTI (autoVTI) in a few seconds only.
Objectives: We designed the present study to compare autoVTI measurements done by experts and trainees to reference manual measurements (VTI-ref) done by experts.
Methods: We studied critically ill patients who required an echocardiographic evaluation during their ICU stay. AutoVTI measurements were performed with the autoVTI software available on the cart-based Venue (GE Healthcare) ultrasound system from an apical 5-chamber view. Automatic VTI measurements done by trainees (autoVTI-trainee) and experts (autoVTI-expert) were compared with VTI-ref measurements done manually by two experts (FAG & JB) in critical care echocardiography. All measurements were done in triplicate and the reproducibility of measurements was calculated as SD/mean and expressed as a percentage.
Results: We enrolled 77 patients in whom transthoracic echo images were possible to obtain. AutoVTI measurements were technically possible in 71 patients (92%). VTI-ref ranged from 14.8 to 32.8 cm (mean 22.2 ± 4.3 cm). AutoVTI-expert ranged from 11.6 to 29.3 cm (mean 20.5 ± 4.4 cm). We observed a close relationship ($r = 0.86$, $p < 0.001$) between VTI-ref and autoVTI-expert. The average difference (bias)

between autoVTI-expert and VTI-ref was -1.7 ± 2.3 cm, with a percentage error (2SD/mean) of 22%. AutoVTI-trainee ranged from 11.6 to 28.4 cm (mean 20.2 ± 4.3 cm). We observed a significant relationship (r = 0.79) between VTI-ref and autoVTI-trainee. The average difference (bias) between autoVTI-trainee and VTI-ref was -1.9 ± 2.8 cm, with a percentage error of 26%. The reproducibility of manual and automatic measurements was comparable: 5.8 ± 3.9% for VTI-ref, 6.1 ± 4.0% for autoVTI-expert, and 5.6 ± 3.9% for autoVTI-trainee.

Conclusion: The automatic assessment of VTI was possible in most patients. It was accurate (low bias) and precise (percentage error < 30%), both for experts and trainees. The reproducibility of measurements was as good for trainees as for experts. Therefore, the AI-enabled autoVTI tool may assist clinicians, in particular trainees, to quickly identify the underlying mechanisms of shock and to assess fluid responsiveness.

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000734

Capillary refill time in healthy volunteers: does the arm position matter?

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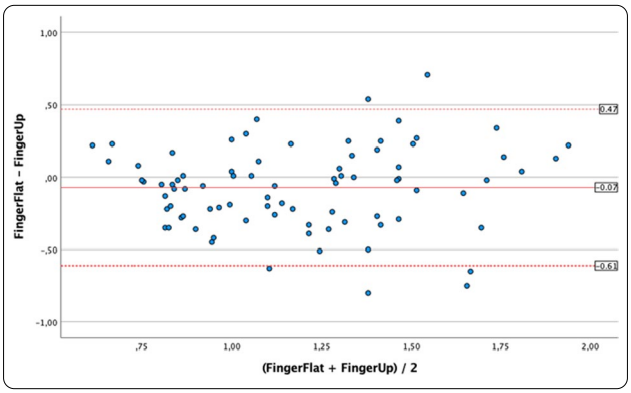
Intensive Care Medicine Experimental 2022, **10(2)**:000734

Introduction: Capillary refill time (CRT) is a marker of peripheral perfusion and activation of the sympathetic nervous system. It has been associated with organ failure and mortality in patients admitted to intensive care unit. Its use has been implemented for the management of critically ill patients and showed promising results. The position of the arm during assessment has not been fully standardized. In particular, as compared to a flat position of the arm, its elevation may reduce venous congestion; however, it remains undefined whether this change in finger position may influence CRT measurements to a clinically significant extent.

Methods: In healthy adult volunteers with no pre-existing medical conditions and lying in semi-recumbent position, we performed a single-center prospective study measuring CRT at the ventral surface of the index finger (distal phalanx level) on the right hand. Two measurements were taken: 1) with the index at the level of the hip ("finger-flat"), and 2) after positioning the finger in a 30° unloaded position for 60 s. CRT was measured by a single operator applying firm pressure with a glass microscope-slide. Pressure was increased until the skin was blank and kept for 15 s. The time for return of the normal skin color was registered with a chronometer. We also video recorded all measurements for subsequent intra- and inter-rater variability and external validation. All together with vital parameters (blood pressure, heart rate, oxygen saturation), we recorded hemodynamic data using Clearsight® (Edwards Lifescience, CA, USA) monitoring. Differences between the two measured CRT were assessed using the Friedman test, then a Bland–Altman analysis was performed to calculate the mean bias and the limits of agreement (LoA). Correlation between measurements was performed with the Spearman test.

Results: We collected data from 82 healthy volunteers, with a median age of 30 years (interquartile range [IQR] 27–35). Median CRT for "finger-flat" group was 1.04 s (IQR 0.8–1.39), whilst "finger-up" CRT was 1.17 s (IQR 0.93–1.41; p = 0.027). As shown in the Bland–Altman diagram (Figure 1), the mean bias between measurements was −0.07 s (standard deviation 0.3) and the LoA were -0.61 (lower) and 0.47 (upper). We found significant correlation with a Spearman rho 0.70 (95% Confidence Interval 0.56–0.80; p > 0.001).



Conclusion: In healthy volunteers, the CRT measured at the finger distal phalanx in unloaded position produces different results as compared to CRT assessment with the index at the level of the hip; however, this difference is small, we found a good accuracy (small mean bias) with a clinically acceptable precision (LoA). Whether these differences are similar in critically ill patients (i.e. septic) remains to be defined.

000748

Risk factors for mortality in patients with heart failure (HF) and COVID-19 at Respiratory Intensive Care Unit (R-ICU) "Dr. Mario Shapiro" American British Cowdray Medical Center

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Intensive Care Medicine Experimental 2022, **10(2)**:000748

Introduction: The coronavirus disease 2019 (COVID 19) rapidly spread around the world becoming a global public health problem with an influx of patients hospitalized with severe acute respiratory syndrome-coronavirus-2 (SARS-Cov2-2). So far more than four hundred millions of confirmed COVID 19 cases can be counted worldwide, with a total of more than six million deaths, as of April 12, 2022, according to the

World Health Organization.1–2. Although COVID 19 was initially considered a respiratory disease, it has rapidly become clear that a multiorgan involvement was common. However, the heart often represents a target organ and patients may develop heart failure (HF). History of HF is a risk factor for a more severe clinical course of COVID 19.3 HF involves more than 10% of population over 70 years in the developed countries, making it a known epidemic that is inevitably shattering with the one currently caused by SARS-CoV-2. 4 There are few studies that discuss the relationship between prognostic factors for HF and COVID-19 in Mexico and Latin America. 5–6. Patients with pre-existing HF are likely at higher risk for adverse outcomes in COVID 19. Whether this pattern of worsened outcomes among patients with heart failure is unique to COVID-19 or similar to that seen in any other systemic inflammatory state is not clear.7 The overall mortality rate of 25% is consistent with that seen in other large registries, whereas a humbling 40% of those with heart failure died during hospitalization. 8–9.

Objectives: Identify factors associated with the death among patients with a history of heart failure (HF) hospitalized with severe coronavirus disease-2019 (COVID-19).

Methods: This study conducted an retrospective longitudinal analysis of 213 patients with a history of HF admitted for Severe COVID-19 at Respiratory Intensive Care Unit in Mexico City between March, 2020 to July 2021.Patients were classified according to the categorical variable of mortality as deceased or not deceased. The categorical and continuous variables were expressed as absolute values and percentages and as medians (ranges), respectively The differences between groups were analysed using Student's t-test or the Mann–Whitney U test for continuous variables or Pearson's chi-squared test for categorical variables. A p-value < 0.05 was considered statistically significant; subsequently. A multivariate logistic regression analysis was performed to identify admission factors associated with mortality expressed as an adjusted odds ratio (OR), with a 95% confidence interval (95% CI). The statistical analysis was conducted with SPSS software. (IBM SPSS Statistics©).

Results: Data from 213 Severe COVID 19 patients admitted to the R-ICU were analyzed. A total of 153 patients (71.8%) had a history of HF prior to admission. Of these 80 patients (52.4%) died during admission. The median age of study participants was 72.4 years (range 62.5–81.7). Among patients with HF hospitalized with COVID 19 who died were significantly older (OR: 4.2 (95% CI: 1.33–12.52; $p = 0.008$), male gender (OR: 2.96 (95% CI: 1.35–7.12; $p = 0.005$), and had higher comorbidity. In addition, there was a higher proportion of diabetics with target organ damage (OR: 1.30; 95% CI: 1.20–1.50; $p = < 0.001$), arterial hypertension (OR: 1.25; 95% CI: 1.07 to 1.46 $p = 0.001$), and kidney failure (OR: 1.26; 95% CI: 1.15 to 1.42 $p = 0.004$) among the deceased.

Conclusion: Patients with HF hospitalized for COVID-19 have a high in-hospital mortality rate. These risk factors mentioned could help clinicians to identify patients with bad prognosis at the intensive care unit.

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Acknowledgements: We would like to thank all the critical care team at intensive care unit "Dr. Mario Shapiro" American British Cowdray Medical Center for his cooperation and support.

000786

Vaso-inotropic score should not be the main determinant for VA-ECMO support decision in post cardiotomy cardiogenic shock

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Intensive Care Medicine Experimental 2022, **10(2)**:000786

Introduction: Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) is a rescue therapy in refractory post-cardiotomy cardiogenic shock (PCS). Currently, there is no consensus about the best timing for implantation of VA-ECMO in this setting. The Vasoactive-Inotropic Score (VIS Score) has been reported to accurately predict adverse outcomes, ECMO-VA support and death in various clinical settings, including PCS.

Objectives: This study was designed to investigate the role of VIS score as determinant of early VA-ECMO implantation in patients with PCS in operating theatre.

Methods: This study is a multicentric retrospective database study conducted at the Cardiovascular ICU of the university-affiliated tertiary hospitals over a fixed period of 3 years. Inclusion criteria were cardiac surgery with cardiopulmonary bypass in adult patients. The main exclusion criteria were: off-pump cardiac surgery, pre-operative VA-ECMO, LVAD, VA-ECMO implantation in ICU, heart transplantation and incomplete data. VIS Score was calculated as follows: dobutamine dose (µg/kg/min) + dopamine dose (µg/kg/min) + norepinephrine dose (µg/kg/min) × 100 + epinephrine dose (µg/kg/min) × 100 + milrinone dose (µg/kg/min) × 10 + vasopressin dose (unit/kg/min) × 10,000. We evaluated risk factors associated with VA-ECMO implantation by using a multivariate logistic regression model with backward process. Then we performed a propensity matching (1:1) without replacement and a calliper distance of less than 0.2. Quantitative and qualitative paired variables were analysed by using the Wilcoxon test and the McNemar test.

Results: Of 2769 patients screened during the study period, 528 patients had PCS and 76 patients were supported by VA-ECMO in operating theatre. Risk factors for VA-ECMO support were age 0.97 (CI95%: 0.944–0.986), BPCIA 5.9 (CI95%: 2.1–17), right ventricular dysfunction 3.4 (CI95%: 1.6–7.2), LVEF < 30% 4,1 (CI95%: 1,9–8,6), pulmonary hypertension 2.2 (CI95%: 1.2–3.8), emergency 3.2 (CI95%: 1.8–5.5), number of procedures 1.8 (CI95%: 1.4–2.4), VIS score 1.09 (CI95%: 1.07–1.1). After matching (65 patients per group), the two groups did not differ significantly in their demographic characteristics, cardiac surgery type and operative characteristics. The VIS score did not differ (29.0 [20.0;65.0] vs 32.0 [17.4;64.6], $p = 0.89$). The VA-ECMO group had higher in hospital mortality (36% (55.4) vs 9% (13.8), $p < 0.001$). In addition, VA-ECMO group had worse clinical outcomes, in terms of acute renal failure, infections, transfusions and abdominal complications (Table 1).

Table 1. In-hospital complications

	NO VA-ECMO	VA-ECMO	p value
Atrial Fibrillation	25 (38.5%)	30 (46.2%)	0.478
Ventricular arrhythmia	6 (9.23%)	23 (35.4%)	0.001
Prolonged intubation	16 (24.6%)	44 (67.7%)	<0.001
ARDS	20 (30.8%)	28 (43.1%)	0.203
Acute Kindney Injury	28 (43.1%)	54 (83.1%)	<0.001
CRRT	7 (10.8%)	27 (41.5%)	<0.001
Septic shock	6 (9.23%)	21 (32.3%)	0.002
Blood transfusion	28 (43.1%)	61 (93.8%)	<0.001
Hemorrhagic shock	5 (7.69%)	38 (58.5%)	<0.001
Mesenteric Ischemia	0 (0.00%)	10 (15.4%)	0.003
ICU LOS	4.00 [2.00;7.00]	9.00 [5.00;15.0]	<0.001
Hospital LOS	9.00 [7.00;18.2]	14.0 [6.00;24.0]	0.300

Conclusion: VIS score was independently associated to ECMO-VA support in operating theatre. When matching patients, no significant differences in VIS Score was demonstrated. Patients supported by VA-ECMO had higher mortality because of ECMO-VA related morbidity. Consequently, despite VIS score being associate to ECMO-VA support, it should not be considered as a main determinant for VA-ECMO initiation in PCS. Physician should take in account other variables.

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000793

Invasive mechanical ventilation induces postcapillary collapse which diminishes the cardiac output and promotes pulmonary edema; An integrated model of the cardiopulmonary interactions

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Intensive Care Medicine Experimental 2022, **10(2)**:000793

Introduction: Mechanical ventilation (MV) can decrease cardiac output (CO) and jeopardizes the patients. The MV effects on right ventricle (RV) preload and afterload are well-known, but the effects on left ventricle (LV) filling are not well-defined. The pulmonary circulation is complex and comprises of two compartments (intrapulmonary and extrapulmonary) with different surrounding pressures.
Objectives: To investigate the effects of the transpulmonary pressure (alveolar minus pleural pressure) on LV filling and CO. To test the hypothesis that higher transpulmonary pressure decrease the intrapulmonary vascular transmural pressure, which decreases the vessels diameters, especially in the pulmonary postcapillary vessels, leading to diminished LV filling.
Methods: A unique integrated model of the cardiovascular and respiratory systems was developed to investigate the cardiopulmonary interactions. The pulmonary circulation is divided into four compartments: extrapulmonary arterial and venous compartments and intrapulmonary precapillary and postcapillary compartments, with the different surrounding pleural and alveolar pressures, respectively. The intrapulmonary vessels are compliant, and their diameters are determined by the transmural pressure gradient. These vessels collapse when the alveolar pressure approaches the intravascular pressure (close to zero transmural pressure).
Results: MV of a normal lung decreases the RV preload, and even decreases the pulmonary artery pressure. Concurrently, the LV filling increases during inspiration, due to the increase in the pressure gradient between the pulmonary bed and the LV. However, an increase in the ventilation pressure in attempt to maintain adequate ventilation of a compromised lung leads to the opposite effect on LV filling. Higher ventilation pressure increases the PVR due to the decline in the vascular transmural pressure. The same alveolar pressure surrounds all the vessels, but postcapillary vessels with the lower intravascular pressure are the most vulnerable, and can collapse during inspiration. The PEEP, Driving pressure and higher inspiration:expiration ratio have synergistic effects on the postcapillary resistance. Postcapillary collapse: (1) decreases the LV filling and CO and shifts lung regions from zone 3 to zone 2, (2) increases the pulmonary artery pressure and the RV afterload, and (3) increases the pulmonary capillary pressure and may intensify pulmonary edema. The latter is due to substantial larger increase in postcapillary resistance than in precapillary resistance.
Conclusion: Optimization of MV is complex, and understanding the underlying cardiopulmonary interactions is mandatory for reaching this goal. The effects of intense MV on the pulmonary circulation may be dominated by the increase in the postcapillary resistance which diminished the CO while it increases the pulmonary artery and capillary pressures.

000808

The skin as diagnostic organ for water balance and vascular tone in septic and cardiogenic shock (SkInShock Study)

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Intensive Care Medicine Experimental 2022, **10(2)**:000808

Introduction: The assessment of volume status is often subject of controversial discussions at the ICU. Clinical examination remains the basis for fluid status estimation, resulting in a wide interobserver variability and nonquantifiable results. Although optimal management of fluid administration is important, especially in shock, the estimation of 24 h fluid balance is often reduced to administered intravenous fluids and urine output. Transepithelial water loss through lungs and skin plays a crucial role for the volume management and is usually estimated with formulas based on body weight and temperature, which often leads to systematic errors and unsatisfactory fluid balances.
Objectives: In the SkInShock study, we aimed to test the hypothesis that the skin as an easily accessible organ could be used for an optimized, noninvasive assessment of vascular tone and fluid balance in septic or cardiogenic shock.
Methods: In this prospective single-center study (German Clinical Trails Register ID: DRKS00027981), we measured transepithelial water loss (TEWL) through the skin on the forehead, upper limbs, trunk, and lower limbs of ventilated patients with cardiogenic or septic shock in a cardiac intensive care unit. For this purpose, we used a Tewameter® (Courage + Khazaka, Germany) which quantifies transcutaneous water evaporation (g/h/m^2) in an open chamber method without affecting the skin microenvironment.Total water loss through the skin per day was calculated either by using the performed TEWL measurements or

the following formula: 6 ml/kg bodyweight/24 h + 20% correction per °C different from 37 °C. As all patients were intubated and ventilated with active humidification, so only skin was considered as relevant for invisble water loss. To correlate skin water loss with vascular tone, systemic vascular resistance index (SVRI) was quantified with PiCCO technology (Getinge, Germany) simultaneously to TEWL measurements.
Results: We are reporting the first results of the SkInShock study (20 measurements in two patients with cardiogenic and three patients with septic shock). TEWL measurements significantly correlated to SVRI, with low TEWL values indicating high SVRI. Statistical significance regarding this correlation was achieved for measurements within each individual patient and for a pooled analysis of all patients ($n = 20$; $R^2 = 0.4$; $p < 0.02$). In addition, calculated 24-h water loss based on TEWL measurements showed a significant correlation with the estimated insensible fluid loss using the accepted formula ($n = 20$; $R^2 = 0.89$; $p < 0.0001$). Notably, our data show that in patients with high TEWL values and low vascular resistance, measured insensible water loss exceeded the formula-based estimate by up to 100%.
Conclusion: The first results of our study show that noninvasive measurements of TEWL seems to correlate with SVRI and therefore can provide additional information on vascular resistance in a simple and rapid approach. Measurement of TEWL may improve clinical assessment of volume status, especially in situations with low vascular tone and consecutive increased transcutaneous water loss. Further results of our study will show whether these initial observations can be confirmed.

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000820

The regulation of O-GlcNAcylation during cardiopulmonary bypass, a potential therapeutic solution for post-operative multi-systemic alteration: assessment in humans and in a rat extracorporeal circulation model

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Intensive Care Medicine Experimental 2022, **10(2)**:000820

Introduction: O-GlcNAcylation is a ubiquitous post-translational modification involved in stress response and cell survival. Its stimulation is beneficial in states of shock in murine models (1). Cardiopulmonary bypass (CPB) a mandatory procedure for cardiac surgery share common pathophysiological mechanism with state of shock potentially leading to death. Despite improvements of both materials and techniques over the past decades, the cardiovascular alteration associated with CPB after surgery remain an unsolved problem.
Objectives: Evaluate the impact of (i) CPB on O-GlcNAc levels both in human and rats and (ii) O-GlcNAc stimulation in a rat model of extracorporeal circulation (ECC).
Methods: A biocollection of human blood samples in adults ($n = 36$) and children ($n = 23$) during CPB central venous placement, aortic declamping, 5–6 and 12 h after declamping. After being anesthetized 24 sprague dawley rats were randomly assigned to receive no therapy (Sham), ECC, and ECC supplemented with NButGT to increase O-GlcNAc levels. ECC was maintained for 1 h. Rats were then evaluated 5 h post ECC weaning. Global proteins O-GlcNAcylation levels were evaluated by Western-blot analysis in human and rat blood and myocardium.
Results: In adults and children undergoing cardiac surgery, CPB was associated with an increase in O-GlcNAc levels 6 h (+29% and +27% respectively $p < 0.05$) and 12 h after declamping. ECC model induced multiorgan and metabolic dysfunction in rats with lower mean arterial pressure at H + 5 (Sham: 95 ± 4; ECC: 70 ± 8 mmHg; $p < 0.01$), higher lactate level at H + 5 (Sham: 1.5 ± 0.3; ECC: 3.9 ± 0.9 mmol/L; $p < 0.01$) and higher creatininemia level at H + 5 (Sham: 0.6 ± 0.06; ECC: 1.48 ± 0.15 mg/dL; $p < 0.0001$). Treatment with NButGT induced a restoration of H + 5 mean arterial pressure, behavior and severity score in rats. This was associated with a correction of lactatemia, creatininemia, blood urea nitrogen and pCO2. Comparatively to ECC, treated rats had higher levels of protein O-GlcNAcylation at H + 5 ($p < 0.01$).

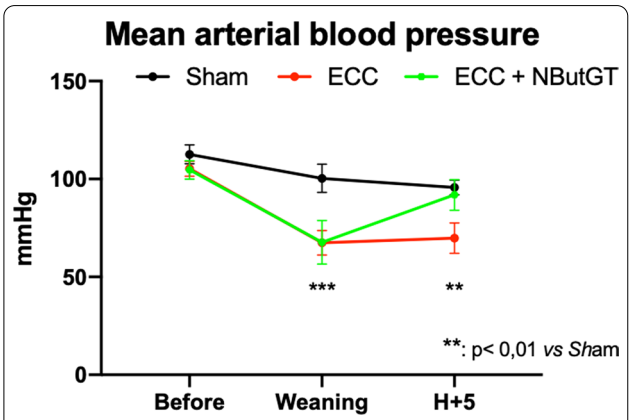

Figure 1: Impact of treatment with NbutGT in rat model of ECC: Mean arterial pressure before ECC, at weaning and at H + 5 after ECC Weaning. Values are presented as mean ± SEM, **p < 0,01 Vs sham; Determined by two ways ANOVA test.

Conclusion: Increase in O-GlcNAc level post ECC in human seems to be a response to stress. Comparison of patient outcome with the evolution of O-GlcNAc level during ECC could be of interest in a larger cohort. Results obtained with O-GlcNAc stimulation in the rat model suggest that the increase in O-GlcNAc level could be a promising strategy for the management of peri-operative period during cardiac surgery in human.

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Cardiovascular Dynamics 4 + Infection 5

001243

Can carotid artery Doppler variations induced by End-expiratory Occlusion manoeuvre predict fluid responsiveness in septic shock patients?

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Intensive Care Medicine Experimental 2022, **10(2)**:001243

Introduction: An increase in cardiac index (CI) during an End-Expiratory Occlusion test (EEOt) predicts fluid responsiveness in septic shock patients admitted to intensive care unit (ICU)[1,2]. However, CI monitoring, which is mandatory to track CI changes, may not always be available. Carotid doppler is a non-invasive, bedside, safe and

easy-to-use ultrasound technique that allows measuring of the systolic peak velocity [3] and the duration of systolic component of each cardiac cycle [4] as surrogates for stroke volume. When invasive cardiac monitoring is not available or when the echocardiographic window is technically difficult, the use of the carotid doppler could be a feasible alternative to track changes in CI.

Objectives: The aim of this study is to investigate whether changes in Carotid Doppler Peak Velocity (CDPV) and in corrected Flow Time (cFT) during an EEOt could predict fluid responsiveness in patients with septic shock ventilated with low tidal volume strategy (6 mL/kg of PBW).

Methods: Prospective, single-center study in adult patients with hemodynamic instability, defined by persisting hypotension requiring fluid administration or vasopressors to maintain a mean arterial pressure of 65 mmHg. The CDPV and cFT on carotid artery doppler and the other hemodynamic parameters using the Pulse Contour Analysis EV1000TM were recorded at baseline, during a 20 s-EEOt and after fluid challenge (500 mL) (Fig 1). Responders were defined as those with an increase in CI ≥ 15% after a fluid challenge.

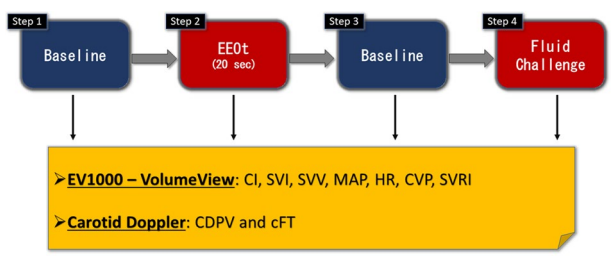

Fig 1. Study protocol

Results: We included 44 measurements on 18 mechanically ventilated ICU patients with septic shock. Fluid responsiveness rate was 43.2%. An increase in CI ≥ 5.35% during EEOt predicted fluid responsiveness with a sensitivity and a specificity of 78.9% and 91.7%, respectively, with an area under ROC curve of 0.85 (p = 0.001). An increase in CDPV ≥ 10.5% during an EEOt predicted fluid responsiveness with 96% specificity and 53% sensitivity with an area under ROC curve of 0.743 (p = 0.006) (Fig 2). The cFT changes during EEOt, instead, did not accurately predict fluid-responsiveness (p = 0.13).

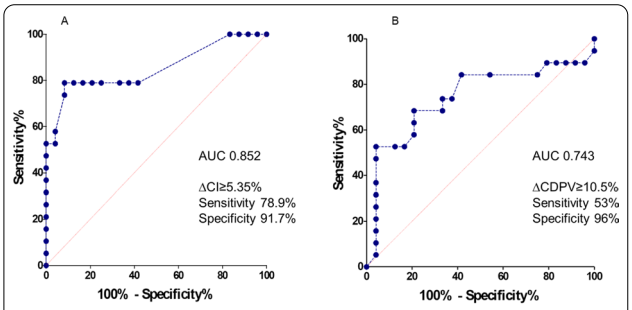

Fig 2 . ROC curve of CI variations (A) and CDPV variations (B) induced by an EEOt in predicting fluid responsiveness.

Conclusion: In adult patients with septic shock and low tidal volume ventilation, an increase in CDPV greater than 10.5% during a 20-s EEOt predicted fluid responsiveness with > 95% specificity and may help optimize preload when invasive hemodynamic monitoring is not available (Clinicaltrials.gov NCT04470856).

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001248

Interpretation and agreement between intensive care unit physicians ability to diagnose atrial fibrillation on single lead ECG traces of critical care patient in the ICU using the MIMIC-III Database

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Intensive Care Medicine Experimental 2022, **10(2)**:001248

Introduction: Atrial fibrillation (AF) affects between 4–14% of all ICU admissions and up to 44% of patients with septic shock [1]. AF with a ventricular response rate can lead to haemodynamic instability, increased ICU and hospital mortality, recurrent AF, and stroke. Despite continuous ECG monitoring, short episodes of AF remain underdiagnosed in critically ill patients [2]. It remains unclear whether a reliable diagnosis of AF is possible using single lead ECGs. In the current study we used 30-s ECG snippets to assess agreement between ICU clinicians' detection of AF.

Methods: A subset of 371 patients from the Medical Information Mart for Intensive Care (MIMIC) III database were used, containing a total count of 603 ECG records. Each ECG record was partitioned into 30-s snippets. A random selection of three snippets were created from each record for assessment by three senior intensivists. Each clinician interpreted 1206 snippets and assigned one of the following diagnostic codes: 'AF', 'Possible AF', 'Sinus Rhythm', 'Other Arrythmia' and 'Uninterpretable'. The primary research objective was to define the interrater variability between diagnostic codes. We implemented a 2/3 validation method with each ECG segment being reviewed independently by 2 clinicians. For disagreement in diagnosis, a final senior cardiologist acted as the tie breaker with the majority vote taking precedent. Cases where three clinicians voted for a different diagnosis were classed as 'Unknown'. Cases where clinicians voted 'AF' and or 'Possible AF' were classified as 'AF'. ECGs which at least one clinicians regarded as 'Uninterpretable', were classified as such, as in real life circumstances the ECG would likely have been discarded and or regenerated.

Results: A total number of 1809 thirty second ECG segments were collected and analysed. We found that only 1,147 (63.41%) of the ECGs had full agreement amongst the 5 class labels, thus over one third of the ECGs needed additional input. When the 'AF' and 'Possible AF' diagnoses were aggregated into one group, agreement between increased to 84.3%. Of the 1809 ECG snippets, 257 (14.21%) were classified as 'AF/Possible AF', 1132 (62.58%) as 'Sinus Rhythm', 217 (12%) as 'Uninterpretable', 169 (9.34%) as 'Other Arrythmia' and 34 (1.88%) as 'Unknown'.

Conclusion: Diagnosis of AF in short 30-s single lead ECG snippets remains challenging in over 15% of cases and may explain why brief episodes of AF (< 30 s) often remain undiagnosed. Classical monitoring devices such as

defibrillators, but also novel patch-based devices or lifestyle gadgets commonly offer single lead ECG monitoring. Interference, patient movement and shivering may impact on ECG quality and hamper readability. 12% of the ECG snippets in our study had inadequate quality for the diagnosis of AF. Further research using diagnostic algorithms based on machine learning is required to address this diagnostic uncertainty.

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001279

Cardiac output using electrical cardiometry correlates with echocardiographic measurments in extracorporeal membrane oxygenation patients

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Intensive Care Medicine Experimental 2022, **10(2)**:001279

Introduction:

- Cardiac output (CO) monitoring is important in patient connected to extracorporeal membrane oxygenation (ECMO) either Veno-Venous (VV) ECMO or veno- arterial (VA) ECMO
- In VV ECMO patient's adequate oxygenation is achieved with ECMO flow above 60% of cardiac output and in VA ECMO patients adequate hemodynamic is maintained with ECMO flow 50–70 ml/kg/min.

Objectives: Validate cardiac output measured by electrical cardiometry (ICON™) using transthoracic echocardiography in patients connected to ECMO (either VA ECMO or VV ECMO).
Methods: CO was estimated using electrical cardiometry (ICON OSYPKA medical, Germany) using bioimbedance technology through 4 electrodes connected to the eft side of the body with good signal quality for accuracy of measurements {signal quality indicator (SQI) ranging from 70 to 100}.

- – Echocardiography measurements were taken using Pulsed Wave (PW) doppler over left ventricular outflow track (LVOT) (2-3 cm away from aortic valve in apical 3 or 5 chamber views) to calculated LVOT Velocity Time Integral (LVOT VTI).
- – Stroke Volume (SV) = LVOT VTI × Cross sectional area (CSA) of LVOT (calculated from parasternal long axis 0.5 cm from aortic valve).
- – CO = SV × Heart Rate (HR)
- – The two measurements were taken at the same time in 10 patients treated with ECMO (6 patients were connected on VV ECMO (675 paired values) and remaining 4 patients on VA ECMO (343 paired values)
- – In VV ECMO patients, CO calculated by echocardiography and estimated by ICON equal native CO
- – While CO estimated by ICON in VA ECMO patients equals native CO measured by echocardiography and ECMO flow

Results: There were significant correlations between cardiac output estimated using ICON compared to echocardiography in both patients connected to VV (4.8 to 12.7 L/min with mean 8.97 L/min ± 2.1 Vs 4.6 to 12.4 L/min with mean 8.42 L/min ± 1.84 by echocardiography) and VA ECMO (4.3.61 to 8.46 L/min with mean 8.535 L/minute ± 1.13 Vs 4.01 to 7.25 L/minute with mean 5.2 L/min ± 0.72 by echocardiography) (**r = 0.915 and 0.808 for VV and VA respectively) (p < 0.001**). Intraclass Correlation coefficient and Cronbach's Alpha analysis were used to assess the agreement between the two measurements and there was a statistically significant agreement (**P value > 0.001**).
Conclusion: ICON is a valuable noninvasive and continuous tool for the assessment of cardiac output in patients supported with ECMO.

001318

Deep vein occlusion and its detrimental effect on hemodynamics are only reversible over time

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Intensive Care Medicine Experimental 2022, **10(2)**:001318

Introduction: Coagulation abnormalities linked to increased inflammation and septic shock enhance the formation of deep vein thrombosis, which increases morbidity and mortality in critical conditions. [1].
Objectives: The goal of this research was to investigate in a long term the macro and microhemodynamic adaptations in animals submitted to acute occlusion of the deep femoral vein.
Methods: Under general anesthesia, 3-month-old female Wistar rats were subjected to a deep femoral vein obstruction and monitored for the flow of veins and arteries, proximal and distal to the site of obstruction (Transonic System Inc. TS420 transit-time perivascular flowmeter). The microcirculation was observed by videomicroscopy and the tissue perfusion by Laser Doppler. The animals were monitored at 60 min, 7, 30, and 90 days after occlusion. As a control, the contralateral limb was used.
Results: There was an immediate and significant reduction in the volume of flow in the veins both above and below the point of occlusion, with no total recovery of venous drainage until 90 days after the procedure. Tissue perfusion distal to the obstruction and the microcirculatory density were reduced partially during the study period, and the recovery was just at 90 days period. The arterial flow of the occluded limb likewise showed a drop, with complete recovery in 90 days. There were no observed alterations in macrocirculation or tissue perfusion in the contralateral limb, but the microcirculatory vascular density showed a mild reduction.
Conclusion: Deep venous thrombosis causes long-term hypoflow in both the vein and the artery in healthy animals, indicating the importance of long-term monitoring of flow. This process can be exacerbated in critical illness because macro and microvascular damage are common occurrences and can further impede the recovery process.

Acknowledgements: FAPESP - Fundação de Amparo à Pesquisa do Estado de São Paulo. Processo 2017/21052-0.

001427

Pulmonary arterial cannulation in Veno-pulmonary-arterial ECMO compared to Protek Duo with an oxygenator in patients with acute right ventricular failure requiring mechanical circulatory support

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Intensive Care Medicine Experimental 2022, **10(2)**:001427

Introduction: Right ventricular [RV] failure [RVF] is a major cause of morbidity and mortality with complex pathophysiology of

several etiologies that would change its outcomes and management options. Causes include ARDS, pulmonary hypertension, LVAD placement, myocarditis, myocardial infarction, valvulopathy, amongst others [1]. Now data is proving a higher prevalence of RV dysfunction amongst COVID paitents making this poor clinical outcome in need of even a wider discussion regarding the available supportive interventions [2]. Poorer clinical outcomes has been proved extensively regardless of RVF cause [3–6]. Medical interventions focuses on optimizing preload, contractility, RV afterload, maintenance of atrioventricular synchrony, and fixing the underlying cause. It is not uncommon for RVF to be refractory to medical treatments necessitating mechanical circulatory support [MCS]. Different right ventricular assist devices [RVAD] are available with extracorporeal membrane oxygenation [ECMO] or sole circulatory support with centrifugal pumps amongst others. ECMO has significantly developed its cannulation modalities to mitigate the many possible negative effects such as bleeding, organ failures, secondary infections, pathlogical hemodynamic syndromes, and death. RV support by accessing the pulmonary artery [PA] is not new [7], but it is becoming more prevalent in the last few years, especially peripherally. Most commonly, accessing the PA was done through a separate cannulation in conjunction with another femoral vein inflow access in the Veno-pulmonary-arterial [VPa] strategy. One of the newer strategies is the use of single cannulation site with the Protek Duo device. Protek Duo is a novel veno-venous percutaneous cannula-within-a-cannula RVAD. First used in 2016 [8], it utilizes a single venous access through the right internal jugular vein with two ports, inflow from the right atrium, and outflow to the PA [9]. Addition of an oxygenator is possible. Its theoretical advantage stems from its singular access site avoiding the additional cannulation site of the conventional VV ECMO and what would ensue of lesser chances of bleeding, thrombosis, and infection [10]. It is a minimally invasive implantation technique sparing surgical cannulations, further re-sternotomies, and is groin-free leaving the area accessible for further future interventions if needed [10]. It provides easier and earlier post-op mobilization reducing the chance of many possible unfavorable outcomes [10]. Despite these theoritcal advantages over other ECMO techniques, we continue to have paucity of data to support them.

Objectives: The first reported case control study to compare the conventional VPa ECMO with the use of Protek Duo amongst patients with medically refractory RVF requiring MCS.

Methods: Retrospective case–control study in a single tertiary care center of 24 RVF patients from 1/1/2017 to 12/31/2021. Cases are 12 who underwent VPa ECMO while controls are 12 who underwent Protek Duo with an oxygenator. Primary outcomes are mortality and hospital discharge. Secondary outcomes are length to discontinue MCS, length of ICU and hospital stays, bleeding, thrombotic events, hemolysis, secondary infections, organ functions.

Results: During the study period, cases were12 RVF patients [83% men; 67% African Americans; mean age 58 ± 22; mean SOFA score of 9 ± 7; mean APACHE II score of 24 ± 18] received MCS with VPa ECMO. Controls were 12 patients [83% men; 50% African American; mean age 53 ± 19; mean SOFA score of 12 ± 6; mean APACHE II score of 24 ± 10] who received MCS with Protek Duo with an oxygenator. MCS was peripheral. Etiology of RVF ranged from post LVAD insertion to ischemia/Infarction to ARDS and others. 6 patients survived their hospitalization and were discharged amongst the VPa group [50%] while only 4 patients survived and discharged amongst the Protek Duo group [33%]. Amongst those on VPa ECMO their mean length of MCS was 10 ± 4 days, while those on Protek Duo they were decannulated was 7 ± 3.

Conclusion: Despite the proposed advantages of Protek Duo MCS over the use of 2 cannulation sites, our study failed to prove better survivability amongst those who received it. This proves yet again the complexity and high mortality rates amongst patients with medically refractory RVF despite the development of novel MCS techniques and devices. We continue to need larger data for a more accurate assessment of outcomes.

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001431

Calculation of beat-to-beat right ventricular ejection fraction from continuous measured right ventricular pressures

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Intensive Care Medicine Experimental 2022, **10(2)**:001431

Introduction: In addition to right ventricular and estimated pulmonary arterial diastolic pressures we evaluated right ventricular ejection fraction and diastolic relaxation time Tau for up to 30 days from continuously measured right ventricular pressures in mechanically ventilated patients with severe COVID-19 ARDS.

Methods: We retrospectively calculated beat-to-beat ejection fraction from continuously recorded right ventricular pressures and dp/dt maximum and minimum in 39 invasively ventilated COVID-19 ARDS patients treated between October 1st 2020 and June 30st 2021. We first performed a stepwise logistic regression with survival as independent variable. Thereafter we divided the patients into two groups, survivors and non survivors based on their 60-day mortality. Primary outcome variables were the values of right ventricular ejection fraction (RVEF) and right ventricular diastolic isovolumetric relaxation time Tau over time after insertion of the right ventricular probe. Secondary outcome variables were right ventricular systolic and diastolic (RVSP; RVDP) pressures and ePAD as described previously.

Results: RVEF increased significantly over time in the survivors (estimate: 0,354; 95% CI: 0,18–0,53; $p < 0,001$). In contrast, RVEF in the non survivors remained unchanged. TAU increased significantly in the non survivors (estimate: 0,001; 95% CI: 0,0004 – 0,0018; $p < 0,002$) but not in the survivors. At the last measurement day RVSP and ePAD were

significantly lower while RVEF was significantly higher in the survivors compared to the non survivors.
Conclusion: In surviving COVID-19 ARDS patients calculation of beat-to-beat RVEF and Tau from continuously measured right ventricular pressures unravelled early contrary trends in RVEF with an increase in the surviving and a decrease in the non-surviving patients. Tau remained unchanged in the surviving but increased in the non-surviving patients over time.

000313

The predictive value of the modified early warning score for ICU admission in patients with a hematologic malignancy – a multicenter observational study

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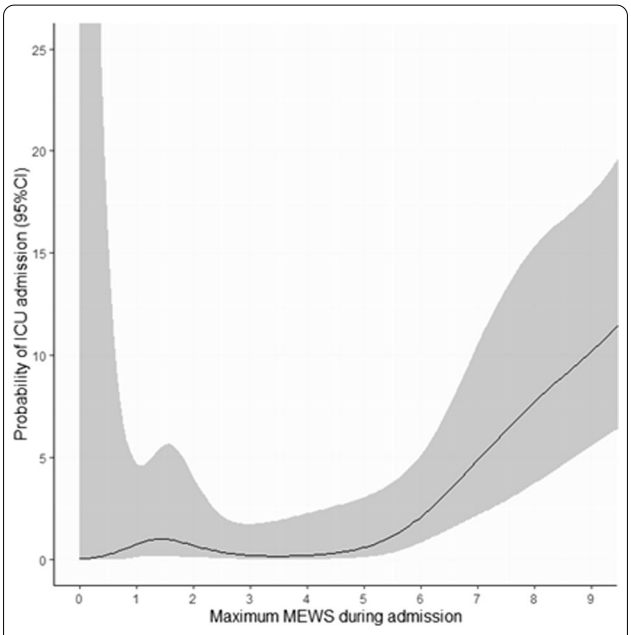
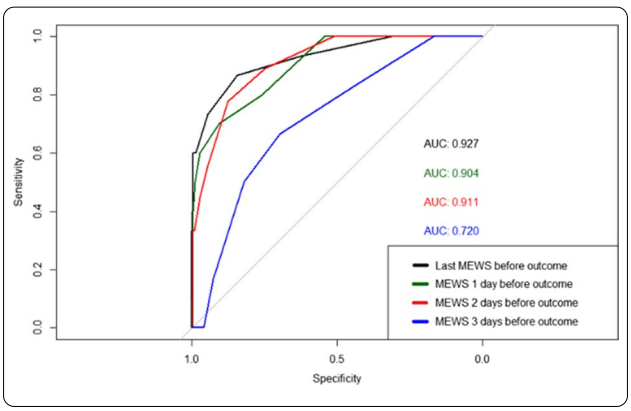
Intensive Care Medicine Experimental 2022, **10(2)**:000313

Introduction: Timely identification of hemato-oncologic patients with an increased risk for clinical deterioration and intensive care unit (ICU) admission has proven to be difficult [1]. Patients with a hematologic malignancy have a high risk to develop infectious and other disease and chemotherapy related complications, hereby these patients have an increased risk of ICU admission [2–5]. Once admitted to the ICU, mortality rates are high [6]. Early recognition of clinical deterioration and timely ICU admission are associated with better outcome [7,8]. The modified early warning score (MEWS) is used to detect clinical deterioration of hospitalized patients [9]. MEWS thresholds for intervention differ between hospitals and patient populations, with conflicting reports about its potential to predict outcomes [10].
Objectives: Our objective was to investigate the predictive value of the MEWS for ICU admission in patients with hematologic malignancies admitted to the ward.
Methods: We performed a multicenter, retrospective, observational cohort study. Data were collected in two university hospitals in The Netherlands between January 1, 2018 and January 1, 2020. All adult patients with a previous or active diagnosis of a hematologic malignancy admitted to the ward were included. We studied the value of the highest MEWS during admission, the largest increase in MEWS in 24 h and MEWS 3 days prior to ICU admission (vs. discharge or death) as predictors of ICU admission. Restricted cubic spline, logistic regression and area under the receiver operating characteristic (AUROC) analyses were performed.
Results: We included 395 patients with 736 hospital admissions; 2% of admissions resulted in ICU admission. A higher MEWS (OR 1.5 (95% CI: 1.3–1.8) and a larger increase in MEWS (OR 1.4 (95% CI: 1.1–1.8)) were associated with ICU admission. To assess the relationship between the highest MEWS during ward admission and the probability of ICU admission, we built a restricted cubic splines model (Figure 1). An evident rise in the probability of ICU admission for MEWS values ≥ 6 was observed. Compared to patients with MEWS < 6, patients with MEWS ≥ 6 had an OR of 22.6 (95% CI: 5.1–101.2) for ICU admission.
The AUROC of MEWS for predicting ICU admission was 0.830. For MEWS ≥ 3, sensitivity was 87% with a specificity of 41% for ICU admission, whereas for MEWS ≥ 6, sensitivity was 87% with a specificity of 78%. The AUROCs in Figure 2 show that MEWS was predictive for ICU admission up to 3 days prior to outcome.



Figures 1 & 2



Conclusion: In this retrospective cohort study, MEWS was a sensitive predictor of hemato-oncology patients at risk for ICU admission. As the specificity for ICU admission increased for a higher MEWS, while sensitivity was preserved, a higher threshold for intervention may be appropriate. Future studies should focus on confirmation of the thresholds and potential additional characteristics, to further enhance identification of the critically ill patient with a hemato-oncological malignancy.

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000611

Use of an innovative cuff pressure control and subglottic secretions drainage system in COVID-19 ARDS patients undergoing pronation

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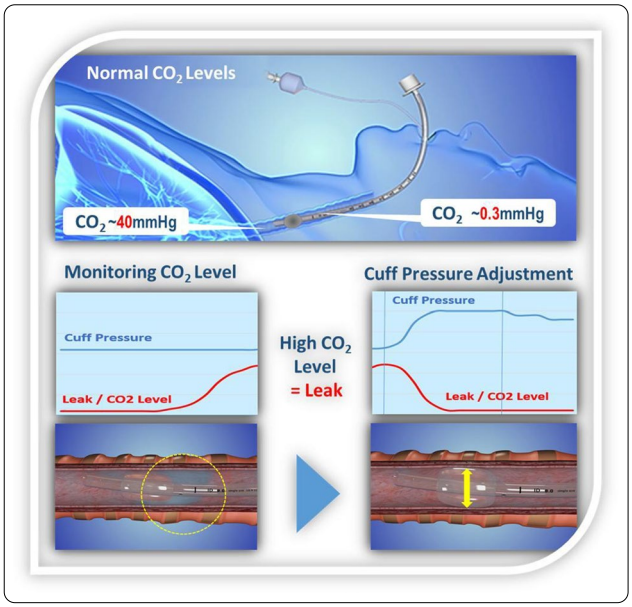
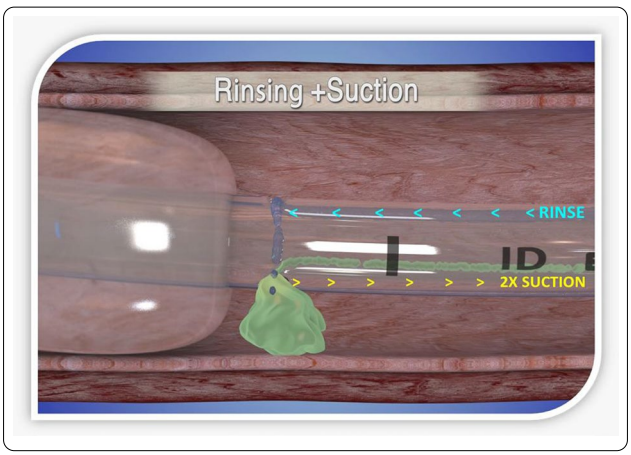
Introduction: Endotracheal tube (ET) cuff pressure (Pcuff) control and subglottic secretions drainage (SSD) are key factors for the prevention of microaspiration and ventilator associated pneumonia (VAP).
Objectives: An observational study to describe microaspiration in patients with Coronavirus disease 2019 (COVID-19) induced Acute Respiratory Distress Syndrome (ARDS) managed with a new Pcuff control and SSD system.
Methods: 15 patients with COVID-19 induced ARDS were intubated with AnapnoGuard (AG) ETs and connected to the AG 100 control unit (Hospitech Respiration LTD). The AG 100 system provides continuous ET Pcuff regulation, detecting air leakage trough the cuff by measuring the carbon dioxide (CO2) level in the subglottic space. Additionally, it evacuates SS with dual suction lines and an extra venting line. Alpha-amylase and pepsin levels were detected from tracheal aspirates (TA) collected in the first 72 h after connection to the AG 100 system.
Results: Among 15 patients, 80% were male; median age, SAPS II and SOFA score were 65 [56–76], 35 [29–44], 4 [4–4], respectively. Main airway management and microaspiration details are described in Table 1. Baseline characteristics of patients and results are shown in Table 1. Alpha-amylase and pepsin were measured in 85 (100%) and 75 (88%) TA, respectively. The median number of tracheal samplings was 6 [4;7] per patient. Pcuff values were stable between 25 and 30 mmHg with a median volume of daily SS drainage of 31 ml. Oropharyngeal microaspiration (alpha-amylase value > 1685 UI/l) was diagnosed in 47 TA (55%) and in nine patients (60%) abundant microaspiration was detected (> 30% with alpha-amylase > 1685 UI/l). Conversely no tracheal secretions samplings showed evidence of gastric microaspiration (pepsin > 200 ng/ml), not even patients with abundant events (> 30% of TA with pepsin > 200 ng/ml). There was no correlation between prone positioning and median alpha-amylase levels (1973 UI/l [1159–2983] in 25 TA during pronation vs. 1899 [1092.75–3156.25 UI/L] in 60 TA in supine position; p = 0.85). The incidence of VAP was 40%, with a median mechanical ventilation time to infection of 8.5 days [7.25–9.75]. Stridor after extubation was observed in two patients. No ET misplacements occurred.





Ventilation and airway management

AG connection (days)	7 [5–10]
Pronations per patient (n)	4 [2–5]
Daily ET Pcuff (cmH2O)	27,3 [1, 8–8]
SS volume per patient	170 [150–275]
SS volume per day	31 [5–37]

Microaspiration and outcome

alpha-amylase level (UI/L)	1905 [1132–3145]
Oropharyngeal microaspiration(n)	47 (55)
Pepsin level (ng/mL)	7,8 [7–21, 45]
Gastric microaspiration (n)	0 (0)
VAP (n)	6 (40)
28-day mortality (n)	4 (27)

* Categorical variables are expressed in count and percentage; continuous variables are expressed in median and interquartile range.
Conclusion: The use of AG 100 system has provided effective Pcuff control and SSD in COVID-19 ARDS patients undergoing pronation. Oropharyngeal and gastric microaspiration rates were lower than

reported with standard ETs. The application of this new technology as a tool for VAP prevention deserves further investigations.

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000833

Minocycline as combination therapy for critically-ill patients with difficult to treat Acinetobacter baumannii ventilator-associated pneumonia

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Intensive Care Medicine Experimental 2022, **10(2)**:000833

Introduction: The prevalence of multidrug resistant (MDR) *Acinetobacter baumanni* (*A. baumannii*) isolates is increasing and treatment options for multidrug resistant *A. baumannii* are limited. The lack of new effective antimicrobial agents has led to reintroduction of old antibiotics like minocycline for the treatment of MDR *A.baumannii.*
Objectives: Our objective was to evaluate the effectiveness of minocycline for the treatment of patients with extensively drug (XDR) and pandrug (PDR) resistant *A.baumannii* ventilator-associated pneumonia (VAP).
Methods: We conducted a retrospective chart review of ICU patients between September 2021 and March 2022. Patients with a diagnosis of VAP due to XDR or PDR *A.baumannii* that had received combination therapy with minocycline were included. Data such as demographics, comorbidities and duration of treatment with minocycline were recorded. Clinical and laboratory data (fever, haemodynamic instability, PaO2/FIO2 ratio, WBC count, CRP, procalcitonin) and cultures of endotracheal aspirates (ETSA) were assessed at the start and after completion of treatment. Minocycline was administered via nasogastric tube at a loading dose of 200 mg followed by 100 mg every 12 h. The primary outcomes were clinical improvement defined as recession of infection and increase of PaO2/FIO2 ratio and microbiological response defined as no, rare or light bacterial growth in ETSA.
Results: Eleven patients (7 males) with a mean age of 70.9 years and a diagnosis of VAP due to XDR or PDR *A.baumannii* were included. All patients had documented severe COVID-19 infection as a primary diagnosis upon ICU admission. Three *A. baumannii* isolates were susceptible (MIC < 4 μg/ml), while 8 had an intermediate susceptibility (MIC 8 μg/ml) to minocycline. The mean duration of hospitalization before VAP was 12 days and the mean duration of treatment with minocycline was 8.5 days. Minocycline was combined with meropenem and/or colistin. All patients had impaired blood gas exchange with a mean PaO2/FiO2 ratio of 96. Six patients had fever and 8 were under vasopressors. Upon completion of treatment PaO2/FIO2 ratio was improved in 9 patients with a mean ratio of 143.6. Remission of fever was noted in all febrile patients (100%) and in 5 out of 8 (63%) hemodynamically unstable patients, noradrenaline was tapered or stopped. ETSA cultures after completion of treatment were available in 10 patients. *A.baumannii* was isolated at rare or light growth in 8 (73%) and was eradicated in 1 patient. Twenty-eight-day mortality was 45% (5 out of 11 patients). However, in only one patient mortality was attributed to *A.baumannii* pneumonia.
Conclusion: The role of minocycline for difficult to treat *A.baumannii* infections needs further exploration. The limited evidence from this study suggests that minocycline might be effective as combination therapy for the treatment of XDR and PDR *A.baumannii* pneumonia. The favourable tissue penetration safety profile and the relative low cost make minocycline an attractive therapeutic option.

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Acknowledgements: None.

000238

Factors related to in-ICU acquired infection in critically ill CoVID-19 patients. Data from the ENVIN-HELICS registry

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Introduction: There is a lack of scientific evidence when it comes to the factors that made the COVID19 patients acquire more in-ICU infections than other respiratory critically ill patients, more specifically relating inmunomodulatung treatments.
Objectives: To determine the pharmacological agents and other factors related to in-ICU infection acquirement in CoVID19 critically ill patients.
Methods: Data from the ENVIN-HELICS registry was used, gathering all CoVID19 patients registered from 2020 to 2021. The registry is voluntary, prospective and multicentric. The studied infections were ventilator-associated pneumonia (VAP), catheter related urinary tract infection (c-UTI), catheter related bloodstream infection (c-BI), which included unknown origin BI, and secondary BI. The analyzed variables were related to demographics, comorbidities, evolution and drugs used for immunomodulation during SARS-CoV2 infection. The univariant analysis was made by Chi square and U-Mann Whitney. The association was measured by binary logistical regression. The Hosmer Lemeshow test and graphical residual analysis were used to measure goodness to fit. Statistical significance p > 0,05. Software R4.1 and SPSS25.
Results: A total of 11,114 patients were studied in 182 ICU all over Spain. 69.1% were male, median age of 62 (IQR 53–70) years old and an APACHEII score of 13 (IQR 9–17) points. 4470 patients (40.2%) developed one or more bacterial infection (891 infections in total). Mortality of 28,5%. In the multivariant analysis the following variables were related to the acquirement of any of the in-ICU infections: male gender, OR 1.2 (CI95% 1.1–1.3); age (50–59 years, OR 1.3, CI95% 1.1–1.4; 60–69 years, OR 1.6, CI95% 1.4–1.8; over 69 years old OR 1.4, CI95% 1.3–1.6); APACHE II (minus age) score (11–15 points, OR 1.4, CI95% 1.2–1.5; 16–20 points, OR 1.8, CI95% 1.6–2.0; over 20 points, OR 1.8, CI95% 1.6–2.0); history of cirrhosis, OR 1.7 (CI95% 1.1–2.7); treatment with corticoids at any dose (low dosage OR 1.3, CI95% 1.2–1.6; medium dosage OR1.2, CI95% 1.0–1.4; high dosage OR 1.6, CI95% 1.3–1.8);

interferon OR 1.2 (IC 1.0–1.5); infusion of hyperimmune plasma, OR 1.6 (CI95% 1.2–2.0). Goodness to fit of 0.75.
Conclusion: In critically ill CoVID19 patients, gender, age, severity at admission, history of cirrhosis and treatment with corticoids, interferon or hyperimmune plasma were related to the acquirement of in-ICU infections.

Acknowledgements: Spanish Agency of Medicines and Medical Devices (Ministry of Health). File number: 2021/48603/001.

Cardiovascular Dynamics 5

000851

Noradrenaline requirements increases in the presence of systemic acidemia

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Intensive Care Medicine Experimental 2022, **10(2)**:000851

Introduction: Acidemia is associated with reduced cardiovascular function in humans. At the same time, there is extensive "in vitro" evidence that acidemia results in altered vasoreactivity, studies investigating the effect of abnormally low pH on the vasopressor requirements in humans have not been reported to date.
Objectives: In the present study, we examined the effect of systemic acidemia on vasopressor requirements.
Methods: This was a prospective multicenter observational cross-sectional study of 297 patients from 6 intensive care units in London, England admitted consecutively between May 2018 and March 2019. We measured various cardiac indices using PiCCO at the lowest plasma pH and concurrently recorded vasopressor requirements and hemodynamic parameters in all eligible patients.
Results: An adjusted logistic regression analysis showed that there is an inverse association between pH and the duration of vasopressor administration (coefficient -55 h, 95% CI -94 to -16; $p = 0.06$), a direct relationship between pH and the dosage requirement of vasoactive drugs with significant values for noradrenaline vasopressin/terlipressin ($p < 0.001$). Additionally, patients with the most severe acidosis received more renal replacement therapy and bicarbonate. In our cohort, the mortality at 28 da was 60.3% among patients in the low pH category (< 7.28) and 25.4% in those included in the higher pH group (> 7.28).
Conclusion: Acidemia is associated with an increase in the requirements for vasopressors in patients admitted to intensive care. These results support an early diagnosis of acid–base abnormalities and a rapid normalization of arterial pH in these patients.

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Acknowledgements: The study was partially supported by unrestricted funds from the UCLA School of Medicine. No other financial support, including any institutional departmental funds, was sought for the study. The authors received no specific funding for this work.

000862

Physiological changes after fluid bolus therapy in cardiac surgery patients: a matched case–control study

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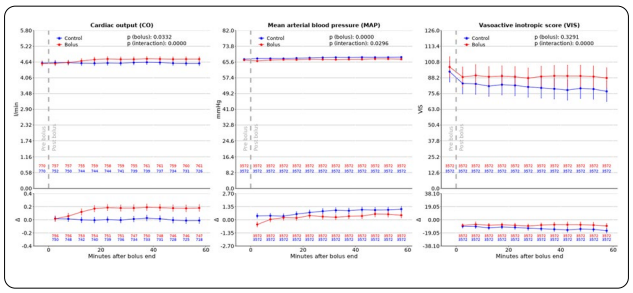
Intensive Care Medicine Experimental 2022, **10(2)**:000862

Introduction: Fluid bolus therapy (FBT) is ubiquitous in intensive care units (ICUs) after cardiac surgery. However, its physiological effects remain unclear [1–3]. A positive response to a fluid bolus (FB) is commonly defined as an increase in cardiac output (CO) by > 10–15%. However, many clinicians also consider an increase in mean arterial pressure (MAP), urinary output, or decrease in blood lactate levels a positive response[4]. Despite its common use, granular data on the physiological effects of FBT in ICU patients are scarce and are limited to the period immediately following a FB [2] and the effect appears to dissipate within minutes [5, 6]. On the other hand, FBT is responsible for a large proportion of the positive fluid balance seen in patients after cardiac surgery [7], which has been associated with increased mortality and higher hospital costs [8].
Objectives: We sought to evaluate the physiological changes associated FBT in patients after cardiac surgery using a large, granular dataset from Electronic Health Records (EHR) of a tertiary academic ICU.
Methods: We performed an electronic health record-based quasi-experimental ICU study after cardiac surgery. We applied propensity score matching and compared the physiological changes within 60 min after FBT episodes to matched control episodes with no FB administration. We defined a FB as the continuous administration of ≥ 250 ml Ringer's Lactate within ≤ 30 min. Control episodes were time epochs preceded by similar hemodynamic baseline characteristics but without fluid administration. Primary variables of interest included CO, Stroke volume (SV), MAP, and vasoactive-inotropic score (VIS) [9]. Secondary outcomes included changes in metabolic variables.
Results: We studied 2,736 patients and 3,572 matched fluid boluses. After FBT, but not in control episodes, CO increased within 10 min, with a maximum increase of 0.2 l/min (95%CI 0.1 to 0.2) or 4% above

baseline after 40 min ($p < 0.0001$ vs. controls) driven by increased SV with a maximum increase of 2.3 ml (95%CI 1.78 to 2.77) above baseline while SV remained unchanged in controls. In contrast, MAP decreased within 5 min after FBT by 0.5 mmHg (95%CI 0.2 to 0.7) and returned to baseline after 10 min compared with a 1.1 mmHg (95%CI 0.8 to 1.4) increase in controls ($p < 0.0001$). The VIS decreased by 9.0 units (95%CI 6.3 to 11.6) after FBT compared with 15.8 units (95%CI 12.5 to 19.1) in controls. FBT did not change acid–base status or oxygen delivery.



Conclusion: In this quasi-experimental comparative ICU study in cardiac surgery patients, FBT episodes were associated with statistically significant but numerically small increases in CO and SV, did not lead to any detectable increase in MAP, and did not affect the acid–base status or oxygen delivery. These findings suggest the need to conduct prospective studies to more clearly define optimal patient selection for the role of FBT in patients after cardiac surgery.

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000901

Change of Strong Ion Gap in the First Six Hours of Intensive Care Admission as a Predictor of Mortality

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Intensive Care Medicine Experimental 2022, **10(2)**:000901

Introduction: Acid–base analysis is a cornerstone in the treatment of critical care patients, and various approaches have been tried, among which the Stewart's physiochemical model stands out. Unmeasured anions, through the measurement of the strong ion gap (SIG), could help guide the management of patients with acid base disorders.
Objectives: To determine the predictive value for mortality of the change in the strong ion gap between two blood gas measurements in the first six hours of the treatment of hospitalized patients in the intensive care unit.
Methods: 146 hospitalized patients from two intensive care units in Colombia with surgical or medical pathologies were included. All patients underwent arterial and venous samples for blood gas analysis upon admission and six hours later, and measurements of acid base variables of the Stewart's model were performed. A logistic regression model was done to identify predictor variables of mortality. Difference in means were evaluated with Student's t test.
Results: We found an average age of 61.5 years with 67.12% men, average APACHE II of 10.68 and SOFA score of 5.28. Mortality was 13.38%. Average SIG at admission 12.8. We found a significant difference in the change of the SIG between survivors and non-survivors, with a decrease in survivors and an increase in non-survivors. (-1.03 vs 1.61, $p = 0.03$). This difference is maintained when lactate is removed from the calculation of the SIG. (-0.74 vs 3.43, $p = 0.0028$). Mortality in patients with less than 10% decrease in initial SIG was 18.92% compared with 7.35% in patients with more than 10% decrease in such value ($p = 0.043$). The decrease in the SIG of less than 10% of the initial value in the first six hours was associated with an increase in mortality in the logistic regression analysis with an OR:6.6 (IC95%:1.24–38, $p = 0.02$) and OR:9.68 (IC95%:1.22–76.4, $p = 0.03$) when lactate is removed from calculation of SIG.
Conclusion: The change in SIG in the first six hours of admission to the intensive care unit is a useful predictor, with a decrease of less than 10% of the initial value associated with an increase in mortality of critical care patients.

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Acknowledgements: Universidad Surcolombiana.

000924

Continuous Stroke Volume (SV) Changes but not Thoracic Fluid Content (TFC) Predict Dynamic Fluid Responsiveness during the Initial Resuscitation of Shock Patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000924

Introduction: Fluid resuscitation is a central component of septic shock treatment but is associated with adverse effects including pulmonary edema. We previously reported that *increasing* thoracic fluid content (TFC) was predictive of subsequent passive-leg raising (PLR)-guided non-invasive stroke volume (SV) responsiveness $\geq$ 10% (ATS 2022) in a prospective septic shock RCT (FRESH, CHEST 2020). It is unknown if this association exists in patients resuscitated for undifferentiated shock under usual care conditions.
Objectives: We hypothesized that Starling derived SV and TFC measurements from 30 min before a PLR or bolus challenge would predict ΔSV fluid responsiveness (ΔSVI $\geq$ 10%) during initial resuscitation of septic and undifferentiated shock.

Methods: Patients in the FRESH intervention arm were assessed for fluid responsiveness before any fluid bolus or increase in vasopressors. Additional patients monitored in a prospective observational study (FRESH-ER) from initial presentation to an ER with undifferentiated[SJ1] shock were included. Non-invasive SV (Starling Monitor ®) was derived from bioreactance signals. Bioimpedance signals are also recorded and are a sensitive reflection of changes in thoracic fluid content (TFC) that correlates with net fluid balance. 30 min of continuous TFC, SV and CO data were isolated from immediately prior to each PLR challenge or crystalloid fluid resuscitation bolus (500 mL). A subsequent challenge-induced SV index (ΔSVI) ≥ 10% was considered fluid responsive and ΔSVI < 10% was considered fluid non-responsive.
Results: Pre and post challenge hemodynamics, PLR and fluid bolus responses were included from 83 FRESH interventions arm patients and 30 FRESH-ER patients, N = 113. Patients (768 challenges) were not fluid responsive (ΔSVI < 10%) in 497 (63.2%) measurements, and responsive (ΔSVI > 10%) in 289 (36.8%). A Boosted Regression Tree was trained on 85 randomly selected subjects and tested on the remaining 28. The model detected fluid non-responsiveness with Sensitivity 67%, Specificity 44% Accuracy 61% (MATLAB 2018b).
Conclusion: In undifferentiated shock pre-bolus trending in CI and SV were moderately accurate in predicting the response to a subsequent challenge-induced SV index (ΔSVI). When combined with undifferentiated shock patients TFC trends amongst septic shock patients were no longer predictive of subsequent PLR-induced ΔSVI ≥ 10%. This highlights that trending SV and CO alone are insufficient to predict dynamic fluid-responsiveness to establish preload effectiveness during the initial resuscitation of undifferentiated shock. Concomitant ΔSVI and TFC measurement could enhance personalized shock resuscitation.

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Acknowledgements: Baxter International, Inc. Unrestricted grant to Denver Health Medical Center, Denver CO.

000947

Breath-dependent changes in the ratio between pressure and pulse wave transit time in the pulmonary artery as a function of heart lung interaction

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Intensive Care Medicine Experimental 2022, **10(2)**:000947

Introduction: Pulse wave transit time (PWTT) was described as a surrogate of systemic and pulmonary arterial pressure (Solà et al., 2009, Proença et al., 2017). In a previous animal experiment, we demonstrated a negative linear relationship between pulmonary arterial pressure (PAP) and PWTT in a model of thromboxane A2- and hypoxia-induced pulmonary hypertension (Müller-Graf et al., 2021). Pulmonary perfusion under non-hypoxic conditions is affected by the relation between alveolar, pulmonary artery and pulmonary venous pressures, characterized as West zones I-III (West et al., 1964). Whether the influence of mechanical ventilation, resulting in a relative rise of less perfused West Zone I and II during inspiration, contributes to changes in PWTT is yet unknown.

Objectives: We aimed to investigate whether fluctuations of PWTT in the pulmonary artery occur under resting conditions within the ventilation-induced changes in PAP.
Methods: Five anesthetized and mechanically ventilated pigs (24.4–48.3 kg) were studied. In order to assess PWTT we positioned in each animal besides a standard pulmonary artery catheter additionally two Millar microtip catheters: one directly behind the pulmonary valve, and the second in a distal branch of the pulmonary artery. All signals were synchronously registered using a dedicated multi-channel platform at a sampling rate of 20 kHz. The arrival of the pulse wave at each catheter tip was determined using a MATLAB-based hyperbolic tangent algorithm for each heartbeat. PWTT was then calculated as the time interval between the arrival times at the two microtip catheters. Data assessment was performed for each animal during continuous ventilation (strictly standardized pressure-controlled ventilation, I:E ratio 1:2, respiratory rate 12/min, and Pinsp for tidal volume of 6 ml/kg) and periods of expiratory apnea.

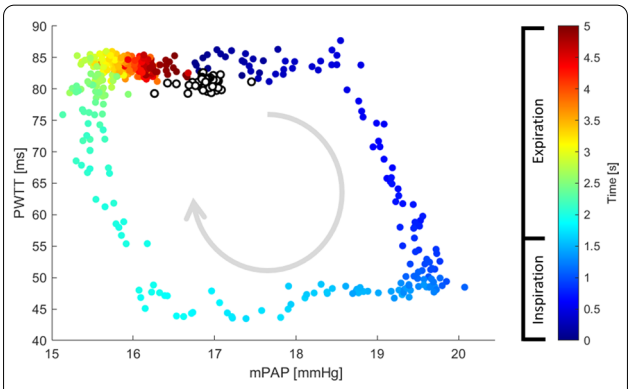

Figure 1: Relationship between PWTT and mPAP with colored dots representing the time of each heartbeat within the respiratory cycle (absolute time and phase of respiratory cycle on the right). Apnea (black open circles).

Results: Ventilation-dependent changes in were seen in both variables, PWTT and PAP. But interestingly, the changes in PWTT were not synchronous with the ones of the PAP. Thus, plotting PWTT as a function of PAP for each heartbeat revealed a characteristic hysteresis (Figure 1, filled dots). Visualizing the respective timepoint of each heartbeat within the respiratory cycle by a color gradient from blue (inspiration) to red (expiration) allowed identifying the dependency of PWTT on both, PAP and the timepoint within the respiratory cycle: at the beginning of inspiration, mPAP rised while PWTT initially remained constant, but then started to decrease rapidly when mPAP was about to reach its plateau. The same time course could be observed during expiration: mPAP decreased to a minimum, which was followed by an increase in PWTT. During apnea this hysteresis disappeared (black open circles).
Conclusion: Changes in PWTT and PAP occur at different times within the ventilatory cycle. The assumed inspiratory increase in West's zones I and II resulted in smaller vessel diameters and in a reduced transcapillary pressure which might explain the inspiratory shortening of PWTT, which occurred delayed compared to the inspiratory rise in PAP. These findings provide novel insights into the mechanisms of heart–lung interaction which warrant further explorations.

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000954

Time for restauration of radial arterial pressure after a transient arm vascular occlusion may reflect vascular reactivity and correlate with outcome in critically ill patients: preliminary results of an observational study

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Introduction: Septic shock is characterized by an impairment of vascular reactivity and an impaired vascular reactivity is associated with a poor outcome in critically ill patients, as assessed by the resaturation slope of the muscular tissue oxygen saturation after a transient vascular occlusion (TVO). Another means for assessing vascular reactivity might be to observe the time of the increase in radial arterial pressure after a TVO at the arm level.
Methods: In mechanically ventilated patients hospitalized in intensive care equipped with a radial artery catheter, a brachial cuff was rapidly inflated to induce a transient arterial stop-flow. Arterial pressure decreased down to the level of mean systemic pressure (PMSarm). After 60 s of occlusion, the cuff was deflated and time to return from Pmsarm to baseline arterial pressure was measured (Trevasc).
Results: We included 45 patients, among whom 31 (69%) where in shock, including 15 (33%) septic shock, 17 (38%) had acute respiratory distress syndrome and 10 (22%) were intubated for neurological impairment. Norepinephrine was infused at a dosage of 0.33 (0.18–1.11) µg/kg/min in patients with shock. Measurements were obtained 3 (1–6) days after onset of mechanical ventilation or vasopressors infusion. Mean arterial pressure was 83 ± 12 mmHg, PMSarm was 29 ± 9 mmHg, central venous pressure was 13 ± 4 mmHg and the (PMSarm-CVP) gradient was 16 ± 8 mmHg, with no difference between patients with or without shock. In the whole population, Trevasc was 26 (20–35) sec, with no difference between patients with or without shock (28 (21–39) sec *vs.* 21 (18–30) sec, respectively, $p = 0.186$). Among patients with shock, Trevasc was longer in patients with septic shock than in the other ones (38 (29–45) *vs.* 21 (13–29) sec, respectively, $p = 0.001$). Trevasc was significantly increased in the 21 (47%) patients who died (18 patients with shock and 9 with septic shock) compared to survivors (35 ± 17 *vs.* 25 ± 12 s, respectively, $p = 0.038$).
Conclusion: In intensive care patients under mechanical ventilation, Trevasc was increased in patients with septic shock compared to patients with non-septic shock or without shock. Mortality was also associated with higher Trevasc. This new variable might indicate vasoreactivity at bedside and, as such, be associated with severity and mortality. More data are needed to confirm these preliminary results and inclusions are ongoing.

000969

Scandinavian survey concerning assessment and treatment of fluid overload in intensive care

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Intensive Care Medicine Experimental 2022, **10(2)**:000969

Introduction: Fluid overload in patients in the ICU is associated with mortality [1]. There are a few randomized controlled trials [2] to aid physicians in treating patients with fluid overload in the ICU, but no guidelines exist.
Objectives: We aimed to elucidate how Scandinavian ICU-physicians a define, assess, and treat fluid overload in the ICU.
Methods: Based on two former surveys [3] [4], we developed an online questionnaire with 18 questions. The questions were pre-tested and revised. Through a network of national coordinators, we aimed to reach as many Scandinavian ICU-physicians as possible. The distribution started January 2022 and ends May 6th 2022.
Results: Preliminarily we have received 981 responses from Denmark, Norway, Finland, Sweden, and Iceland. 628 respondents completed all questions. When assessing fluid status, respondents applied clinical parameters such as cumulative fluid balance, bodyweight, and urine output more frequently compared to cardiac/lung ultrasound, radiological appearances, and cardiac output monitoring. Respondents agreed that a > 10% increase in body weight from baseline supported the diagnosis of fluid overload better than a > 5% increase (88% vs 59% answered agree/strongly agree). The preferred de-resuscitation strategy was diuretics (91%), followed by minimisation of maintenance (76%) and resuscitation fluids (71%). The majority (84%) would not abstain treatment of fluid overload and would continue diuretics despite mild hypotension, mild hypernatremia, and ongoing vasopressor treatment. 36% of the respondents deemed no upper limit for noradrenaline infusion, when using diuretics to treat fluid overload.
Conclusion: Self-reported practice among Scandinavian ICU-physicians varies broadly when assessing, diagnosing, and treating fluid overload. Physicians favoured clinical parameters to assess, define and diagnose fluid overload and the preferred de-resuscitation strategy was diuretics.

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000979

Prognostic markers in cardiogenic shock. A retrospective observational study

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Introduction: Cardiogenic shock(CS) is a major complication of acute myocardial infarction with a high motality rate.Emergent Coronary revascularisation reduced mortality but despite this therapeutic, a number of patients present a persistent and severe cardiac dysfunction.
Objectives: The objective of this study was to collect and analyze pronostic markers of patients with cardiogenic shock after a coronary revascularisation for acute myocardial infarction.
Methods: We conducted a retrospective observational study and collected data of of patients with CS admitted in University ICU between 2015 and 2019. We divided the patients into 2 groups:
A first group of survivors.
A second group of non survivors.
All The patients, in the 2 groups were 73 + −8 years old, were monitored invasively with arterial femoral line and internal jugular line, mechanically ventilated and received norepinephrine. We used Picco device and echocardiography to measure cardiac output and hemodynamic parameters.
We recorded in the 2 groups the following parameters: Svco2 at T0, T48H, blood lactate at T0, T48H, systolic arterial pressure(SAP), Mean arterial pressure (MAP), cardiac index at T0,T24H,T48H T72H(CI), ejection fraction (EF), heart rate (HR) and serum creatinine at T0 and T 96 h.
Results: Statistics used Mann Whitney test and results expressed as Mean + -STD deviation. Table 1.
Table 1. Variables related with outcome in survivors and non survivors of CS

	Survivors	Non-survivors	P
SVCo2% T 48H	60 ± 5	40 ± 2	< 0.001
Lactates mmol/l T0	3.5 ± 0.3	5.5 ± 0.3	< 0.001
MAP mmHG T48H	65 ± 3	60 ± 4	< 0.09
CI T 72H (l/mn/m^2)	3 ± 07	2 ± 0.4	< 0.001
HR T72H (F/mn)	115 ± 10	150 ± 6	< 0.001
Creatinine T96H (mg/l)	20 ± 5	37 ± 3	< 0.001

Conclusion: We observed in this retrospective study that pronostic markers in CS following myocardial infarction were useful to predict outcome[1,2].Early identification of survivors from non-survivors enables better, patient tailored therapy.

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Acknowledgements: Thanks to my colleagues of Algiers University for their collaboration.

000988

The role of the Intensivist as part of the Pulmonary Vascular Disease Unit

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Introduction: Pulmonary hypertension (PAH) is a hemodynamic disorder defined by abnormally high pulmonary artery pressure which may lead to RV dysfunction and/or severe hemodynamic impairment. Right-sided heart catheterization is essential to evaluate and characterize it effectively, prior to starting therapy, and can not be replaced by noninvasive imaging. The specific treatment depends on the disease group. In high-risk patients, initial combination therapy should include parenteral prostanoids, with epoprostenol, having the highest recommendation because of mortality reduction. Nowadays, multidisciplinary units have been created in order to improve the management of these patients.
Objectives: The aim of this study is to analyze:
- The clinical profile and hemodynamics of the patient who undergoes a right heart catheterization.
- The role of the intensivist as part of the pulmonary vascular disease unit.
Methods: Retrospective observational study conducted in the polivalent Intensive Care Unit of a regional Hospital. All the patients admitted to the ICU, with the echocardiographic diagnosis of PAH, in whom, subsequently, was placed a Swan-Ganz catheter, from January 2017 to April 2022, were included. We analyzed demographic variables, underlying pathologies, CVRF, functional class, hemodynamic parameters and mortality. Statistical analyses were performed using SPSSv22 software. The cuantitative variables are represented as media ± SD and the cualtative ones as percentage.
Results: We included 51 patients, mean age 69,37 ± 13,3 years and predominantly women (60,8%). Among the CVRF presented: smoking 33,3%, Hypertension 62,7%, DLP 31.4% and DM 23,5%. Other noteworthy background: AF 23.5%, PE 11,8%, Deep vein thrombosis 7,8%, renal failure 13,7%, Valvular heart disease 52,9%, Pericardial disease 3,9%. 49% had pulmonary pathology (27,5% IPF, 7,8% UIP, 11,8% COPD) and 19,6% had a connective tissue disease (CREST 3,9%, SLE 3,9%, dermatomyositis 3,9% and scleroderma 7,8%). At the time of diagnosis, their NYHA functional class was: II (41,2%), III (45,1%) and IV (13,7%), with requirement of home oxygen therapy in 33,3% of the cases. 2 fluid challenges and 10 pulmonary vasoreactivity tests were performed (88.9% were responders). Likewise, the implantation of Hickman catheter (3) or PICC (3) was requested for epoprostenol infusion. Of the 51 diagnostic catheterizations performed, 17,6% ruled out PAH. Within the hemodynamic classification, 39,2% presented precapillary and 43,1% postcapillary PH. 13,7% of the patients included in the analysis died.

Conclusion:

- The predominant clinical profile was a middle-aged woman with cardiovascular risk factors and underlying valvular disease; being the pulmonary pathology the main etiology that conditioned precapillary pulmonary hypertension. It is also remarkable the high rate of responders to the pulmonary vasoreactivity test, that we found in our series.
- The intensivist plays a fundamental role in this multidisciplinary unit, being responsible for the confirmation of the echocardiographic suspicion of pulmonary hypertension, through right heart catheterization; as well as collaborating in the implantation of long-lasting vascular accesses.

001013

Effectiveness of Pulmonary Artery Catheter Monitoring in Cardiogenic Shock According to Shock Etiology: Meta-analysis and Systemic Review

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Introduction: The mortality and morbidity of cardiogenic shock are still significant. The invasive hemodynamic monitoring with pulmonary artery catheterization (PAC) can help assessing the changes of

cardiac function and hemodynamics. However, the benefits of the use of PAC for each etiology of cardiogenic shock are not known exactly.
Methods: We performed a systemic review and meta-analysis with observational studies and randomized controlled trials about comparing PAC and no-PAC groups in cardiogenic shock with each shock etiology. Studies were searched from MEDLINE, EMBASE, and Cochrane CENTRAL. We reviewed articles including abstract data and evaluated the quality of evidence using the GRADE framework. We used a random-effect model in order to compare in-hospital mortality in each study.
Results: In total twelve studies in our meta-analysis, we compared in-hospital mortality between PAC use group and non-PAC use group according to shock etiology. The apply of PAC in cardiogenic shock showed no significant difference in non-use of PAC (RR 0.86, 95% Confidential interval 0.73 – 1.02, I^2 = 100%; p < 0.001). Two studies of cardiogenic shock due to acute decompensated heart failure shows the lower in-hospital mortality in PAC use group than non-PAC use group (RR 0.49, 95% CI 0.28 to 0.87; I^2 = 45%, p = 0.18). Six studies of CS with non-specific etiology show the lower in-hospital mortality in PAC use group than non-PAC group (RR 0.84; 95% CI 0.72 to 0.97, I^2 = 99%, P < 0.01). However, no significant difference in in-hospital mortality between PAC use group and non-PAC use group in CS with acute coronary syndrome (ACS) (RR 1.01, 95% CI 0.81 to 1.25, I^2 99%, P < 0.01).
Conclusion: The use of PAC in CS with ACS was not associated with lower in-hospital mortality. On the other hand, in CS with acute decompensated heart failure, the use of PAC is associated with lower in-hospital mortality.

Cardiovascular Dynamics 6

001017

Effects of rapid fluid infusion on hemoglobin concentration: A systematic review and meta-analysis

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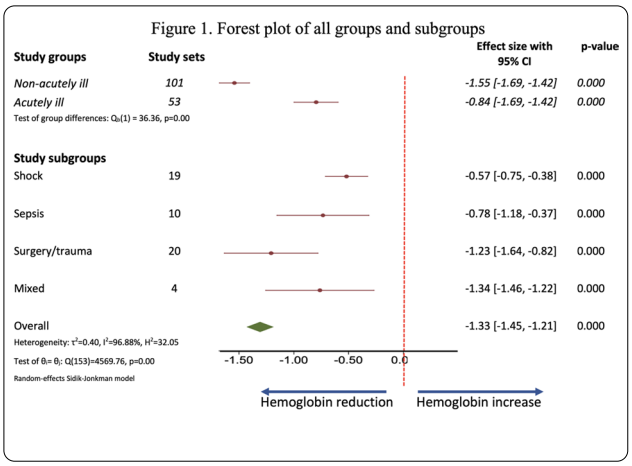
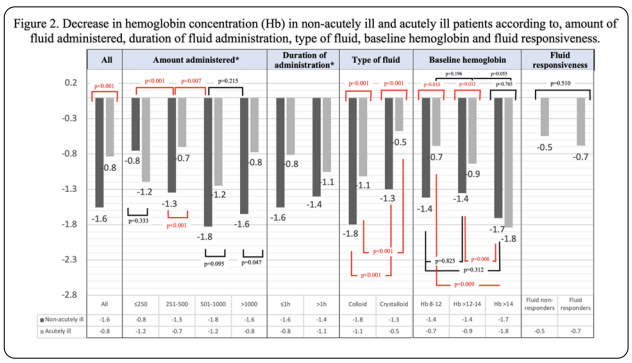
Introduction: The main objective of fluid administration in acutely ill patients is to correct hypovolemia and increase cardiac output and oxygen delivery (DO2), to restore adequate tissue perfusion. However, rapid fluid administration may decrease hemoglobin concentration by a diluting effect, which could limit the increase in oxygen delivery (DO2) expected with a positive response to fluid challenge in critically ill patients. Despite the several reports and clinical perception of Hb reduction after fluid administration, the magnitude of hemodilution in different clinical scenarios has not been objectively assessed.
Objectives: Our aim was to quantify the decrease in hemoglobin concentration after rapid fluid administration.
Methods: We searched PubMed, the Cochrane Database and Embase from inception until February 15, 2022. We selected studies that reported hemoglobin concentration before and after rapid fluid administration with non-blood fluids in adults, without language restrictions. Studies were divided according to whether they involved non-acutely ill or acutely ill(surgical/trauma, sepsis, circulatory shock or severe hypovolemia, and mixed conditions) subjects.
The mean hemoglobin difference and, where reported, the DO2 difference before and after fluid administration was extracted. Meta-analyses were conducted to assess differences in hemoglobin concentrations before and after rapid fluid administration in all subjects and across subgroups. Risk of bias was evaluated using validated tools.
Results: We included 65 studies from 1011 citations that met our inclusion criteria, 40 in non-acutely ill and 25 in acutely ill subjects. Across all studies, the hemoglobin concentration decreased significantly after fluid administration by a mean of 1.33 g/dL [95% CI -1.45 to -1.12; p < 0.001; I2 = 96.88]. In non-acutely ill subjects, hemoglobin decreased by a mean of 1.56 g/dL [95% CI -1.69 to -1.42; p < 0.001; I2 = 96.71] and in acutely ill patients by a mean of 0.84 g/dL [95% CI -1.03 to -0.64; p = 0.033; I2 = 92.91]. The decrease in hemoglobin concentration was less marked in patients with sepsis than in other acutely ill patients. There was a significant difference in the change in DO2 between fluid responders (67.76 [95% CI46.11 – 89.40]) and non-responders (-16.30 [95% CI -31.52 – -1.09]) (p < 0.001).





Conclusion: Hemoglobin concentration decreased consistently after rapid fluid administration. This effect may limit the positive effects of fluid challenges on oxygen delivery and thus on tissue oxygenation.

001027

Dynamic arterial elastance predicts volume responsiveness in patients with hemodynamic instability and irregular heart rhythm: results from a pilot study

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Introduction: Prediction of volume responsiveness in mechanically ventilated patients with hemodynamic instability remains challenging especially in conditions where usability of standard dynamic tests is significantly limited due to irregular heart rhythm.
Objectives: The aim of our study was to assess a relationship between the values of dynamic arterial elastance (EAdyn) and hemodynamic response to leg raise test in patients with circulatory shock and irregular heart rhythm.

Methods: Mechanically ventilated patients with combined cardiogenic and septic shock treated with vasopressors (noradrenalin and/or vasopressin) and inotropes (dobutamine and/or milrinone) and with irregular heart rhythm were eligible for the study. Pulse pressure variation (PPV), stroke volume variation (SVV), EAdyn, cardiac output (CO), stroke volume (SV) and mean arterial pressure (MAP) were continuously monitored from pulse wave analysis. The values of PPV, SVV and EAdyn were recorded before standard passive led raise test (LRT) and analyzed for correlation with the change (after LRT – before LRT) in CO (dCO), SV (dSV) and MAP (dMAP).
Results: Ten hemodynamically unstable patients were enrolled (mean age 54 years, females 4/10). Irregular heart rhythm was caused by atrial fibrillation (7/10) or frequent premature complexes (3/10). Admission diagnoses were acute myocardial infarction (5/10), pulmonary embolism (2/10), COVID-19 (1/10), cardiac arrest (1/10) and cardiac tamponade (1/10). All were treated with inotropes and vasopressors. A significant correlation was observed between EAdyn and dCO (Spearman $r = 0.801$, $P = 0.013$) as well as between EAdyn and dSV ($r = 0.684$, $P = 0.048$) but not between EAdyn and dMAP ($P = 0.178$). The values of PPV and SVV did not correlate with any of the changes.
Conclusion: Our pilot results indicate that EAdyn could be used as a predictor of volume responsiveness in mechanically ventilated patients with circulatory shock and irregular heart rhythm.

Acknowledgements: This study was supported by an Institutional grant MH CZ-DRO (Nemocnice Na Homolce - NNH, 00023884) IG150501.

001031

Incidence and prognostic impact of myocardial dysfunction in septic shock – An observational cohort study

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Introduction: Recent sepsis guidelines endorse myocardial dysfunction as a major contributor to shock in sepsis. Sepsis induced cardiomyopathy is known to be biventricular which is both acute as well as reversible. The aim of this study was to assess the incidence, spectrum, and prognostic impact of myocardial dysfunction in patients with septic shock.
Objectives: The primary outcome was to evaluate the effect of myocardial dysfunction on the 28 day mortality. The secondary outcomes were to assess the effect of 1. Left ventricular dysfunction, right ventricular dysfunction or both on 28-day mortality.2) Myocardial dysfunction on ventilator free days, duration of vasopressor use and ICU length of stay.
Methods: This was a prospective observational cohort study, conducted between December 2019 to September 2021 in adult patients with septic shock. We excluded those having improper window for transthoracic echocardiography (TTE), known cardiac diseases, pregnancy, or post cardiac arrest status. Patients fulfilling the inclusion criteria underwent TTE within the first 24 h of ICU admission, and if abnormal a repeat scan was repeated on 7th day. TTE was used to assess systolic and diastolic function of both ventricles based on the criteria recommended by the American Society of Echocardiography. Patient demographic data, hemodynamic monitoring data, vasopressor use, APACHE II/ SOFA scores and patient outcomes were also recorded. Patients were followed up till day 28 or death.
Results: Echocardiographic evidence of myocardial dysfunction was present in 39 out of 71 patients (54.9%). Diastolic dysfunction was more common than systolic dysfunction(47.89% vs 28.17%).The mortality in patients with myocardial dysfunction was 74.36% versus 31.25% in patients without myocardial dysfunction($P < 0.0003$). In subgroup analysis of the type of myocardial dysfunction, only right ventricular dysfunction alone significantly increased the 28 day mortality. Myocardial dysfunction also led to increase in duration of mechanical ventilation, vasopressor use and ICU stay ($P < 0.0001$). The predictors of mortality were APACHE II, SOFA scores, e' and E/e'.
Conclusion: In our study, septic cardiomyopathy was associated with significant increase in 28 mortality, vasopressor use, duration of mechanical ventilation and length of ICU stay. Echocardiographic parameters like e' and E/e' need to be evaluated as prognostic markers in septic cardiomyopathy.

References: None.

Acknowledgements: None.

001037

Serial evaluation of myocardial function using echocardiography in rodent endotoxemia model

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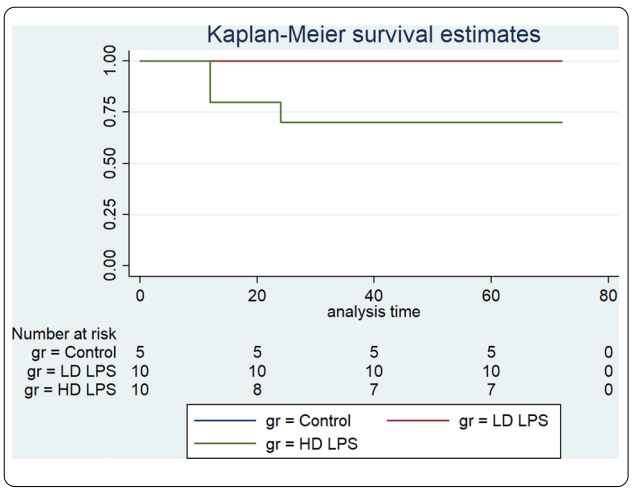
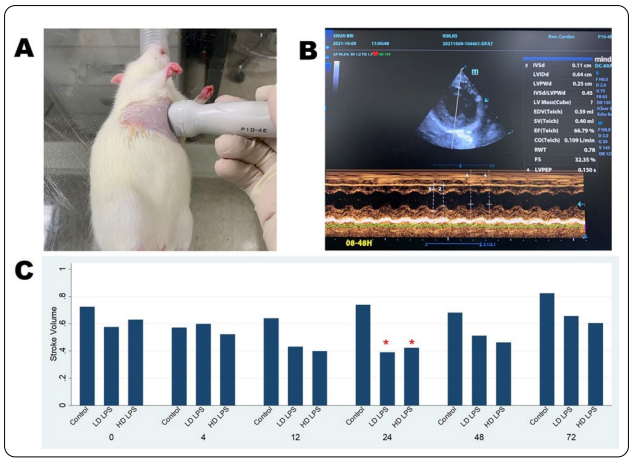
Introduction: Sepsis-induced cardiomyopathy (SICM) is a transient cardiac dysfunction frequently encountered in sepsis patients.
Objectives: To investigate the pathophysiology of SICM, we have evaluated myocardial function serially in rodent endotoxemia model.
Methods: Twenty-five rats were grouped into control (n = 5), low dose lipopolyssaccharide (LD-LPS, n = 10), and high dose lipopolyssaccharide (HD-LPS, n = 10) group. Animals were anesthetized using 15 mg/kg of Zoletil and 1% ~ 2% of inhaled isoflurane. Baseline transthoracic echocardiography was performed. Same volume of normal saline (control group), 5 mg/kg of E.coli LPS (LD-LPS group), and 10 mg/kg of E.coli LPS (HD-LPS group) were administered through tail vein, respectively. Serial echocardiography was performed at 4 h, 12 h, 24 h, 48 h, and 72 h after injection. Survival status was checked at each time point and rats were euthanized under deep anesthesia after 72 h of observations. All processes were approved by Institutional Animal Care and Use Committee.
Results: During 72 h of observations, only 3 animals of HD-LPS group died and there was no statistically significant difference among 3 groups ($p = 0.082$) (Fig 1).



Among echocardiographic findings, stroke volume at 24 h were significantly lower in both endotoxemia groups (LD-LPS and HD-LPS) than control ($p = 0.007$) (Fig 2).



Conclusion: In rodent endotoxemia model, stroke volume decreased significanlty at 24 h after LPS injection and recovered thereafter. Further molecular biologic analysis at 24 h after LPS injection would be helpful to understand the pathophysiology of SICM.

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Acknowledgements: This work was supported by the National Research Foundation of Korea Grant funded by the Korean Government (NRF-2021R1A2C101324412).

001065

Incidence and risk factors of weaning-induced cardiac dysfunction: results from a multicenter, observational study

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Intensive Care Medicine Experimental 2022, **10(2)**:001065

Introduction: Weaning-induced pulmonary edema (WiPO) is one of the main reasons for weaning failure. Nevertheless, the reported incidence of WiPO is variable and mainly in monocentric studies with small sample sizes.

Objectives: The objective of this study is to evaluate the incidence and risk factors of WiPO in a large mixed population of critically ill patients.

Methods: Adult critically ill patients receiving invasive ventilation were included once the attending physicians decided to perform a spontaneous breathing trial (SBT). Patients with tracheostomy were excluded. The duration and modalities of the SBT (T-tube or pressure support ventilation (PSV) with or without positive end-expiratory pressure (PEEP)) were decided by attending physicians. The consensual diagnosis of WiPO was made a posteriori by five experts based on the patient characteristics, hemodynamic and echocardiographic variables, and biochemical results.

Results: From July 2019 to February 2021, 634 SBTs performed in 500 patients (65 (55–74) y.o., 64% male) from twelve intensive care units, were prospectively included. The median SOFA score and SAPS II score are 8 (5–11) and 52 (40–66). The main indication for intubation was acute respiratory failure or shock or sepsis in 347 (69.4%) patients, neurological failure in 77 (15.4%) patients, interventional procedure in 47 (9.4%) patients and resuscitated cardiac arrest in 29 (5.8%) patients. Regarding the modalities of the SBT, T-tube was used in 358 (56.5%) cases of SBTs, PSV with low PEEP (PSV-PEEP) was used in 85 (13.4%) cases, and PSV without PEEP (PSV-ZEEP) was used in 191 (30.1%) cases. In total, 79 WiPO (36%) was identified in 217 failed SBTs (34%). Among 217 failed SBTs, WiPO occurred in 54 (25%) of SBTs performed with a T tube, 18 (8%) with PSV-ZEEP, and 7 (3%) with PSV-PEEP. Compared to patients without WiPO (n = 434), patients with at least one WiPO (n = 66) had a higher prevalence of chronic obstructive pulmonary disease (COPD) (24% *vs.* 10%, respectively; p = 0.001), and previous cardiopathy (dilated and/or hypertrophic and/or valvular disease, 52% *vs.* 25%, respectively; p < 0.001). A logistic regression analysis found that, COPD (odds ratio (OR): 4.4, [95% confidence interval: 1.6–12.3]), and previous cardiopathy (OR: 3.3 [1.5–7.4]) were independent risk factors for developing WiPO.

Conclusion: In a large mixed population of critically ill patients, WiPO accounts for 36% of SBT failure. COPD and a previous cardiopathy were independent risk factors for developing WiPO.

001108

Validation of prognostic scales in patients supported with VA ECMO

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Intensive Care Medicine Experimental 2022, **10(2)**:001108

Introduction: Cardiogenic shock is still one of the major causes of mortality despite therapeutic advances developed in recent years. Among these new therapies we found devices for cardiorespiratory support such as ECMO. Developing mortality predictive scales would help to predict the survival of patients with cardiogenic shock and VA ECMO.

Objectives: To validate the prognostic scales for the prediction of mortality in patients in refractory cardiogenic shock requiring VA ECMO.

Methods: Retrospective observational study from January 2011 to November 2021 in an Intensive Care Unit of a tertiary care hospital. All patients with cardiogenic shock who required a VA ECMO implantation were included. Demographic variables, personal history, aetiology of cardiogenic shock, SAVE and Cardshock scores, as well as SCAI scale, SOFA and APACHE II were collected. Qualitative variables were described by frequencies; Quantitative by mean and interquartile range. X2 test was performed for qualitative variables and U Mann Whitney for quantitative variables.

Results: A total of 105 patients were included, of whom 51 (48.57%) survived. Demographic characteristics, personal history, reason for VA ECMO implantation and prognostic scales are shown in Table 1. Statistically significant differences were observed in the prediction of mortality with the use of SOFA and SAVE score scales, with no difference on the rest of the prognostic scales used.

Table 1 Analysis of demographic characteristics, history, etiology of cardiogenic shock and prognostic scales according to mortality. BMI, body mass index

Variables	Survivors (n = 51)	Non-survivors (n = 54)	p
Male; n (%)	32 (62.74)	30 (55.55)	0.454
Age; median (IR)	47 (37; 57)	58 (48; 66)	0.002
Arterial hypertension; n (%)	22 (43.14)	27 (50)	0.481
Diabetes; n (%)	9 (17.65)	12 (22.22)	0.558
BMI; median (IR)	26.2 (22.85; 29.40)	27.34 (24.92; 31.58)	0.309
Cardiogenic shock aetiology; n (%)			0.044
Acute myocardial infarction	14 (27.45)	25 (46.30)	
Postcardiotomy shock	17 (33.33)	15 (27.78)	
Acute myocarditis	8 (15.69)	4 (7.41)	
Primary graft failure	5 (9.80)	2 (3.70)	
Others	7 (13.73)	8 (14.81)	
Prognostic scales; median (IR)			**p**
APACHE II	15 (10; 19)	16 (12; 21.50)	0.06
SOFA	9 (7; 12)	11 (9; 13)	**0.037**
SAVE score	− 1 (− 6; 2)	− 4 (− 7.50; − 1)	**0.019**
Cardshock score	3 (2, 4)	3 (2, 5)	0.408
SCAI scale			
A	0 (0)	0 (0)	
B	4 (7.84)	1 (1.85)	
C	5 (9.80)	7 (12.96)	
D	18 (35.29)	15 (27.78)	
E	24 (47.06)	31 (57.41)	0.291
INTERMACS	1 (1;1)	1 (1;1)	0.246

Conclusion: The use of mortality predictor scales could be very useful for the management of patients with cardiogenic shock who need VA ECMO implantation for cardiorespiratory support. Among the available scales, only SOFA and SAVE score have demonstrated their prognostic validity in our population.

001152

Animal model of haemodynamic effect of a large arteriovenous fistula during VA-ECMO

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Intensive Care Medicine Experimental 2022, **10(2)**:001152

Introduction: Arteriovenous fistulas (AVF) represent a low-resistant circuit. Their opening leads to increase in cardiac output, decrease of peripheral vascular resistance and other haemodynamic changes. Competition in perfusion of AVF and other organs has been observed before and was described in our previous series of experiments (1). The aim of this study was to describe effect of AVF opening during VA-ECMO support with preserved cardiac output on systemic haemodynamics. This could be particularly important for chronic kidney disease patients with patent AVF in critical states, as it is still unknown how large is the proportion of cardiac output stolen by AVF during extracorporeal circulatory support.
Methods: The experiments were performed on domestic pigs in general anaesthesia. The pigs were sedated, intubated, and catheters were inserted. VA-ECMO was inserted using femoro-femoral approach. AVF was created by connecting another two ECMO cannulas, also by femoro-femoral approach. The measurements were performed during following ECMO flow: 500 ml (baseline, to prevent clotting), 1 L/min, 2 L/min, 3 L/min, 4 L/min with maintained cardiac output (CO), and maximum ECMO flow during ventricular fibrillation. Total systemic flow (TSF) was calculated as CO + ECMO flow. Carotid artery flow was measured by perivascular ultrasound probe. Frontal lobe tissue blood flow was measured by laser Doppler microvascular probe. Cerebral tissue oxygen saturation (rSO2) was measured by near-infrared spectroscopy. Coronary artery flow velocity was measured using Doppler flow wire.
Results: Combination of ECMO support with maintained normal cardiac output creates a hyperperfusion state. Surprisingly, the percentage of total systemic flow running through AVF decreases with higher total systemic flow. This was enabled by hyperperfusion of the brain—carotid artery flow continuously increased with increasing total flow—and possibly also of other organs. However, almost in all levels of ECMO support, opening of an AVF increases total systemic flow due to CO increase, but significantly decreases effective systemic perfusion (TSF – AVF flow). This led to a significant decrease of carotid artery flow (with P-value less than 0.05), frontal lobe tissue flow, and cerebral rSO2 after AVF opening regardless the current ECMO flow. Coronary artery flow velocity was proportional to current cardiac output and increased after opening of the AVF.
Conclusion: Opening of a large AVF increases cardiac output even when part of perfusion is maintained by ECMO support. Proportion of systemic flow stolen by AVF decreases even during increased total output state. A high-flow AVF opening significantly steals systemic perfusion leading to decrease in cerebral flow and oxygenation. Cardiac perfusion remains regulated mainly by metabolic demands of the myocardium.

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Acknowledgements: This work was supported by grant n. GA20-25429S of Czech Science Foundation.

001156

Factors of poor prognostic in patients with cardiogenic shock supported with VA ECMO

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Intensive Care Medicine Experimental 2022, **10(2)**:001156

Introduction: New devices have been proposed for the management of refractory cardiogenic shock in the last few years. The use of venoarterial extracorporeal membrane of oxygenation (VA ECMO) has been increased in recent years as alternative to conventional therapies. Identifying those factors associated to mortality in these patients is crucial in order to improve the rates of survival in patients with refractory cardiogenic shock.
Objectives: To describe risk factors associated with increased mortality in patients with refractory cardiogenic shock requiring VA ECMO.
Methods: Observational retrospective study from 2011 to 2021 in an Intensive Care Unit (ICU) of a tertiary care hospital. Patients with cardiogenic shock in need of VA ECMO were included. Demographic variables, medical history, lactate levels, development of cardiorespiratory arrest and acute kidney failure, Length of stay at ICU and vasoactive amines dosage were collected. Qualitative variables were described by frequencies; quantitative by mean and interquartile range (IR). X2 test

was performed for qualitative variables and U Mann Whitney for quantitative variables.
Results: A total of 105 patients were included, with an overall survival of 48.8%. Medical history, lactate levels, development of cardiorespiratory arrest and acute kidney failure and vasoactive amines dose are described in Table 1.
Conclusion: To identify those factors associated with increased mortality in cardiogenic shock requiring mechanical support with VA ECMO may be useful for their therapeutic management. The need of higher doses of amines or hyperlactatemia despite of VA ECMO implantation are, among others, the poorest prognostic factors in our population.

001225

End-Expiratory Occlusion Test (EEOT) to assess Fluid Responsiveness in critically ill patients with shock: a preliminary report

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Intensive Care Medicine Experimental 2022, **10(2)**:001225

Introduction: Fluid overload may harm critically ill patients with shock.1 It is, in fact, recommended that fluid administration should be guided by the assessment of fluid responsiveness.2 Several dynamic tests for fluid responsiveness have been proposed: all of them aim at assessing hemodynamic changes induced by transient changes in cardiac preload.3 All these tests have been validated in mechanically ventilated patients with a tidal volume $\geq$ 10 ml/kg IBW, which is not applied in routine practice.4 The End-Expiratory Occlusion Test (EEOT) is a dynamic test during which changes in cardiac preload is caused by a respiratory maneuver performed on the ventilator.5
Objectives: Our study object that EEOT could predict fluid responsiveness in shocked patients who were ventilated with a tidal volume < 8 ml/kg ideal body weight (IBW).
Methods: This was a prospective observational study conducted in a general intensive care unit (ICU) in Italy. Inclusion criteria were: need for fluid resuscitation as assessed by the attending physician, analgo-sedation, lung-protective volume-controlled ventilation with Vt 6–8 ml/kg IBW, hemodynamic monitoring (pulse-contour metho with MostCare -Vygon SA, Ecouen, France). All patients underwent the EEOT dynamic test with evaluation of Cardiac Output (CO) before and after administration of a 15-min fluid challenge (FC) of 6 mL/kg with crystalloids. Patients were deemed as "responders" when post-bolus CO improved $\geq$ 15%, as compared with baseline.
Results: Eighteen patients were enrolled and 11 (61%) were "responders", with a significant average post-bolus CO increase from 3.2 (2.68–3.6) to 4.7 (3.8–5.1) $p = 0.0001$. In "responders", average post-EEOT CO at baseline showed a significant predictivity of fluid responsiveness from 3.2 (2.68–3.6) vs 3.8 (3.2–4.5) $p = 0.0299$. EEOT exhibited an 83% sensitivity and a 100% specificity in predicting fluid responsiveness as assessed with FC.
Conclusion: Despite the small sample size, in our population EEOT proved to be a reliable dynamic test of fluid responsiveness even in patients with low tidal volume ventilation.

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Acknowledgements: None.

Data Science 1

000039

Hospital Length of Stay and 30-day Mortality Prediction in Stroke: A Machine Learning Analysis of 17,000 ICU Admissions in Brazil

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Intensive Care Medicine Experimental 2022, **10(2)**:000039

Introduction: Hospital length of stay and mortality are associated with resource use and clinical severity, respectively, in patients admitted to the ICU with acute stroke.
Objectives: We proposed a structured data-driven methodology to develop length of stay and 30-day mortality prediction models in a large multicenter Brazilian ICU cohort.
Methods: We analyzed data from 130 ICUs from 43 Brazilian hospitals. All consecutive adult patients admitted with stroke (ischemic or non-traumatic hemorrhagic) to the ICU from January 2011, to December 2020, were included. Demographic data, comorbidities, acute disease characteristics, organ support, and laboratory data were retrospectively analyzed by a data-driven methodology, which included seven different types of machine learning models applied to training and test sets of data. The best performing models, based on discrimination and calibration measures, are reported as the main results. Outcomes were hospital length of stay and 30-day in-hospital mortality.
Results: Out of 17,115 ICU admissions for stroke, 16,592 adult patients (13,258 ischemic and 3,334 hemorrhagic) were analyzed. 4,298 (26%) patients had a prolonged hospital length of stay (> 14 days), and 30-day mortality was 8% (N = 1,392). Prolonged hospital length of stay was best predicted by the Random Forests model (Brier Score = 0.17, AUC = 0.73, PPV = 0.61, NPV = 0.78). Mortality prediction also yielded

the best discrimination and calibration through Random Forests (Brier Score = 0.05, AUC = 0.90, PPV = 0.66, NPV = 0.94). Amongst the twenty strongest contributor variables in both models were: (1) premorbid conditions (i.e., functional impairment), (2) multiple organ dysfunction parameters (i.e., hypotension, mechanical ventilation) and (3) acute neurological aspects of stroke (i.e., Glasgow coma scale on admission, stroke type).
Conclusion: Hospital length of stay and 30-day mortality of patients admitted to the ICU with stroke were accurately predicted through machine-learning methods, even in the absence of stroke-specific data such as the NIHSS or neuroimaging findings. The proposed methods using general intensive care databases may be used for resource use allocation planning and performance assessment of ICUs treating stroke. More detailed acute neurological and management data, as well as long-term functional outcomes, may improve the accuracy and applicability of future machine-learning based prediction algorithms.

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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.

000061

Score-Based Prediction for Severe Vitamin D Deficiency in Critically Ill Patients

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Intensive Care Medicine Experimental 2022, **10(2)**:000061

Introduction: Severe vitamin D deficiency (SVDD) with 25-hydroxy-vitamin D (25(OH)D) concentration below 12 ng/mL (or 30 nmol/L) dramatically increases the risk of mortality, infections, and many other diseases (1). Our previous multicenter observational study showed a high prevalence of vitamin D deficiency in critically ill patients (2). Several prediction models of vitamin D deficiency had been built for the general population but not patients admitted in intensive care units.
Objectives: This multicenter cohort study aimed to develop and validate a score-based prediction model of SVDD in critically ill patients.
Methods: This study reviewed the data of our previous multi-center, prospective, observational cohort study, and the critically ill patients were enrolled between August 2018 and July 2020. SVDD was measured and defined as a serum 25(OH)D level < 12 ng/mL (or 30 nmol/L). Patient characteristics, admission season, hemodynamic data, laboratory data were recorded. The data were divided into a derivation cohort (first 80% of the data set based on chronology) and a validation cohort (the remaining data set). Multivariable logistic regression (MLR) was performed to generate a predictive model for SVDD via the derivation cohort. In addition, we developed a score-based calculator (SVDD score) from the MLR model. The model performance and calibration were then tested in the validation cohort. The area under the receiver operating characteristic curve (AUROC), the area under precision recall curve (AUPRC) and the Hosmer–Lemeshow test were calculated.
Results: The prevalence of SVDD was 16% and 26% in the derivation cohort and the validation cohort, respectively. The final MLR model involved 14 predictors (age, gender, body mass index, sepsis, post-operation, mean arterial pressure, heart rate, lactic acid, albumin, sodium, potassium, white blood cell count, hemoglobin and platelet count) and had an AUROC of 0.761 (95% CI, 0.650–0.873), an AUPRC of 0.603 (95% CI, 0.521- 0.676) in the validation cohort. The score-based calculator was built with 7 predictors (as Table 1 and Figure 1) and had

an AUROC of 0.804 (95% CI, 0.708–0.900) and an AUPRC 0.612 (95% CI, 0.551–0.677).

	Addition to the SVDD score												
Age (years)	<50 +0	50-54 +7	55-59 +6	60-64 +4	65-69 +2	70-79 +0	80-84 +1	85-89 +2	>=90 +3				
Mean arterial pressure (mmHg)	<60 +0	60-69 +1	70-79 +2	80-89 +3	90-99 +4	100-109 +5	110-119 +6	120-129 +7	>=130 +8				
Albumin (g/dL)	<1.5 +7	1.5-1.9 +6	2.0-2.4 +5	2.5-2.9 +4	3.0-3.4 +3	3.5-3.9 +2	4.0-4.4 +1	>= 4.5 +0					
Heart rate (/min)	<55 +13	55-89 +15	90-105 +16	105-109 +14	110-114 +12	115-119 +10	120-124 +8	125-129 +6	130-134 +4	135-139 +2	>=140 +0		
Gender	Male	+0	Female	+4									
Sepsis	No	+0	Yes	+4									
Post-operation	No	+2	Yes	+0									

Table1*. Score-based calculator.*

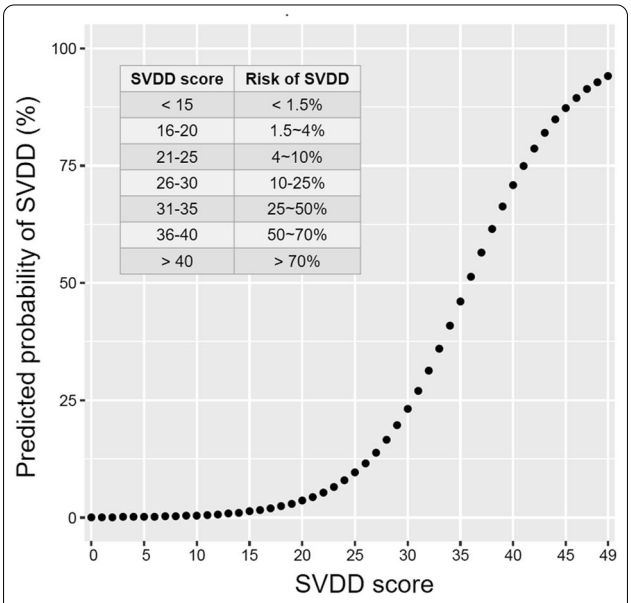

Figure 1*. Score-based prediction model with predicted probabilities of SVDD for each SVDD score in an individual.* (Abbreviations: SVDD, severe vitamin D deficiency)

All the predictive models demonstrated adequate goodness-of-fit. There was no significant difference between the MLR model and the score-based model in the ROC curves. When using a score of 29 as a threshold for predicting outcome, the sensitivity was 73%, the specificity was 80%, the positive predictive value was 54%, and the negative predictive value was 91%.

Conclusion: This study demonstrated a simple score-based prediction model for SVDD in critically ill patients.

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000108

Regional indicators in COVID-19 lethality in Brazil: a descriptive analysis

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Intensive Care Medicine Experimental 2022, **10(2)**:000108

Introduction: With a rapid international expansion, on December 31, 2019, the first cases reported to the World Health Organization (WHO) of the disease were received, which, until then, was defined as a "pneumonia of unknown origin", associated with principle to individuals who worked in the Seafood market, in the city of Wuhan, Chinese province of Hubei (OLIVEIRA et al., 2020). Soon after, given the high repercussion and incidence, which broke the geographical. Regarding Brazil, according to data made available by the Coronavirus Brazil portal (https://covid.saude.gov.br/) developed by the Ministry of Health (MS), the different regions of the country have high averages in the Mortality Index for each 100,000 inhabitants, with the North region, with 80.3, the one with the highest death rate to date; followed by the Midwest region with 75.3; Southeast with 72.4; Northeast with 67.7; and the South region with the lowest mortality rate with a rate of 39.0. As for the Brazilian states with the highest Mortality Rates for every 100,000/inhabitants, there are Rio de Janeiro with 105.7; Roraima with 105.2; Ceará with 97.6; Sergipe with 87.7; Holy Spirit with 86.8; and Pernambuco with 85.3 (BRAZIL, https://covid.saude.gov.br/, updated on Sept. 26, 2020).

Objectives: The objective of the research was to compare the mortality and lethality rates of the different regions and states of the federation (UF) with their respective human development indices, socioeconomic levels and with the investments received to fight the disease.

Methods: A documentary, retrospective, statistical and descriptive research was carried out through the collection and correlation of data available on the official websites of the Ministry of Health, the State Health Departments, the Department of Informatics of the Brazilian Unified Health System (DATASUS) and the Coronavirus Panel (https://covid.saude.gov.br/), in order to tabulate the data made available between the months of April 2020 and January 2021. Through the results obtained from the analysis, we sought to verify the causes that denote the discrepancy and variation in mortality and lethality rates by COVID-19 in the State of Tocantins. The sample included the number of confirmed, recovered, follow-up cases and the deaths of individuals affected by COVID-19, in the State of Tocantins, between April 2020 and January 2021.

Results: It was possible to observe the relationship between the analyzed variables. The first one, between the positive correlation of mortality data and confirmed cases, which resulted in 0.955, revealing that the more cases were confirmed, the greater the data referring to mortality in the period. In the correlation between the total number of beds and the mortality rate, it showed a positive result equivalent to 0.558, something surprising, as it was expected that with a greater availability of beds, there would be a drop in mortality rates, however, which what was observed was a positive relationship in which even with a greater number of beds available, there was no reduction in mortality rates. This is justified by the positive relationship that occurred between the total number of available beds and the number of confirmed cases in the period, which was equivalent to 0.684, demonstrating that the supply of beds may have increased due to the increase in the number of cases, which consequently also increased the mortality rate. On the other hand, between the ratio of total number of beds and the lethality rate, this resulted in a negative correlation of -0.524, meaning that with the increase in the availability of beds, there was a reduction in the lethality rate during the period evaluated.

Conclusion: It was observed that in the first year of the COVID-19 pandemic, there were discrepancies between the availability of beds and the number of cases, that there is a direct relationship between the spread of the disease and its mortality, and that the availability of beds tends to to reduce lethality. Other studies should be carried out based on the months following this study for further conclusions about public health policies.

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000115

Community-based suicide prevention programs are effective in preventing emergency medical utilization after self-harm: a nationwide registry-based study

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Intensive Care Medicine Experimental 2022, **10(2)**:000115

Introduction: Over the past few decades, suicide has become a serious public health concern worldwide. The World Health Organization has endorsed national and community-based suicide prevention (SP) programs (SPPs). Deliberate self-harm is defined as a non-fatal self-injury act that may lead to suicide. In order to implement a community-based program and evaluate its effectiveness, it is imperative to understand epidemiological characteristics of self-harm.
Methods: Data including age, sex, type of injury, and outcome of emergency care were collected from the National Emergency Department Information System (NEDIS) data panel in Korea for patients seen after self-harm. Socioeconomic factors related to self-harm were collected from Statistics Korea. Variables representing SP activities were collected from the Korea Foundation for SP.
Results: Incidence rates of self-harm (IRSHs) were higher in young population (15- to 34-year-old) than in the elderly (65 and older) at almost all measurement points. Annual IRSH exceeding 100 per 100,000 people were most frequently observed in rural areas. In elderly males aged 65 and older, suicide rates were closely correlated with socioeconomic factors. Socioeconomic factors affected young population more than elderly population regardless of sex. As a result of analysis of the SPPs, increasing the number of mental health providers resulted in lower IRSHs in the entire population as well as in both young and elderly populations. In addition, an increase in mental health budget led to a significant reduction in IRSH. However, the number of SPPs per 1000 km2, a measure of geographical accessibility, did not have any significant association with IRSH.
Conclusion: The IRSH among young people and elderly males is strongly influenced by socioeconomic factors. It is important to reduce poverty and social inequity to prevent self-harm. There is substantial evidence that community-based SPPs are effective in preventing self-harm injuries.

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Acknowledgements: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

000150

The effect of age on vital sign changes in patients hospitalised with infection

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Introduction: Bacterial infections are a common reason for hospital and intensive care unit (ICU) admission, leading to significant morbidity and mortality. Older patients suffer worse outcomes compared to younger patients (Yoshikawa 2019). Vital signs taken at hospital admission guide decisions around escalation of care. However, evidence of how age affects the relationship between vital signs and patient outcomes is limited.

Objectives: To examine how age affects the association between admission vital signs and patient outcomes in patients hospitalised with bacterial infection.
Methods: This retrospective cohort study used a large database of routinely collected patient data from four hospitals in one NHS Trust. We included emergency hospital admissions between 1st January 2016 and 31st December 2017 of patients aged 18 and over with suspected bacterial infection. Suspected bacterial infection was defined by diagnostic coding and antibiotics prescribed within the first 24 h of admission (Inada-Kim 2017). We excluded admissions without a recording of each vital sign (heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, temperature, oxygen saturation, mental status and oxygen use) within 24 h of admission. The first of each recorded vital sign was selected as the admission vital sign. The primary outcome was in-hospital mortality within five days of admission. The secondary outcome was a composite of cardiac arrest, unplanned ICU admission or death within five days of admission.
We used Generalised Additive Models (GAMs) to estimate distributions of admission vital signs (heart rate, respiratory rate, systolic blood pressure, temperature) across all ages. We also used GAMs to model the relationship between age, vital signs and the primary/secondary outcomes.
Results: We included 19,936 admissions, of which 580 (2.9%) and 809 (4.1%) experienced the primary and secondary outcome respectively. Increasing age was associated with a reduction in median heart rate and temperature and an increase in median systolic blood pressure and respiratory rate at admission. After adjusting for age, the relationships between admission heart rate and respiratory rate, and odds of 5-day in-hospital mortality, changed significantly with patient age. We found a similar age-dependent association between heart rate, respiratory rate, temperature, systolic blood pressure and the composite outcome. For example, a heart rate of 131 beats/minute (the cut-off used in the NEWS2 early warning score) increased odds of the composite outcome by 7.5 (95% CI 4.6–12.3) in 30 year-olds but only by 2.5 (1.7–3.8) in 90-year-olds.
Conclusion: Age affects the relationship between vital signs and outcomes in patients admitted to hospital with bacterial infections. Our results have implications for how vital signs are used to identify patients who would benefit from critical care. In particular, failing to incorporate age in current early warning score systems could likely disadvantage older patients.

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000193

Full-context modelling of traumatic brain injury in the ICU: data-driven trajectories of ordinal prognosis for dynamic interpretation

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Intensive Care Medicine Experimental 2022, **10(2)**:000193

Introduction: Traumatic brain injury (TBI) patient trajectories in the ICU are highly variable and poorly understood [1]. Without an evidence-based understanding of disease trajectory evolution after TBI, our ability to individualise time-sensitive ICU treatments and predict their effects will be limited.
Objectives: Previously, we developed artificial intelligence (AI) which could read a TBI patient's full clinical record up to 24 h after ICU admission to predict individual levels of functional recovery (on the Glasgow Outcome Scale – Extended [GOSE]) at 6-months post-injury [2]. In this work, we aimed to extend this strategy to dynamically interpret all clinical events in real-time to model the longitudinal evolution of TBI patient prognoses over ICU stay. Using ordinal GOSE prognosis as a proxy for the patient's condition, this model would then identify important ICU events and simulate individualised treatment effects (ITE).
Methods: From a prospective cohort ($n = 1{,}550$, 65 centres with adherence to national and EU ethical approval) in the ICU stratum of the CENTER-TBI dataset [3], we extracted all clinical information collected during ICU stay (1,152 variables) as well as 6-month GOSE scores. We trained recurrent neural-network (RNN) models on a token-embedded time series representation of all variables [4] to return ordinal prognoses every 2 h. With repeated k-fold cross-validation (20 repeats, 5 folds) and bias-corrected bootstrapping, we evaluated ordinal discrimination and calibration, with 95% confidence intervals, over ICU stay. Furthermore, we implemented TimeSHAP [5] to calculate the contribution of clinical events and prior time periods towards automatically detected moments of changing prognosis for individual patients.
Results: Our model achieves adequate calibration (slopes: 1, fit curve [6]) at 8 h post-admission and its best ordinal discrimination (ordinal c-index [7]: 0.73 [0.72–0.74]) at 32 h post-admission. In Fig 1, we demonstrate a sample trajectory of patient prognoses over time during the ICU. Based on TimeSHAP values, we highlight clinical events that had the highest contribution to the change in prognosis. While clinically relevant effects varied significantly across the study population, we found changes in pupillary reactivity, neurofilament light chain and sedation to be the three most frequently important clinical events.

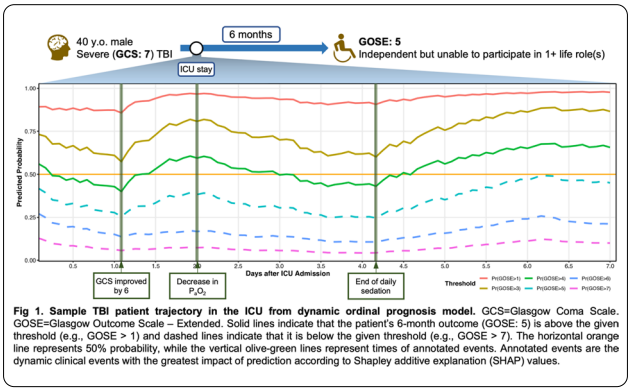

Fig 1. Sample TBI patient trajectory in the ICU from dynamic ordinal prognosis model. GCS=Glasgow Coma Scale. GOSE=Glasgow Outcome Scale – Extended. Solid lines indicate that the patient's 6-month outcome (GOSE: 5) is above the given threshold (e.g., GOSE > 1) and dashed lines indicate that it is below the given threshold (e.g., GOSE > 7). The horizontal orange line represents 50% probability, while the vertical olive-green lines represent times of annotated events. Annotated events are the dynamic clinical events with the greatest impact of prediction according to Shapley additive explanation (SHAP) values.

Conclusion: Our results validate the application of AI modelling for mapping TBI trajectories in the ICU. Our next step is to perform ITE calculations and validate applications for dynamic, targeted decision support.

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Acknowledgements
1. CENTER-TBI was supported by the European Union 7th Framework programme (EC grant 602,150). Additional funding was obtained from the Hannelore Kohl Stiftung (Germany), from OneMind (USA), and from Integra LifeSciences Corporation (USA). We are grateful to the patients of our study for helping us in our efforts to improve TBI care and outcome. We gratefully acknowledge interactions and support from the International Initiative for TBI Research (InTBIR) investigators.
2. S.B. is currently funded by a Gates Cambridge fellowship.

000418

Performing Clustering analysis in the Emergency Department to improve patient flow

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Introduction: This preliminary study uses the k-means algorithm to cluster emergency department (ED) patients into admission or discharge subgroups based on demographic and lab data.
Objectives: Aim of this clustering analysis is to assess the performance of an unsupervised algorithm in the ED. Implementing such a model into triage practice could theoretically assist healthcare professionals in decision making during ED triage, and possibly improve patient flow and reduce ED overcrowding.
Methods: During the year 2020, 13,991 overall ED visits for routine laboratory testing were recorded. We selected the pneumonology Dept and Covid dept visits to perform the cluster analysis and compare the results of the clustering method between these two departments. The dataset of the analysis included 13 lab exams, age, and ED outcome (admission or discharge). For missing data imputation, we applied the Multiple Imputations by Chained Equations (MICE) approach. For cluster analysis we used the R programming environment (version 4.1.1) in RStudio IDE (version 2021.09.0) and in particular the *dplyr*, *ggpubr*, and *factoextra* packages along with the *k*-means algorithm. The *k*-means clustering method takes as input a number of observations, *n*, and an integer, *k*, indicating the preferred number of clusters into which these *n* observations will be partitioned so that each observation is assigned to the cluster with the closest mean. The *k*-means algorithm's iterative approach minimizes the distance between each observation and the mean of the related cluster. To improve the clustering quality we applied the R function *FeatureImpCluster()*, which measures feature importance in *k*-means clustering. The importance of a feature is measured by the misclassification rate relative to the baseline cluster assignment due to a random permutation of feature values. The parameters picked out by this process were Age, C-Reactive Protein (CRP), hemoglobin (Hgb), neutrophil count (neut%), lymphocyte count (lym%), and Urea.
Results: Cluster allocation of the ED visits to the Pneumonology and to the Covid Dept, based on *k*-means and relative to actual hospital admission, is shown in Tables 1,2. Ideally, each row and each column of the tables would contain only one non-zero element.
Table 1. The allocation of the 2787 ED visits to the Pneumonology department relative to the hospital admission

	Clusters		
Admission	**1**	**2**	**Sum**
Yes	250 (10%)	1106 (40%)	1356
No	826 (30%)	605 (20%)	1431
Sum	1076	1711	2787

Table 2. The allocation of the 717 ED visits to the COVID department relative to the hospital admission

	Clusters		
Admission	**1**	**2**	**Sum**
Yes	55 (∼10%)	317(40%)	372
No	182 (25%)	163 (25%)	345
Sum	237	480	717

Conclusion: In this study, we used an unsupervised machine learning technique to compare the clustering results regarding admission/discharge of Pneumonology/Covid ED patients by means of age and lab exams. Cluster allocation performance did not differ between Covid and non-Covid patients. The discrepancy between cluster allocation and real-life scenarios in both departments, is mainly due to the lack of clinical indices in the dataset. Nevertheless, if we reduce the numbers described in the individual tables to percentages, we observe that the 2 departments are very similar. Maybe this just confirms that lab inputs are inadequate, but at least consistent across the board.

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Acknowledgements: None.

000517

Detecting Atrial Fibrillation on Unlabeled, Continuously Streamed Data Using Weak Supervision

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Intensive Care Medicine Experimental 2022, **10(2)**:000517

Introduction: Despite a wealth of physiologic data being collected in ICUs, a hurdle faced by clinician-scientists is that events not expressly denoted by the electronic health record or device alerts are cumbersome to annotate and thus difficult to study. Weakly supervised machine learning has been efficacious previously in identifying ectopic beats without need for labeled electrocardiogram data (Goswami 2021), thus decreasing the time and annotation effort required to create an effective detection model. However, atrial fibrillation is

more difficult to delineate, leading to many current detectors being trained and evaluated on curated, publicly-available databases. Atrial fibrillation (AF) is associated with significant morbidity and mortality (Bosch 2018, Lip 2018), and its detection using real-world data and weak supervision has not been rigorously explored.
Objectives: We aim to utilize real-world, high-frequency telemetry data to demonstrate the ability of weak supervision to yield a reasonable AF detection algorithm while minimizing expert annotations and data pre-processing.
Methods: We utilized high-frequency waveform data collected from 72 beds in a tertiary care center using a commercial monitoring system. Features describing instantaneous heart rate distribution/variability over 10-s telemetry segments were calculated. Clinicians derived rules based on these features to distinguish AF from other rhythms, which informed a weakly supervised model to detect AF. An iterative model-improvement process took place with a curated, clean evaluation set containing segments of AF, sinus rhythm, and specifically challenging rhythms. After revisions, a separate testing set enriched with segments with high heart rate variability was annotated for model evaluation on unseen data.
Results: Over 10,000 segments of telemetry data from 657 ICU patients were used to train our weakly supervised model. Our model applied to the hand-picked, clean evaluation set yielded precision of 0.76 and recall of 0.95 for AF and 0.97 and 0.86, respectively for other rhythms (accuracy: 0.89). Our testing set enriched with high heart rate variability segments demonstrated reduced performance (precision of 0.51, recall of 0.90 for AF; precision of 0.97, recall of 0.79 for other rhythms; accuracy: 0.81).
Conclusion: We demonstrated an accessible, time-saving means of model creation using weak supervision and real-world telemetry data to detect AF. Though the model performed reasonably on clean, hand-curated segments, performance faltered when adjudicating non-AF segments with noise artifact or higher degrees of heart rate variability such as sinus arrhythmia and ectopy. Applying available signal quality indices (Zhao 2018) coupled with additional heuristics that better delineate AF from irregular non-AF rhythms in order to improve our weakly supervised model could allow for better results without excessive efforts and costs.

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Acknowledgements

1. Dr. Clermont and Dr. Al-Zaiti are MPIs on National Institutes of Health grant R01 NR013912-08 (Predicting Patient Instability Noninvasively for Nursing Care-Two (PPINNC-3)).
2. This study was supported by National Institutes of Health grant R38 HL150207. SR
3. The University of Pittsburgh holds a Physician-Scientist Institutional Award from the Burroughs Wellcome Fund. SR
4. Dr. Clermont is a MPI on National Institutes of Health grant R01DK131586 (AI-driven Acute Renal Replacement Therapy (AID-ART)).

000644

Clinical profile and outcomes of 13,575 patients with COVID19 respiratory failure requiring Renal Replacement Therapy: A Machine Learning analysis

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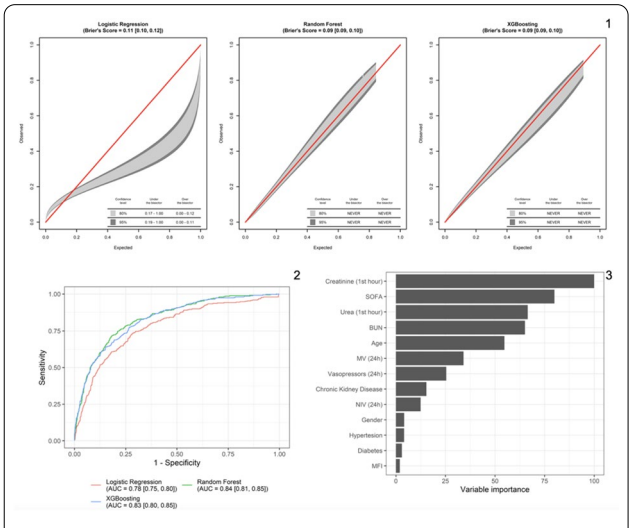
Intensive Care Medicine Experimental 2022, **10(2)**:000644

Introduction: Acute kidney injury (AKI) is a frequent and severe complication of Covid-19 infection in ICU patients associated with high resource use and poor outcomes.
Objectives: To propose a structured data-driven methodology and develop a model to predict the use of renal replacement therapy (RRT) for patients on respiratory support with Covid-19 in 126 ICUs from 42 Brazilian hospitals.
Methods: Adult ICU patients admitted from March 2020 to December 2021 with confirmed SARS-CoV-2 infection and under need of ventilatory support (invasive or NIV) in the first 24 h admission in the ICU. Main outcome was the need of RRT. We estimated three prediction models: Logistic Regression (LR), Random Forest (RF) and XGB Boosting. As predictors, we selected 14 variables based on the literature: age, gender, Modified Frailty Index, SOFA, diabetes, chronic kidney disease, hypertension, urea, creatinine, BUN, mechanical ventilation, noninvasive ventilation and use of vasopressors. Models were derived in the training set and evaluated in the test set following an 80/20 split ratio, and models' parameters were selected using fivefold cross-validation. We evaluated and selected the best model in terms of discrimination (AUC) and calibration (Brier's Score). Variable importance was estimated for each predictor variable.
Results: 13.575 ICU patients with need of respiratory support, of which 1.828 (14%) needed RRT. ICU and hospital mortality were respectively 15.7%, 20.3% (non-RRT) and 54.3%, 69% (RRT). Mean age was 63.9 and 55.3 years (RRT vs non-RRT). Mean ICU LOS was 27.8 vs. 12 days, in RRT vs non-RRT. Regarding severity of illness, patients RRT vs non-RRT presented the following (averages): Charlson's Comorbidity Index (1.55; 0.8); Modified Frailty Index (1.8; 1.11), SAPS-3 (65.01; 50.26), SOFA (7.01; 2.98).
RF and XGB models both showed higher discrimination performance compared to LR (95% confidence interval [95% CI]: 0.84 [0.81–0.85] and 0.83 [0.80–0.85] vs 0.78 [0.75–0.80]). RF and XGB models presented similar calibration (Brier's Score: ([95%CI]: 0.09 [0.09–0.10] and 0.09 [0.09–0.10]), which was also better than in LR (0.11 [0.10–0.12]). The final model (RF) showed no sign of under or overestimation of predicted probabilities in calibration plots. Physiological variables in the 1st hour (Urea, Creatinine and BUN), Age and the use of invasive MV in first 24 h were the most important variables in the model.



1 – Calibration belts for Logistic Regression (LR), Random Forest (RF) and eXtreme Gradient Boosting (XGB); 2 – Receiver Operating Characteristic (ROC) and Area Under the Curve (AUC) curves; 3 –Variables' importance for the Random Forest model.

Conclusion: The need of RRT among patients on respiratory support diagnosed with Covid-19 was accurately predicted through machine learning methods. RF and XGB based models using data from general intensive care databases provides an accurate and practical approach for the early prediction of use of RRT in Covid-19 patients.

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000663

Perioperative morbidy and mortality of patients with COVID-19 who required addmision to the ICU, after surgical procedures

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Intensive Care Medicine Experimental 2022, **10(2)**:000663

Introduction: There are few publications on the mortality of patients with COVID-19, who required surgical interventions.
Objectives: To study the postoperative morbidity and mortality of surgical patients with COVID-19, who required admission to the Surgical Intensive Care Unit (SICU), compared with patients without COVID.
Methods: Retrospective and observational study of patients admitted to the SICU, from October 2020 to May 31 2021 (second, third and fourth waves). We analyzed demographic variables, morbidity and mortality. T-Student was applied for continuous variables and X2 and Fisher test for qualitative variables.
Results: During the study period, 42 postoperative patients with COVID-19 and 1,319 COVID-19 negative patients were admitted to the SICU. There were no significant differences in demographic variables. Postoperative mortality was 26.2% in COVID-19 patients, compared to COVID-19 negative subjects. There were also statistically significant differences in the incidence of septic shock, ARDS, pulmonary thromboembolism, stroke, and acute myocardial infarction (Table 1). The incidence of acute renal failure was similar.
Table 1.

Postoperative complications	COVID-19 positive	COVID-19 negative	P value
Pneumonia	47,6%	15,2%	0,0001
ARDS	33,3%	9,4%	0,0001
Septic shock	35,7%	11,9%	0,001
AKI	25,5%	22,9%	N.D
Pulmonary embolism	16,6%	0,6%	0,001
Stroke	16,6%	2,3%	0,001
Myocardial infaction	14,3%	3,1%	0,001
Mortality	26,2%	6,9%	0,0001

Conclusion: COVID-19 is associated with an increased risk for serious postoperative morbidity and mortality.

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Acknowledgements: Not applicable.

Data Science 2 + Translational Biology 2

001078

Finding the Physiologic Switch to initiate weaning from mechanical ventilation: testing the water

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Introduction: Weaning from mechanical ventilation following recovery of acute respiratory failure is performed in all intensive care units globally. There has been a vast number of clinical studies and consensus about the initiation of weaning from invasive mechanical ventilation. (1) However, initiation of weaning from mechanical ventilation remains a process of trial and error. Numerous times clinicians need to stop weaning and change strategy as patients 'do not cope' with the initial reduction of ventilatory support. Furthermore, failed extubation is reported as high as 44% (2, 3).
This study set out to investigate if there are features of importance from a composite of clinical variables such as modes of mechanical ventilation, physiology, and use of sedation that could help to identify the switch to initiate weaning from mechanical ventilation.
Methods: Data were extracted from 926 patients admitted to the intensive care unit at two hospitals in London. Twenty-two clinical features were grouped into 4 categories 1) physiological data, 2) ventilatory parameters, 3) laboratory results and 4) sedative drugs.

We used an hourly synchronized method to align different medical events. To investigate their statistical relationship, we used imputation methods including the last observation carried forward for 24 h, and mean value imputation. We used three explorative algorithms to gain a better understanding of clinical variables commonly used to wean from mechanical ventilation to identify the ones that could be used as a switch to initiate weaning from mechanical ventilation. The three algorithms used were the Logistic Regression Model, the Decision Tree Model, and the Random Forest Model. The training was performed with 70% of the data and the remaining 30% was used for testing the model (Figure 1). The Random Forest and Logistic Regression Model were used to explore further the significant features identified by the Decision Tree algorithm.

Results: Following feature selection and handling of missing values. A dataset of 780 cases was used to test our hypothesis. The algorithms identified that the clinical features which most strongly contributed to the prediction of unsuccessful weaning were Mean Airway Pressure (MAP), Ventilatory Ratio, Minute Ventilation (MV), Respiratory Rate and P/F ratio, SpO2, PaCO2, and age. Using the above variables, the Logistic Regression Model, Decision Tree Model, and Random Forest Model achieved negative predictive values of 81.22%, 79.69%, and 80.82% respectively (Table 1).

Conclusion: Our constructed statistical models were unable to predict the successful initiation of weaning from mechanical ventilation. However, all three models were good at predicting unsuccessful weaning. Furthermore, we were able to identify features of importance that could confidently contribute to the prediction. Clinical features of interest should be treated cautiously due to the small sample size. Further work is needed before clinical interpretation is made.

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001105

Attitude towards artificial intelligence of intensive care unit professionals and their perceived barriers for implementation: A survey study

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Intensive Care Medicine Experimental 2022, **10(2)**:001105

Introduction: Over the past years, artificial intelligence (AI) has been increasingly studied for use in the intensive care unit (ICU) but to date only a handful of clinical studies have been conducted (1). Given the exponential growth rate and the emergence of guidelines and frameworks to guide AI from bytes to bedside (2), it is expected that more clinical ICU-AI studies may be conducted in the upcoming years. However, little is known about the attitude and experience of the healthcare professionals who ultimately need to use these technologies at bedside.

Objectives: To determine the attitude towards AI among healthcare professionals working in the ICU. Specifically, we aimed to assess their prior knowledge of AI, attitude towards AI, and perceived barriers for clinical implementation.

Methods: A cross-sectional survey study was performed in the ICU of the Erasmus Medical Center, the largest tertiary academic referral hospital in Rotterdam, The Netherlands between January 25, 2022 and February 25, 2022. The survey consisted of 22 questions and was distributed via email and in person among all intensivists and ICU nurses. Questions were related to: consent and demographics, prior AI knowledge, attitude towards AI, potential applications of AI and perceived implementation barriers. Attitude towards AI was specifically measured on a five-point Likert scale (ranging from 1: completely disagree to 5: completely agree) within five constructs described in literature: perceived mistrust in AI (3), perceived liability issues (4), perceived risks (5), perceived benefits (6) and intention to use AI (7).

Results: A total of 125 respondents (38.2%) completed the survey of which 92 (73.6%) were nurses. More than half of the respondents (74 [59.2%]) reported only to have heard of AI but not more than that. In general, we found a positive overall attitude towards AI when combining the five constructs, with a mean score of 3.3 (95% confidence interval [3.20, 3.31]) which did not substantially differ between subgroups (for example, we compared nurses versus intensivists and good versus poor prior AI knowledge). Importantly, the majority of the respondents (90 [72.0%]) had the intention to use AI in clinical practice, most frequently to lower the administrative burden (97 [77.6%]), when technology is ready. Nevertheless, most respondents (102 [81.6%]) also reported at least one or more implementation barriers, which were structured around lack of knowledge, high workload, and a lack of clear policy.

Conclusion: Most ICU professionals foresee many possible applications and are willing to use AI but they are in need of adequate information. To responsibly implement AI, ICU professionals should first have a general understanding of AI and as such commonly used terminologies and principles may need to be demystified by means of educational programs. In addition, hospitals need to draw up a policy for safe and responsible AI use (if not done already) and, in particular, be clear in their communication towards the healthcare professionals at bedside.

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Acknowledgements: There were no funding sources.

001139

COVID-19 ICU Admissions Pattern Throughout the Pandemic Across 10 US HHS Regions

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Introduction: COVID-19 pandemic is well studied, but it's impact on ICU admission pattern is still unclear. We aim to study the ICU admission pattern throughout the COVID-19 pandemic across 10 US Health and Human Services (HHS) regions.
Methods: This study was conducted using two publically and freely available databases; 1. The COVID Tracking Project- manually aggregated data from available sources from official, public state government sites, and 2. The US Department of HHS – state wise patient impact and hospital capacity data. The state wise ICU admission data was extracted and collated by noting ICU admission for the complete time range (from March 1, 2020 to March 7th, 2021) for dataset-1 and data reported between the dates of March 7th, 2021, to March 12th, 2022, for dataset-2. The HHS wise regional ICU admissions were then calculated by adding the respective daily state statistics and scaled to per 100,000 population. A 7-day moving average filter was finally applied to the data before visualization and analysis, to account for repeated days of missing recordings in the data sources. No patient and hospital identifiers were utilized; thus, study was IRB exempted.
Results: Based on proximity of the spikes in each wave, data visualization tools grouped, HHS regions 1, 2, 3, 5 in group A; regions 4, 6, 9 in group B, and regions 7, 8. 10 in group C. The visualization of data determined total 6 spikes till date. The start and end of spikes were determined by placing a threshold (1 case per day per 100,000 population) on the number of daily ICU admissions. The spikes were further divided when a given start/end date pair has multiple clear peaks. Maximum number of days difference observed between the occurrence of COVID-19 peaks in number of ICU admissions, were 48 days for spike-3 for HHS regions in group A (Compared to 4 and 14 days in group B and C, respectively). For Spike-5 it was highest in group C as 82 days (compared to 27 and 4 days in group A and B, respectively).

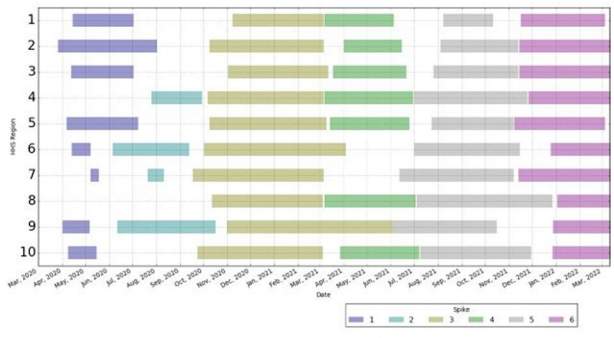

Figure 5: Timeline of spikes in COVID-19 ICU admissions in the US, by HHS region

Conclusion: In a latest COVID-19 ICU admission data analysis, after normalization of data, states in HHS regions, 4, 6, and 9 have the closest spikes throughout the pandemic. These regions included three most populous states of US (Florida, Texas, California) among others and consisted of 67 M (region 4), 42 M (region 6) and 51 M (region 9) people, total of roughly 50% US population.

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Acknowledgements: NA.

001250

Insertion cites of central venous catheter in adult hospitalized patients: a systematic review and network meta-analysis

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Introduction: Central venous access is a commonly performed procedure, accounting for approximately 8% of hospitalized patients requiring central venous access. The anatomic site chosen for central venous catheterization, including jugular, subclavian and femoral vein, influences complication risks. Recently, peripherally inserted central venous catheters have been used as a substitute for central venous catheters in an increasing number of hospitalized patients. Based on the current literatures, it is not conclusive which site is the most acceptable for central venous access considering various complications in hospitalized patients.
Objectives: We conducted a network meta-analysis to assess the clinically important complications of four sites including infectious, thrombotic, and mechanical complications.
Methods: The Cochrane Central Register of Controlled Trials, MEDLINE, Web of Science, Ichushi databases, Clinicaltrials.govand International Clinical Trials Registry Platform were searched. Studies including adults aged ≥ 18 years and RCTs that compared two different central venous access sites (internal jugular, subclavian, femoral, and peripheral vein) were selected. A frequentist-based approach with multivariate random-effects meta-analysis was used. The outcomes were clinically important catheter related infection, symptomatic venous thrombotic events, and clinically important mechanical complications which included pneumothorax, hemothorax, hematoma, and bleeding.
Results: Among the 5,819 records initially identified, 13 studies (6,201 patients) were included for a network meta-analysis. For clinically important catheter related infection, subclavian insertion was significantly associated with the lower risk than internal jugular insertion (risk ratio [RR], 0.30; 95% confidence interval [CI], 0.11–0.81). In addition, peripheral insertion decreased the infectious complication, compared with internal jugular (RR 0.06; 95% CI, 0.01–0.32); subclavian (RR 0.21; 95% CI, 0.05–0.77); and femoral insertion (RR 0.08; 95% CI, 0.02–0.40). For symptomatic venous thrombotic events, we did not find significant differences among insertion sites. For clinically important mechanical complications, femoral insertion decreased the complication risk, compared with internal jugular (RR 0.42; 95% CI, 0.21–0.82) and subclavian insertion (RR 0.33; 95% CI, 0.16–0.66). Peripheral insertion was also associated with the lower complication risk compared with internal jugular (RR 0.39; 95% CI, 0.18–0.85) and subclavian insertion (RR 0.31; 95% CI, 0.13–0.75).
Conclusion: The insertion site of central venous access that is most likely to cause the fewest complications should be selected, considering complication risks in individual cases, since baseline risks also depend on the operator experience, the expected duration of catheter placement and patient risk factor. Peripheral insertion may be a preferable site considering the lower risk of infectious and mechanical

complications. Further studies that directly compare peripheral insertion and centrally insertion are required for robust evidence.

001306

Awareness on workplace violence against healthcare professionals – An Emergency Medicine Perspective

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Intensive Care Medicine Experimental 2022, **10(2)**:001306

Introduction: Over the last few years, there have been several accounts of the rising incidence of violence against healthcare professionals in the developing world especially in emergency and critical care setting.The issue of violence in healthcare settings as a law and policy issue and its awareness continues to remain relevant.

Objectives:

1. To know what percentage of healthcare workers working in emergency medicine department have been affected by physical violence and verbal abuse.
2. To know what impact it has had on their emotional health and working capabilities.
3. To know if the healthcare workers are aware of the proper protocol to be followed in case of violence by patients / attendants.
4. To assess the basic knowledge of Indian Penal Code sections and medical acts involved in violence against healthcare professionals.

Methods: A questionnaire was answered by 250 medical and paramedical professionals.Questions were designed to assess 4 major parameters ie—Basic awareness of violence experienced in emergency services, legal discourse, essential IPC sections doctors should be aware of and personal experience and impact it had after experiencing verbal abuse and physical violence.

Results: Following are few of the basic observations noted in the study:

1. The awareness of legal discourse amongst resident doctors [1], consultants and under graduates were satisfactory. Nursing officials were not aware of legal provisions that safeguard healthcare professionals in the line of duty.
2. Amongst all physicians, residents [2] and nursing officers had experienced some or other form of violence in form of physical scuffle or verbal threat during their line of work.
3. The Knowledge of IPC sections was poor amongst all the participants except consultants.
4. Basic awareness on the prevalence of violence amongst healthcare professionals worldwide and in India was also poor amongst all study participants except consultants.
5. Healthcare workers who faced verbal and physical altercation18.7% reportedly had no impact on their mental health, 6.7% had been diagnosed as having clinical depression by a psychiatrist and 74.6% have experienced low mood ranging from a few hours to many days after the episode.
6. Assessing the impact violence and verbal threats have on healthcare workers we noted: 67.6% stated that it did not affect them, 24.3% reported that it affected their outlook towards all patients, 8.1% of health care workers reported that this affected their outlook only towards a particular group of patients / attendants who had a predilection to violence, identifiable by some abstract characteristics set.

Conclusion: The awareness of legal aspects on violence against healthcare professionals is low amongst resident physicians, undergraduates and nursing officers. It is recommended to include this topic in their core curriculum or competency assesment.

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Acknowledgements: No Grants recieved.

001353

RUPTURED- Retrospective analysis undertaken for Patients Treated for Unexplained Retroperitoneal/abdominal pain in Emergency Department

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Intensive Care Medicine Experimental 2022, **10(2)**:001353

Introduction: Acute abdominal pain is one of the commonest reasons for presentation to ED. Older individuals carry a higher mortality rate, with complex pathologies. Despite improvements in the management of older/ geriatric patients in ED, they continue to be a clinical challenge for ED physicians. There is considerable evidence to classify geriatric patients as high-risk emergency presentations, leading to RCEM standard elaborating that abdominal pain of more than 70 years requires a consultant sign off. However, there is scant data from within the UK which outlines the epidemiology of abdominal pain, the spectrum of presentations and the course in hospital following an emergent presentation to ED in older adults. Moreover, there is considerable mortality in older adults more than 50 years with an equally similar trend.

Objectives: To compare the variation in abdominal presentations to AE in the 50–69-year-olds to 70 years and above. For primary outcome measure, we sought to ascertain the leading cause of presenting complaints according to different diagnostic groups – abdominal pain, renal colic and back pain. For secondary outcome measures, we also assessed the representation rates in both age categories within 72 h of presentation and the all-cause mortality in 30 days.

Methods: Retrospective analysis of the patients of all patients over the age of 50 who presented to AE between January 2021 and July 2021. Data was collected from the AE presentation data and the trust intranet. Baseline characteristics, performance status, treatment received, complications sustained, relevant investigations performed and subsequent follow-up plan as well as representation rates were obtained. The demographics will then be analysed to assess the trend of disease presentation, re-presentation rates, admission rates, duration of AE stay, and allcause mortality at 30 days.

Results: A total of 920 patients presented to ED with complaints of abdominal pain at Blackpool Vicotria hospital between Jan and June 2021. The majority of the patients spent around 4–12 h in AE: (606/920). Overall, 32.5% were discharged with conservative measures, 60.7% were admitted, 1.6% were self discharged, and 0.7% were transferred to a tertiary centre. Around 3.2% died within AE. The total all-cause mortality at 30 days was 52 of the 920 presentations. In the study population, 53.6% were 50–70 years of age (Group 1) and 46.4% were older than 70 years (Group 2). There were more women (55.7%) than men in the study population and in Group 1 it was 54.97% and in Group 2 it was 57.61% of women.73.63% of patients in Group 1 and 78.69% of group 2 presented with abdominal pain. Most patients had abdominal pain for 1–2 days –49.49% in Group 1 and 51.05% in Group 2. In Group 1, 73.63%, and 21.1% 5.27%of patients presented with abdominal pain, flank pain and renal colic respectively. In group 2 the percentage was 78.69%, 17.56% and 3.75% respectively. The time spent in ED was most often 4–12 h in both groups (65.52% in Group 1 and 66.28% in Group 2). The biliary disease was the most common cause of pain accounting for 9.68% and 12.96% in Group 1 and group 2 respectively. The rate of admission was 64.91% and 69.09% in Groups 1 and 2 respectively. The most common cause for admission in both groups was biliary disease. The mortality rate in ED was 0.61% in Group 1 and 6.32% in Group 2. The specialist consults needed most often were surgery and urology (44.02%) in Group 1 and Medical (32.79%) in Group 2. Only 3.85% of patients in Group 1 and 4.92% in Group 2 presented again in 72 h. All-cause mortality in 30 days was 1.83% in Group 1 and 10.07%in Group 2.

Conclusion: In our retrospective analysis, the leading cause of abdominal pain was due to biliary disease. in both groups as well as the most common cause for admission. More women than men presented in both the age group, with higher all-cause mortality in women across all age groups. Although group 1 (50–69 years), had a higher representation rate within 72 h, the all-cause mortality in 30 days was higher in group 2 (70 years and above). Interestingly, in the patients that were represented- cholecystitis was most common and only 2 of the 920 patients (0.2%) required critical care admission.

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001198

Remdesivir Metabolite GS-441524 Effectively Inhibits SARS-CoV-2 VOC Infections in human lung organoids

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Introduction: Growing evidence indicates breakthrough infections in certain vaccinated individuals infected with SARS-CoV-2 variant of concern (VOC), especially Omicron variants [1–5]. To understand the mechanisms underlying SARS-CoV-2 infection and discover effective antiviral, appropriate models that can be used to faithfully mimic viral infection in the human body are urgently needed. Lung organoids are a 3-dimensional (3-D) organ-simulating system that contains airway-like structures surrounded by lung mesenchymal cells and other cell types from multiple germ layers including cells that express specific lung epithelial markers and recapitulate specific organ functions thus mimicking mature human lung [6] We hypothesized that human lung organoids are permissive to SARS-CoV-2 VOC infections and GS-441524, a fast-acting metabolite of Remdesivir, acts a potential therapeutic antiviral agent against breakthrough SARS-CoV-2 VOC infections.
Objectives: We established human induced pluripotent stem cell (iPSC)-derived lung organoids to investigate the infection and cytopathic effects and to examine the potency of GS-441524 against SARS-CoV-2 VOC.
Methods: Human lung organoids are generated from iPSCs based on a stepwise directed differentiation protocol [7]. We first performed single cell RNA sequencing to characterize and validate our lung organoids. We then infected the lung organoids with SARS-CoV-2 D614G, and SARS-CoV-2 VOCs including alpha, beta, delta variant at MOI 0.1 for 1 h, and Omicron BA.1 at MOI 0.2. We next administered GS-441524 (0.01 μM to 100 μM) in the infected lung organoids for assessment of viral gene copies and viral load 72 h post infection (hpi).
Results: Using immunostaining analysis, we validated our human lung organoids with surface expression of NKX2-1, pro-SP-C. Our single sequencing results showed 8 cell phenotypes in the iPSC-derived human lung organoids, including alveolar type II (AT2) and type I cells, airway epithelial cells, pulmonary neuroendocrine cells, fibroblasts, non-lung epithelial cells, proliferative cells and undifferentiated cells. At 72 hp, Median Tissue Culture Infectious Dose (TCID50) assay showed significant amounts of virus progeny in infected lung organoids infected with D614G ($P = 0.003$), alpha ($P = 0.006$), beta ($P = 0.062$), delta ($P = 0.0028$) and omicron ($P = 0.0006$) (student's t-test $^*P < 0.05$, $^{**}P < 0.001$), respectively. Immunostaining of the spike protein confirmed robust SARS-CoV-2 infection. Cytopathic effect was observed in the infected lung organoids characterized by swelling, detachment and shedding as compared to control lung organoids. We noticed a "ballooning" effect in the infected lung organoids resulting in uneven density throughout the organoids and these changes were attenuated with GS-441524 treatment. Moreover, GS-441524 reduced viral titer to near undetectable levels at 72 hpi ($P = 0.05$; student's t-test $^*P < 0.05$). We also observed reduced viral RNA in the lung organoids at 72hpi with GS-441524 ($P = 0.0304$; student's t-test $^*P < 0.05$).
Conclusion: Our human iPSC-derived lung organoids 1) pose similar cellular sources and microenvironment present in human lung, 2) are sensitive to SARS-CoV-2 VOC infection but responded differently to the VOCs in terms of cytopathic effects, and 3) can serve as an effective ex vivo lung model for drug testing against SARS-CoV-2 infection.

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Acknowledgements:
1. Canada 150 Research Chairs Program F18-01336
2. Canadian Institutes of Health Research COVID-19 grants F20-02343 and F20-02015.
3. Canadian Institutes of Health Research (OV3-170344, SBC-171482 and VS1-175560 to H. Z.)

001260

The effect of neutrophil depletion on endothelial activation in acute lung injury

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Introduction: The importance of neutrophils in development of acute respiratory distress syndrome (ARDS) is supported by investigations that have established a link between neutrophil recovery, vascular compromise, ARDS development and death (1,2). This would imply a protective effect of neutrophil depletion which is supported by preclinical data where therapeutic inhibition of neutrophil-dependent processes (i.e. CXCR2, IL8, P-selection, neutrophil elastase inhibition) protect against acute lung injury (3–7). Yet we know ARDS, with pathological findings of diffuse alveolar damage and hyaline membranes, develops in subjects during prolonged neutropenia, with autopsy sections in these subjects confirming no neutrophils in the lung parenchyma (8,9).
Objectives: We previously reported that neutropenic ARDS is associated with a plasma signature of immune dysregulation (increased tumor necrosis factor receptor 1, TNFR1) and vascular activation (increased intercellular adhesion molecule 1, ICAM1) (10). We sought to build on this finding by characterizing the plasma vascular proteome of neutropenic ARDS and ARDS control subjects. Next, in vivo, to understand if neutrophil depletion directly activates the endothelium, we used a murine model of neutropenic indirect lung injury to measure the impact of "neutropenic inflammation" on lung vascular injury responses.
Methods: To quantify the circulating vascular proteome, we performed exploratory plasma proteomics on Neutropenic ARDS (N = 6) and ARDS control subjects (N = 54) enrolled in the Weill Cornell Biobank of Critical Illness (BOCI) using O-Link through the Proteomics Core of Weill Cornell Medicine-Qatar. The O-link assays were performed using Inflammation (v.3021), Cardiovascular II (v.5005), and Cardiovascular III (v.6113) panels (O-link, Uppsala, Sweden). In vivo, C57BL/6 mice age 8–12 weeks were injected intraperitoneally (IP) with 240 ug of either Ly6G IA8 clone or LTF-2 isotype control (both BioXcell, Lebanon, NH) 24 h prior and immediate following high grade cecal ligation and puncture (CLP). Mice were sacrificed 24 h after CLP for organ harvest.
Results: Neutropenic ARDS subjects enrolled in the Weill Cornell Biobank of Critical Illness (BOCI) demonstrated a plasma signature of exaggerated immune signaling (TNFR1, Padj = 0.022) and vascular injury (Angiopoietin 2/Angiopoietin 1 (ANGPT2/ANGPT1) ratio, Padj < 0.001) compared to ARDS control subjects. In vivo, intraperitoneal Ly6G 24 h prior to high grade cecal ligation and puncture (CLP) and again immediately after surgery depleted the mature neutrophil population in the blood (99.6% depletion of Ly6Chigh Gr1high neutrophils) and lung (89.3% of CD11bhighGr1high neutrophils). Importantly, neutrophil depletion did not result in body temperature differences at organ harvest (32.4 versus 31.4 degrees Celsius, P = 0.64), highlighting that targeted neutrophil depletion would not impact our phenotype through differences in infection severity. Despite similar severity of illness, the neutropenic CLP mice phenocopied our human data. We isolated lung endothelial cells from Ly6G and isotype control mice after CLP and evaluated endothelial activation cytokines using a proteomic array (R&D, ARY028). Strikingly, neutrophil depletion led to increased endothelial derived inflammatory cytokines including endothelial IL-6, CXCL1, CXCL2, and RANTES, demonstrating altered endothelial responses in neutropenic conditions. Specifically, Ly6G depletion increased gene expression of the vascular injury/permeability factor angiopoietin 2 (ANGPT2) in the mouse lung after neutropenic CLP, recapitulating the high vascular injury (ANGPT2) environment of human neutropenic ARDS.
Conclusion: Neutropenic ARDS is associated with a plasma signature of immune dysregulation and vascular injury that is recapitulated in neutrophil deplete mice. Given the known role of inflammation in initiating vascular responses, our data bring forth the idea that the neutropenic environment is ideally suited to study the link between inflammation and vascular injury.

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Acknowledgements: D.R.P is supported by grants from NIH (US) (T32HL134629-01A1) and Stony Wold-Herbert Fellowship Fund (US).

001301

SARS-CoV-2 Variant of Concern – Challenge and Strategies

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Introduction: There have been more than 510 million confirmed cases of COVID-19, including over 6.2 million deaths, reported to WHO, as of May 1, 2022(1). The emerging SARS-CoV-2 variant of concern (VOC) is particularly challenging. A recent Canadian study found that with Delta infections, the risks of hospitalization jumped to 108% higher than non-VOC cases, with the risk of admission to ICU 235% higher and the risk of death 133% higher than the original virus (2). Since the first half of January 2022, the globe entered Omicron predominant period and the weekly growth rate reached 80.5% in April 2022 (3). Moreover, Omicron variant sub-lineages have shown increased transmissibility,

rose COVID-19 re-infection rate and lowed vaccine effectiveness and expanded breakthrough infections.
Objectives: The study is to offer the State-of-the-Art of potential therapeutic strategies against breakthrough infections.
Methods: Based on the viral structure and the mechanisms of its interaction with host cells, we are testing several potential therapeutic strategies against SARS-CoV-2 infection and its VOC in human lung organoids and humanized mice. The approaches include, but not limited to, using decoy viral particles, decoy host receptors and blockage of host receptor complex, as well as targeting the SARS-CoV-2 conserved non-structured protein regions and interrupting viral genome from which VOC with mutative spike proteins may escape.
Results: We have observed significant decreases in viral load, clinical manifestation scores, lung injury scores using recombinant human angiotensin converting enzyme 2 (ACE2) in humanized mice infected with SARS-CoV-2. We also demonstrated a potential prophylactic role of recombinant ACE2 and SARS-CoV-2 varus-like particles as decoys, as well as a CRISPR/Cas-13 single guide RNA to attenuate the numbers of viral gene copy and cytopathic effects in human lung organoids infected with Delta and Omicron (BA.2) variants.
Conclusion: The decoy host receptor, decoy virus-like particles and gene editing technique and perhaps drug repurposing have shown promising results that will facilitate the development of effective prophylactic and treatment capability against breakthrough SARS-CoV-2 infections.

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Acknowledgements: This work was supported by the Canadian Institutes of Health Research (OV3-170344, SBC-171482 and VS1-175560).

001434

Inflammatory versus resolutive responses and endothelial dysfunction in critically ill patients: differences in cardiogenic shock, septic shock and critical COVID-19 profiles

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Introduction: Precision medicine envisions that identification of biological "phenotypes" will lead to personalized treatment and improved outcomes (1). COVID-19 proof-of-concept of modulation of inflammatory response for an infectious insult (2) poses into question whether promoting resolution could be an attractive option (3). Also, the post-mortem analysis of the lungs from patients with Covid-19 showed severe endothelial injury compared with influenza A (4). The recognition of biological patterns is a rare strategy in literature but could illuminate putative therapeutic design pathways.
Objectives: Our team aimed to evaluating the inflammatory versus pro-resolutive responses and endothelial dysfunction in common diagnosis in ICU differentiating, in particular, cardiogenic shock (CS), septic shock (SS) and COVID-19 diseases.
Methods: We evaluated inflammatory response and endothelial dysfunction biomarkers in CS (n = 25), SS (n = 20) and critical COVID-19 (n = 34) patients in blood samples collected at days 1–2 (admission), 3–4 and 5–8. Blood donors were used as controls (n = 45). Tumour necrosis factor alpha (TNF-α), interleukin 1 beta (IL-1β), interleukin 6 (IL-6), resolvin D1 (RvD1), resolvin E1 (RvE1), endocan, intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) and E-selectin, were determined by immunoassays.
Results: Admission TNF-α was increased in SS and COVID-19 compared to controls and CS. Along hospitalization, TNF-α remained higher in COVID-19 but not in SS. Admission IL-1β was increased in COVID-19 compared to controls, CS and SS. During hospitalization, IL-1β remained higher in COVID-19 compared to CS and SS. Admission IL-6 and IL-10 were increased in all patients' groups and were reduced only in CS and SS during hospitalization. COVID-19 had lower RvD1 and higher RvE1 than controls, CS and SS at admission and throughout hospitalization. Along hospitalization, no differences in RvD1 were observed within each patient group, but RvE1 increased only in COVID-19. Admission endocan and VCAM-1 were higher in all patients' groups, with COVID-19 patients exhibiting lower endocan than CS patients. A decreasing profile during hospitalization was observed only in SS for endocan and in SS and COVID-19 groups for VCAM-1. Admission ICAM-1 was increased in CS and SS, but not in COVID-19 when compared to controls, and again it decreased only in SS during hospitalization. Admission E-selectin was higher in SS patients compared to controls, CS and COVID-19 patients and remained higher in SS during hospitalization.
Conclusion: COVID-19 patients appear to have exacerbated and prolonged inflammation and remarkable dysregulated proresolving responses which are not counteracted by early measures. Although endothelial dysfunction is present in all patients' groups, endocan and E-selectin appear to be more related to CS or SS pathogenesis, respectively. Moreover, endothelial dysfunction seems to be more difficult to treat in CS.

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Acknowledgements: FCT/COMPETE, PTDC/MEC-CAR/32188/2017 and RESEARCH4COVID-19-Proj 519-613690173.

Data Science 3

000692

Development of an image-based electrocardiographic biomarker for COVID-19 prognostication

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Intensive Care Medicine Experimental 2022, **10(2)**:000692

Introduction: Coronavirus disease 2019 (COVID-19) infection can result in cardiovascular involvement, with such patients having a significantly higher morbidity and mortality rate. Electrocardiogram

(ECG) is a simple and non-invasive diagnostic modality that has a substantial clinical impact on investigating the severity of cardiovascular diseases. However, it is very high dimensional data and difficult to interpret and quantify. We aimed to develop easily interpretable single numeric value using artificial intelligence (AI) from ECG image to prognosticate the critically ill patients with COVID-19 infection.
Methods: We retrospectively analyzed all COVID-19 patients admitted from February 2020 to March 2021 to the Intensive Care Unit of single tertiary academic hospital. Initial 12-lead ECG images performed within 3 days after admission were used. A CNN-based encoder, named Quantitative Cardiography (QCG) was used to covert each ECG image into a fixed-size vector (244 elements). The CNN-based encoder was originally developed as a part of a smartphone-based AI ECG analyzer using smartphone Camera. The dataset made of the vector output were split into train and test dataset with split ratio of 3:1. A random forest classifier using only the vector output was fit to the train dataset and evaluated in the test dataset. The primary goal of this model was to predict poor outcomes, defined as death during admission or initiation of Extracorporeal Membrane Oxygenation.
Results: A total of 167 patients were included. The median age was 67 (IQR: 58–76) and the number of male patients were 89 (53.3%). Forty-six patients (27.5%) were classified as poor outcome group. Among non-ECG predictors, initial Troponin I level (AUC: 0.787) and SOFA score (AUC: 0.777) were the strongest predictors. Among the QCG vector elements, element-147 showed best performance (AUC: 0.816) followed by element-3 (AUC: 0.791). Combining the ECG vector elements as a single biomarker using a random forest classifier fitted in the training dataset resulted in an AUC of 0.865. The biomarker's sensitivity, specificity, positive and negative predictive values in predicting the main outcome were 91.6%, 56.6%, 45.8% and 94.4%, respectively, when optimal cutoff value (0.350) determined in the training dataset were used.
Conclusion: Electrographic biomarker demonstrated good power to predict poor outcomes in critically ill patients with COVID-19 infection. Deployment of the digital biomarker could potentially inform clinical triage where expedient and reliable decision-making is key.

000718

Implementation of the WHO sentinel surveillance system for influenza-like infection (ILI) and severe acute respiratory infections (SARI) in Ziauddin Group of Hospitals Karachi

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Intensive Care Medicine Experimental 2022, **10(2)**:000718

Introduction: Influenza viruses are a leading cause of severe acute respiratory infections (SARI) and influenza-like infection (ILI), especially in middle-aged and young adults (1). Thus, surveillance is essential for identifying new strains, detecting atypical symptoms, and determining the disease burden. Identifying populations with a more significant illness burden can help direct preventative activities and assist towards more effective resource allocation.
Objectives: The overarching aim was to maintain a database of patients presenting with ILI/SARI at the Ziauddin Hospital sites for WHO-ILI/SARI sentinel surveillance. Secondary objectives included investigating the descriptive epidemiology of patients with ILI/SARI and identifying potential patient populations based on trends found.
Methods: A prospective observational study was conducted using a case report form for the survey adapted from the existing Global Influenza Surveillance and Response System (GISRS). Ziauddin University Hospitals served as the sentinel location. All patients reporting at Ziauddin University Hospital with a history of fever and cough for the last ten days were included. Ethical approval was obtained from the Ethics Review Committee (ERC) of the Ziauddin University, and the data was collected and recorded in the Research Electronic Data Capture (REDCap) database. Every day, all patients who meet the above-mentioned inclusion criteria were recruited for ten months. Data were collected per the WHO ILI and SARI Case Reporting Proforma (COVID-19) CRF. A coordinator was trained to lead local implementation by supporting data collection and dashboard navigation. Data were analyzed using STATA (16.1, StataCorp LLC, College Station, TX) and SPSS (24.0, IBM Corp, Armonk, NY, USA). For categorical variables, numbers and percentages were computed. Whereas continuous variables with normal and non-normal distributions were reported as mean (SD) and median [inter-quartile range (IQR)], respectively. The data extraction sheets have been password protected and stored at the workplace of the principal investigator.
Results: Among 27854 screened patients, ILI/SARI has been confirmed in 306 (1.1%) cases. The highest numbers detected were in the month of May (n = 78, 25.5%) and Aug (n = 59, 19.3%). Other than fever and cough, most detected symptoms were sore throat (n = 30, 9.8%), nasal discharge (n = 23, 7.5%) and headache (n = 22, 7.2%). The majority had the risk factor of living with family members who had flu like symptoms (n = 224, 73.2%). Out of 221 ILI/SARI cases, 160 (72.4%) were COVID-19 positive. A total of 282 (92.1%) cases were from within the city.
Conclusion: The ILI/SARI cases peaked and coincided with the COVID-19 wave in Karachi. This surveillance helped identify ILI/SARI burden, which can contribute to more efficient resource allocation, demonstrating its importance in Pakistan.
Amendment
UK Foreign, Commonwealth and Development Office and Wellcome funded (222,048/Z/20/Z), enabling ISARIC Clinical Characterisation Protocol (CCP) roll out in LMICs, including Pakistan, through Pakistan Registry of Intensive Care (PRICE).

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Acknowledgements: WELCOME trust funded the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) to support the roll out of the ISARIC WHO Clinical Characterisation Protocol (CCP) across LMICs including Pakistan through Pakistan Registry of Intensive Care (PRICE).

000769

Salzburg Intensive Care database (SICdb) - A Preliminary Outcome Analysis

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Intensive Care Medicine Experimental 2022, **10(2)**:000769

Introduction: The flood of data generated during medical care, especially in the setting of critical care is underutilized and often wasted.1,2 To make medical data more widely assessable and easier to utilize numerous databases containing data from different ICUs have been created.3–6.
Objectives: The aim of SICdb is to create a database that provides a simple and efficient way to analyze critical care data generated at the Department of Anesthesiology and Intensive Care Medicine at the University Hospital Salzburg (SALK).
Methods: SICdb provides insight to over 27.000 intensive care admissions, including therapy and data during preceding surgery. Data was collected between 2013 and 2021 from 4 different ICUs at one single tertiary care institution. The dataset contains, amongst others: case information, scoring, laboratory values, medication, monitor and respirator signals as well as configuration data. SICdb provides highly granulated once per minute data and is preprocessed hourly. The

database is populated with data collected with MetaVision (iMDSoft, Tel Aviv, Israel) patient data management (PDMS) software. Additionally, exports from ORBIS (Dedalus Healthcare GmbH, Bonn, Germany), containing admission, discharge and ICD—10, are included. SICdb is fully approved by the local ethical commission of the Land Salzburg, Austria. (EK Nr: 1115/2021). The exporting and processing procedures are repeatable and allow for incremental updates. All data is pseudo anonymized as defined by the European General Data Protection Regulation, Article 4(5). (The European Parliament, 2016) The deidentification strategy additionally complies with the 'Guidance Regarding Methods for De-identification of Protected Health Information in Accordance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule'. Only deidentified raw data is processed to the final database. The SICdb server software provides data as multiple entities and prepares data for export to numerous statistical software solutions.

Results: The SICdb dataset, version 1.0.1 contains 27,386 admissions to an ICU at the Department of Anesthesiology and Intensive Care Medicine at SALK and the Paracelsus Medical University (PMU). Overall Length of stay was 3.50 [SD 6.49] days. 26,446 [96.55%] patients were alive at ICU discharge and 25,252 [92.20%] were alive at hospital discharge, respectively. Table 1 shows further examples of demographic data included in SICdb.

Table 1: Demographic data/diagnosis of the SICdb population

Demographic Data	
Sex female (n [%])	17,092 [62.41%]
Sex male (n [%])	10,285 [37.56%]
Sex unknown/diverse (n [%])	9 [0.03%]
Simplified Acute Physiology Score III (SAPS III) (mean [SD])	44.67 [14.81]
Mechanically ventilated > 24 h (n [%])	2406 [8.79%]
CRRT during stay (n [%])	1027 [3.75%]
Most common ICD-10 diagnosis	
I25.X (ischemic heart disease) (n [%])	1930 [7.05%]
I70.X (atherosclerosis) (n [%])	1352 [4.94%]
I35.X (non-rheumatic aortic valve disease) (n [%])	1186 [4.33%]
I71.X (aneurysm or dissection of aorta) (n [%])	863 [3.15%]
I65.X (occlusion of cerebral artery) (n [%])	741 [2.71%]
S72.X (femur fracture) (n [%])	544 [1.98%]

Conclusion: SICdbis one of the largest, high granulated ICU datasets available today. To our knowledge only two comparable (and accessible) databases do exist in Europe.5,6 Our first outcome analysis shows short length of stay and a low overall mortality. We believe that SICdb will develop to a valuable tool for further research, as we intend to continuously develop the dataset and make it available to external researchers in the near future.

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000860

Mining Association Rules in the antibiotic resistance profile of critically ill patients in the Intensive Care Unit

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Intensive Care Medicine Experimental 2022, **10(2)**:000860

Introduction: Machine learning (ML) techniques are progressively gaining ground in biomedical sciences, modifying medical routine. Association rule mining (ARM), is an unsupervised ML method that detects patterns, links, or interesting relationships within large databases.

Objectives: The aim of this preliminary study is to use an unsupervised ML technique in the antimicrobial susceptibility dataset of critically ill patients in the Intensive Care Unit (ICU), in order to extract the most important association rules among the selected variables.

Methods: Data from the Microbiology Laboratory of patients admitted to the ICU of a Greek public tertiary hospital over 12 months (2019) were studied. We investigated the existence of association rules in the antibiotic resistance profile of two frequently encountered gram-negative multidrug-resistant bacteria (MDR)-*Klebsiella Pneumoniae* and *Acinetobacter baumanii*.The 4,515-instance data set contains the attributes of gender (binary), bacterial species (categorical–*K. pneumoniae, A.baumanii*), antibiotics (categorical- 30 antibiotics), specimen (categorical—Respiratory secretions, Pus, Peritoneal (ascitic) fluid, Blood, Urine, Tissue, Catheter tip, Pleural fluid), and the binary class attribute (antimicrobial susceptibility—Resistant, Sensitive) obtained by the culture process. We used the R programming language, specifically the '*arulesViz*' and '*arules*' packages, as well as the Apriori algorithm. The *Apriori* algorithm, which mines frequent itemsets and interesting associations in transaction databases, is the most popular association rule mining tool.

Results: The association rules that can be inferred based on the given antimicrobial susceptibility data set can be parametrized according to the knowledge that clinicians want to extract from the database. For example, by setting *minsup* and *minconf* thresholds to 0.001 and 0.50, respectively, the first four rules sorted by decreasing order in respect of confidence are presented in the following sample outputs.

Table 1 The first four rules for *K.pneumoniae* sorted by decreasing order in respect of confidence

LHS				**RHS**	**Measures**		
Gender	**Type**	**Bacteria**	**Antibiotic**	**Susceptibility**	**Support**	**Confidence**	**Lift**
F	Blood	*K.pneum*	Cefta/avi	S	0.0014	1,00	2.8351
F	Resp	*K.pneum*	Cefta/avi	S	0.0037	1,00	2.8351
M	Resp	*K.pneum*	Cefta/avi	S	0.0066	1,00	2.8351
M	Blood	*K.pneum*	Gentamycin	S	0.0019	1,00	2.8351

Table 2. The first four rules for *A. baumanii* sorted by decreasing order in respect of confidence

LHS				RHS	Measures		
Gender	**Type**	**Bacteria**	**Antibiotic**	**Suscep-tibility**	**Support**	**Confi-dence**	**Lift**
F	Blood	*A.baumanii*	Tigecycline	S	0.0013	1,00	16.3219
M	Blood	*A.baumanii*	Tigecycline	S	0.0021	1,00	16.3219
M	Resp	*A.baumanii*	Tigecycline	S	0.0014	0,85	13.8736
M	Blood	*A.baumanii*	Colistin	S	0.0017	0,57	9.3268

For example, the first row of Table 1 can be stated as follows: IF the patient is female AND the sample type is Blood AND the bacteria detected is *K.pneumoniae* AND the antibiotic used is Cefta/Avi, THEN the susceptibility testing will show that this bacteria is sensitive to Cefta/Avi.

Conclusion: Association rule mining is an evolving technique that combines statistics and ML to discover interesting correlations among items in aggregated data. We applied ARM in an antibiotic susceptibility dataset, to reveal the most meaningful rules in the antibiotic resistance profile of ICU patients with MDR infections, as a new option to explore data relationships. Limitations are the small sample size and the limited time-frame.

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Acknowledgements: None.

000868

Causal inference in the intensive care unit: preliminary results of a methodological systematic review

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Intensive Care Medicine Experimental 2022, **10(2)**:000868

Introduction: The majority of the developed prediction models in the intensive care unit (ICU) domain, often presented as clinical decision aids, remain within the prototyping phase.[1] We hypothesize that this slow clinical adoption is partly because an accurate prediction of a patient outcome does not tell us *what to do if* we want to change that outcome. In other words, accurate predictions are not necessarily actionable. Unlike prediction, causal inference considers outcomes under different courses of action,[2] which is key in decision making in the ICU. Randomized trials are currently the gold standard for causal inference but could be impractical and findings sometimes fail to generalize [3]. Under certain assumptions, causal inference is possible based on observational data. However, inappropriate use of methodology and unmet assumptions may lead to false conclusions. Therefore, good reporting is important and assumptions and findings should be validated where possible.

Objectives: To emphasize the importance of causal inference in clinical decision making, stress the difference compared to prediction, and systematically review and appraise the quality of published causal inference studies in the ICU domain.

Methods: We searched six databases (MEDLINE, EMBASE, Web of Science, Google Scholar, medrXiv and biorXiv) to find causal inference studies (1) in the adult ICU domain, (2) based on observational data, (3) which examine time-varying exposures. The first reviewer (JS) performed title-abstract screening for eligibility. Studies for which doubt remained will be screened full-text by the first reviewer and sample checks will be carried out by two other reviewers (JK and MvG). For each eligible study, we will collect study characteristics and judge the quality based on reproducibility, reporting of modeling assumptions and study findings.

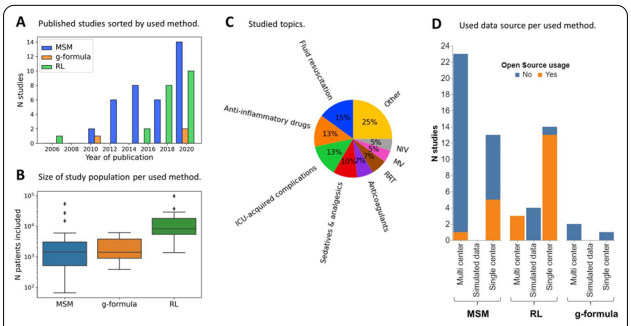

Figure 1. Characteristics of the thus far included studies.
MSM=marginal structural model, RL=reinforcement learning, ICU=intensive care unit, RRT=renal replacement therapy, MV=mechanical ventilation, NIV=non-invasive ventilation

Results: 1714 studies were identified after duplicate removal. Based on title and abstract screening, we included 60 studies and doubt remained for 66 studies (now staged for full-text screening). Figure 1 summarizes the (thus far) collected study characteristics. Marginal structural models (MSMs) were applied most (36), followed by RL (21) and the g-formula (3). Studies that used RL generally included more patients compared to studies using MSMs and the g-formula. The most studied topic (15%) was fluid resuscitation and 36.6% of the studies utilized one or multiple open source ICU databases.[4–6] The MSM studies mostly used multi-center data (64%). In contrast, RL studies mostly used a single-center open-source database [4] (67%). Further screening, item collection and quality assessment is currently in progress.

Conclusion: Recently, the number of causal inference studies using observational ICU data is rising and their findings should be carefully interpreted. This review will provide an overview and critical appraisal, discuss current limitations in methodology and point out areas for future research.

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000882

Modelling the number of mechanically ventilated COVID-19 beds in the UK using neural net autoregression (NNAR)

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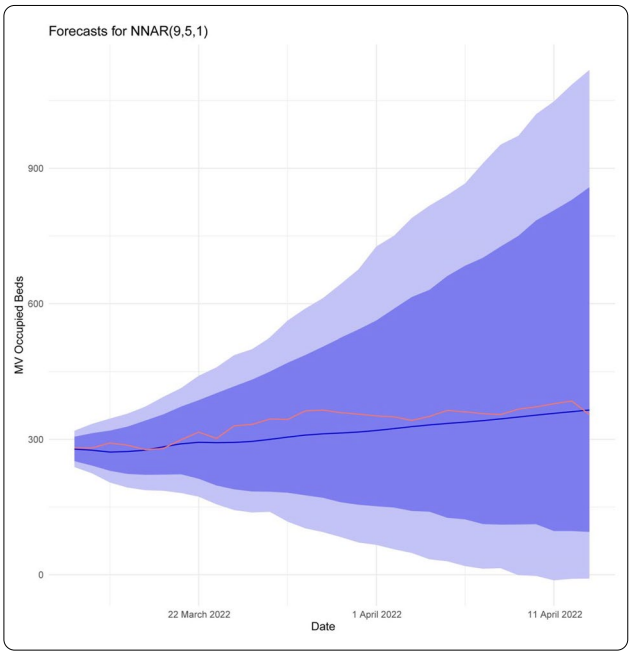
Introduction: Throughout the pandemic in the UK, the pressure on providing mechanically ventilated (MV) beds to patients with critical COVID-19 has been incredibly high. Various forecasting methods can be employed to model and predict the need for MV beds. NNAR models can be regarded as a network of neurons or nodes that represent complex nonlinear relationships and functional systems. This and other forecasting models have already been successfully applied to COVID-19 data from other countries (ArunKumar et al.). Forecasting using the absolute number of MV beds may be considered a more robust measure of how the COVID-19 pandemic affects critical care services in the UK.
Objectives: Our aim was to assess the ability for NNAR to model the observed data for MV occupied beds in the UK and test the accuracy of a 30-day prediction using the most recent and available data.
Methods: Freely available data was downloaded from the COVID-19 Gov.UK website (https://coronavirus.data.gov.uk/). Daily records of MV occupied beds were available from 02/04/2020 to 13/04/2022. The training set utilised the data between 02/04/2020 to 14/03/2022 (713 days). The test set for the 30-day prediction was taken from 15/03/2022 to 13/04/2022. Measures of accuracy used to assess the performance of the training and test model data included root mean squared error (RMSE), mean absolute percentage error (MAPE) and the mean absolute scaled error (MASE). The NNAR model was generated using the *nnetar()* function from the *forecast* package (Hyndman et al.) that is part of the R environment (version 4.1.3, Austria, Vienna).
Results: The NNAR(9,5,1) model for observed and expected values was highly accurate as demonstrated by the MAPE and MASE that were lower than 10 and 1 respectively (Table 1). The 30-day value predicted by the NNAR (9,5,1) model was 365 occupied beds, and the actual observed number of beds was 355 (see Figure – blue line: expected, red line: observed, dark blue area: 80% prediction intervals; light blue area: 95% prediction intervals). This represented an absolute error of + 10 (2.7%) MV occupied beds.

Table 1

NNAR(9,5,1)	RMSE	MAPE	MASE
Observed	21.05145	2.56027	0.55758
Expected	27.43573	6.68583	0.89967



Conclusion: We have demonstrated that NNAR is capable of accurately modelling and predicting the number of MV occupied beds in the UK. Similar models have also yielded accurate results for forecasting the need for both hospital and MV COVID-19 beds. The use of NNAR and other forecasting models can assist healthcare service delivery providers in determining the ongoing need for MV beds, purchasing protective equipment for staff and patients, and workforce requirements for example. However, given the highly dynamic nature of the COVID-19 pandemic, longer term predictions (i.e. > 30-days) should be applied cautiously, and these methods of forecasting are best used to inform short-term decision-making processes.

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Acknowledgements: Nil grant.

000888

Predicting adverse long-term neurocognitive outcomes after pediatric intensive care unit hospitalization

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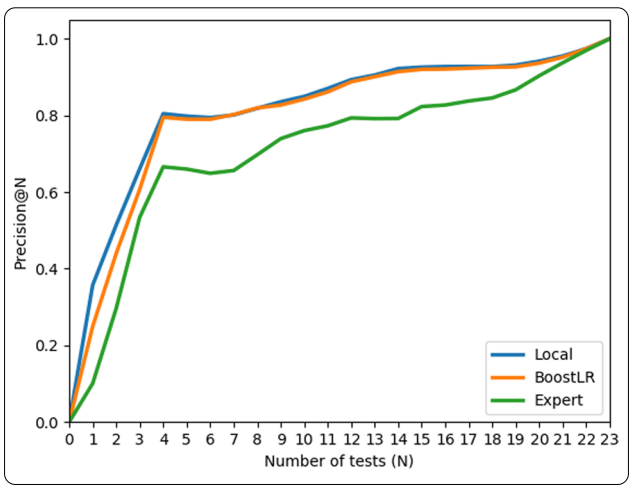
Introduction: Critically ill children often suffer from impaired neurocognitive functions years after paediatric intensive care unit (PICU) discharge, which severely hinders their overall quality of life [1]. These functions can be assessed during a follow-up evaluation where the patients are subjected to a fixed order of clinically and internationally validated tests [1]. However, this evaluation can be arduous, since it requires the concentration of patients for approximately 4 h, leading often to interrupted evaluations. In this work, we employ machine learning to predict a personalized order of tests which aims to reduce the number of tests required to identify the most severe neurocognitive deficiencies.
Objectives: Our objective consists of building a machine learning model that predicts a personalized sequence of tests for each patient. This sequence prioritizes tests associated to neurocognitive functions that are expected to be affected, and, differently from the approach currently employed in clinical practice, considers the features of each patient, providing valuable clinical validation for the use of individualized follow-up after PICU discharge.
Methods: We employed data obtained in a 2 years follow-up from the PEPaNIC-RCT (ClinicalTrials.gov-NCT01536275 [1,2]. The dataset includes 786 previously hospitalized patients and 405 healthy control individuals, and was collected in three PICUs located in Leuven, Rotterdam and Edmonton. It contains 23 features, including age, gender, socioeconomic status, STRONGkids risk score, PELOD score, duration of ICU stay, mechanical ventilatory support, among others [1]. These features are available at discharge from the PICU. Furthermore, it presents 5 groups of outcomes: intelligence (measured with 3 outcomes), visual motor coordination (1 outcome), alertness (4 outcomes), motor coordination (4 outcomes) and memory (11 outcomes), resulting in 23 tests. We adopted a normalization procedure, where outcomes of patients are transformed from absolute values to values relative to the outcomes of the control individuals, thus generating a new dataset. We

also proposed a novel method, named Local, that first builds 5 random forests, one per group of outcomes, that rank only the labels within their group, and then combines the rankings. Using the transformed dataset, we compared our approach against two approaches: i) Expert: the fixed order currently employed in clinical practice [1] and ii) BoostLR: a recently proposed machine learning method for label ranking [3]. As the evaluation measure, we employed Precision@N which measures the proportion of correctly predicted tests in the top-N predicted tests [4]. All experiments were repeated using 5 times tenfold cross-validation.



Results: As shown in the Figure, our proposed method, Local, was mostly associated with better performance where its performance raises faster than the others, surpassing its competitor methods. A visible difference is perceivable with 4 tests where our method reaches 80% of precision, whereas the Expert achieves only 66%, meaning that Local predicts on average 3.2 out of 4 outcomes correctly. The difference between Local and BoostLR is mostly noticeable when a small number of tests and age-restricted sub-analysis are considered. Furthermore, as the feature importance reveals, the age of the patients was considered the most relevant feature, which was also identified in other studies from the literature [5].
Conclusion: Machine learning methods are capable of accurately predicting the neurocognitive outcomes expected to be most affected in PICU patients based on (pre-)PICU features. These methods can be used to shorten the length of follow-up assessment, assessing only those outcomes that are affected. This provides a step towards enabling preventive, tailored care, starting immediately after discharge, rather than curative care at a later moment during follow-up.

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Acknowledgements: This work was supported by Research Fund Flanders (through research project G080118N) from the Flemish Government (AI Research Program); by European Research Council Advanced Grants (AdvG-2012-321670 from the Ideas Program of the European Union 7th framework program and AdvG-2017-785809 from the Horizon 2020 Program to GVdB); by the Methusalem program of the Flemish government (through the University of Leuven to GVdB, METH/08/07 and to GVdB and IV, METH14/06); by the Institute for Science and Technology, Flanders, Belgium (through the University of Leuven to GVdB, IWT-TBM150181 and IWT-TBM110685); by the Sophia Research Foundation (SSWO to SV); by the Stichting Agis Zorginnovatie (to SV); Nutricia Research B.V (to SV); by the Erasmus Trustfonds (to SV); and by an European Society for Clinical Nutrition and Metabolism (ESPEN) research grant (to SV).

001016

Cardioversion of new-onset atrial fibrillation in a non-cardiac and non-obstetric post-operative MIMIC-IV cohort

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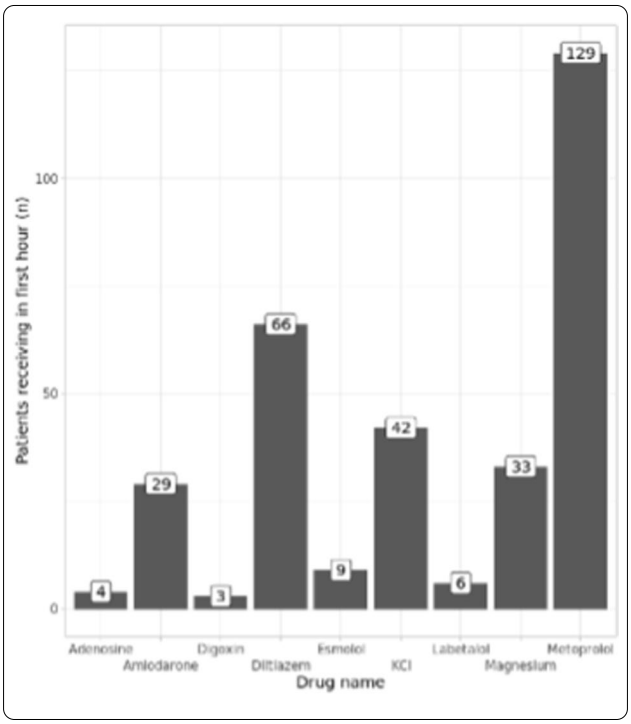
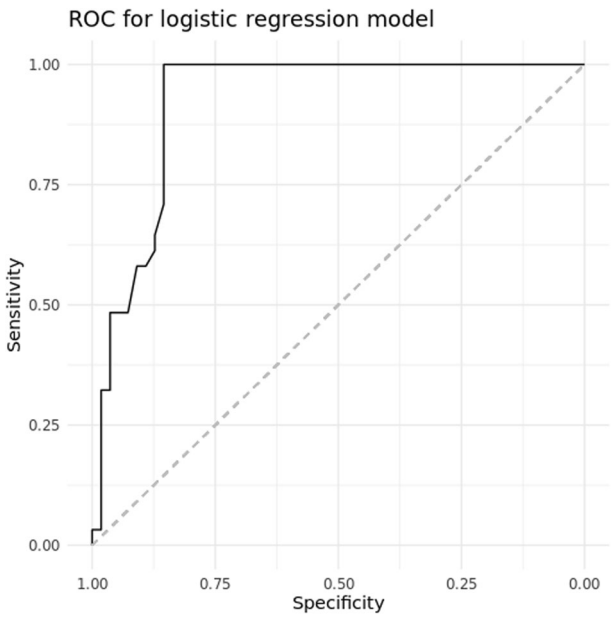
Intensive Care Medicine Experimental 2022, **10(2)**:001016

Introduction: New-onset atrial fibrillation (NOAF) is a common problem on intensive care (ICU) among post-operative surgical patients; risk factors include age and degree of physiological disturbance(1). Strategies to control the rate and rhythm are well described with different focusses depending on the clinical scenario(2).
Objectives: To identify factors predicting NOAF resolution in post-operative ICU patients.
Methods: A time-limited subset of post-operative non-cardiac and non-obstetric ICU patients was selected from the MIMIC-IV database(3), excluding patients with pre-existing AF. Rate of NOAF resolution and the time to resolution were calculated. Drugs administered from the onset and the following hour were identified and analysed with multivariate logistic regression.



Results: 12,756 post-operative ICU patients were identified from the dataset, of whom 6,181 were identified as not having developed AF prior to ICU admission and had sufficient further data. 433 (7%) developed AF during their ICU stay. The median time to AF from admission was 16.2 h (IQR 4.8–37.5). 312 (72%) of these reverted to a non-AF/flutter rhythm. The median time to resolution was 180 min (IQR 60–540). Figure 1 shows the frequency of relevant medications in the first hour after NOAF. The most administered medications were metoprolol and diltiazem.



A logistic regression model was trained on 80% of the dataset, which revealed significant associations with the administration of amiodarone ($p < 0.001$), diltiazem ($p < 0.001$), labetalol ($p < 0.01$) and metoprolol ($p < 0.001$). Administration of potassium chloride and magnesium sulfate were each associated with cardioversion (both $p < 0.01$). No association with adenosine, digoxin or esmolol was seen, nor with gender and age 75. The model was tested against the remaining 20% of the dataset demonstrating 85% sensitivity and 90% specificity and ROC AUC 0.922.

Conclusion: This study supports the administration of amiodarone, diltiazem, labetalol or metoprolol as predictors of cardioversion following the development of NOAF and additionally the supplementation of electrolytes with this aim. Further work could further develop a model predicting patient-related outcomes such time to discharge from ICU or hospital, inpatient stroke and mortality.

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Intensive Care Medicine Experimental 2022, **10(2)**:001029

001029

Performance of a prediction model for elevated intracranial pressure in traumatic brain injury: a prospective observational study

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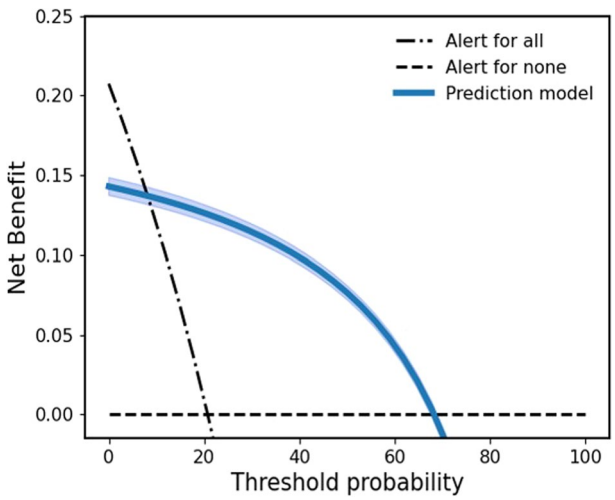
Introduction: In traumatic brain injury (TBI), the 'ICP dose', defined as the combination of intensity and duration of an event of elevated intracranial pressure (ICP) carries relevant clinical information [1]. The early identification of such potentially harmful ICP events may improve clinical practice. With this objective, we previously developed a machine-learning (ML) model that predicts events of potentially harmful ICP dose (as identified in previous studies [1–3]), 30 min ahead. This model presented good performance when externally validated on the CENTER-TBI dataset [4] (unpublished data). A prospective clinical trial is a necessary step towards the implementation of this ML model at the bedside.

Objectives: In this prospective, observational, single-center study, we evaluated the prediction model for harmful ICP doses on real-time patient data and performed a pilot analysis of the performance of the model when applied in this setting.

Methods: Patients with severe TBI and invasive ICP monitoring admitted to the intensive care unit of the University Hospitals Leuven, Belgium, between January 2020 and April 2021, were included in the study. Minute-by-minute ICP and mean arterial blood pressure signals were collected and predictions of harmful ICP doses were computed and retrospectively compared with the true labels, namely whether the patient experienced such harmful ICP event, or not. Model performance was assessed with respect to accuracy, precision, sensitivity and specificity. In addition, we evaluated the potential clinical usefulness of the model with decision curve analysis.

Results: Fourteen patients with severe TBI were included in this prospective study, with a median monitoring time of 5 days [IQR 3–10]. In this cohort, the model presented an accuracy of 0.87, precision of 0.68, sensitivity of 0.69 and specificity of 0.91 (alerting threshold = 0.50). Clinical usefulness was demonstrated for the risk thresholds [0.09–0.65] (Figure 1).

Figure 1 Decision curve of the prediction model for harmful ICP doses when used in a clinical setting.



Conclusion: In this prospective observational study, the ML model for the prediction of harmful ICP doses demonstrated good discrimination, specificity, and clinical usefulness for a broad range of risk thresholds. The choice for a model with high specificity, at a cost of a lower sensitivity, was deliberate, when considering potential alert fatigue in a real-time clinical setting. The observed good performance in this study, warrants the use of the model in a future interventional study.

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Acknowledgements: Research Foundation Flanders (FWO), internal KU Leuven funds (C2 project [C24/17/072]). GC performed this research while receiving funding from the Research Foundation, Flanders (FWO) as a PhD fellow.

Ethics 1

000206

Opting for intensive care unit admission in advanced age? Preliminary data from a survey among very elderly Norwegians

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Intensive Care Medicine Experimental 2022, **10(2)**:000206

Introduction: Despite high and rising numbers, the benefit of admitting very elderly patients to an intensive care unit (ICU) remains controversial (1). Age, frailty and comorbidity have been shown to be of independent prognostic value (2) and are regularly considered. In clinical decision-making, priority setting, and policymaking, the patients' wishes and values are paramount, but knowledge about very elderlies' ICU admission pReferences is scarce.

Objectives: The primary objective of this study is to describe the very elderly (≥ 80 years) Norwegian outpatients' pReferences regarding ICU admission in a hypothetical event of acute critical illness. The secondary objective is to assess whether factors commonly used in clinical decision-making affect the choices made by the very elderly respondents themselves.

Methods: We developed, tested, and validated a survey tool exploring very elderly patients´ ICU admission pReferences. We report preliminary data from a purposive sample of very elderly Norwegian outpatients regarding their treatment choices in three hypothetical scenarios, randomly selected from 20 clinical vignettes. The possible ICU outcome is presented either as survival or mortality. The questionnaires also include demographics, frailty (3), comorbidity and polypharmacy (4) of the respondent.
Results: One hundred very elderly outpatients (55% females) made choices regarding three hypothetical clinical scenarios, resulting in 289 decisions (11 missing answers). Most respondents (74%) made the same choice in all three presented scenarios. Of all choices made, 38% were in favor for and 42% against ICU admission. Framing the ICU outcome as mortality increased the likelihood of the respondent opting against ICU admission (Table 1).

Vignette outcome framing \ Respondent preference	Opting for ICU admission (N=108)	Opting against ICU admission (N=123)	Wishing not to engage in the decision (N=58)
Survival	44%	35%	22%
Mortality	30%	52%	18%
Total	**38%**	**42%**	**20%**

Table 1: Very elderly respondents' ICU admission preferences depending on framing of the ICU outcome in an hypothetical event of critical illness

Figure 1 shows the proportion of decisions made by the very elderly respondents stratified by age, frailty and comorbidity/polypharmacy.

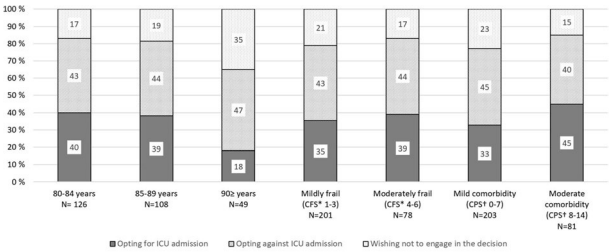

Figure 1: Very elderly respondents' ICU admission preferences stratified by age, frailty and comorbidity
* Clinical Frailty Scale (3); † Comorbidity Polypharmacy Score (4)

Conclusion: In this purposive sample, 74% very elderly Norwegian respondents expressed a consistent preference regarding ICU admission in the event of acute critical illness; equally many opted for and against ICU admission. Whether the outcome is presented as mortality or survival appeared to be important for the very elderly; however, increasing age, frailty and comorbidity did not appear to influence the proportion opting against ICU admission.

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Acknowledgements: This study is supported by Helse Vest RHF (the Western Norway Regional Health Authority).

000296

Satisfaction among family members of patients in the Intensive Care Unit during the COVID-19 pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000296

Introduction: The number of patients that survive an admission in the Intensive Care Unit (ICU) has increased. The ICU is one of the places in a hospital where family members suffer most, especially when

prognosis is poor, exposing family members to damaging psychological consequences that can last several years after the ICU. The COVID-19 pandemic increased the separation between families and their loved ones not only in the ICU but also in other inpatient services. This situation may then exacerbate these psychological changes as more families are prevented from visiting their relatives in the ICUs.
Objectives: Assess the degree of satisfaction of family members of patients admitted to the Intensive Care Unit before and during the COVID-19 pandemic. Understand whether certain characteristics of patients and their families have an impact on their satisfaction.
Methods: This is an observational, single-center and mixed study developed at the Unidade de Cuidados Intensivos Polivalentes of the Centro Hospitalar Universitário do Porto, carried out between the 1st of January 2020 and the 31st of July 2020. A version of the Critical Care Family Needs questionnaire was applied during a telephone call, in order to assess the satisfaction of family members regarding their experience at the ICU. Furthermore, demographic and clinical data were collected from the patients' electronic (Sclinico) process. All data collected were processed and analyzed using the SPSS program, version 27.
Results: Of the 162 potential participants, 87 (53.7%) family members were included. The group of family members with the most positive answers in almost all questions is the group of family members of patients hospitalized with COVID-19. The questions related to the provision of care, the accurate transmission of the clinical situation are the ones with the most positive answers, in all groups. The questions related to the concern and support given to the family by the medical team, the explanation of the equipment used in the ICU and the comfort of the waiting room were the questions with the least positive answers.
Conclusion: This study outlines the hypothesis that the period of time with more restrictions was the time when communication, even at a distance, was more effective, leading to a high degree of family satisfaction. It would be interesting to see what changes positively impacted patients and their families during their experiences in hospitalization during a pandemic time so that they could be implemented on a lasting basis.

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000326

High prevalence of treatment limitations in two Swedish ICU´s – female patients more likely to be involved in the decision-making process

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Intensive Care Medicine Experimental 2022, **10(2)**:000326

Introduction: The use of treatment limitations (TL) is common in intensive care units (ICU) in Sweden, but there are indications that patients and next of kin are not adequately involved in the decision-making process. The primary aim of this study was to study the prevalence, documentation and patient involvement in treatment limitations in two Swedish ICUs.
Methods: All ICU admissions at two Swedish hospitals in 2019 were included. Patients were identified using the Swedish Intensive Care Registry (SIR) and patient characteristics and outcome data were extracted. The hospital charts of all patients with a TL were reviewed to investigate patient involvement and documentation. Uni- and multivariate logistic analysis was performed to investigate associations with the presence of TL.
Results: 1019 patients were admitted to the ICU, 45.5% were women and the mean age was 62.9 years. 26.5% of the patients had one or more TLs. 82% of the patients that died in the ICU had a TL at the time of death. Women were more likely to have been involved in the decision process and the next of kin to women with a TL were more often involved and informed of the TL.
Conclusion: TL are common in Swedish ICUs but only 17% of the patients were involved in the decision process and 64% of the next-of-kin were informed. Women were more likely to be involved in the decision process and next-of-kin to women that received a TL were more likely to be informed.

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000367

Research in the potential organ donor after circulatory death: Determining public opinion

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Intensive Care Medicine Experimental 2022, **10(2)**:000367

Introduction: There remain unanswered questions regarding factors affecting the quality of organs donated for transplantation after circulatory death (DCD). It is proposed that physiological changes occurring in the donor in the period between treatment withdrawal and circulatory death are responsible for the elevated incidence of poor graft function in the recipient. To answer this question a study was proposed that involved intensive study of the donor during the period of treatment withdrawal. Consent for the study would involve seeking 'Personal consultee' consent for study inclusion. This consent mechanism is standard in patients who cannot consent (1). However, such a study has never been undertaken in the dying patient, and we sought to understand if public opinion would consider such research acceptable.
Objectives: Objectives were two fold: To determine public opinion regarding the appropriateness of research undertaken in the potential DCD organ donor in the period between treatment withdrawal and death. Then to determine if public opinion supported the use of Personal consultee consent for patient involvement in a study of this nature.
Methods: A sample of hospital outpatient attenders, their family members, and members of the general public on the street in central Cambridge were asked to complete a survey. The survey instrument included a summary of the proposed research study, an explanation of the purpose of the study and a questionnaire. All survey documents were worded in lay terminology and took between 5 and 20 min to describe to most participants. Participants were then asked some basic demographic information, and the two core survey questions in a verbal interview format:
Question 1: Would you be willing to consent for your relative to be involved in this study?
Question 2: Would you find your next of kin/ Personal Consultee giving consent for your involvement in this research study acceptable?
Survey participants responses to questions using a five-point Likert scale, with available responses of 'Absolutely not, Probably not, Neutral, Probably yes and Absolutely yes. The demographic information was also collected.
Data were analysed using Prism (Graphpad Software, La Jolla, CA, USA).

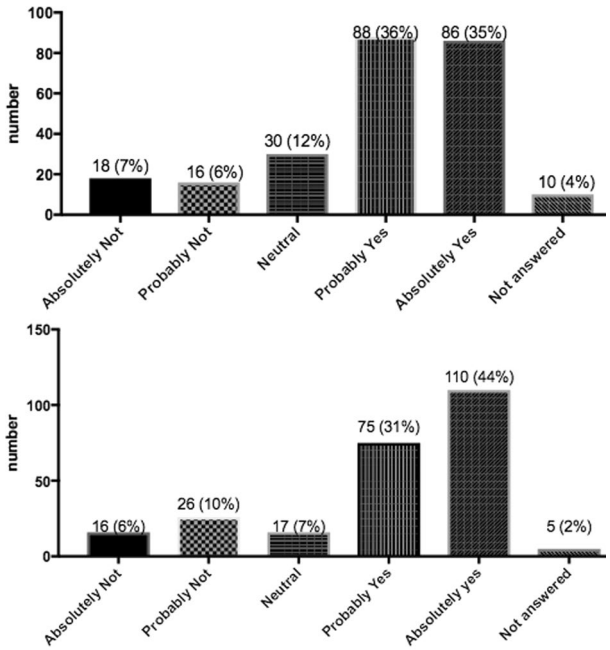

Figure 1:(top) *Willingness to consent for a relative being involved in this research study.(bottom) Acceptability of consent for research being provided a 'personal consultee' for a patient who cannot give consent. Total respondents 248*

Results: Two hundred and forty-eight participants completed the survey. 36 people were approached and declined to take part in the survey. Figure 1 demonstrate the survey participants responses on willingness to consent for a relative being involved in the research study (top) and the appropriateness of a person consultee giving consent for involvement in research (bottom). Of 248 respondents 71% were positive with regard to providing consent for a relative to be involved in this research study (answering probably yes or absolutely yes). With regards to the acceptability of a personal consultee providing consent for involvement in a research study for someone who is unable to consent 75% responded positively.
Conclusion: Our results suggest that the majority of members of the public would find premortem study of potential DCD organ donors agreeable. Furthermore, it shows that our proposed method of seeking next of kin/Personal consultee consent is considered acceptable by the majority of the group surveyed. Given the results of this survey, we suggest consent rates for research in potential DCD donors would be high. Indeed, were Personal Consultees to adopt the attitude that consent for research in this patient cohort represents an extension of the patient's altruistic wishes to help others, research consent for studies such as ours may exceed standard research consent rates.

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Acknowledgements: This work was funded by the NIHR Blood and Transplant Research Unit.

000370

Understanding medical students' perception of end of life care

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Intensive Care Medicine Experimental 2022, **10(2)**:000370

Introduction: Palliative care is an important aspect of a clinician's duties and within the ICU, decisions around end of life (EOL) can be made daily. The General Medical Council (GMC) of United Kingdom has not only outlined guidance for the treatment and care towards the end of life but has also stipulated that medical graduates are expected to recognise and deliver the appropriate care for dying patients [1]. A 2019 systematic review identified that junior doctors feel unprepared in caring for these patients and that undergraduate or postgraduate rotations with a palliative care focus can help bridge the knowledge gap [2]. As clinicians working in ICU of a university affiliated hospital, we play an important role in preparing students to face and care for the terminally ill. To help support the students through their clinical learning and experience, we have looked at their perception of EOL care and their experience so far.

Objectives:

1. Creating an objective questionnaire to analyse understanding and experience of EOL care among medical students
2. To identify gaps in their learning and experience during their clinical placement

Methods:

1. Objective anonymous questionnaire which uses a mixture of multiple choice, short answer and checkboxes.
2. Questionnaire initially shared among 3rd and 5th year medical students on their ICU placement.
3. Questions looking at current/previous experience, perception, relevant university/placement teaching of EOL care, management of psychological impact.
4. Further questions would be discussed in the presentation.

Results: Almost 95% of them agree that EOL care is very important. Key themes of their perception were about comfort, compassion and least distressing treatments. Oncology and hospice placements were identified as other clinical departments which provided insight into EOL care. About three quarters of the students have not witnessed any EOL discussions with patients or their family. They received a variety of teaching but only about 11% of them stated having practical experience during their clinical placements. It is also recognised this can be emotionally or ethically distressing for the medical students.

Conclusion: The findings highlight that although students received formal teaching sessions, this can be difficult to translate into practical experience. One of the changes proposed to be implemented would be work on bridging the gap between formal teaching and real-life clinical experience by involving medical students around various decisions in the treatment and care in EOL. This could be taken a step further by coordinating existing formal teaching or e-learning materials to be consolidated on the shopfloor.

Along with augmenting their practical experience of the care of palliative patients, psychological support can be provided in the form of debriefs sessions with various stakeholders such as clinical supervisors, learners support and the medical school.

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Acknowledgements: No grant acknowledgement required.

000459

Análisis of decision making in the context of end of life in hospitalización plants during the first wave of the SARS COV2 pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000459

Introduction: In the context of first wave of SARS COV2 pandemic; our aim was to describe the decision making process at the end of life situation in a 3rd hospital.

Objectives: To describe the decision-making process at the end of life of patients admitted to the ward for COVID pneumonia during the study period.

Methods: Descriptive, observational and retrospective study through the analysis of medical records of the patients under study from March 15 to April 15, 2020.

Results: 150 patients died in the study period. Age 81 ± 9.7, 53% male, mean stay 7.7 days ± 7.2, Charlson index 4.355 ± 2.6. 52% dependent for AVBD, 11% totally dependent. 39% cognitive impairment. Use of validated severity prognostic scales 2%. Use of validated functionality scales 10%. Listed as non-subsidiaries of UCI 98%. Decision not to support admission to the Intensive Care Unit (ICU): Staff doctor 80% ICU doctor 20% Family/patient 0%. Non-competent patient 68%. 92% of competent patients do not participate in decision-making. Patient not informed of the decision 72% of competent patients. The family does not participate in decision making in 92%. Family informed of the decision 96%. Reasons for not considering admission to the ICU/no CPR include: age 44%, associated comorbidities 38%, lack of care resources 16%, agony 12%, no record 8%. Age as the only cause of ICU admission refusal was considered in 12% (with an age of 85.7 ± 4.7 years). The lack of resources as the only reason for exclusion was 4% and the combination of both reasons was 6%.

Conclusion: The average age of patients who are not candidates for admission to the ICU is high. Most of the non-candidates for admission to the ICU are dependent for daily activities. There is a low percentage of use of validated prognosis and functionality scales. The staff physician was the one who most frequently decided not to be admitted to the ICU. A high percentage of patient exclusion was detected both in decision-making and in information about it. The family was also excluded in decision-making in a high percentage, however, they mostly received information. Age was the most argued reason for exclusion, however, it was the only reason in a low percentage of patients who had a high chronological age. Lack of resources as the sole reason for exclusion was rare.

000463

Aspects related to care and the end of life in no candidates to ICU admission during first wave of the SARS COV2 pandemic

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Intensive Care Medicine Experimental 2022, **10(2)**:000463

Introduction: During first wave of SARS COV2 pandemic, rate of hospital admission was extremely high, as well as the mortality rates, our objective is to describe the care related to the end of life in patients who were not candidates to ICU admission during this time.

Objectives: To describe the care related to the end of life of patients admitted to the ward for COVID pneumonia, not candidates for admission to the Intensive Care Unit (ICU) during the study period.

Methods: descriptive, observational and retrospective study through the analysis of medical records of the patients under study from March 15 to April 15, 2020.

Results: 150 patients died in the study period. Age 81 ± 9.7, 53% male, mean stay 7.7 days ± 7.2, Charlson index 4.355 ± 2.6. 52% dependent for AVBD, 11% totally dependent. 39% cognitive impairment. No care measure was carried out at the end of life in 5.4%. Palliative sedation was administered to 97% of patients, of whom 2.2% received midazolam infusion only, 33% received continuous infusion of opioid (morphine), and 64.8% received benzodiazepine and opioid infusion. 85.7% of the relatives were informed of the patient's death, and 30% were able to receive family support during the end-of-life process. The death of the patient occurred alone in 94% of them. The patient received psychological assistance during the process in 2.2% of cases,

and the family in 19%. Spiritual assistance during the process by 2%. Among the reasons for starting palliative sedation, in all of them it was carried out due to dyspnea, and in 7.5% because they were also in an agonizing situation.
Conclusion: Most of the patients died alone, without family support at the time of death. A minority received family support during the end of life process. Information about the death to a high percentage of family members, and a very low percentage of psychological or spiritual assistance for both the patient and family members.

000613

Current status of Physician Orders for Life-Sustaining Treatment of patients with cancer admitted to the intensive care unit

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Intensive Care Medicine Experimental 2022, **10(2)**:000463

Introduction: The Life-sustaining Treatment (LST) Decisions Act has been implemented for the refusal of meaningless life-prolonging treatment and a death with dignity in Korea since 2018. The purpose of this study is to investigate how the physician orders for Life-Sustaining Treatment (POLST) is actually applied to patients with cancer who have been admitted to the intensive care unit (ICU).
Methods: The medical records of patients who received POLST among cancer patients admitted to the medical ICU from February 2018 to June 2020 were retrospectively reviewed.
Results: A total of 1049 cancer patients were admitted to the medical ICU, 604 of those patients who received POLST were included during this study period. Hematologic malignancy (32.3%) was the most common disorder before ICU admission. Respiratory failure (40.9%) was the most common cause for the admission to ICU. Among them, 29 patients (4.8%) received POLST before admission to the ICU, and 575 patients (95.2%) obtained POLST after admission to the ICU. The average time from the assessment for the patient at the End Stage of Life to the verification of Decision of patient or patient family was about 0.54 days and the assessment and verification was done on the same day in 583 patients (96.5%). The decision on LST plan were done by the patient's family in 466 patients (77.2%) and only 138 patients (22.8%) determined the LST plans by themselves. In the 142 patients (23.5%), POLST was received within 48 h after the admission to the ICU. 488 patients (80.8%) received mechanical ventilation treatment during ICU stay, and vasoactive agents were administered to 552 patients (91.4%). The withdrawal of current therapy occurred in 19.2% of the patients. 227 patients or patients' family members (37.6%) agreed with maintaining the intensive care only except cardiopulmonary resuscitation, and 301 (49.8%) refused mechanical ventilation.
Conclusion: In most cases, even after the establishment of POLST, the decision whether to participate in the LST plan or not, is determined by the patient's family. Despite the patients and their families agree to participate in POLST, the majority of them want to maintain intensive care. There appears to be a disconnect between the LST decision system and the medical environment.

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000620

A review of critical care end-of-life care practices during Coronavirus disease 2019 pandemic focusing specifically on visiting policies, chaplaincy support and the effect of depersonalisation of patients in the prone position

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Intensive Care Medicine Experimental 2022, **10(2)**:000620

Introduction: The Coronavirus disease 2019 (COVID-19) pandemic has had a significant impact on patient and relatives' experiences of end-of-life care, as well as changing the provision of these services in Intensive Care Units across the world. [1–7] Established methods for assisting relatives through the grieving process have required modification due to the unique features and circumstances surrounding deaths from this disease.
Methods: This mixed methods study from the United Kingdom, aims to review data from 173 patients who died on a large Intensive Care Unit at University Hospital (the surge capacity for more than 100 ventilated patients), over the course of approximately one-year. The inpatient noting of these patients was reviewed specifically for details of visiting practices, chaplaincy support and patient positioning (prone versus supine) prior to death.
Results: 119 (68.8%) patients had visitors attend them in the 48 h immediately prior to their passing. 45 patients (26.0%) had no visitors and 9 (5.2%) had visitors attending their bodies after their death. Of those who visited within 48 h of death, 84 visitors (70.6%) were present at the time of death. 135 (78.0%) patients were placed in the prone position during their ICU stay, based on clinical need. Review of case notes identified that prone positioning was mentioned in communications with relatives of 119 patients. 16 of these 119 patients were still in the prone position when visited in the end of life. Chaplaincy support was sought for 55 patients (31.8%) during their ICU stay. This was initiated by the family members of 29 of the patients (52.7%), more than double the number of requests initiated directly by ICU staff (11 (20.0%)). It could not be determined from the inpatient noting who initiated chaplaincy support in 14 (25.5%) of cases. There was 1 case, where chaplaincy support was initiated by the pandemic family liaison service. The median number of days prior to death that chaplaincy support was initiated was 0 (IQR 0–4). There was no difference in the mean number of days prior to death in which families-initiated chaplaincy support (7.3 days) compared with when this was done by ICU staff (6.9 days) ($p = 0.95$).
Conclusion: Using this data, recommendations are made to improve end-of-life care services. To allow relatives the opportunity to attend the Intensive Care Unit, there is a need for early recognition of patients approaching the end of life. The need for clear explanations of the need for prone positioning and increased access to chaplaincy services were also identified.

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000727

Prospective multicenter observational cohort study on time to death in potential controlled donation after circulatory death donors; development and external validation of prediction models. The DCD III study

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Introduction: Acceptance of organs from controlled donation after circulatory death (cDCD) donors depends on the time to circulatory death.
Objectives: Here we aimed to develop and externally validate prediction models for circulatory death within 1 or 2 h after withdrawal of life-sustaining treatment.
Methods: In a multicenter, observational, prospective cohort study, we enrolled 409 potential cDCD donors. For model development, we applied the least absolute shrinkage and selection operator (LASSO) regression and machine-learning artificial intelligence (AI)-analysis. Our LASSO models were validated using a previously published cDCD cohort. Additionally, we validated three existing prediction models using our dataset.
Results: For death within 1–2 h, the area under the curve (AUC) of the LASSO models were 0.77 and 0.79, while for the AI-models these were 0.79 and 0.81. We were able to identify 4–16% of the patients that would not die within these timeframes with 100% accuracy. External validation showed that the discrimination of our models was good (AUC 0.80 respectively 0.82), but were not able to identify a subgroup with certain death after 1–2 h. Using our cohort to validate three previously published models showed AUCs ranging between 0.63–0.74. Calibration demonstrated that the models over- and underestimated predicted probability of death.
Conclusion: Our models showed a reasonable ability to predict circulatory death. External validation of our and three existing models illustrated that their predictive ability remained relatively stable. We accurately predicted a subset that died after 1–2 h preventing starting unnecessary donation preparations, which however needs external validation in a prospective cohort.

Ethics 2

000834

End of life care in critically ill patients - qualitative study on the challenges faced by anaesthesiology residents in Singapore

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Introduction: Doctors undergo rigorous training with an emphasis on restoring health and function but are seldom prepared for care of the dying. In Singapore, sicker and older patients are being admitted to the intensive care unit (ICU), but still face mortality rates of about 10–20% despite aggressive interventions. Patients and their families are often unprepared for conversations which may lead to the limitation of their care. Many patients have not done advance care planning. Anaesthesiology senior residents (SRs) (United Kingdom—Specialist Trainee Year 4–5 equivalent) are the main points of contact when a critically ill patient is deteriorating. Our qualitative study aims to gain deeper understanding, exploring SRs' attitudes on and experiences in caring for end of life patients in the ICU.
Methods: Study participants: A purposive sample of 12 SRs in Singhealth Anaesthesia (Singapore's largest public healthcare cluster) with at least 6 months of SR experience participated in the study. IRB approval was granted prior to starting the study. Data Collection: An in-depth face-to-face individual semi-structured interview was done. Participants were encouraged to respond in their own words and set their own emphases while providing a frame orientation. Participants engaged in reflective dialogue about their experiences, which were audio-recorded, anonymized and transcribed. Data analysis: Thematic analysis is a method of identifying, analysing and reporting patterns within data. It organizes and describes data in detail and interprets various aspects of the research topic. Core values of reflexive thematic analysis (Braun and Clarke 2006) are theoretical flexibility, rigorous procedural focus and emphasis on the reflexive contribution of the researcher. We applied the six phases of reflexive thematic analysis. NVIVO software version 12 (QSR International) was used for coding and data analysis.

Results: In Singapore, various cultural, religious, social, moral and legal practices come into play. Patient and family values and dynamics differ in our local Asian population, where cultural taboos on the subject of death and dying are prevalent. We found that anaesthesiology residents perceived that caring for dying patients was a daunting task and encountered personal, patient, and situational challenges. Lack of personal experiences and limited knowledge in caring for dying patients result in low confidence levels and self-doubt. Cultural taboos on the subject of death and dying are prevalent. The patient's family is heavily involved in treatment discussions and decision-making processes. Cognitively intact patients frequently deferred decision making to their next of kin. Collusion and non-disclosure may prevent the medical team from knowing the patient's care pReferences. Finally, a misplaced perception of filial piety may result in family members requesting for extraordinary life support even at the end of life. Conflicts arise when interprofessional opinions differ, or when the patient's family disagrees with the medical team's care plan. Negotiating for a consensus while maintaining the patient's best interests requires great skill and tact.
Conclusion: Addressing the needs of critically-ill patients is emotionally and logistically taxing. Amidst high emotions, the anaesthesiology resident must navigate the complexities of care determinations. Further training and education intervention would help to improve knowledge and confidence levels.

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Acknowledgements: Academic Medicine Education Institute (AMEI) Duke NUS Education - Program Development Grant.

000887

Impact of routine ECPR service on availability of donor organs

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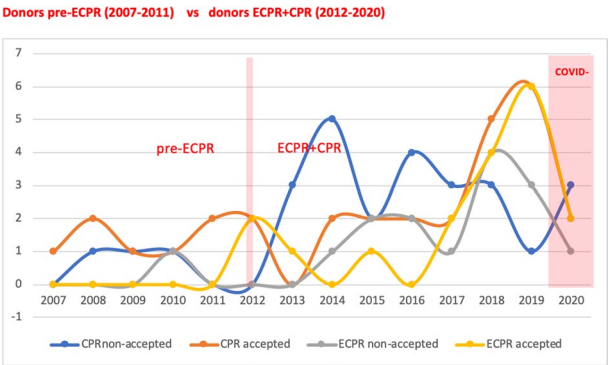
Intensive Care Medicine Experimental 2022, **10(2)**:000887

Introduction: In refractory cardiac arrest, extracorporeal cardiopulmonary resuscitation (ECPR) may increase the chance of survival. However, in brain death or donation after cardiac death scenario, ECPR may provide an important source of organ donors.
Objectives: We hypothesized that 1/ the implementation of ECPR into the daily routine of a high volume cardiac arrest center might increase the availability of organ donors, and 2/ ECPR might assure the same long-term function of donated organs as non-ECPR care.
Methods: We retrospectively evaluated pre-ECPR (2007–2011) and ECPR (2012–2020) periods in terms of donors recruited from the out-of-hospital cardiac arrest population. We assessed the number of donors referred, the number of organs harvested, and their one- and five-year survival.
Results: In the pre-ECPR period, 11 donors were referred, of which 7 were accepted. During the ECPR period, the number of donors increased to 80, of which 41 were accepted. The number of donated organs in respective periods were 18 and 119, corresponding to 3,6 vs 13,2 (p = 0.033) organs per year harvested. One-year survival of transplanted organs was 94.4% vs 99.2%, and five-year survival was 94.4% vs 95.9%, in relevant periods. Survival of organs obtained from donors after CPR and ECPR at one year (98.8% vs 97.8%) and five years (89.5% vs 88.9%) was the same. Graft failure was not the cause of death in any single case.



Conclusion: Establishing a high volume cardiac arrest/ECPR centre may lead to a higher number of potential and subsequently accepted organ donors. The length of survival of donated organs is high and comparable between ECPR vs non-ECPR cardiac arrest donors.

Acknowledgements: No grant.

000912

The role of High Flow Nasal Cannula oxygen delivery in palliative and end of life care

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Introduction: High Flow Nasal Cannula (HFNC) oxygen therapy is a mode of non-invasive ventilatory (NIV) support that allows for delivery of heated and humidified oxygen, at predictable FiO2. HFNC has emerged as a safe and useful supportive therapy in many clinical situations and is considered a valuable tool in enhancing patients' comfort and oxygenation [1,2].
In the current pandemic, HFNC oxygen has been used in the management of acute hypoxaemic respiratory failure (AHFR) secondary to COVID-19 pneumonia [3]. However, some patients receiving HFNC will not improve and may transition from purely curative to palliative care (PC). Patients with AHFR and established ceilings of treatment will often be treated with HFNC or other forms of NIV. Concerns have been raised that the burdens of NIV may outweigh potential benefits and could extend the dying process without improving the quality of death [4]. The evidence around the use of HFNC in end-of-life (EoL) scenarios remain limited.
Objectives: To assess the number of patients receiving HFNC along palliative and EoL care during the Covid-19 pandemic, the indications for its use, and any beneficial and/or unintended effects.
Methods: We conducted a retrospective observational study of all ward patients that received HFNC around their end of life, over 10 months (December 2020 –September 2021), in a 950 bedded, tertiary London hospital, with an established outreach service. We reviewed electronic patient records and collected patient demographics, COVID-19 status, indications for HFNC initiation, response to treatment, including adverse events and EoL decision-making.
Results: During the study period, 183 patients received HFNC with 40 (21.8%) receiving it for palliative or EoL care. Mean age was 77 y/o (IQR 50–92), 55% were male and 60% tested SARS-CoV-2 positive. The commonest indication for HFNC initiation was hypoxia (60%). Signs of treatment success were measured by decreased respiratory rate (32.5%) and increased SpO2 (32.5%). In 60% of cases there were no adverse events associated with HFNC, however 27.5% of patients expressed general discomfort and 7.5% were intolerant of heated humidification. Only 4 patients (10%) were recognised as EoL at initiation of HFNC, whilst 31 patients (77.5%) had a change in their goals of care after the HFNC failed to improve their condition. HFNC was removed in 52.5% of patients before death. The main reason HFNC was not weaned off was for comfort (42.5%). Details on HFNC use around EoL are shown in Table 1. Referral to PC was made in 90% of EoL patients.
Table 1: End of Life Decision Making

Variables (N = 40)	n (%)
Determination of end-of-life status	
Before HFNC commenced	4 (10)
After HFNC commenced	26 (65)
After HFNC failure	5 (12.5)
Patient never recognised as at end of life	4 (10)
HFNC practices around end of life	
Discontinued	21 (52.5)
Not discontinued	8 (45)
Reasons for not discontinuing HFNC	
Comfort	17 (42.5)
Patient/family refusal	2 (5)
Patient not recognised as EoL	1 (2.5)
Death considered as imminent	3 (7.5)
Not documented	9 (22.5)

Conclusion: Approximately 22% of HFNC therapy during the pandemic was for COVID-19 positive patients. The majority of patients showed signs of improvement with no adverse effects, and approximately 50% died on HFNC therapy. More than 40% of patients needed HFNC alongside PC involvement for comfort around EoL. The traditional comfort measures warrant further evaluation in the context of Covid-19 infection.

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000981

End of life in a peripheral Portuguese ICU – Can we do better?

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Intensive Care Medicine Experimental 2022, **10(2)**:000981

Introduction: Intensive Care Medicine is the medical specialty that provides life-sustaining therapies with the goal of restoring or maintaining organ function to patients who are critically ill. On the other hand, Palliative Care Medicine optimizes the patient's quality of life by anticipating, preventing and giving comfort when therapeutic "cures" are futile.1
Objectives: The aim of this study was to evaluate the quality of end-of-life care applied in a peripheral Portuguese Intensive Care Unit (ICU).
Methods: We performed a retrospective study in which we consulted clinical records concerning patients who died in a peripheral Portuguese ICU between 2019 and 2021 with a length of stay of at least 48 h.
Results: A total of 206 clinical files were analysed, of which the majority were male patients (75.7%). The mean age of patients was 68.43 ($\pm$ 12.67) years old, ranging from 33 to 96 years old; the average length of stay was 8.81 ($\pm$ 8.38) days. APACHE II average value was 26.82 ($\pm$ 8.29) points.
From the analysis of the total 206 clinical records at admission, 124 (60.2%) had a therapeutic limit during their stay, 125 (60.7%) patients had been suspended from curative treatments and 148 (71.8%) patients were placed in comfort care before they died. Only 2 patients were admitted considering organ donation. From those who were admitted for a 48 h ICU trial, 29 of them were considered to have a therapeutic limit. Treatment suspension and end-of-life comfort were offered to 52.9% of patients and terminal extubation was performed in 8 patients. As the family is concerned, 74.3% were informed about end-of-live measures, but only 51.5% were offered a terminal visit. That offer was refused by 8.5% of relatives. In all of 206 patients, we couldn't find any reference to religious or psychological support offered.
Conclusion: Death is frequent in ICUs and end-of-live measures should be adequately implemented. However, it is well recognized that most clinicians do not deal appropriately with terminal issues and palliative care, with significant consequences for terminal patients. Our results show that most of our patients were submitted to palliative care before they died, although we might consider that the prevalence of such measures should be increased. One explanation might be related to the lack of palliative care specialists in our hospital, although the authors consider that lack of information and medical education explains some of the findings. The authors recognized that a considerable improvement is needed as families are concerned. Their involvement should be greater and earlier, and more education should be done. End-of-life care should be discussed, considered in advance and probably aggregated to everyday discussion of all patients, allowing timely institution of such measures with clear benefit to patients as well as to their families.

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000995

Limitation of Life-sustaining Treatments in adult patients in Indian ICUs: Data from the second Indian Intensive Care Case Mix and Practice Patterns Study (INDICAPS-II)

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Intensive Care Medicine Experimental 2022, **10(2)**:000995

Introduction: Clinicians in Indian intensive care units (ICUs) face uncertainty while making end-of-life (EoL) decisions. This may be due to socio-cultural and legal considerations surrounding withholding (WH) and withdrawal (WD) of life support. In INDICAPS, performed between 2010-2011in 4038 adult patients from 120 ICUs, terminal discharge (TD) from the ICU was common, and accounted for 183 (25%) of 729 non-survivors (patients dying in the ICU and TDs). INDICAPS-II was a large multicentre, observational, point-prevalence study capturing practice patterns in Indian ICUs in 2018–19. In this sub-study, we evaluate the patterns of contemporary EoL decisions in Indian ICUs.
Objectives: The primary objectives are to determine the proportion of patients who died in the ICU without any limitation of treatment (No-LIM), those who died in the ICU after limitation of life support (LIM), and the proportion of patients who were terminally discharged from ICU (TD). The secondary objectives are to determine the patient and organizational characteristics associated with No-LIM, LIM, and TD.
Methods: An observational, 4-day point prevalence study was performed between 2018 and 2019, including 4669 adult patients ($\geq$ 16 years) in 132 Indian ICUs. ICU outcomes were recorded till 30 days after the study day. For patients who died in ICU, we recorded whether they had No-LIM, or LIM (including full treatment but no cardiopulmonary resuscitation (CPR), WH or WD of life-support). We also recorded whether patients were TD from ICU. Patients who died in ICU and TDs were counted as non-survivors. Multivariable logistic regression analyses were performed to determine patient and organizational characteristics associated with No-LIM, LIM, and TD.
Results: Mean age and APACHE II scores were 56.9 $\pm$ 17.41 years, and 16.7 $\pm$ 9.8, respectively, with 36.3% female patients. There were 1092 non-survivors (23.4%), including 737 deaths in ICU (15.8%) and 355 TDs (7.6%). 55.9% of patients died with No-LIM, and 32.5% of non-survivors were TDs. LIM occurred in 127 patients (11.6%); of these, 39 patients (3.6%) had no CPR; 73 (6.7%) had WH and 15 (1.4%) had WD of life-support. Factors independently associated with No-LIM, LIM and TD are shown in the Table.

EOL decision Factors	Odds ratio [95% confidence interval]
No-LIM	
Self-paying patient	0.55 [0.42–0.72]
APACHE-II	1.013 [1.001–1.026]
Male gender	1.30 [1.01–1.68]
LIM	
Any cancer	2.03 [1.32–3.12]
Age	1.018 [1.005–1.031]
APACHE-II	1.04 [1.02–1.06]
TD	
Private hospital	5.24 [1.16–23.59]

EOL decision Factors	Odds ratio [95% confidence interval]
Self-paying	1.71 [1.28–2.29]
Closed ICU	1.45 [1.04–2.04]
APACHE-II	0.96 [0. 95–0.0.98]
Any cancer	0.49 [0.31–0.75]

Conclusion: Practice of TD is widespread while WH and WD of life-support are uncommon. LIM is more likely in older, sicker patients and those with cancer. Cancer patients more likely to have LIM rather than TD. The association of TDs with self-paying patients, private hospitals, and lower APACHE-II scores as well as the association of No-LIM with non-self-paying patients suggest that financial issues play a role in the decision for TD.

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Acknowledgements: Indian Society of Critical Care Medicine.

001293

Improving end of life care in critical care – why everyone matters

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Intensive Care Medicine Experimental 2022, **10(2)**:001293

Introduction: The pandemic has resulted in increased challenges to End of Life (EoL) care. Staff have suffered high moral distress due to increased mortality, lack of family visiting, social restrictions, virtual communication and the challenges of PPE. Evidence indicates provision of effective care at EoL is a vital component of Intensive Care Medicine(1). The Guidelines for provision of intensive care services V2 (GPICSV2) has set out definitive standards and recommendations for care at EOL (2,3). In order to conform with the standards and recommendations set out in GPICSV2, an End of Life Quality Improvement (EoL QI) group was formed at a DGH with the aim to improve both staff and patient EoL experiences, whilst adhering to Institute of Healthcare Improvement`s Model for Improvement.
Objectives:
1. Improve prescribing practices at EoL
2. Enhance patient and family centred care
3. Enhance staff wellbeing
4. Enhance multidisciplinary cooperation
5. Provide targeted and relevant staff training

Methods: An audit of EoL prescribing practices, and a staff survey investigating EoL experiences were undertaken. The survey highlighted three key areas of need – prescribing consistency, psychological support for staff and education and training in EOL care. The prescribing data was initially collected over a twelve month period studying 78 deaths on the unit across this period. Two exclusion criteria were applied—patients who had died within one hour of arrival on the unit or those who had experienced a sudden, unexpected death—41 patients satisfied the criteria. The process was repeated seven months later following a period of staff education with involvement from the palliative care team, yielding a total data set of 49 patients for the following audit cycle. The staff survey was an anonymous questionnaire with both Likert scale responses and 'white space' questions. There were 33 respondents covering the whole multidisciplinary team.
Results: With many aspects of the EoL QI group work, it is difficult to quantify the improvement but surrogate measures that show evidence of improvement include:
1. Appropriate end of life prescribing (61% compliance with EoL prescribing improved to 70% after initial QI)
2. Implementation of a notice board with signposting of resources for education, training and psychological support
3. Increased use of syringe drivers and collaboration with palliative care team
4. Palliative care education via ECHO from ACCORD hospice for staff
5. Engagement of multidisciplinary team with psychologists
6. Participation of spiritual care lead at debriefs
7. Ensuring equity of access to debriefs with the clerk and housekeeper joining in along with doctors and nurses
8. Engagement of families in memory making including keepsakes
9. Informal feedback from staff accessing bereavement support and attending death debriefs has been overwhelmingly positive.

Conclusion: Although there are still improvements to be made the EoL QI group has no doubt enhanced EoL care for both patients and staff. It is a multidisciplinary team which has demonstrated modest improvements in prescribing practices at EoL, improved staff wellbeing, implemented staff education and created an environment where everyone strives to provide the best EoL care possible. A repeat survey and evaluation of all key areas of EoL care is planned.

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001345

Treatment Escalation Plans in Intensive Care: Discussion and Documentation

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Intensive Care Medicine Experimental 2022, **10(2)**:001345

Introduction: Treatment Escalation Plans (TEPs) are essential to holistic care and encompass complex legal and ethical concepts4. Use increased in the COVID-19 pandemic3, attracting public attention2. Communication changed and there were fewer conversations2. Doctors in training played a greater role despite feeling unprepared and overwhelmed2. In response, the CQC published "Protect, Respect, Connect" to guide TEP implementation and communication1. The report emphasised consistent, informed, and individualised decision making1.
Objectives:
1. Assess changes in implementation of TEPs in an Intensive Care Unit (ICU) of a District General Hospital (DGH) since the COVID-19 pandemic
2. Improve implementation and communication of TEPs
3. Improve experiences of doctors in training involved

Methods: Anonymised data were collected in 2021/22 on TEPs throughout admission for two one-month periods before and after interventions at a DGH ICU. When there was a change in TEP, communication to relatives (who and how) was analysed. Doctors in training were anonymously surveyed on their experiences in TEP communication. Data were analysed with MS Excel. Chi-squared was used for

comparing periods. P < 0.05 was deemed statistically significant. Interventions were a trust-wide departmental teaching session on TEPs, inclusion of TEP in the 'A-I' daily ward round assessment, and distribution of posters and consultant-led emails encouraging senior-led communication.
Results: There were 32 and 41 ICU admissions in periods 1 (P1) and 2 (P2) respectively. TEP documentation before ICU admission increased from 6% (2/32) in P1 to 63% (26/41) in P2 (P < 0.001). All patients, except one in P2, had TEP documentation on ICU admission. Documentation during ICU significantly improved in P2, with at least one mention of TEP in 68% (28/41) compared with 16% (5/32) in P1 (P < 0.001), and 54% (22/41) documentation at least every other day compared with 3% (1/32) (P < 0.001). Per period, 7 patients had a TEP change, and 6 had documented communication with relatives. Consultant-led communication increased from 4/6 in P1 to 5/6 in P2. In P2, the other conversation was started by the relative to a doctor in training but followed up with a consultant-led discussion. Method of communication remained mostly via telephone. There were 8 survey responses: 5 in P1 and 3 in P2. In P1, 40% (2/5) of doctors felt supported with TEP discussions compared with 100% (3/3) in P2. Confidence in raising concerns to seniors about TEP discussions also increased.
Conclusion: These results are in keeping with national findings of low TEP documentation and doctors in training feeling unsupported2. We demonstrate the importance of addressing pandemic-related changes to improve services. Further improvements are still needed. However, our interventions focussing on senior-support, raising awareness, and regular prompting led to significantly increased documentation of TEPs and senior-led discussions, translating to greater confidence and feeling supported amongst doctors in training.

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Acknowledgements: None to Declare.

001371

Characteristics and outcomes of palliative care patients at the intensive care unit: a retrospective single center cohort study

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Intensive Care Medicine Experimental 2022, **10(2)**:001371

Introduction: Knowledge on characteristics and outcomes of palliative care patients admitted to the intensive care unit (ICU) is crucial to ensure a high quality of care (1,2). Nevertheless, available information on the degree of palliative care development and outcomes in Brazil is limited.
Objectives: To describe clinical characteristics, the use of advanced life support, and outcomes of palliative care patients admitted to the ICU of a private hospital in Brazil.
Methods: Retrospective single center cohort study conducted in a medical-surgical, open ICU of a private, quaternary care hospital located in São Paulo, Brazil. All adult (≥ 18 years) patients on palliative care admitted to the ICU or who benefited from palliative care implementation during the ICU stay between January 1, 2014 and December 31, 2018 were eligible for this study. Palliative care patients were categorized according to the time of palliative care implementation: before or within 24 h of ICU admission (Group Early) and after 24 h of ICU admission (Group Late). Comparisons were performed between the groups.
Results: During the study period, 12,074 patients were admitted to the ICU. Out of those, 4.2% (503/12,074 patients) received palliative care. Palliative care was implemented before or within 24 h of ICU admission in 37.8% (190/503) of patients and was implemented after 24 h of ICU admission in 62.2% (313/503) of patients. The median (IQR) age of included patients was 83 (70–88) years, 50.7% male, SAPS III score of 63(54–72) points and SOFA score of 5(2–7) points. Compared to Group Late, Group Early was older [86(79–92) vs. 78(64–86) years; p < 0.001], had a lower modified frailty index [2 (1–3) vs.3(2–4) points; p < 0.001], had immunosuppression less frequently [13.2% (25/190) vs.21.1%(66/313); p = 0.034)] or hematologic cancer [2.1% (4/190) vs.12.1%(38/313); p < 0.001)] and received invasive mechanical ventilation (MV) at ICU admission less frequently [18.9%(36/190) vs.31.6%(99/313); p = 0.003)]. During the ICU stay, Group Early received less red blood cell transfusion [14.2%(27/190) vs.43.5%(136/313); p < 0.001], less parenteral nutrition [2.6%(5/190) vs.12.5%(39/313); p < 0.001], less MV [30.0%(57/190) vs. 74.4%(233/313); p < 0.001], less vasopressors [44.7%(85/190) vs.71.2%(223/313); p < 0.001] and less renal replacement therapy [6.8%(13/190) vs.30.7%(96/313); p < 0.001] than Group Late. Additionally, Group Early exhibited a lower ICU [35.3%(67/190) vs.70.3%(220/313); p < 0.001] and hospital [61.6%(117/190) vs.85.6%(268/313); p < 0.001] mortality and had a shorter length of ICU [2(1–3) vs.7 (4–14) days; p < 0.001] and hospital [12(5–23) vs.17(8–34) days; p < 0.001] stay compared with Group Late.
Conclusion: Palliative care prior to admission to the ICU was associated with better outcomes and a lower resource use. Therefore, efforts should be made to increase availability of palliative care services at the ICUs in Brazil in order to improve the quality of palliative care provision.

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Acknowledgements: None.

001127

Delayed graft function and survival after five years of renal transplantation in controlled asystole donation

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Intensive Care Medicine Experimental 2022, **10(2)**:001127

Introduction: Renal transplantation remains the best treatment for patients with chronic renal failure. Controlled asystole donation has considerably increased the number of possible transplants with satisfactory results, which is why its practice is growing in Spain.

Objectives: The aim of this study is to know the results obtained in a sectorial coordination area Granada-Jaén following the patients for five years after the procedure.
Methods: Descriptive, retrospective, observational study. Data were collected on renal transplants in controlled asystole donations performed between April 2010 and December 2016 with normothermic abdominal perfusion by extracorporeal circulation system (PAN-ECMO) as the extraction method. Patients who died during follow-up and those who underwent other extraction methods were excluded. Subjects were followed up for the subsequent five years by measuring annual creatinine and collecting primary graft failure, delayed function and graft survival after the period.
Results: Seventy-four patients were selected out of 109 transplanted in that period with a mean age of 48 years. There were 14 patients (18.9%) with primary dysfunction, 20 (27%) with delayed graft function and a five-year graft survival of 90.55% (67 patients). During the five-year follow-up, patients had the following mean creatinine levels:

- At one month: 2.41 mg/dL
- At one year: 1.59 mg/dL
- At second year: 1.54 mg/dL
- At third year: 1.53 mg/dL
- At fourth year: 1.39 mg/dL
- At year five: 1.34 mg/dL

Conclusion: This study shows that the asystole donation programme in the Granada-Jaén region obtains viable kidneys for transplantation with high graft survival at five years of follow-up. A trend towards improvement in renal function over the years is noteworthy.

001148

DNR orders in SARS-CoV-2 patients: a retrospective validation study in a Swiss COVID-19 Center

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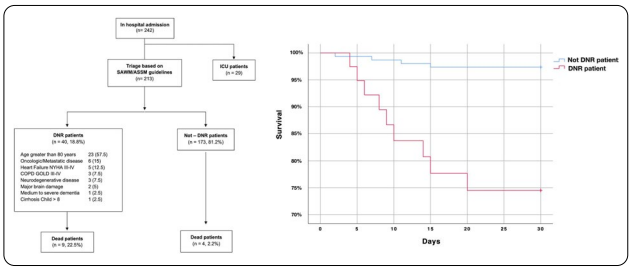
Intensive Care Medicine Experimental 2022, **10(2)**:001148

Introduction: In early 2020, the world witnessed the first pandemic of COVID-19. This dramatic situation forced many hospitals to improve their skills, and in some countries such as Switzerland, some hospitals became dedicated centers to provide specific management of patients with COVID-19, following government instructions. In this context, the Swiss Academy of Medical Sciences, a bridge builder between science and society, organized national guidelines to identify Do-Not-Resuscitate (DNR) patients to reduce futile ICU admissions and resource abuse. However, the practical impact of this standardized protocol has not yet been evaluated.
Objectives: In our COVID-19 center, we studied the characteristics and mortality of DNR patients identified according to the standardized national protocol, compared with non-DNR patients, to retrospectively validate the effectiveness of the Swiss national standard protocol in a pandemic emergency situation characterized by low resource availability.
Methods: A pilot retrospective validation study of consecutive COVID-19 patients admitted to the hospital. The primary outcome was the 30-day survival of DNR patients compared with the control group. Secondary outcomes reported the quality of treatment of deceased patients, especially with regard to agitation/sedation and dyspnea, using the RASS-PAL and modified Borg Scale.
Results: From March to April 2020, 213 consecutive patients were triaged. At 30-day follow-up, 9 patients (22.5%) died in the DNR group, 4 (2.2%) in the control group; the higher mortality rate in the DNR group was further confirmed by Log- Rank Mantel-Cox (23.104, $p < 0.0001$). In patients who died in the DNR group, end-of-life support was performed with oxygen (100%), opioids (100%), and sedation (89%), improving the mean RASS- PAL from 2.2 to -1.8 ($p < 0.0001$) and the Borg scale from 5.7 to 4.7 ($p = 0.581$).



Conclusion: The high mortality rate in COVID-19 patients increases the importance of identifying the subpopulation at highest risk of short-term death in a pandemic situation with limited resources. In this setting, the validation analysis we performed supported the role of the Swiss national standardized protocol in identifying DNR patients. Early access to specialist care should be mandatory, especially for this subgroup of patients, in order to improve long-term management and at the same time reduce the social impact of these pandemics.

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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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