Oral Sessions
Improving treatment and outcome in respiratory failure: 0955–0959

0955

NONINVASIVE VENTILATION USEFULNESS AND EFFECTIVENESS IN H1N1 INFLUENZA A VIRUS RESPIRATORY FAILURE: 144 SPANISH ICUS EXPERIENCE

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INTRODUCTION AND OBJECTIVES. It remains controversial the role of non invasive ventilation (NIV) in patients with acute respiratory failure. The objective of this study was to evaluate the usefulness and effectiveness of NIV to manage influenza A (H1N1) respiratory failure in Spanish ICUs.

METHODS. Prospective, observational, multicenter study in 144 Spanish ICUs. Data were obtained from GTEI/SEMICYUC register (June 15 and December 31, 2009). All adult patients with influenza A (H1N1) confirmed by rt-PCR were included and only patients treated with NIV were considered in the analysis. We evaluated the use and failure of NIV, as well as demographic data, comorbidities and severity scores. The analysis (SPSS 18.0, Inc. Chicago, IL) was performed using Chi square or Fisher exact tests for categorical variables and Student or Mann–Whitney tests for continuous variables. Significant variables from univariate analysis were included in the multivariate model (logistic regression). Differences of $p < 0.05$ were considered statistically significant.

RESULTS. Among 938 patients registered in the GTEI/SEMICYUC, 632 (67.4%) had completed their ICU admission and was the source of this analysis. Of the 449 (71%) who received mechanical ventilation, 157 (24.8%) were treated with NIV. NIV failed in 92 patients (58.6%) and they had to be subsequently intubated (control group = IT). Sixty-five (41.4%) patients responded to NIV (study group = NIV). The IT group had a higher APACHE II (16.1 ± 7.3 vs. 11.9 ± 6.0, $p < 0.01$) and SOFA (7.1 ± 3.8 vs. 4.2 ± 2.8 $p < 0.01$) compared to the NIV group. No significant differences in age, comorbidities and LDH levels were observed. Time from onset of symptoms to hospitalization (4.2 vs. 4.1 days) or ICU admission (1.0 vs. 1.0 days) was similar between groups. Shock occurred more frequently in the IT (66.1 vs. 15.6%, $p < 0.01$), and they also had more quadrants affected in the thorax X-ray (2.6 ± 1.1 vs. 1.9 ± 1.3, $p < 0.01$). Pneumonia (viral and bacterial) was more frequent in the IT (87.0% vs. 72.3%, $p < 0.05$) whereas COPD exacerbation was similar (4.9 vs. 10.9%, $p = 0.11$). The presence of shock (OR = 3.0 95% CI 1.61–5.69, $p < 0.01$) and pneumonia (OR = 1.2 95% CI 1.01–1.58, $p < 0.05$) were independently associated with NIV failure in the multivariate analysis. Mortality was significantly higher in IT compared to NIV (35.2 vs. 4.7%, $p < 0.01$).

CONCLUSIONS. NIV is not recommended as an alternative to invasive ventilation in patients affected by influenza A(H1N1) virus pneumonia with severe multiorganic failure or shock. In spite of this, selected patients with mild acute respiratory failure might benefit from this alternative therapy.

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NAVA ENHANCES VENTILATORY VARIABILITY AND DIAPHRAGMATIC ACTIVITY/TIDAL VOLUME COUPLING

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INTRODUCTION. Neurally Adjusted Ventilatory Assist (NAVA) is a new ventilatory mode in which ventilator settings are adjusted based on the electrical activity detected in the diaphragm (Eadi). This mode offers significant advantages in mechanical ventilation over standard pressure support (PS) modes, since ventilator input is determined directly from patient ventilatory demand. Therefore, it is expected that tidal volume (Vt) under NAVA would show better correlation with Eadi compared with PS, and exhibit greater variability due to the variability in the Eadi input to the ventilator.

OBJECTIVES. To compare tidal volume variability in PS and NAVA ventilation modes, and its correlation with patient ventilatory demand (as characterized by maximum Eadi).

METHODS. A comparative study of patient-ventilator interaction was performed for 22 patients during standard PS with clinician determined ventilator settings; and NAVA, with NAVA gain set to ensure the same peak airway pressure as the total pressure obtained in PS. A 20 min continuous recording was performed in each ventilator mode. Respiratory rate, Vt, and Eadi were recorded. Tidal volume variance and Pearson correlation coefficient between Vt and Eadi were calculated for each patient. A periodogram was plotted for each ventilator mode and each patient, showing spectral power as a function of frequency to assess variability.

RESULTS. Median, lower quartile and upper quartile values for Vt variance and Vt/Eadi correlation are shown in Table 1. The NAVA cohort exhibits substantially greater correlation and variance than the PS cohort.

TABLE 1 VARIANCE AND CORRELATION FOR PS AND NAVA

	Variance in Vt		Correlation (Eadi vs. Vt)	
	PS	NAVA	PS	NAVA
Lower quartile	793	5,218	0.0405	0.5971
Median	3,043	10,798	0.2563	0.6618
Upper quartile	5,398	23,715	0.3517	0.7618

Power spectrums for Vt and Eadi are shown in Fig. 1 (PS and NAVA) for a typical patient. The enlarged section highlights how changes in Eadi are highly synchronized with NAVA ventilation, but less so for PS.

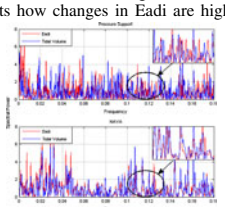

Fig. 1 Power Spectrum under PS and NAVA

CONCLUSIONS. There is greater variability in tidal volume and correlation between tidal volume and diaphragmatic electrical activity with NAVA compared to PS. These results are consistent with the improved patient-ventilator synchrony reported in the literature.

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AN ALGORITHM TO ADJUST THE PERCENTAGE OF ASSISTANCE IN PAV+ BASED ON AN ESTIMATION OF THE PATIENT'S RESPIRATORY EFFORT

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INTRODUCTION. With proportional-assist ventilation (PAV) the pressure delivered is proportional to instantaneous flow and volume and to respiratory muscles pressure (Pmus). This requires knowing the elastance and resistance of the respiratory system. PAV with load-adjustable gain factors (PAV+) has a software which automatically measures these values. The clinician simply adjusts a gain representing the percentage of the total pressure supported by the ventilator. From the observed peak airway pressure (Paw_{peak}) and the gain set on the ventilator it becomes possible to estimate the value of peak Pmus ($Pmus_{peak}$).

OBJECTIVES. We assessed the feasibility of targeting a Pmus estimate from Paw_{peak} to adjust the gain in PAV+.

METHODS. Multicenter prospective observational study. Patients under assisted controlled ventilation (ACV) were enrolled as soon as they triggered ventilator breaths, until extubation or complications. $Pmus_{peak}$ was calculated as $=(Paw_{peak} - PEEP) \times (100 - gain)/gain$, and was available on a grid at bedside. A simple gain adjustment algorithm was defined to target a $Pmus_{peak}$ between 5 and 10 cmH_2O in order to keep muscle pressure-time product (PTPmus) between 50 and 150 cmH_2O s min^{-1}. Additional recommendations were available in case of hypo- or hyper-ventilation despite a $Pmus_{peak}$ in the target interval. Ventilator data were recorded every minute and were used to calculate PTPmus after later processing. Adherence to the algorithm and patients' outcomes were collected. Results are given as median [25th–75th percentiles].

RESULTS. 52 patients, 67 year-old [57–74] with a SAPSII of 52 [40–63], were enrolled in five ICUs. Main causes for intubation were ARDS and septic shock. Patients spent 5 [3–7] days under ACV before inclusion. At baseline, PaO_2/FiO_2 ratio was 207 [173–261], PEEP 5 [5–6] cmH_2O, static compliance 36 [32–44] mL/cmH_2O and resistance 14 [9–17] $cmH_2O/L/s$. Gain at inclusion was 50 [50–60]%. Patients remained 3 [1–5] days under PAV+. Gain was adjusted 1 [0–2] time per day, according to $Pmus_{peak}$ in 85% of cases, because of hypo- or hyper-ventilation in 10, and 5% out of the protocol. Thirty-three patients were extubated, with a gain set at 50 [35–60]% at time of extubation. The other 19 were switched back to ACV for clinical worsening independent of PAV+, except for one patient. Patients spent 79 [67–85]% of the time in the PTPmus target interval.

CONCLUSIONS. For the first time the level of assistance was directly adjusted to target a given patient's respiratory effort. In PAV+, this method is feasible, and most often sufficient to ventilate patients until weaning.

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NEURALLY ADJUSTED VENTILATORY ASSIST CAN IMPROVE ARTERIAL OXYGENATION

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INTRODUCTION. Neurally Adjusted Ventilatory Assist (NAVA) [1] is a new spontaneous-assisted ventilatory mode which uses the diaphragmatic electrical activity (Eadi) to pilot the ventilator. Eadi is used to initiate the ventilator's pressurization and cycling off. Delivered inspiratory assistance is proportional to Eadi. NAVA can improve patient-ventilator synchrony [2] compared to pressure support (PS), but little is known about its effect on minute ventilation and oxygenation.

OBJECTIVES. To compare the effects of NAVA and PS on minute ventilation and oxygenation and to analyze potential determinant factors for oxygenation.

METHODS. Comparison between two 20-min periods under NAVA and PS. NAVA gain (proportionality factor between Eadi and delivered pressure) set as to obtain the same peak pressure as in PS. FIO_2 and positive end-expiratory pressure (PEEP) were the same in NAVA and PS. Blood gas analyses were performed at the end of both recording periods. Statistical analysis: groups were compared with paired t tests or non parametric Wilcoxon signed-rank tests. $p < 0.05$ was considered significant.

RESULTS. [Mean ± SD]: 22 patients (age 66 ± 12 year, 7 M/15F, BMI 23.4 ± 3.1 kg/m^2), 8 patients with COPD. Initial settings: PS 13 ± 3 cmH_2O, PEEP 7 ± 2 cmH_2O, NAVA gain 2.2 ± 1.8. Minute ventilation and $PaCO_2$ were the same with both modes ($p = 0.296$ and 0.848, respectively). Tidal volume was lower with NAVA (427 ± 102 vs. 477 ± 102 ml, $p < 0.001$). In contrast respiratory rate was higher with NAVA (25.6 ± 9.5 vs. 22.3 ± 8.9 cycles/min). Arterial oxygenation was improved with NAVA (PaO_2 85.1 ± 28.9 vs. 75.8 ± 11.9 mmHg, $p = 0.017$, PaO_2/FIO_2 210 ± 53 vs. 195 ± 58 mmHg, $p = 0.019$). Neural inspiratory time (Tin) was comparable between NAVA and PS ($p = 0.566$). Among potential determinant factors for oxygenation, mean airway pressure (Pmean) was lower with NAVA (10.6 ± 2.6 vs. 11.1 ± 2.4 cmH_2O, $p = 0.006$), as was the pressure time product (PTP) (6.8 ± 3.0 vs. 9.2 ± 3.5 $cmH_2O \times s$, $p = 0.004$). There were less asynchrony events with NAVA (2.3 ± 2.0 vs. 4.4 ± 3.8, $p = 0.009$).Tidal volume variability was higher with NAVA (variation coefficient: 30 ± 19.5 vs. 13.5 ± 8.6, $p < 0.001$). Inspiratory time in excess (Tiex) was lower with NAVA (56 ± 23 vs. 202 ± 200 ms, $p = 0.001$).

CONCLUSION. Despite lower Pmean and PTP in NAVA, arterial oxygenation was improved compared to PS. As asynchronies may be associated with an increased work of breathing and a higher oxygen consumption, their decrease in number with NAVA could be an explanation for oxygenation improvement. Another explanation could be the increase in VT variability. Further studies should now be performed to confirm the potential of NAVA in improving arterial oxygenation and explore the underlying mechanisms.

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IS ICU DISCHARGE TO THE WARD WITH A TRACHEOSTOMY CANNULA A RISK FACTOR FOR MORTALITY?

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INTRODUCTION. Between 10 and 40% of patients with prolonged mechanical ventilation (MV) undergo tracheostomy. Decannulation during the ICU stay is commonly advocated based on some studies reporting higher mortality in cannulated patients in the ward.

OBJECTIVES. To analyze the impact of discharging patients from the ICU to the ward without decannulation on ward survival in non-experimental conditions.

METHODS. Prospective survey of all patients admitted to 31 ICUs during a 3-month period in which data were collected for the validation of the Sabadell Score. At ICU discharge, we recorded demographic variables, severity score, and ICU treatments, with special attention to tracheostomy. Follow-up variables included ICU readmission and hospital survival. Statistics: Univariate and multivariate analyses for ward mortality, with Cox proportional-hazard ratio adjusted for propensity score for ICU decannulation.

RESULTS. We included 4,132 patients, 1996 (48%) of whom needed MV. Of these, 260 (13%) were tracheostomized, and 59 (23%) died in the ICU. Of the 201 ICU tracheostomized survivors, 60 (30%) were decannulated in the ICU and 141 (70%) were discharged to the ward with cannulae in place. Variables associated with ICU decannulation [non-neurologic disease (85 vs. 64%), vasoactive drugs (90 vs. 76%), parenteral nutrition (55 vs. 33%), acute renal failure (37 vs. 23%), and good prognosis at ICU discharge (40 vs. 18%)] were included in a "propensity score" model for decannulation. Crude ward mortality was similar in decannulated and non-decannulated patients (22 vs. 23%), but after adjusting for propensity score, vasoactive drugs, acute renal failure, and Sabadell Score, the presence of tracheostomy cannula seemed to be a protective factor, with an odds ratio of 0.5 [0.22–0.99] ($p = 0.048$).

CONCLUSIONS. In hospitals with good ward performance, ICU discharge before decannulation is not a risk factor. The possibility that it can be a protective factor would need further confirmation.

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SMARTCARE/PS DECREASES TOTAL VENTILATION TIME IN PATIENTS AFTER CARDIAC SURGERY

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INTRODUCTION. The automated weaning system SmartCare/PS (SC, Dräger Medical AG and Co. KG, Lübeck, Germany) provides an automatic control of the pressure support level. It has already been shown that this system may be equal efficient [1, 2] or even faster [3] in weaning patients from mechanical ventilation when compared to usual care or weaning protocols. In this a priori defined subgroup analysis of a randomized controlled trial [1] we analyzed patients after cardiac surgery (clinicaltrials.gov ID00445289).

OBJECTIVE. To assess the association of SC with total ventilation time in patients following cardiac surgery.

METHODS. After IRB approval and written informed consent, patients were included into the study when being ventilated for longer than 9 h and when none of the following exclusion criteria were fulfilled: cerebral surgery/trauma, age <18 years, do-not-resuscitate-order, preventilation time >24 h. After inclusion patients were randomly assigned either to be weaned by SC or according to a weaning protocol.

RESULTS. Baseline characteristics of the 132 included patients showed no significant differences between groups. Total ventilation time was 24 (18–57) h [median (25th–75th interquartile range)] compared to 34 (20–94) h in the protocol group respectively ($p = 0.037$) (Fig. 1).

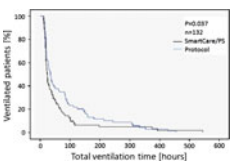

Fig. 1 Total ventilation time

Outcome parameters (Table 1) and complications of mechanical ventilation (Table 2) did not differ significantly between the two studied groups.

TABLE 1 MAIN OUTCOME PARAMETERS

Variable	SmartCare/PS group (n = 62)	Protocol group (n = 70)	p value
Length of stay in intensive care unit (days)	2.1 (1.2–4.5)	2.4 (1.3–8.5)	0.133
Length of stay in hospital (days)	12.6 (8.6–23.8)	14.3 (8.7–23.7)	0.510
90-day-mortality, n (%)	7 (11.3)	7 (10)	0.810

TABLE 2 COMPLICATIONS OF MECHANICAL VENTILATION

Complication	SmartCare/PS group (n = 62)	Protocol group (n = 70)	p value
Reintubation, n (%)			0.290
1	3 (4.8)	8 (11.4)	
2 or more	2 (3.2)	4 (5.7)	
Tracheostomy, n (%)			0.250
1	3 (4.8)	8 (11.4)	
2	0 (0.0)	1 (1.4)	

CONCLUSIONS. Patients after cardiac surgery may profit from weaning with SC. This has to be re-evaluated in a further randomized controlled trial.

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THE MEASUREMENT OF PAIN IN INTENSIVE CARE UNIT: COMPARISON OF 5 SELF-REPORT INTENSITY SCALES

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INTRODUCTION. Contrary to wards, where chronic and acute pain are regularly managed, comparisons of the most commonly used self-report pain tools have not been reported for the Intensive Care Unit (ICU) setting.

OBJECTIVES. To compare the feasibility, preference, validity and performance of 5 current self-report intensity scales for the assessment of pain in critically ill patients: the Visual-Analog-Scale (horizontal (VAS-H) and vertical (VAS-V) line orientation), the Verbal-Descriptor-Scale (VDS), the 0–10 oral Numeric-Rating-Scale (NRS-O) and the 0–10 visually enlarged laminated NRS (NRS-V).

METHODS. Psychometric study, approved by Sud-Mediterranee II Ethic Committee, in consecutive patients admitted in a medical-surgical ICU during 1 year. Informed written consent by patient or next of kind. Inclusion criteria: alert or only drowsy patients (RASS > -2) able to follow simple commands. Exclusion criteria: previous self-report pain assessment without the presence of investigator. Pain assessment using the 5 scales in random order at baseline (T1) and after (T2) administration of an analgesic, or during a nociceptive procedure, in absence of pain at baseline. Evaluated parameters: psychometric properties of scales (feasibility, validity, responsiveness and preference). Non parametric tests and Spearman's coefficients were used for statistical analysis (Statview 5.0). Data are expressed in median [25th–75th].

RESULTS. One hundred patients were included 24 [12–96] h after their admission to ICU: age 58 [48–69] years, SAPS II (admission) 39 [32–48], SOFA (admission) 7 [3–9], medical admission (49%), intubation before inclusion (76%), at time to inclusion (50%). The rate of any response obtained both at T1 and T2 (success rate) was significantly highest for NRS-V (91%) compared with NRS-O (83%), VDS (78%), VAS-H (68%) and VAS-V (66%). The NRS-V was considered as the easiest, most accurate and preferred scale for future use by respectively 62, 59 and 64% of patients who were able to answer. Pain intensity measured with the 5 scales changed significantly between T1 and T2 ($p < 0.01$) showing a good discriminative validity. Correlation between the 5 scales was important (Spearman's coefficients between the scales ranged from 0.75 to 0.96, $p < 0.001$). Responsiveness was very good for each of the 5 scales, either after an analgesia and a nociceptive procedure (effect size >0.8). The negative predictive value calculated from true and false negatives defined by real and wrong absence of pain was highest for NRS-V (90%).

CONCLUSIONS. In conclusion, among these 5 current self-report intensity scales which are all valid and responsive tools for the assessment of pain in communicant ICU patients, the NRS-V should be the tool of choice because it is the most feasible and discriminative.

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A OBSERVER BLIND, RANDOMIZED, PARALLEL GROUP, COMPARATIVE, STUDY TO EVALUATE SAFETY AND EFFICACY OF DEXMEDETOMIDINE HCL VERSUS PROPOFOL FOR POSTOPERATIVE SEDATION IN THE INTENSIVE CARE UNIT

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INTRODUCTION. The a2 agonist dexmedetomidine is a new sedative analgesic agent known to have both sedative and analgesic properties and has been licenced for <24 h sedation.

OBJECTIVES. To evaluate safety and efficacy of dexmedetomidine HCL versus propofol for postoperative sedation in the intensive care patients.

METHODS. 100 patients requiring short term ventilation (6–24 h) were randomized to receive either dexmedetomidine—Group A (Bolus 1 mcg/kg over 10 min followed by a maintenance infusion of 0.2–1 mcg/kg/h, $n = 50$) or propofol—Group B (loading dose of 1 mg/kg followed by infusion of 1–2 mg/kg/h, $n = 50$). Ramsay Sedation Scale (RSS) was used to maintain adequate depth of sedation (RSS 2–4). Analgesia was provided with intravenous fentanyl boluses of 1 mcg/kg as required. Intravenous midazolam boluses (40 mcg/kg) were used as rescue sedation. Cardiovascular, respiratory, biochemical and haematological data were obtained during the drug infusion and 24 h thereafter. The overall quality of sedation was also assessed by patients and doctors on a scale of 0–10. The total requirement of analgesics and rescue medications, time from stopping sedation to awakening and extubation, need for reintubation and adverse events were recorded.

RESULTS. 100 patients completed the study (50 in each group).There was no difference in the demographic variables between the 2 groups. No significant difference in the heart rate, blood pressure or respiratory rate, temperature, oxygen saturation or investigations between the groups. There was an insignificant trend towards lower hear rate in Group A. None of the patients were reintubated. Use of rescue sedation was significantly less in Group A versus Group B (10 patients vs. 23 patients, $p < 0.05$). The average dose of fentanyl required in mcg/kg/h was also significantly lower in Group A (0.53 ± 0.28 vs. 1.18 ± 0.53, $p < 0.05$).Though there was no difference in the total time to extubation, the time to awakening in minutes after stopping sedation was significantly lower in Group A (5.20 ± 1.81 vs. 8.40 ± 5.41, $p < 0.05$.) There were 4 deaths (1 Group A and 3 Group B) which were unrelated to the study and 3 adverse events in Group B (rise in urea, creatinine and lactate).The global assessment of safety and satisfaction by the physician and patient was significantly better in Group A.

CONCLUSIONS. Dexmedetomidine HCL is safe and acceptable sedative agent for postoperative short term sedation producing superior quality of sedation and reduced time to awakening compared to propofol. At comparable sedation levels dexmedetomidine HCL reduces the requirement of opioid analgesia.

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INTRAOPERATIVE CEREBRAL DESATURATION AS PROGNOSTIC FACTOR FOR THE NEUROCOGNITIVE OUTCOME AND THE PROLONGED HOSPITALIZATION AFTER CORONARY ARTERY BY PASS GRAFTING SURGERY

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AIM. The aim of this study was to evaluate whether cerebral desaturation episodes (CDE) during coronary artery bypass grafting surgery (CABG) are related to the postoperative neurocognitive outcome and to an increased risk of prolonged intensive care unit (ICU) and hospital stay.

METHOD. Sixty patients who underwent elective CABG procedure were assessed. Cerebral regional oxygen saturation (rSO_2) was continuously monitored intraoperatively with near-infrared spectroscopy. All CDE were recorded; cerebral desaturation episode was defined as a >20% decrease of baseline rSO2 values, for at least 1 min. Patient's neurocognitive status was evaluated preoperatively, prior to discharge and at 3-month follow-up, employing a broad range of neurocognitive tests for visual-spatial perception, executive functions, complex scanning, visual tracking, attention, working, short- and long-term memory, anxiety and depression. A decrease of 1 standard deviation (based on normative data relative to preoperative value) in performance on ≥1 neuropsychological tests was defined as neurocognitive decline (NCD).

RESULTS. The frequency of NCD and CDE was compared with χ^2 tests used for categorical variables. This resulted in a more common cognitive decline prior to discharge to those patients who had at least one CDE intraoperatively ($p = 0.01$). Moreover, decline in more than one neuropsychological test was also more frequent to the patients who had at least one CDE ($p = 0.01$). Likewise, NCD 3 months after surgery, was related with at least one CDE ($p = 0.04$). Linear regression models were conducted in order to assess the relationship between NCD and intensive care unit and hospital stay. The results showed that patients with NCD 3 months after surgery, had a significantly higher risk of prolonged stay in the ICU (>3 days) ($p = 0.02$) and in-hospital postoperatively (>10 days) ($p = 0.007$).

CONCLUSIONS. This study demonstrates the importance of continuous cerebral oximetry monitoring during coronary surgery. It shows that even a single desaturation episode intraoperatively affects postoperative cognitive outcome and patient's performance on more than one cognitive functions (tests). Neurocognitive decline 3 months after surgery is related to prolonged ICU stay and hospitalization.

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0964

TRADITIONAL AND HIGH TIDAL VOLUMES ARE ASSOCIATED WITH PROLONGED MECHANICAL VENTILATION AND ORGAN FAILURE AFTER CARDIAC SURGERY

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INTRODUCTION. High tidal volumes in mechanically ventilated patients with ARDS lead to baro/bio-trauma and increase mortality. Also, it was recently shown that ventilation with high tidal volumes is a risk factor for "acquired ARDS" in a medical population.

OBJECTIVE. We evaluated the impact of high tidal volumes after cardiac surgery.

METHOD. We analysed the prospectively recorded data of 3,434 consecutive patients who underwent cardiac surgery from 2002 to 2005. We predefined 3 groups of patients based on the tidal volume delivered immediately after surgery: (1) low: 7–9.9, (2) "traditional": 10–12.9, (3) high: above 13 ml/Kg of predicted body weight (PBW). We assessed the risk factors for organ dysfunction (prolonged mechanical ventilation, hypoxemia, hemodynamic failure and renal failure) by univariate and multivariate analysis, including the initial tidal volume in the models.

RESULTS. Mean tidal volume/actual weight and tidal volume/PBW was 9.2 ± 1.3 and 11.1 ± 1.5 in men ($P < 0.0001$), 9.1 ± 1.4 and 12.5 ± 2.2 in women ($P < 0.0001$). 411 patients (12%) were ventilated with low tidal volumes, 2,194 (63.9%) with "traditional" TV and 829 (24.1%) with high TV. The mean body mass index in the 3 groups was 23.8 ± 4.0, 27.0 ± 4.1 and 31.5 ± 5.4 respectively ($P < 0.0001$). With increasing BMI, the tidal volume/actual weight decreased while the tidal volume/PBW increased (Figure). The percentage of women was 12.2, 20.8 and 52.2% respectively for low, "traditional" and high TV ($P < 0.0001$). High tidal volumes were associated with prolonged intubation (>48 h) (1.5 vs. 2.7 vs. 4.3%, $P = 0.009$), renal failure (8.8 vs. 9.9 vs. 13.5%, $P = 0.007$) and prolonged use of inotropes/vasopressors (5.8 vs. 7.4 vs. 113%, $P = 0.004$). In a multivariate analysis, use of high tidal volumes was an independent risk factor for mechanical ventilation >48 h (traditional vs. low: OR: 2.2 [0.8–6.0], $P = 0.13$ and high vs. low: OR: 3.1 [1.1–8.6]), $P = 0.04$ and prolonged use of inotropes/vasopressors (traditional vs. low: OR: 1.7 [0.9–3.0], $P = 0.11$ and high vs. low: OR: 2.4 [1.2–4.5], $P = 0.01$.

CONCLUSION. Traditional and very high tidal volumes are associated with prolonged mechanical ventilation and organ dysfunction after cardiac surgery and use of high tidal volumes is an independent risk factor. "Prophylactic" protective ventilatory strategy should be provided in this population with inflammatory state at risk to develop ventilator induced pulmonary edema. Women and patients with high BMI are more at risk to be ventilated with injurious tidal volumes.

Education and training in intensive care: 0965–0969

0965

DEVELOPMENT, RELIABILITY, AND CONTENT VALIDATION OF THE OBSERVATIONAL SKILL-BASED CLINICAL ASSESSMENT FOR RESUSCITATION (OSCAR)

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INTRODUCTION. Evidence shows that clinicians' non-technical skills (behavioural and cognitive skills) have a significant impact on teamworking, patient safety, efficiency of care provided and potentially patient outcomes (1). Such skills are key for Cardiac Arrest Teams (CATs), which are multi-professional (Anaesthetists, Physicians and Nurses) and normally function under high pressure. To date, most tools to assess nontechnical skills in healthcare have focused on surgery (2) and anaesthesia (3). No validated, robust tools are currently available for assessing non-technical skills in CATs.

OBJECTIVES. To develop and validate an Observational Skill-based Clinical Assessment tool for Resuscitation (OSCAR). This should be psychometrically robust for use in both training and assessment contexts.

METHODS. OSCAR was based on a well-validated tool for surgery (OTAS) (4) and was developed in phases. Six behaviours were included in the assessment: Communication, Cooperation, Coordination, Monitoring, Leadership and Decision-Making. Observable behavioural exemplars were derived for each one of these behaviours across the three CAT subteams—Anaesthetists, Physicians and Nurses (Phase 1). Quantitative expert consensus methodology was employed to assess content and face validity and observability of the exemplars (Phase 2). Two clinician observers used OSCAR to blindly rate eight CATs performance in a series of simulated cardiac arrests. Psychometric analyses of these ratings were used to determine observable behaviour applicability, internal consistency, and inter-rater reliability (Phase 3).

RESULTS. 15 of 18 OSCAR behaviours demonstrated high internal consistency (Cronbach $\alpha = 0.736–0.970$). Psychometric analyses dictated removal of three behavioural exemplars (two in Anaesthetic group; one in Physician group) to significantly improve internal consistency. Inter-rater reliability was also high (inter-observer Pearson $r = 0.661–0.911$, all $p < 0.005$). Inter-observer reliability analyses revealed a learning curve between the two observers, with significant reduction in scoring discrepancies from the first to the eighth observed resuscitations.

CONCLUSIONS. OSCAR is a psychometrically robust (reliable, content- and face-valid) tool for the assessment of teamworking skills in cardiac arrest events. The tool is feasible to use and can be employed for both training and assessment purposes.

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0966

ASSESSMENT OF EDUCATIONAL METHODS: FULL SCALE SIMULATION TRAINING VERSUS PAPER CASE BASED SEMINARY ROUNDS

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INTRODUCTION. Different educational methodologies are used to teach basic skills in emergency medicine. High-fidelity patient simulation offers an ideal venue for presentation of critical events that can be managed by medical students without risk to a patient. Therefore full scale simulation training could be superior to paper case based seminary rounds to achieve these specific educational objectives.

OBJECTIVES. The aim was to compare simulation to a standard education measured by multiple choice questionnaire.

METHODS. After written informed consent and approval of the institutional research ethics board 160 fifth year medical students were included in the survey. They took part in the compulsory emergency medicine curriculum of Charité Universitätsmedizin Berlin. The students completed a basic multiple question tests on day 1 including 25 questions concerning the topic of "acute coronary syndrome" (ACS). On day 2 for the topic "ACS" half the group was assigned a 45 min session simulation training while half the group was assigned a 45 min session paper case training. On day 3 groups were reversed and the topic "AIC" was taught in either simulation training or paper case seminary round. The test of day 1 was repeated after each training sessions. Results of the tests were evaluated using SPSS(TM) 18. The Mann Whitney U test was used to show any significant differences in reaching educational objectives in the test ($\alpha < 0.05$ was considered significant).

RESULTS. There was an even distribution of men and women among the two groups. The test results showed no significant difference between the two groups on day 1. On day two for the topic "ACS" the group with simulation training achieved significantly better test results. For the topic "ACS" on day 3 there was no difference while students received further training in ACS not using a high fidelity simulator. The results were not linked to specific teachers.

CONCLUSIONS. Students in the simulation training group on the topic "ACS" scored better tests results on day 2. The results of the survey cannot be linked to gender nor the lecturer and corroborate Steadman et al. findings. The survey was conceived to show the positive effects of simulation training over paper case seminary rounds in teaching skills in acute coronary syndrome.

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0967

CRITICAL CARE ANAESTHESIA: DRUGS, EQUIPMENT AND MONITORING OUTSIDE THE OPERATING ROOM

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INTRODUCTION. Rapid sequence induction (RSI) involves loss of spontaneous breathing and mandates airway control. Steps to reduce adverse incidents include adherence to minimum monitoring standards, appropriate drug selection, access to difficult airway equipment and presence of skilled anaesthetists. There is substantial evidence that appropriate monitoring reduces risk by detecting the consequences of errors, and by giving early warning of patient deterioration.
OBJECTIVES. To assess conduct of emergency anaesthesia (monitoring and drugs) for critically ill patients not in an operating theatre (OR) administered by intensive care doctors.
METHODS. Prospective analysis of RSI for critically ill patients in a UK NHS Acute Hospital over 1 month. OR based practice was excluded. Reason for anaesthesia, location, drugs administered, monitoring modalities, adverse events and access to airway equipment were recorded.
RESULTS. Data from 26 patient episodes were collected: predominantly in the emergency department (38%) and intensive care unit (27%) for respiratory failure (46%), reduced consciousness (19%) and to facilitate investigations (19%). The most common induction agent was propofol (52%); thiopentone (26%) and etomidate (11%) were less frequently used. Suxamethonium (73%) was preferred for initial neuromuscular blockade. During induction most doctors used pulse oximetry, electrocardiography and blood pressure monitoring. Only 24% used capnography. No doctor used minimum monitoring to Association of Anaesthetists of Great Britain and Ireland (AAGBI) standards.[1]
Rescue airway equipment immediately available is shown in Fig. 1. Complications occurred in 12 cases (Fig. 2). Patients that had a hypotensive episode during induction all had thiopentone or propofol used as induction agents. 15% of patients had a period of desaturation, and 23% required more than one attempt for successful intubation. In cases with complications, rescue airway equipment was unavailable in >60 and 75% did not achieve UK minimum monitoring standards.

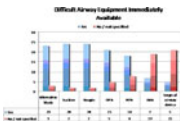

Figure 1

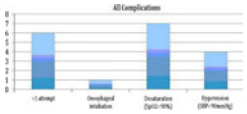

Figure 2

CONCLUSIONS. Shortcomings during emergency anaesthesia were recorded including monitoring, access to rescue airways and physiological disturbance. Procedural guidelines and training are to be developed for emergency anaesthesia; access to capnography and alternative airway equipment will be assured. These issues are unlikely to be unique to our Trust and assessment of practice is recommended.

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0968

BASIC CRITICAL CARE ECHOCARDIOGRAPHY: VALIDATION OF A CURRICULUM DEDICATED TO NONCARDIOLOGIST RESIDENTS

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INTRODUCTION. Critical care echocardiography (CCE) is performed and interpreted by the intensivist at the bedside to establish diagnoses and guide the management of patients with circulatory or respiratory failure in the ICU. Competence in basic and advanced CCE has been recently defined [1], but no curriculum to reach the required cognitive and technical skills has yet been elaborated.
OBJECTIVES. To assess the efficacy of a limited, tailored training program for noncardiologist residents without experience in ultrasound to reach competence in basic CCE.
METHODS. Six noncardiologist residents (Anaesthesiology: n = 5, Pneumology: n = 1) without previous experience in ultrasound participated to the study during two 3-month periods. The curriculum consisted in 4 h of didactics, 2 h of interactive clinical cases and 6 h of tutored hands-on. Color Doppler mapping was excluded from the training. After completion of the training program, all eligible patients underwent subsequently a transthoracic echocardiography (TTE) performed in random order by a recently trained resident and an experienced intensivist with expertise in CCE who was used as a reference. In each patient, the resident and the experienced intensivist answered binary "rule in, rule out" clinical questions covered by basic CCE [1]: global left ventricular (LV) size and systolic function (eye-ball evaluation of ejection fraction), homogeneous or heterogeneous LV contraction pattern, global right ventricular (RV) size and systolic function, identification of pericardial fluid and tamponade, and assessment of both the size and respiratory variations of the IVC. In case of undetermined interpretation, the corresponding clinical question was considered not addressed. The agreement between responses to clinical questions provided by the two investigators who independently interpreted the TTE study at bedside was used as an indicator of effectiveness of the tested curriculum.

RESULTS. In this prospective descriptive study, 201 consecutive patients [mean (±SD) age: 61 ± 16 years; SAPSII: 37 ± 17; 145 ventilated patients] who required a TTE were studied. Residents performed a mean of 33 TTE during the study period (range: 29–38). Experienced intensivists had significantly less unaddressed clinical questions than residents [61 (5.1%) vs. 114 (9.5%) of 1,206 clinical questions: $p < 0.0001$]. Residents accurately identified dilated left ventricle (Kappa: 0.90; CI 95%: 0.80–1.0), dilated right ventricle (Kappa: 0.76; CI 95%: 0.64–0.89), dilated inferior vena cava (Kappa: 0.79; CI 95%: 0.63–0.94), pericardial effusion (Kappa: 0.79; CI 95%: 0.58–0.99) and diagnosed two cases of tamponade.

CONCLUSIONS. A 12-h training program blending didactics, interactive clinical cases and tutored hands-on sessions dedicated to noncardiologist residents without experience in ultrasound appears well suited for reaching competence in basic CCE.

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0969

A SINGLE-DAY COURSE DESIGNED WITH A MODIFIED DELPHI METHOD PRECEDING A CRITICAL CARE POST IMPROVES "NOVICE" TRAINEES' PERFORMANCE AND CONFIDENCE

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INTRODUCTION. Modern postgraduate medical training in the United Kingdom requires a large proportion of graduates to work within a "Critical Care" setting. The level of support available to trainees may vary with local resources but risk management and national guidelines stipulate that close supervision is provided to junior doctors in high stake decisions and procedures until deemed competent at the relevant tasks[1]. Furthermore, substantial ongoing reduction in working hours places further limitations on training; both majors can impact adversely on junior doctors service output and experience. A modified Delphi method was used 2 years ago to design a task focused single-day course on the theoretical basis of critical care and provide lab-based training in Delphi identified high risk procedures and interventions[2].

OBJECTIVES. Assess the impact of the course on the following:

Trainee confidence and the start of the "novice" Critical Care post
Trainee performance in comparison to peers
Perceived educational benefit from their training post compared to peers

METHODS. 30 junior doctors attending the course were enrolled in the study and matched for graduation year and medical school to 30 junior doctors who did not attend similar training prior to commencing their post. Data was collected through anonymous standardized forms on the day of the course, first day of the job, end of week 1, week 6 and 4 months into the post. Trainee confidence and self perceived competence were assessed on a ten point scale. In addition, trainees were requested to maintain a log of 3 interventions: 1—ultrasound guided central venous catheter insertion, 2—arterial catheter insertion, 3—ventilation problem solving.

RESULTS. Candidates attending the course demonstrated greater confidence at multiple points within their post as well as higher performance, satisfaction and educational value scores.

CONCLUSIONS. Critical Care trainees benefit from a task focused orientation to the fundamentals of critical care before commencing first post in this setting.

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Improving nursing care: 0970–0974

0970

RANDOMIZED CONTROL TRIAL COMPARING ORAL CARE METHODS AND VAP

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INTRODUCTION. Mechanically ventilated patients in ICU have 10–30% risk to develop VAP (ventilated associated pneumonia). It has been found that tooth plaque is one of the causes of VAP. Published literature shows that evidenced based nurse driven oral care protocols can lower the incidence of VAP

OBJECTIVES. The objective of our study was to reduce the incidence of VAP in our unit using an evidenced based protocol for oral care

METHODS. Prospective randomized control trial comparing standard oral care to evidenced based oral care protocol. Adult ventilated patients were randomized according to their order of admission on alternate days to the ICU. Control group received oral care standard—mouth sponge soaked with Chlorhexidine 02%, 3 times daily. Study group received oral care protocol of tooth brushing, toothpaste and suction, 3 times daily.

RESULTS. 100 enrolled 50 patients in each group. No differences in age and gender. Incidence of VAP-study group 8.8% compared to control group 28.8% p value 0.004. VAP per 1,000 hospital days: control—29.5% compared to study—10.2% p value 0.06; average days in ICU control—14.97 compared to study—11.8, p value 0.151; average ventilated days, control—12.68 compared to 8.9, p value 0.044; average antibiotic use in days control—9.7 compared to study—7.2, p value 0.413.

RESULTS

Variable	Control group	Study group	p value
Incidence of VAP	28.80%	8.80%	0.004
VAP per 1,000 hospital days	10.60%	26.6	0.06
Average days in ICU	14.97	11.8	0.151
Average ventilated days	12.68	8.9	0.044
Average antibiotic use days	9.7 days	7.2 days	0.413

CONCLUSIONS. Evidenced based nurse driven protocols can successfully reduce the incidence of ICU VAP, ventilation days, antibiotic use, hospital and ICU stay. Nursing interventions influence patient outcomes. Recommendations: Evidenced based nursing oral care protocols can be successful in reducing incidence of ICU VAP. Nurses can successfully perform clinical randomized control trials.

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0971

DIARRHOEA, ENTERAL NUTRITION AND INTESTINAL FLORA RELATIONSHIPS IN CRITICALLY ILL PATIENTS: A PROSPECTIVE CORRELATION COHORT STUDY

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INTRODUCTION. Diarrhoea occurs in 46–60% of critically ill (CI) patients. The causes of diarrhoea in CI are debatable. Potential causes include antibiotics (AB) and other medications, enteral tube feeds (ETF), hypoalbuminaemia and changes in intestinal flora (IF). Little research has examined IF, ETF and diarrhoea relationships in CI patients.

OBJECTIVES. To examine relationships between IF, ETF and diarrhoea in CI adult patients.

METHODS. A single centre repeated measures, correlation cohort study of 101 patients was conducted in a 22 bed adult ICU of a tertiary hospital. Diarrhoea and ETF risk factors were examined. Patients were included if they were (1) ETF; (2) emergency admission and not admitted to another hospital/ward; (3) ≥18 years; (4) ICU length of stay >24 h. Patients were excluded if they (1) suffered burns, severe perianal trauma; (2) elective post operative patients. Diarrhoea was defined as a loose/liquid stool ± stool weight >200 g/day using the Bristol Stool Chart. IF were collected from rectal swabs at ICU admission, discharge and diarrhoea.

RESULTS. Diarrhoea was experienced by 53% (n = 53) of patients, reported on 143 (16%) of 925 patient admission days and observed 326 times. The mean APACHE II score was 28 and mean ICU LOS was 9 days. The average delay from ICU admission to initial bowel activity was 90 h. Patients received aperients (n = 81, sd = 0.4; 80%), prokinetics (n = 78, sd = 0.42; 77%), AB (n = 87, sd = 0.35; 86%) and sedation (n = 98, sd = 0.17, 97%). Hypoalbuminaemia (<30 g/L) (n = 96, 95%) and hyperglycaemia (n = 92, 91%) were highly prevalent. Diarrhoea duration was associated with (1) delay to bowel activity (β −0.01, $p = 0.02$); (2) duration of AB (β −0.106, $p < 0.001$), aperients (β 0.062, $p < 0.001$), opioids (β 0.219, $p < 0.001$), hyperglycaemia (β 0.177, $p = 0.004$), hypoalbuminaemia (β 0.265, $p < 0.001$), elevated white blood cells (WBC) (β 0.223, $p < 0.001$); (3) ICU LOS (β 0.126, $p < 0.001$); (4) diarrhoea incidence (β 0.369, $p < 0.001$). Diarrhoea incidence was associated with (1) delay to bowel activity (β −0.023, $p = 0.035$); (2) duration of AB (β −0.224, $p < 0.001$), ETF (β 0.527, $p < 0.001$), aperients (β 0.137, $p = 0.002$), opioids (β 0.534, $p < 0.001$), hyperglycaemia (β 0.511, $p < 0.001$), hypoalbuminaemia (β 0.654, $p < 0.001$), elevated WBC (β 0.588, $p < 0.001$); (3) ICU LOS (β 0.336, $p < 0.001$). IF changes were not associated with increased diarrhoea duration (β −0.018, $p = 0.962$) or incidence (β 0.357, $p = 0.545$). Diarrhoea duration was not associated with IF changes in faecal test one (FT) (X_4^2 4.813, $p = 0.307$) or FT two (X_3^2 2.546, $p = 0.467$). Diarrhoea incidence was not associated with IF changes in FT one (X_4^2 3.703, $p = 0.448$) or FT two (X_3^2 3.482, $p = 0.323$).

CONCLUSIONS. No significant relationships between diarrhoeal duration, incidence, IF and ETF were observed. Strategies to reduce ETF diarrhoea in CI patients must be explored and addressed to optimise recovery from a CI experience.

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0972

LONG-TERM QUALITY OF LIFE AND COGNITIVE FUNCTIONING IN DELIRIUM IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Delirium is associated with long-term cognitive decline and poor health related quality of life (HRQOL). Little is known about long-term differences on these aspects between delirious and non-delirious critically ill patients.

METHODS. We performed a health related quality of life (HRQoL) survey 18 months after discharge in patients that were admitted to a general ICU. An HRQoL survey, the SF-36v1, the Checklist Individual Strength (CIS) and the Cognitive Failure Questionnaire (CFQ) was sent out to 1,292 ICU patients with (n = 272, 21.1%) and without (1,020, 78.9%) delirium during their ICU admission. We compared the results of the delirious and non-delirious patients. Covariance analysis was performed to correct for age, APACHE-II score, and sepsis.

RESULTS. 915 (71%) out of 1292 patients responded of which 170 patients (18.6%) had been delirious during ICU admission (age 63 ± 15, APACHE-II score 18 ± 6) and 745 patients (81%) had not been delirious (age 62 ± 13, APACHE-II score 13 ± 5). After adjustment for age, APACHE-II score and sepsis, the delirious group evaluated their physical functioning (SF-36v1) significantly worse compared with the non-delirious patients at 18 months after ICU discharge (Table 1). Delirious patients also reported significant higher fatigue levels (CIS) than the non-delirious patients. No differences were found on the other HRQL dimensions (SF-36v1) or cognitive functioning (CFQ) between the two groups.

CONCLUSIONS. 18 months after ICU discharge, patients that suffered from delirium during their ICU stay had significantly more problems with physical functioning and fatigue than patients that did not suffer from delirium. Other HRQL dimensions and cognitive functions were not different between the two groups.

TABLE 1 RESULTS ON DIMENSIONS OF HRQOL

	Delirious patients (N = 170)	Non-delirious patients (N = 745)	*p* value
SF36 (mean ± SD)			
Physical functioning	20.7 ± 6.3	23.3 ± 5.8	***<0.004***
Body pain	11.4 ± 1.6	11.5 ± 1.5	*0.70*
Role-physical	5.7 ± 1.6	6.1 ± 1.7	*0.05*
General health	15.4 ± 4.6	16.3 ± 4.5	*0.31*
Vitality	15.2 ± 3.9	16.2 ± 42	*0.13*
Social functioning	7.6 ± 2.0	8.1 ± 2.0	*0.14*
Role-emotional	5.0 ± 1.2	5.2 ± 1.2	*0.47*
Mental health	22.8 ± 4.8	23.8 ± 4.7	*0.15*
CIS	40 ± 15	36 ± 15	***0.01***
CFQ			
Tolal score of CFQ	32.5 ± 18.0	34.2 ± 18.2	*0.28*
Absent-mindedness	8.0 ± 5.7	8.8 ± 5.6	*0.14*
Absent-mindedness in social situations	5.5 ± 3.5	5.9 ± 3.7	*0.35*
Names and words	6.1 ± 2.9	6.3 ± 2.9	*0.21*
Orientation	2.3 ± 2.5	2.6 ± 2.7	*0.26*

0973

DO NURSE CONSULTANT TEAMS PREVENT MECHANICAL VENTILATION ASSOCIATED PNEUMONIA AND CATHETER-RELATED BLOODSTREAM INFECTION IN THE ICU? THE SABADELL EXPERIENCE

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INTRODUCTION. Nosocomial infections are the most common in-hospital complications with high morbidity and mortality. Educating healthcare professionals is an important prevention measure.

OBJECTIVE. To analyze the impact of a nurse consultant team on nosocomial infections prevention in the ICU, the improvement in prevention knowledge of the nurse staff, and its impact in the application of the prevention measures in the daily practice.

METHODOLOGY: The nurse referent team was constituted by 8 nurses. The study subjects were all the staff ICU nurses and all the patients admitted during pre and post-intervention phases. The study was conducted in our medical-surgical ICU (16 beds) in 3 phases:

1 Pre-interventional (15/01/09–15/02/09)
Observational. Record of the accomplishment of 12 CDC recommended variables about mechanical ventilation associated pneumonia (VAP) and catheter related bloodstream infection (CR-BSI) prevention measures.

2 Interventional (1/03/09–1/10/09)
Eight educational meetings with the nurses staff groups to teach the most important aspects of the nosocomial infections prevention. Before and after lectures every nurses answered an anonymous questionnaire about their knowledge in those subjects. A poster with the most important reminders was place in every ICU patient room.

3 Post-interventional (15/01/10–15/02/10)
Observational. New record of the same 12 CDC pre-interventional variables. We compared the accomplishment of these variables before and after the interventional phase as well as the number of correct questionnaire answers. Statistics were made with SPSS software.

RESULTS. During the interventional phase 70% of the staff nurses attended the educational meetings. The number of correct answers increased significantly after the conference (77.1 vs. 55.2% p < 0.0001). Regarding to the daily practice, we observed a significant increase in the accomplishment in most of the variables (see table below), while in 3 of them no improve was observed and in 2 the improvement was not statistically significant. During the study period we observed a decrease in the incidence of VAP (6.7–14.9 episodes/1,000 MV days) and CR-BSI (2.1–4.8 episodes/1,000 catheter days).

VARIABLES

Variables	PRE	POST	p
Not in-use catheter removal or change after 72 h	61.6	88.6	<0.001
IV dressing removal after 72 h	83.8	92.2	<0.001
Last dressing change record	55.8	87.4	<0.001
Emergency catheter removal within 24 h	59.9	90.7	<0.001
Iv line kit date record	62.4	85.4	<0.001
OT tube external fix control	70.1	76.9	0.1
3-way ports IV line cleaning	94	96.6	0.05
IV and arterial lines dressing maintenance	94.4	92.1	0.1
Daily update of the catheters number in paper chart	97.2	98.8	0.05

CONCLUSIONS. Nurse consultant teams are an effective tool for improving nurse knowledge and kills in nosocomial infection prevention. The role of these teams could be important to reduce the incidence of VAP and CR-BSI in the ICU, as well as to improve daily practice.

0974

A CLUSTER CONTROLLED IMPLEMENTATION PROJECT OF INTENSIVE INSULIN THERAPY (IIT): AFFECTS ON BLOOD GLUCOSE CONTROL AND INCIDENCE OF SEVERE HYPOGLYCEMIA (SH)

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INTRODUCTION. IIT is a complex intervention involving several steps which may all contain potential sources of variability. Changing practice in complex multidisciplinary environments is difficult. In addition, it is undecided whether IIT should be applied by nurses and physicians, or nurses alone. We implemented IIT using a conceptual implementation framework and compared overall blood glucose control and incidence of SH [blood glucose level (BGL) <40 mg/dl] before and after implementation.

METHODS. 3 ICUs developed and implemented an evidence-based guideline for IIT; 3 ICUs with no change in blood glucose control served as control ICUs. In the guideline ICUs, the IIT practice-change composed of 2 periods: in the first year after implementation of the guideline, physicians and nurses used the guideline together; in the second year the guideline was applied solely by nurses. BGL collection and analysis included the 1 year before implementation of the guideline. Analysis was performed using statistical process control (SPC).

RESULTS. IIT guideline: the new guideline emphasized on fast correction of high BGLs, acceptance of low BGLs and frequent BGL measurements (up to 1/h).

Blood glucose control: BGLs of approximately 8,000 patients were collected and analyzed. Case mix was similar in guideline and control ICUs, and did not change over time. No change in overall blood glucose control or incidence of SH was observed in the control ICUs. In the guideline ICUs the median number of daily blood glucose measurements increased from 4/patient (3–7) to 9/patient (5–12) (P < 0.001). Median morning BGL declined in guideline ICUs, from 114 mg/dl (96–139) to 100 mg/dl (85–123) (P < 0.001). The change in blood glucose control was accompanied by a rise of the incidence of SH, from 7 to 13% (P < 0.001). SH, however, did never cause short-term harm (no death or coma). Nurses alone performed equally well with regard to overall blood glucose control, and even showed a decline of incidence of SH, for details see Fig. 1.

CONCLUSIONS. Implementation of an evidence-based IIT guideline improves blood glucose control, but increases the incidence of SH. IIT can be applied by nurses alone.

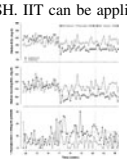

Figure 1

Nutritional support in the critically ill: 0975–0979

0975

EVALUATING SMALL BOWEL FUNCTION IN PATIENTS WITH MULTI ORGAN DYSFUNCTION SYNDROME USING A CITRULLINE GENERATION TEST

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INTRODUCTION. Malabsorption, arbitrarily defined as an intestinal absorption of 85% or less, is believed to be a frequently occurring problem in intensive care units (ICU). It is a problem of great concern, particularly in patients suffering from sepsis or multiple organ dysfunction. Small bowel dysfunction may lead to malnutrition and may predispose to sepsis and multi organ dysfunction syndrome (MODS). However, there are no simple, validated tests to assess intestinal function. A recently developed test, the citrulline generation test (CGT), exclusively measures the enterocytes' conversion of administered glutamine into citrulline and therefore represents enterocyte (small bowel) function [1].

OBJECTIVES. The aim of this study was to apply CGT in patients with MODS in order to evaluate small bowel function. Secondly, we wanted to compare the CGT results of the patients with MODS to a group of stable ICU patients.

METHODS. We compared the MODS group, defined as having 2 or more dysfunctioning organ systems, to a group of stable ICU patients defined as an ICU patient who is mechanically ventilated but not on other organ support (inotropes, renal support, etc.). After a 5 h fast 20 g of glutamine-alanine (Dipeptiven®) was administered intravenously after which, during 3 h, citrulline levels were measured at fixed time points. The measurement was performed by reverse-phase high-performance liquid chromatography (HPLC). The MODS patients were tested twice, the first time on day 1 and the second time on day 5.

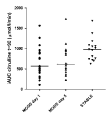
RESULTS. We studied 19 MODS patients (5 females/14 males) and 16 stable ICU-patients (9 females/7 males).

RESULTS

Parameter	MODS day 1		STABLE ICU		P value
	Median	IQR	Median	IQR	
Age (years)	69.0	64.0–76.0	62.5	53.3–67.8	<0.05
APACHE II score	28.0	20.0–34.0	24.5	19.5–26.8	0.2
SOFA score	10.0	8.0–14.0	4.0	3.0–4.8	<0.0001
Citrulline T = 0 (μmol/l)	36.6	23.3–45.3	30.6	25.1–38.4	0.5
Peak citrulline (μmol/l)	45.7	32.0–64.5	51.5	37.1–59.1	0.8
iAUC T = 90 citrulline (μmol/l/min)[a]	571.5	409.5–961.0	977.0	739.8–1084.0	<0.05
Slope[b]	0.17	0.1–0.25	0.22	0.19–0.3	<0.05

[a]iAUC T = 90 is defined as the increment of the area under the curve of citrulline at T = 90 min

[b]Slope is defined as (peak citrulline − citrulline at T = 0)/time to peak



iAUC citrulline T = 90

CONCLUSIONS. MODS patients displayed a markedly decrease of small bowel function, as defined by citrulline iAUC at t = 90 min, when compared to a stable control group. MODS patients also showed a markedly decrease in the speed of citrulline generation as defined by the slope of the graph.

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0976

THE IMPACT OF REAL TIME CONTINUOUS GLUCOSE MONITORING ON GLUCOSE VARIABILITY IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Glucose variability has been found to be associated with mortality in critically ill patients, independent of mean glucose concentration [1].

OBJECTIVES. The aim of this analysis was to assess the impact of real time continuous glucose monitoring (CGM) on glucose variability in critically ill patients receiving intensive insulin therapy (IIT).

METHODS. This is the post-hoc analysis of a prospective, randomized, controlled trial [2]. Data of 124 patients admitted to the ICU either receiving IIT according to a real time CGM system (Guardian®, Medtronic, Northridge, CA, USA) (n = 63) or according to an algorithm (n = 61) with selective arterial blood glucose measurements (simultaneously blinded CGM) for 72 h were analysed. Insulin infusion rates were guided according to the same algorithm in both groups. Mean glucose and standard deviation, as a marker of glucose variability, were calculated for the first 24 h (Glu_{MEAN1}, Glu_{SD1}) and for the whole study period (Glu_{SD}). Statistical comparison of parameters between study groups and between ICU survivors (n = 94) and non-survivors (n = 30) was performed using student's t test.

RESULTS. The variability of sensor glucose during the entire study period was comparable between the real time CGM group and controls (21.51 ± 1.10 vs. 23.44 ± 1.26 mg/dl; p = 0.243). Although the mean sensor glucose during the first 24 h in ICU showed a trend towards lower values in the intervention group (real time CGM vs. control: Glu_{MEAN1}: 104.40 ± 2.00 vs. 109.23 ± 1.96 mg/dl; p = 0.087), variability of sensor glucose during the first 24 h did not differ significantly (real time CGM vs. control: Glu_{SD1}: 18.46 mg/dl vs. 20.85 mg/dl; p = 0.201). Glu_{SD} tended to be lower in ICU survivors (ICU survivors vs. non-survivors: 21.61 ± 8.60 vs. 25.10 ± 10.55 mg/dl; p = 0.071) whereas Glu_{SD1} (19.06 ± 9.32 vs. 21.41 ± 13.21 mg/dl; p = 0.282) and Glu_{MEAN1} (106.39 ± 14.83 vs. 108.00 ± 18.44 mg/dl; p = 0.627) were not different between ICU survivors and non-survivors.

CONCLUSIONS. IIT guided by real time CGM did not result in reduced glucose variability compared to IIT according to an algorithm with selective arterial blood glucose measurements. Although mean sensor glucose during the first 24 h tended to be lower in the real time CGM group, glucose variability was not different between the two groups. Glu_{SD} tended to be lower in ICU-survivors irrespective of glucose monitoring.

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0977

DRAMATIC CHANGES IN THE GUT FLORA IN CRITICAL ILLNESS IMMEDIATELY AFTER SEVERE INSULT

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INTRODUCTION. In the gastrointestinal tract, the gut flora which comprises several hundred grams of bacteria is crucially involved in host homeostasis through their metabolic, trophic, and protective activities. However, the immediate changes in the gut flora in critical illness following severe insults are unknown.

OBJECTIVES. To investigate the changes in the gut flora at an early phase of severe insult in critically ill patients.

METHODS. Fifteen patients who experienced a sudden and severe insult including trauma, out-of hospital cardiac arrest, and cerebral vascular disease were studied, along with 12 healthy volunteers as the control group. Two fecal samples were acquired from the subjects by swabs of the rectum within 6 h after admission to the emergency room (day 0). Samples were serially collected from patients on day 1, 3, 5, 7, 10, and 14. Samples were collected from control subjects.

RESULTS. Total bacterial counts, especially various obligate anaerobes and total *Lactobacillus*, significantly decreased in comparison to those of the control subjects on day 0. In addition, on day 0, the total organic acid levels of the patients were significantly lower than those of the control subjects; particularly acetic acid, propionic acid, and butyric acid. The levels of these acids remained low throughout the 14 days period of study. The total bacterial counts did not recover to normal levels during the 14 day study period. Obligate anaerobe counts of the patients did not improve until day 14. Total *Lactobacillus* counts were low on day 0 and increased gradually thereafter, but did not attain the levels found in controls. The counts of pathogens (*Enterococcus* and *Pseudomonas*) increased during the study period.

CONCLUSIONS. Gut flora in critically ill patients can change drastically immediately after a severe insult, and may not recover for up to 14 days. At the same time, the number of harmful bacteria can increase.

TABLE FECAL FLORA ON DAY 0

	Control Subjects	Patients	P value
Total bacteria	10.1 (9.8–10.4)	7.5 (6.7–8.0)	<0.001
Obligate anaerobes			
Clostridium cocades group	9.4 (9.0–9.7)	6.1 (5.4–7.0)	<0.001
Clostridium leptam subgroup	9.2 (9.0–9.7)	6.5 (6.1–7.3)	<0.001
Bacteroides fragilis group	9.4 (9.0–9.8)	6.8 (5.9–7.6)	<0.001
Bifidobacterium	9.2 (8.9–9.4)	6.0 (<5.0–6.9)	<0.001
Atopobium cluster	9.0 (8.5–9.5)	6.0 (<5.1–7.1)	<0.001
Prevotella	8.8 (8.5–9.1)	<5.0 (<5.0–6.0)	<0.001
Clostridium perfnngens	<3.5(<3.5–<3.5)	<3.5	NS
Facultative anaerobes			
Total *Lactobacillus*	5.7 (4.5–6.9)	<25 (<2.5–2.7)	<0.001
Enterobacteriaceae	5.9 (5.5–6.4)	5.5 (<5.4–6.4)	NS
Enterococcus	5.2 (4.3–5.8)	4.6 (<2.9–5.5)	NS
Staphylococcus	3.8 (3.4–4.5)	<4.0 (<4.0–4.4)	NS
Obligate aerobes			
Pseudomonas	<3.0	<3.0	NS

All measurements was presented as Log_{10} counts/g and median (interquartile range 25–75%)

0978

SERUM 25-HYDROXYVITAMIN D STATUS OF CRITICALLY ILL PATIENTS IS PREDICTIVE OF HOSPITAL MORTALITY INDEPENDENT OF SAPS II

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INTRODUCTION. Whether widespread vitamin D deficiency which is mainly due to geographic latitude, diet and life-style contributes to clinical outcome in the hospital is unclear. Because of the pleiotropic effects that vitamin D may have on immune function, calcium metabolism, muscle and cardiac function, the role of low vitamin D baseline levels as well as that of vitamin D supplementation in an ICU setting has recently attracted interest.

OBJECTIVES. Aim of the present study was to investigate a possible relationship between hospital mortality and vitamin D status of patients at different intensive care units of our institution.

METHODS. From September 2008 until April 2010, 25-hydroxyvitamin D [25(OH)D], serum calcium and parathyroid hormone (PTH) levels were assessed in 577 patients at different ICUs of our tertiary care center (medical, cardiothoracic, mixed surgical and neurological ICUs). Because of seasonal variations of 25(OH)D levels we formed month-specific tertiles with the highest 25(OH)D tertile being the reference category.

RESULTS. Mean serum 25(OH)D level was 18.9 ± 10.9 ng/ml. By current definitions the majority of patients (62.5%) were vitamin D deficient (<20 ng/ml) and 24.9% were vitamin D insufficient (≥20 and <30 ng/dl). Normal 25(OH)D levels (>30 ng/ml) were present in 12.6%. Table 1 provides information on clinical and laboratory findings in the three 25(OH)D groups. Both lower 25(OH)D tertiles were associated with increased hospital mortality after adjustment for age, sex and SAPS II. For 330 patients both 25(OH)D and PTH levels were available. Adjusting the Cox regression analysis also for PTH and dialysis status increased the HR for hospital mortality to 2.3 (1.1–4.7) and 2.1 (0.99 and 4.4) for the two lower 25(OH)D tertiles. In addition tertiles of PTH and serum calcium levels suggested higher mortality rates for patients in the highest PTH (P = 0.09) and those in the lowest calcium tertile (P = 0.12).

TABLE 1

25(OH)D tertiles	Lowest tertile (n = 201)	Medium tertile (n = 192)	Highest tertile (n = 184)	P value
Age (years)	65 (55–77)	61 (49–73)	63 (53–74)	0.04
Male (%)	58	66	62	NS
SAPS score	32 (23–37)	28 (18–33)	29 (19–34)	0.01
25(OH)D (ng/ml)	10.1 (8.0–11.3)	17.2 (13.1–21.4)	30.0 (22.7–34.6)	0.001
Serum calcium (mmol/L)	2.08 (1.97–2.20)	2.12 (1.98–2.23)	2.16 (2.06–2.27)	0.001
Serum phosphate (mmol/L)	1.25 (0.92–1.49)	1.14 (0.87–1.28)	1.15 (0.85–1.33)	NS
Parathyroid hormone (pg/ml)	87 (35–101)	75 (33–76)	54 (28–61)	0.001
Hospital mortality (%)	25.2	20.6	12.3	
Hospital mortality HR (95% CI)	1.67 (1.01–2.75)	1.71 (1.02–2.88)	Ref	

CONCLUSIONS. Our results demonstrate that independent of baseline SAPS II, age and sex, critically ill patients with low 25(OH)D levels seem to be at increased risk for hospital mortality. Whether a rapid correction of vitamin D status may be beneficial in the ICU setting remains to be further explored in randomized controlled trials.

0979

EFFECTS ON NUTRITION THERAPY ON THE OUTCOME OF PATIENTS WITH SEVERE SEPSIS: RESULTS FROM THE VISEP TRIAL

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INTRODUCTION. The optimal route and amount of nutrition therapy remains to be up for debate which is reflected in the most recent nutrition guidelines by the European (ESPEN) and American (ASPEN) societies [1, 2]. Enteral nutrition (EN) should be preferred over parenteral nutrition (PN). While ASPEN recommends permissive underfeeding with EN only and avoid PN in the first days of ICU stay, ESPEN proposes an early complementary parenteral approach.

OBJECTIVES. Our aim was to identify the route and amount of nutrition provided and its possible association to outcome parameters in a large population of patients with severe sepsis/septic shock.

METHODS. Daily nutrition data was collected within the framework of the "Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis" study [2]. Categorical data are reported as absolute or relative frequencies where appropriate. Median and interquartile range are presented for continuous data. The Chi-square, Kruskal–Wallis H test and logistic regression were applied to compare categorical and continuous variables as appropriate. SAS 9.1.3 (SAS Institute Inc., Cary, NC, USA.) was used for all data analyses.

RESULTS. In 477 patients with severe sepsis/septic shock, 107 patients received EN, 62 PN, 272 patients mixed and 36 no nutrition (none). The median total energy amount was 1,066 (569–1,511) kcal/day. 761 (388–1,173) kcal/day were provided by EN, 844 (454–1,472) kcal/day by PN and 1,263 (875–1,668) kcal/day by mixed nutrition ($p < 0.001$). Groups were well balanced regarding epidemiologic data. Patients with PN had a lower APACHE II score (17 [13–22]) compared to EN (20 [17–24]), mixed (20 [16–24]) and no nutrition (21 [15–27]). While morbidity (infection, renal replacement, mechanical ventilation) was not increased in patients with PN, 28-day mortality was significantly higher (EN: 18.7%, PN: 29.0%, mixed: 25.4%, none 50.0%, $p = 0.003$). The effect remained after multivariable adjustment (odds ratio and 95% confidence interval: EN versus PN 0.3 (0.1 to 0.7; mixed vs. PN: 0.5 (0.2–1.0); PN vs. none: 1.6 (0.6–4.2).

CONCLUSIONS. Despite a lower APACHE II score and comparable caloric intake and morbidity an increased risk of mortality was observed in nourished patients receiving PN. The highest mortality risk was observed in patients without nutrition. Our results support once more the importance of nutrition therapy. If nutrition therapy is required, PN seems to be an attributable factor affecting outcome. Hence, the concept of permissive underfeeding with EN only may be more appropriate than early complementary PN.

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Poster Sessions
Echocardiography in the ICU: 0980–0993

0980

CARDIOVASCULAR EFFECTS OF AUTONOMIC STORM AFTER BRAIN DEATH: ECHOCARDIOGRAPHIC EVALUATION OF POTENTIAL CARDIAC TRANSPLANT DONORS AND OUTCOME AFTER IMPLANT

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INTRODUCTION. In 2008, 480 hearts were offered in Spain for transplant, only 292 were implanted (36% were lost for several reasons). One of the main reasons for his rejection, in previously good organs, was the damage of the contractility after the locking of the brainstem, and the surgeons inspection. The manifestations of the cellular damage after autonomic storm are widespread. In the heart, there is focal myocyte necrosis especially of the subendocardial area, a hypercontractile state of the sarcomere, and coagulative myocytolysis associated with a mononuclear cell infiltrate.

OBJECTIVES. The aim of the study is to know the incidence of cardiac dysfunction induced by brain death, the most common echocardiographic changes and the repercussions after implant.

METHODS. We reviewed donor heart patients from the last 5 years, in those patients with an previous echocardiographic exam to brain death and without previous hemodynamic support, expected to be optic donors.

RESULTS. We found 23 heart potential donors, 5 of them (24%) were rejected by a severe cardiac damage after brain death; the resting 76% (18 hearts) were donors. In 13 heart donor (72%) a reported autonomic storm were treated and 5 hearts donor did not suffer any hemodynamic alteration after brain death. The most common echocardiographic new alterations were a reduction in ejection fraction by Simpson 4C (25%), new hypokinesis (18%), a slight elevation of EDLV area (10%) and a reduction of TAPSE values (15%).

There were important consequences in the postoperative period with no increase in mortality rates (below 10%). 25% of heart receptor suffered transitory left ventricular failure and 15% of heart receptor had a right ventricle damage. The clinical consecuences appeared were a delay extubation (20%), prolonged use of inotropoes (more than 7 days) and a 20% used of IABP.

CONCLUSIONS. • Brain death has serious consequences in heart function carrying a lost of 25% of potential hear donors.

- The autonomic storm after brain death must be early diagnosed and treated with a standardized protocol including hormone therapy
- The consequences of autonomic storm in the postoperative period is related with an increase in complications

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0981

THE EFFECT OF CENTRAL VENOUS PRESSURE ON EXPERIMENTAL ACUTE RIGHT VENTRICULAR AFTERLOAD INCREMENT

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INTRODUCTION. Central venous pressure (CVP) as well as delta CVP is known to be a poor parameter for fluid responsiveness [1].

OBJECTIVES. We tested the effect of acute right ventricular afterload increment on CVP in a porcine model, with open pericardium and closed pericardium.

METHODS. 14 pigs were instrumented, 8 underwent acute right ventricular afterload increment with an open pericardium and 6 with a closed pericardium. On the main pulmonary artery, an ultrasonic flowprobe (MA14PAX, Transonic) was positioned to obtain pulmonary flow. Distally, a balloon-occluder was positioned facilitating gradual constriction of the pulmonary artery. All pigs received 2 pulmonary artery catheters: one in the pulmonary artery distal from the occluder and one with the tip in the right ventricle. Delta CVP (dCVP) is computed as CVP minus baseline CVP and delta right ventricular diastolic pressure (RVdia) as RVdia minus RVdia at baseline. Occluder resistance (OR) is computed as the systolic right ventricle pressure minus systolic pulmonary pressure divided by cardiac output times 79.9.

RESULTS. Cardiac output varied between 4.8 and 0.5 l/min in open pericardium and between 5.2 and 0.8 l/min in closed pericardium. There was only a very weak correlation between dCVP and OR ($r^2 = 0.11$, $p < 0.05$) in open pericardium as well as in closed pericardium ($r^2 = 0.13$, $p < 0.05$).

CONCLUSIONS. We did not observe a CVP increment during experimental acute right afterload increment. We hypothesize that this is due to the high compliance of the vena cava.

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0982

LEFT VENTRICULAR PERFORMANCE ASSESSED BY ECHOCARDIOGRAPHY AND UNCALIBRATED PULSE CONTOUR METHOD IN CRITICALLY ILL PATIENTS

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AIMS. Left ventricular (LV) performance is often quantified by echocardiography (EC) in critically ill patients. It has been suggested that pulse contour methods (PCMs) could complement EC in the continuous monitoring of cardiac function in these patients. We studied the value of an uncalibrated PCM (MostCare, Vytech Health, laboratoires pharmaceutiques Vygon, Ecouen, France) compared with EC in the monitoring of LV performance in critically ill patients.

METHODS. We enrolled 21 patients admitted to a 31-bed university hospital medico-surgical ICU who required an EC evaluation and who were equipped with a standard arterial catheter-line for invasive arterial pressure monitoring. We simultaneously assessed the LV ejection fraction (LV-EF%) by EC and the cardiac cycle efficiency (CCE) by the MostCare system. The CCE is an index of arterial-ventricular coupling that represents the equilibrium between preload, afterload, arterial elastance, and contractility. It is obtained from the ratio between the ideal pressure wave form and the form actually detected. The CCE is a dimensionless variable that ranges from −1 (the worst) to +1 (best possible LV efficiency). Linear correlation analysis was applied.

RESULTS. LV-EF% (by EC) ranged from 20 to 77% (mean 57.4 ± 17%) and CCE from −0.31 to +0.45 (mean 0.22 ± 0.18). The correlation coefficient between LV-EF% and CCE was 0.88 ($r^2 = 0.78$, $p < 0.001$). The linear correlation analysis was CCE = 0.01EF − 0.34.

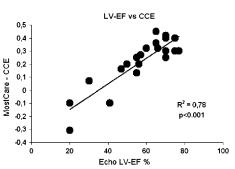

Figure 1

CONCLUSIONS. CCE obtained from the MostCare system was well correlated with a wide range of LV-EF% values obtained by EC. CCE monitoring may allow continuous assessment of LV function in critically ill patients.

REFERENCES: Romano SM, Pistolesi M. Assessment of cardiac output from systemic arterial pressure in humans. Crit Care Med 2002.

0983

CORRELATION BETWEEN SYSTOLIC PULMONARY ARTERY VALUES ESTIMATED WITH DOPPLER ECHOCARDIOGRAPHY AND MEASURED WITH PULMONARY ARTERY CATHETER IN PATIENTS WITH SUSPECTED PULMONARY ARTERY HYPERTENSION

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INTRODUCTION. Because the existence of structural and manpower facilities Intensive Care Unit (ICU) may be a good place to perform some minor haemodynamic studies. Here we show some results in the field of pulmonary arterial hypertension (PAH).

OBJECTIVES. To analyze the correlation between systolic pulmonary arterial pressure (SPAP) values estimated with Doppler-echocardiography (DE) and those directly measured with pulmonary artery catheter (PAC) among patients with high PAH suspicion.

METHODS. Patients undergo an ICU PAH study in order to confirm or rule out the existence of PAH. The study includes PAC measure. We analyze patients with previously measured SPAP by using DE. We performed a correlation study in order to obtain R Pearson coefficient and a correlation equation between both methods. Residuals were analyzed in order to rule out non spherical perturbations in the model. Results are showed as mean and standard deviation for quantitative variables and frequencies for categoric data. We have used *Minitab* statistical packet.

RESULTS. 43 patients were recruited during the period 24/04/2008–08/07/2009. Mean age was 53.8 years (SD 15.7) and 30.2% were males. SPAP directly measured with PAC was 54.4 mmHg (SD 27.3) while the same variable measured by using DE was 64.6 mmHg (SD 23.9). Pearson's R coefficient was 0.81 ($p = 0.000$) and the equation was SPAP (PAC) = $-5.18 + 0.923 \times$ SPAP (DE). The residual analysis showed no model perturbations.

CONCLUSIONS. In high PAH suspicion patients, DE estimated values are well correlated with those measured with PAC and a good correlation equation may be derived.

0984

DOPPLER ECHOCARDIOGRAPHY IN PREDICTING SPONTANEOUS BREATHING TRIAL AND WEANING FAILURE

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OBJECTIVES. Left ventricular (LV) dysfunction may play a critical role in weaning failure. Thus, we tested whether assessing LV function and filling pressures by means of Doppler echocardiography during a spontaneous breathing trial (SBT) could predict SBT and/or weaning failure.

METHODS. The present prospective study included 50 consecutive ICU patients (age: 52.38 ± 18.34 years), hemodynamically stable and in sinus rhythm, who fulfilled previously accepted criteria for a 30-min-SBT through T-tube. SBT was considered successful when patients experienced no respiratory or hemodynamic complications and they were extubated. Transthoracic Echocardiography (TTE) was performed before SBT, and repeated either in 30 min in patients with successful SBT, or before reconnection in patients with unsuccessful SBT. Transmitral flow diastolic velocities were recorded by pulse wave Doppler; TDI intrinsic myocardial velocities were recorded at the borders of mitral annulus. Doppler-derived indices of global (myocardial performance index, Tei index), systolic (lateral S') and diastolic (E/A, E/lateral E′, E/Vp) LV function were prospectively tested. Weaning was considered successful when the patient had successful SBT and sustained spontaneous breathing >48 h after extubation.

RESULTS. 23 patients failed SBT and 5 failed extubation. Increased pre-trial Doppler surrogates of LV elevated filling pressures (E/E′, E/Vp) predicted SBT failure: for E/E′, area under the curve (AUC) (95% CI) was 0.78 (0.64–0.92) ($P = 0.001$); for E/Vp was 0.71 (0.55–0.87) ($P = 0.013$). The diagnostic performance of E/E′ and E/Vp for weaning failure were 0.86 (0.75–0.97) ($P < 0.001$) for E/E′ and 0.75 (0.6–0.9) ($P = 0.003$) for E/Vp, respectively. Notably, AUCs (95% CI) of rapid shallow breathing index (RSBI), were 0.74 (0.59–0.88) ($P = 0.004$) and 0.75 (0.61–0.88) ($P = 0.003$) for SBT failure and weaning failure, respectively. Finally, acute changes in Doppler parameters of LV function during SBT were neither statistically significant, nor correlated to SBT or weaning outcomes.

CONCLUSIONS. Our study showed that the diagnostic performance of cardiac Doppler indices may be helpful in the prediction of SBT and weaning outcome.

0985

MONITORING OF CARDIAC OUTPUT WITH ECHOCARDIOGRAPHY AND MOSTCARE SYSTEM IN PATIENTS WITH TRAUMATIC BRAIN INJURY

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INTRODUCTION. Cardiac output (CO) monitoring is important in critically ill patients in order to avoid a low output syndrome. Echocardiography is a valuable and non-invasive technique, but it is not a continuous bedside monitoring system. Intensivists today have an outfit of several new techniques that provide for continuous and minimally invasive hemodynamic assessment. CO can be obtained by a pulse contour method that does not need any kind of calibration or preloaded data: the MostCare (Vytech Health,Laboratoires Pharmaceutiques Vygon, Ecouen, France).

OBJECTIVES. We compared the CO values assessed by the MostCare system (MC-CO) and transthoracic echocardiography (TTE-CO) in patients with traumatic brain injury (TBI).

METHODS. 22 patients (10 female, mean age 45 ± 20) with TBI admitted to a 13-bed university hospital medico-surgical ICU were prospectively enrolled. Exclusion criteria were patients <18 years old. Simultaneous determinations of CO were obtained by TTE and MostCare at two times: baseline (T0), and after a fluid challenge of 250 ml colloids (T1). Linear correlations and Bland Altman analysis were performed.

RESULTS. 42 paired CO values were obtained. TTE-CO values range from 3.83 to 7.28 l/min, and MC-CO from 4.14 to 7.32 l/min. At T0 the mean bias between the two techniques was 0.07 l/min (SD 0.46 l/min) and the percentage of error (PE) was 19%. At T1 the mean bias was 0.02 l/min (SD 0.04 l/min), and PE was 10%. Pearson's correlation coefficients (R) between TTE-CO and MC-CO were 0.9 and 0.87, at T0 and T1, respectively. Overall, the mean bias between the two techniques was 0.07 l/min (SD 0.24 l/min) (Fig. 1), PE was 9%, and R was 0.84.

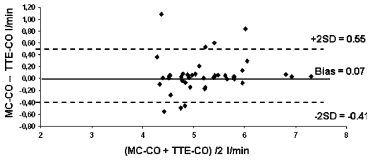

Figure 1

CONCLUSIONS. MC-CO well correlated with a wide range CO values obtained by TTE-CO. MostCare and TTE seemed to be interchangeable in monitoring the CO of TBI patients. This pulse contour system could be a helpful technique in earlier detecting a low output state in critically ill patients.

REFERENCE(S). Romano SM, Pistolesi M. Assessment of cardiac output from systemic arterial pressure in humans. Crit Care Med. 2002;30(8):1834–41.

0986

CORRELATION OF FILLING PRESSURES BY ECHOCARDIOGRAPHY AND INVASIVE MEASUREMENT IN VENTILATED PATIENTS

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INTRODUCTION. The use of filling pressures of the right atrium and left atrium is normal in the monitoring of critically ill patients undergoing mechanical ventilation. This monitoring is done through an invasive catheter placed in the superior vena cava and pulmonary artery, which is not free of complications. The ability to make measurements of these parameters in a non invasive way, makes the echocardiography an useful and essential tool when monitoring critically ill patients

OBJECTIVES. We focus the study on validate the reliability of noninvasive measurements by echocardiography and invasive measurement catheters of filling pressures

METHODS. We conducted a prospective observational study relating the filling pressures, between central venous pressure (CVP) with the diameter of the inferior vena cava and left atrial pressures with the values of the ratio E/e′. The filling pressure variables were only discriminated as high or low. Low values were accepted when invasive measurement of CVP was <6 and <4 mmHg in the LAP; and by echocardiography when the diameter of the IVC was <12 mm and the ratio E/e′ <8. High values were accepted when the measurement of CVP was higher than 10 and 8 mmHg in LAP and in echocardiography when the diameter of the IVC >16 mm and the ratio E/e′ >15. We collected data from 38 patients in the immediate postoperative period, under mechanical ventilation (Vt 8–9 ml/kg, FiO_2 50%, PEEP 3), sinus rhythm, good cardiac function and without postoperative drug support. All of them had a central venous line and right atrium catheter as habitual monitoring of postoperative cardiac patients. We performed an echocardiography when the patient presented hypotension, with low values of CVP and LAP, and we repeated the measurements after the infusion of the habitual fluid protocol (500 ml HES 6% in 30–45 min). The data we record were: diameter of IVC and ratio E/e′ by echo and CVP and LAP values by invasive catheters.

RESULTS. • The relationship of a low CVP with a small IVC diameter was close to 0.987 in the Pearson correlation with a 0.045 significance

- The relationship of high CVP with a greater diameter of IVC was 0.877 in the Pearson correlation with a 0.067 significance
- The relationship of a low LAP with a E/e′ ration <8 was 0.893 in the Pearson correlation with a 0.058 significance
- The relationship of a high LAP with a E/e′ ration >15 was 0.946 in the Pearson correlation with a 0.041 significance.

CONCLUSIONS. Filling pressure variables measured by echocardiography have a very precise correlation with invasive measure variables, especially when those values are high or low.

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0987

EVEN A MODERATE INCREASE IN PEEP IN ALI/ARDS PATIENTS COULD HAVE A REAL IMPACT ON RIGHT VENTRICULAR FUNCTION

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INTRODUCTION. Positive end-expiratory pressure (PEEP) is a widely used technique to maintain alveolar patency [1], but its beneficial effects must be balanced against its harmful effects as increase in intrathoracic pressure may compromise right heart function [2]. Classic echocardiographic parameters as right ventricular diameter area (RVDA), RV/LV ratio area and paradoxical septum permit to detect right ventricular (RV) failure but only when evolved [3].

OBJECTIVES. Aim of the study is to evaluate ability of right myocardial performance index (rMPI), tricuspid annular plane systolic excursion (Tmta) and peak systolic velocity of tricuspid annulus (Sta) to detect right ventricular dysfunction induced by a moderate increase in PEEP in patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS).

METHODS. Sedated ventilated patients presenting an ALI/ARDS with PaO_2/FiO_2 <300, bilateral chest infiltrates were included. Respiratory, hemodynamic, echocardiographic measurements and arterial and central venous blood gas analysis were performed twice: at baseline and 15 min after the increase in 5 cmH_2O of PEEP. This increase in PEEP must have kept the Pplat under 30 cmH_2O.

RESULTS. Twenty consecutive patients were included. PEEP increase was associated with deterioration in RV function, as indicated by the significantly changes in right MPI, Tmta and Sta (Tables 1, 2). By contrast, there are no significant changes during the increase in PEEP for RVDA, RV/LV ratio area and paradoxical septum. The increase in PEEP was also associated with an increase in systolic pulmonary arterial pressure and a decrease in cardiac output. No improvement of arterial blood gas was noted.

CONCLUSIONS. RV systolic function is sensitive to a moderate increase in PEEP in ALI/ARDS patients. Sta, Tmta and rMPI could detect earlier changes in right heart function than classic echographic parameters.

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TABLE 1 VENTILATION AND HEMODYNAMIC PARAMETERS

	Baseline	PEEP + 5 cmH2O	p value
Ventilation parameters			
Tidal volume, ml	485 ± 57	485 ± 57	1
Total PEEP, cmH2O	6.2 ± 0.4	11.8 ± 2.3	0.0001
Plateau pressure, cmH2O	18 ± 4	24 ± 4	0.0001
Hemodynamic parameters			
SAP, mmHg	139 ± 32	137 ± 36	0.37
DAP, mmHg	68 ± 12	69 ± 12	0.93
MAP, mmHg	87 ± 27	87 ± 28	0.70

TABLE 2 ECHOCARDIOGRAPHIC DATA

	Baseline	PEEP + 5 cmH2O	p value
Cardiac output, l/min	4.59 ± 1.78	4.32 ± 1.7	0.01
LVEF, %	62.4 ± 10.1	65.1 ± 10.4	0.3
E, cm/s	73.6 ± 18.7	66.2 ± 16	0.003
RV/LV ratio area	0.59 ± 0.15	0.65 ± 0.17	0.14
Paradoxical septum	0	0	1
SPAP, mmHg	34.2 ± 11.1	39.7 ± 8.4	0.04
Right MPI	0.24 ± 0.14	0.35 ± 0.18	0.0004
Tmta, mm	23.2 ± 5.4	20.3 ± 4	0.01
Sta, cm/s	16.7 ± 4.2	15.5 ± 4	0.05

0988

DOBUTAMINE STRESS ECHOCARDIOGRAPHY UNMASKS MYOCARDIAL DYSFUNCTION IN EARLY RODENT POLYMICROBIAL SEPSIS

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INTRODUCTION. An attenuated cardio-hemodynamic response to dobutamine is associated with a poor outcome in established human sepsis [1,2]. Establishing a sensitive method to identify early cardiac dysfunction in both experimental and human sepsis would be a useful tool to explore time-sensitive mechanisms further.

OBJECTIVES. To assess myocardial responsiveness to dobutamine in early sepsis.

METHODS. All procedures were in accordance with UK Home Office laboratory animal legislation. Under isoflurane anaesthesia, male adult Wistar rats underwent left common carotid and right internal jugular venous cannulation for blood sampling/continuous BP monitoring and fluid administration respectively. Rats received either 1.8 ml caecal slurry (Sepsis; n = 8) or 1.8 ml saline (sham; n = 8) ip, before fluid resuscitation (0.9% saline 10 ml/kg/h) and conscious monitoring was commenced. After 4 h, rats were re-anaesthetized with isoflurane and transthoracic echocardiography was performed. Stroke volume was optimised with saline boluses prior to an incremental dobutamine infusion (1.25–20 mcg/kg/min). Data are presented as mean (SD); analyzed with 2-way ANOVA and post-hoc Tukey test.

RESULTS. Figure 1 summarizes hemodynamic changes after sepsis, fluid resuscitation and dobutamine infusion.

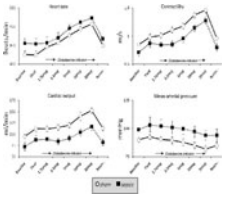

Figure 1

Baseline parameters were similar after echocardiography-guided fluid resuscitation, with contractility and stroke volume restored in septic rats to sham values. Septic rats demonstrated an enhanced chronotropic response to dobutamine compared to sham ($p < 0.002$). Both peak velocity and cardiac output were attenuated by ≥25% in sepsis ($p < 0.0001$). In sepsis, baseline MAP was higher but neither sham nor septic MAPs were affected by dobutamine infusion.

CONCLUSIONS. Dobutamine stress echocardiography is a sensitive, reproducible, dynamic physiological probe that reveals early cardiac dysfunction in septic rats with apparently similar baseline cardiovascular physiology.

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0989

SUBCLINICAL RIGHT VENTRICULAR DYSFUNCTION IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME, AN ECHOCARDIOGRAPHY STUDY WITH DOPPLER TISSUE IMAGING

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INTRODUCTION. The evaluation of right ventricular (RV) function is clinically useful in patients with acute respiratory distress syndrome (ARDS) because the presence of RV failure has large prognosis implications. The purpose of the current study was to compare right ventricular myocardial strain imaging parameters with conventional echocardiographic indices evaluating right ventricular function during ARDS.

OBJECTIVES. We hypothesized that peak systolic strain would be more sensitive than conventional echocardiographic parameters in detecting subclinical right ventricular systolic dysfunction in patients with ARDS.

METHODS. In total, 10 patients with ARDS and with normal right ventricle function assessed by two dimensional echocardiography and 10 age matched subjects under mechanical ventilation without heart or pulmonary disease were included in the present study. Conventional echocardiography parameters for RV function assessment like RV fractional area change (RVFA) or the tricuspid annular plane systolic excursion (TAPSE) were measured and compared to Tissue Doppler imaging parameters with strain value obtained from the right ventricle free wall.

RESULTS. Strain values were reduced in the RV free wall of the patients with ARDS compared with the control group (23.45% ± 3.8 vs. 31.8% ± 2.8 $p = 0.005$) Moreover no significant difference was observed in conventional two dimensional parameters evaluating RV systolic function between these two groups of patients. In patients with ARDS a significant relationship was shown between peak systolic strain at basal free wall and arterial carbon dioxide tension ($rho = -0.79$ $p = 0.017$) and with the end inspiratory pressure ($rho = -0.67$ $p = 0.04$).

CONCLUSIONS. During the ARDS, Doppler tissue imaging parameters can determine RV dysfunction that is complementary to conventional echocardiographic indices and is correlated with respiratory parameters. On Doppler Tissue imaging, patients with ARDS exhibit abnormal RV systolic function even in patients with normal RV function assessed with conventional echocardiographic parameters.

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0990

IMPACT OF OPEN LUNG VENTILATION ON RIGHT VENTRICULAR OUTFLOW IMPEDANCE ASSESSED BY TRANSESOPHAGEAL ECHOCARDIOGRAPHY

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INTRODUCTION. Open lung concept ventilation (OLV) is a method of ventilation intended to maintain end-expiratory lung volume by increased airway pressure.

OBJECTIVES. Studying the effect of OLV on RV outflow impedance during inspiration and expiration using transesophageal echo-Doppler in a trial to differentiate the RV consequence of increasing lung volume from those secondary to increasing airway pressure during mechanical ventilation.

METHODS. Thirty stable patients on mechanical ventilation because of different causes were enrolled prospectively in this single center, cross sectional clinical study. Each patient was firstly subjected to conventional ventilation (CV) with volume controlled ventilation, followed by open lung concept (OLC) ventilation by switching to pressure controlled mode, then recruitment maneuver applied until PaO_2/FiO_2 >375 torr. Hemodynamic (mean arterial pressure "MAP", central venous pressure "CVP" and heart rate "HR") and respiratory (total and intrinsic PEEP, peak, plateau and mean airway pressure and total and dynamic lung compliance) measurements were recorded before, 20 min after a steady state of CV and 20 min after a steady state of OLC ventilation. Also, transesophageal ECHO Doppler was performed at end of inspiration and end of expiration to calculate the mean acceleration (AC_{mean}), as a marker of the RV outflow impedance, 20 min after a steady state of CV and 20 min after a steady state of OLC ventilation.

RESULTS. During inspiration, AC_{mean} was significantly lower during CV compared to OLC ventilation (p value <0.001). Inspiration didn't cause a significant decrease in AC_{mean} compared with expiration during OLV (p value <0.001) but did do so during CV. In comparison to baseline and CV, OLC ventilation was associated with a statistically significant higher CVP (p value <0.001 for both), higher total quasi-static lung compliance (p value <0.001 for both) and dynamic lung compliance (p value 0.001 for both). Moreover, PaO_2/FiO_2 ratio of OLV was significantly higher than in baseline and CV (p value <0.001 for both).

CONCLUSIONS. OLC ventilation does not change RV afterload during inspiration and expiration as RV afterload appears primarily mediated through the tidal volume. Moreover, OLC ventilation provide a more stable hemodynamic condition and better oxygenation and lung dynamics.

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0991

CAN MEAN ACCELERATION OF THE PULMONARY ARTERY BE USED FOR RIGHT VENTRICULAR AFTERLOAD?

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INTRODUCTION. Mean acceleration (MA) has been used for right ventricular (RV) afterload but has never been validated. In a previous study we found a good correlation between MA and RV afterload in an experimental, open pericardium pig model[1]. The purpose of this study was to evaluate the correlation between MA and RV afterload in a pig model with a closed pericardium.

METHODS. Six anesthetized pigs were instrumented for the measurement of arterial blood pressure, central venous pressure, RV and pulmonary pressure. On the main pulmonary artery, an ultrasonic flowprobe (MA14PAX, Transonic) was positioned to obtain pulmonary flow. Distally, a balloon-occluder was positioned facilitating gradual constriction of the pulmonary artery. The mean pulmonary acceleration and cardiac output were calculated from the pulmonary flow curve derived from the ultrasonic flowprobe. Occluder resistance (OR) is computed as the systolic right ventricle pressure minus systolic pulmonary pressure divided by cardiac output times 79.9. All measurements were performed in triple and averaged.

RESULTS. Cardiac output varied between 5.2 and 0.8 l/min. The correlation between MA and OR was -0.550 ($p < 0.001$).

CONCLUSIONS. Mean acceleration also correlates well with RV afterload in a closed pericardium pig model.

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0992

ESOPHAGEAL DOPPLER: ACCELERATION OF THE AORTIC BLOOD FLOW AS AN INDEX OF LEFT VENTRICULAR SYSTOLIC FUNCTION

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INTRODUCTION. Among indices provided by the analysis of aortic blood flow through esophageal Doppler, mean acceleration (Acc) is supposed to reflect the left ventricular (LV) systolic function, but this has been poorly validated. In particular, Acc could be influenced by loading conditions of the LV.

OBJECTIVES. To test whether Acc actually behaves as an indicator of LV systolic function by testing if

1. it increased with inotropic stimulation,
2. it was not altered by fluid loading,
3. it correlated with the echographic LV ejection fraction (LVEF) and it reliably tracked the changes in LVEF during therapeutic intervention.

METHODS. In 37 patients with cute circulatory failure (SAPSII 59 ± 18, age 64 ± 10 years, 26 receiving norepinephrine), we administered either a volume expansion (500 mL saline over 20 min in 24 patients) or dobutamine (5 μg/kg/min in 13 patients). We simultaneously measured Acc (CardioQ, Deltex Medical) and LVEF at baseline and after therapeutic intervention.

RESULTS. Volume expansion significantly altered neither LVEF (from 56 ± 12 to $58 \pm 12\%$) nor Acc (from 9.5 ± 3.2 to 9.9 ± 3.1 cm/s^2) while dobutamine infusion significantly increased LVEF by $27 \pm 15\%$ and Acc by $44 \pm 27\%$. Considering the 74 Acc/LVEF pairs of measurements, an Acc <8.2 cm/s^2 predicted a LVEF $\leq 45\%$ with a sensitivity of 77% (95% CI [56–91%]) and a specificity of 68% (95% CI [52–80%]). The changes in LVEF and in Acc during fluid and dobutamine administration were significantly correlated ($r = 0.64$, $p < 0.05$).

CONCLUSIONS. Acc fulfilled the criteria required from a clinical indicator of LV global systolic function. A given value of Acc allowed detecting a low LVEF with a modest accuracy. By contrast, the treatment-induced relative changes in Acc were reliable for tracking the treatment-induced relative changes in LVEF.

0993

ECHOCARDIOGRAPHIC E/E′ RATIO AT ICU ADMISSION IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: DOES IT PREDICT CARDIAC COMPLICATIONS BETTER THAN LEFT VENTRICULAR EJECTION FRACTION?

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INTRODUCTION. Transthoracic echocardiography enables measurement of systolic and diastolic functions. In recent studies, diastolic dysfunction in patients after myocardial infarction has been shown to have predicting value for cardiovascular events.

OBJECTIVES. To compare the relationship between systolic or diastolic dysfunction at ICU admission and the incidence of cardiologic complications and mortality at sixth months.

METHODS. Prospective study of forty consecutive patients diagnosed of Acute Myocardial Infarction (AMI) (23 NSTEMI, 17 STEMI) who were admitted in the ICU of University Hospital Puerto Real (Cadiz, Spain) from 1st May 2009 to 30th September 2009. Studied variables: Age, gender, type of AMI (NSTEMI, STEMI), Left Ventricular Ejection Fraction (LVEF) by biplanar Simpson's rule, Diastolic function (ratio E/E′ of the mitral annulus included), incidence of cardiac complications (acute pulmonary oedema, atrial fibrillation with hemodynamic instability and cardiogenic shock) and mortality at sixth month. Echocardiographic studies were performed with a GE Vivid 7 Pro(R) by an intensivist who had performed up to 500 Doppler studies in critical patients. All studies were remeasured by a second observer in an echocardiographic workstation with no statistical difference in measured velocities. Patients were classified according to their LVEF in (a) preserved (>55%), (b) mildly depressed (45–55%), (c) moderately depressed (30–45%) and (d) severely depressed (<30%); and according to their E/E′ ratio in (a) normal E/E′ ratio (<10) and (b) elevated E/E′ ratio ($\geq$ 10). The results were statistically analysed with Chi-square test and odds ratio calculus.

RESULTS. Diastolic dysfunction measured with E/E′ ratio was associated with high incidence of cardiac complications (Chi^2 test CL 95% $p < 0.001$, OR 24). Systolic dysfunction measured by LVEF was also associated with more complications but with less strength of statistical association (Chi^2 test CL 95% $p < 0.05$, OR 8.25). There were no significative statistical difference between LVEF and E/E′ ratio in mortality at sixth month.

CONCLUSIONS. In our study, diastolic and systolic dysfunctions in patients with AMI at ICU admission were associated with high incidence of cardiac complications, with more strength of statistical association in patients with diastolic dysfunction. The small sample volume didn't allow us obtaining significative statistical differences in mortality at sixth months.

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Assessment of volume responsiveness: 0994–1007

0994

ANIMAL VALIDATION OF A NEW TRANSPULMONARY THERMODILUTION METHOD TO ASSESS GLOBAL END-DIASTOLIC VOLUME AND EXTRAVASCULAR LUNG WATER

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INTRODUCTION. A new method has been developed to assess global end-diastolic volume (GEDV) and extravascular lung water (EVLW) from a transpulmonary thermodilution curve. Our goal was to compare this new method to the established method currently in clinical use, over a wide range up to extreme pathophysiological conditions.

OBJECTIVES AND METHODS. 11 anesthetized and mechanically ventilated pigs (90–110 kg) were instrumented with a central venous catheter and a right (5F PulsioCath, Pulsion, Munich, Germany) and a left (5F VolumeView, Edwards Lifesciences, Irvine, CA) thermodilution femoral arterial catheter. The right femoral catheter was connected to a PiCCO2 monitor (Pulsion) and used to measure COp, GEDVp and EVLWp using the old method based on the equation: $GEDV = COp \times (MTt - DSt)$. The left femoral catheter was connected to the new EV1000 monitor (Edwards) and used to measure COe, GEDVe and EVLWe using the new method based on the equation: $GEDVe = f(S2/S1) \times COe \times MTt$, where S1 and S2 are respectively the maximum up- and down-slopes of the dilution curve, respectively. 137 measurements were done during inotropic stimulation (DOBU), during hemmorhage (HYPO), during fluid overload (HYPER), and after inducing oleic acid-acute lung injury (ALI).

RESULTS. Overall, COp and COe ranged from 3.1 to 15.4 and from 3.4 to 15.1 l/min, respectively. COp and COe were closely correlated ($r^2 = 0.99$), mean bias ($\pm$ SD) was 0.18 ± 0.29 l/min and %error was 7%. GEDVp and GEDVe ranged from 701 to 1,629 and from 774 to 1,645 ml. GEDVp and GEDVe were closely correlated ($r^2 = 0.79$), mean bias was -11 ± 78 ml and %error was 14%. EVLWp and EVLWe ranged from 507 to 2,379 and from 495 to 2,222 ml. EVLWp and EVLWe were closely correlated ($r^2 = 0.97$), mean bias was -5 ± 72 ml and %error was 15%. Parameters over the study period are presented in the table (*$p < 0.05$ Intervention vs. BASE or HYPER).

TABLE

*p < 0.05	BASE1	DOBU	BASE2	HYPO	BASE3	HYPER	ALI
COp, l/min	7.5 ± 0.9	10.8 ± 1.4*	7.5 ± 0.7	4.7 ± 0.3*	7.9 ± 1.2	11.7 ± 2.1*	6.7 ± 3.3*
COe, l/min	7.6 ± 0.8	11.0 ± 1.6*	7.6 ± 0.8	4.8 ± 0.2*	8.0 ± 1.2	12.0 ± 2.1*	6.9 ± 3.4*
GEDVp, ml	1077 ± 149	1059 ± 134	1110 ± 147	925 ± 84*	1173 ± 120	1326 ± 140*	1070 ± 191*
GEDVe, ml	1052 ± 94	1023 ± 102	1093 ± 124	931 ± 66*	1153 ± 100	1299 ± 162*	1089 ± 174*
EVLWp, ml	622 ± 86	691 ± 112*	653 ± 106	609 ± 72*	644 ± 82	754 ± 117*	1587 ± 380*
EVLWe, ml	621 ± 82	642 ± 68	635 ± 85	624 ± 68	624 ± 80	749 ± 128*	1571 ± 335*

CONCLUSION. In animals, and over a very wide range of values, the new VolumeView transpulmonary thermodilution method is at least as reliable as the PiCCO method to track changes in cardiac output, cardiac preload and lung water induced by inotropic stimulation, bleeding, volume loading, and lung injury.

0995

MICROCIRCULATORY EFFECTS OF FLUID INFUSION IN INTENSIVE CARE UNIT PATIENTS

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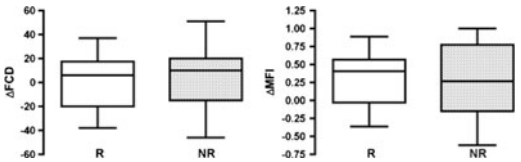
INTRODUCTION. Fluid resuscitation is a major therapy in ICU. Various mechanisms are involved in the regulation of the microcirculation and the macrocirculation.

OBJECTIVES. The goal of this study is to assess the sublingual microcirculatory changes in response to fluid challenge in preload-responsive and non preload-responsive patients.

METHODS. After approval by our local Institutional Review Board, 18 patients in surgical ICU have been included in an observational study. Each patient was monitored by an arterial catheter and an oesophageal Doppler. The decision of fluid infusion was taken by the physician in charge of the patient. Preload-responsive patients were defined by variations in cardiac index (CI) $\geq$ 15%. Sublingual microcirculation videos were obtained using the orthogonal polarized spectral (OPS) imaging technology. Functional capillary density (FCD, cm cm^{-2}) and microcirculatory flow index (MFI) were collected. The macrocirculatory and microcirculatory measurements were obtained before, during and after the infusion of 500 mL of saline. Five sublingual sites were recorded before and after the fluid resuscitation. The ventilator settings and sedative and vasoactive drugs infusion rates were kept constant throughout the procedure.

RESULTS. Patients were admitted in ICU for acute brain trauma (n = 5), hemorrhagic shock (n = 4), septic shock (n = 4), acute brain hemorrhage (n = 3) and acute pancreatitis (n = 2). The average age of the patient was 44 $\pm$ 17. The mean values of CI and mean arterial pressure (MAP) before the fluid therapy were respectively 2.7 $\pm$ 1.2 L/min/m^2 and 80 $\pm$ 15 mmHg. Nine patients responded to fluid infusion (CI $\geq$ 15%.). About the microcirculation, there was no significant difference between responders (R) and non-responders (NR) concerning the variations of MFI (0.4 [$-$ 0.1; 0.6] vs. 0.3 [0.0; 0.7] respectively, $p = 0.85$) and the variations of FCD (6 [$-$ 13; 13] cm.cm^{-2} vs. 10 [$-$ 9; 17] cm.cm^{-2} respectively, $p = 0.65$) after the fluid challenge.



FCD and MFI changes

CONCLUSIONS. These results emphasize the dissociation between the microcirculatory and macrocirculatory response to fluid therapy. This observation encourages us to assess the microcirculation further and to guide volume expansion on microvascular parameters in the future.

0996

PASSIVE LEG RAISING DETECTS PATIENTS WHO WILL NOT BENEFIT FROM FLUID LOADING

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INTRODUCTION. Passive leg raising (PLR) was shown to discriminate hemodynamically unstable patients who will benefit from subsequent fluid administration or not.[1] Concerned by the possibility of harmful hypotension starting the PLR maneuver from a 45° semirecumbent position, in a previous study, we found that raising patients' legs from a supine position, we were not able to predict fluid responsiveness in a heterogeneous cohort of medical intensive care unit (ICU) patients.[2]

OBJECTIVES. To investigate whether starting PLR maneuver from a 45° semirecumbent position would better predict volume responsiveness without harmful hypotension in spontaneously breathing critically ill medical ICU patients.

METHODS. Fluid responsiveness was tested in 27 consecutive patients (14 sepsis, 4 respiratory failure, 5 heart failure, 4 others) with a mean arterial pressure (MAP) <60 mmHg and/or a cardiac index (CI) <2.4 L/min/m^2. Heart rate (HR), mean arterial pressure (MAP), global end-diastolic volume index (GEDVI), cardiac index (CI) and stroke volume index (SVI) were recorded using the PiCCO method. Patients were stable in a semirecumbent (45°) position when first measurements were taken (baseline 1). For the PLR maneuver, patient's bed was tilt to have the lower limbs raised to a 45° angle while the patient's trunk was then in a supine position. Changes after 2 min were recorded. The patient was then brought into a supine position, and heamodynamic measurements were recorded when stable (baseline 2). Thereafter, 500 mL of 0.9% NaCl were administered over 15 min. Positive predictive values (PPV) and negative predictive values (NPV) of the PLR maneuver were calculated using a cut-off value of 15 % increase for CI and SVI and 10 % increase for MAP.

RESULTS. Patients' median age was 60 (29–82) years and their SAPS score 59 (16–90). All patients received vasopressors and/or inotropes. Baseline hemodynamics and changes after PLR and fluid challenge are shown in Table 1. Results are given as median (range); n/a = not available, *p < 0.05 versus baseline. PPV and NPV for CI were 50 and 86%, for SVI 20 and 77% and for MAP 12 and 80%, respectively.

TABLE 1

Parameter	Baseline 1	After PLR	Baseline 2	After 500 mL 0.9 % NaCl
HR (1/min)	102 (54–149)	104 (53–145)	102 (51–145)	99 (58–139)*
MAP (mm Hg)	61 (48–104)	69 (54–106)*	70 (50–107)	69 (52–114)
GEDVI (mL)	712 (495–1107)	n/a	n/a	714 (450–1172)
CI (L/min/m^2)	3.3 (1.3–6.8)	3.2 (1.7–6.9)*	3.2 (1.4–6.4)	3.5 (1.7–7.3)
SVI (mL/m^2)	32 (18–76)	33 (19–76)*	32 (18–69)	36 (19–78)*

CONCLUSIONS. In our hands, PLR was not useful identifying fluid responders in this heterogenous population of severely ill medical ICU patients, the starting semirecumbent position being associated with a potentially harmful decrease in MAP. However, it was helpful to detect patients who will not benefit (or even suffer harm) from further fluid administration.

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0997

ADEQUATE FLUID INFUSION ENHANCES LEFT VENTRICULAR RELAXATION IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Diastolic function is of crucial importance in the setting of intensive care. Recently, some studies suggested that an impaired diastolic function is a predictive factor of mortality in patient with shock. It is not already known whether fluid infusion could improve diastolic function.

OBJECTIVES. The aim of the study was to determine the impact of rapid fluid infusion on diastolic function.

METHODS. After acceptance by the local ethic committee, 94 ICU patients were prospectively included. Volume expansion (VE) by 500 ml of saline was performed by the intensivist in charge. Transthoracic Doppler echocardiography was performed before and after fluid infusion. Stroke volume (SV), early diastolic transmitral velocity (E), early diastolic mitral annular velocity (Ea) and E/Ea ratio (reflect of LV filling pressure) were studied. Patients were divided in 2 groups according to their SV' increase: Responders (R) (those who increased their SV by at least 15 %) and Non-Responders (NR). Wilcoxon Rank sum test was performed to compare data before and after VE. Data are presented in median (IQR)

RESULTS. Fifty-three (56 %) patients were R and 41 (44%) were NR. In the overall population, Ea increased significantly with VE [from 12.8 (4.5) to 13.9 (5.3) cm/s, p = 0.002]. In the R group Ea increased significantly [from 12.6 (4.1) to 14.6 (4.9) cm/s, p = 0.01] and E/Ea did not change significantly [from 6.1 (2.1) to 6.3 (2.3), p = 0.4]. However in the NR group, Ea did not change significantly [from 12 (5) to 12.7 (6.6) cm/s, p = 0.47] while E/Ea increased significantly [from 6.7 (2.8) to 8.5 (3.9) cm/s, p = 0.008].

CONCLUSIONS. According to these results, adequate fluid infusion seemed to enhance LV relaxation without increasing LV filling pressure while inadequate fluid infusion did not affect relaxation but increased LV filling pressure.

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MEASUREMENT OF ACUTE CARDIAC OUTPUT (CO) VARIATIONS IN CRITICALLY ILL PATIENTS UNDER NOREPINEPHRINE: A COMPARISON BETWEEN DOPPLER ECHOCARDIOGRAPHY AND THE LAST VERSION OF VIGILEO-FLOTRAC® SYSTEM (V3.01)

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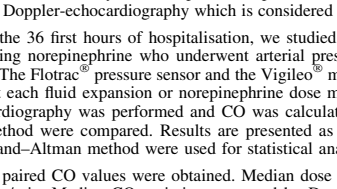
INTRODUCTION. Recently, improvements were made concerning the calculation of CO by the uncalibrated arterial pressure waveform analysis (Vigileo-Flotrac®, Edwards Lifescience, Irvine, USA).

OBJECTIVES. The aim of our study is to compare the rapid variation of CO measured by Vigileo-Flotrac® with Doppler-echocardiography which is considered as a reference method.

METHODS. During the 36 first hours of hospitalisation, we studied 16 mechanically ventilated patients receiving norepinephrine who underwent arterial pressure monitoring via a radial artery catheter. The Flotrac® pressure sensor and the Vigileo® monitor were connected to the arterial line. At each fluid expansion or norepinephrine dose modification a transthoracic Doppler-echocardiography was performed and CO was calculated. Variations for CO measured by each method were compared. Results are presented as median (IQR). Linear regression and the Bland–Altman method were used for statistical analysis.

RESULTS. Sixty six paired CO values were obtained. Median dose of norepinephrine was 1.06 [0.67–1.21] µg/kg/min. Median CO variation measured by Doppler echocardiography and FloTrac-Vigileo® were respectively 0.09 l/min [$-$ 0.15 to 0.31] vs. $-$0.00 l/min [$-$ 0.5 to 0.3]. Linear regression revealed: r = 0.69 [0.54–0.80], p < 0.0001. Bias was 0.1 l/min and limits of agreement were $-$1.6 and +1.8 l/min (Fig. 1).



Bland-Altman graph

CONCLUSIONS. Concerning critically ill patients under norepinephrine treatment, acute CO variations measured by the last version of FloTrac®Vigileo® were well correlated with Doppler-Echocardiography. Despite a limited bias, limits of agreements were still high.

0999

APPLICABILITY OF STROKE VOLUME VARIATION (SVV) AND PULSE PRESSURE VARIATION (PPV) IN AN INTERNAL ICU: A PROSPECTIVE STUDY EVALUATING 1575 TRANSPULMONARY THERMODILUTIONS (TPTD) IN 77 CONSECUTIVE PATIENTS

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INTRODUCTION. Appropriate assessment of preload and volume responsiveness are cornerstones of intensive care. In several recent trials comparing *pressure-based* (CVP, PAWP), *volume-based* (ITBI, GEDI) and *variability-based* (SVV, PPV) preload parameters, CVP and PAWP had the lowest predictive capabilities. The variability parameters were slightly more predictive than the volume-based. However, the use of variability parameters is restricted to patients with sinus rhythm (SR) and controlled (CV) mechanical ventilation. Furthermore, some recent studies indicate that ventilation with low tidal volumes (<7 ml/kg) might reduce the predictive capabilities of SVV and PPV.

OBJECTIVES. Therefore it was the aim of our prospective study to investigate the prevalence of SR, CV and tidal volumes >7 ml/kg in all hemodynamic TPTD measurements in 77 consecutive patients equipped with the PiCCO-device.

METHODS. Over 6 months prevalence of SR and CV as well as tidal volume per kg were prospectively documented in all 1,575 TPTD-measurements of 77 consecutive patients equipped with PiCCO monitoring. Statistics: SPSS 18.0.

RESULTS. Mean age 62.1 ± 13.8 years, 26 female, 51 male, APACHE-II 23.8 ± 8.3. Underlying diseases: 9/77 (12%) sepsis/SIRS, 23/77 (30%) liver cirrhosis, 4/77 (5%) gastrointestinal bleeding, 17/77 (22%) pneumonia/ARDS; 24/77 (31%) varia. Patients were under catecholamines in 658/1575 measurements (42%). The prevalence of both SR and CV was 280/1575 (17.8%). In 950/1575 (60.3%) of the measurements, the patients had SR, but were not on CV. In 59/1575 (3.7%), the patients were on CV, but they were arrhythmic. In 286/1575 (18.2%), the patients were neither on CV nor they had SR.

Among the 280 measurements with SR and CV, GEDI ($r = 0.375$; $p < 0.001$), CVP ($r = 0.315$; $p < 0.001$ and SVV ($r = -0.179$; $p = 0.005$) significantly correlated to Cardiac Index CI (Spearman). These associations of GEDI ($p < 0.001$; standardized coefficient $\beta = 0.264$), CVP ($p = 0.006$; $\beta = 0.174$) and SVV ($p = 0.009$, $\beta = -0.161$) to CI were confirmed in multiple regression analysis ($R = 0.401$). Regarding the r-, p- and β-values, GEDI had the most significant impact on CI, whereas SVV was associated to CI to a minor degree.

In 217/280 (77.5%) of the measurements with SR and CV, the tidal volume was below 7 ml/kg which might have reduced the predictive capabilities of SVV. Analysing the remaining 63 measurements (4% of 1,575 measurements) with SR, CV and a tidal volume ≥7 ml/kg did neither result in an improved association of SVV and CI in univariate ($r = -0.189$; $p = 0.149$) nor in multivariate analysis ($p > 0.05$).

CONCLUSIONS. The variability parameters SVV and PPV cannot be used in a high percentage of measurements in an internal ICU. The main reasons are arrhythmias and/or the absence of CV. Therefore, in high risk patients the availability of monitoring of volumetric parameters such as GEDI, echocardiography and in certain patients the use of pressure based parameters should be warranted.

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COMPARISON OF THE IN VITRO AND IN VIVO MICRORHEOLOGY EFFECTS OF CRYSTALLOID AND COLLOID INTRAVENOUS FLUIDS

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INTRODUCTION. Erythrocyte aggregation and deformability are important determinants of microcirculation.

OBJECTIVES. To evaluate the influence of different IV solutions on rheological properties of erythrocytes in vitro and in vivo in patients with trauma.

METHODS. For the *in vitro* experiments blood of 20 healthy donors was incubated (in the ratio 5:1) with one of the following solutions: Ringer solution, Ringer-lactate solution, modified gelatin (Gelofusin); hydroxyethyl starch (HES) 130/0.42. After incubation, the following parameters of erythrocyte aggregation were measured: T1 and T2—characteristic times of spontaneous erythrocyte aggregation; β—hydrodynamic strength of aggregates; $I^{2.5}$—index of strength of the largest aggregates at shear rate 2.5 s^{-1}. RBC deformability at various shear stresses was determined by ektacytometry. In vivo study on 60 patients with trauma treated randomly with either only crystalloids (group 1; n = 20), or crystalloids + HES 130/0.42 (group 2; n = 20) or crystalloids + Gelofusin (group 3; n = 20) over 7 days, the same parameters as in vitro study were determined at day 1–7. Twenty healthy men and women were included as controls. For statistical analysis the statistical package SPSS version 15.0 was used. Statistical significance was considered at $p < 0.05$.

RESULTS. In vitro study in the final analysis effects of different colloids on RBC aggregation and deformability were considered as increasing impact (↑), decreasing impact (↓) and no impact (–) (Table 1).

TABLE 1 IN VITRO MICRORHEOLOGY EFFECTS OF IV SOLUTIONS

	Ringer	Ringer-lactate	Gelofusin	HES 130/0.42
Deformability	–	–	–	↑
Aggregation	↑	↑	↑	↓

In vivo study significant microrheological disturbances were detected at day 1 after admission. Deformability index was lower in patients compared with controls (0.39 ± 0.012 vs. 0.44 ± 0.016; $p = 0.017$). Simultaneously, the patients showed erythrocytes hyperaggregation compared with control (↓T1, ↓T2; ↑$I^{2.5}$, ↑β). In the first group (crystalloids) described violations persisted throughout the study time. In group 2 (crystalloids + HES), the deformability was higher than in the 1st group, from 3 days till the end of the study, attaining the normal range, and also higher than in the third group (crystalloids + gelofusin). In the third group, deformability index was not significantly different from group 1.

According aggregatometrical data in the first group hyperaggregation syndrome remained the entire period of observation. HES adding (group 2) decelerated aggregate formation (↑T1, ↑T2; ↓$I^{2.5}$). In contrast, modified gelatin adding enhanced erythrocyte aggregation (↓T1 ↑$I^{2.5}$, ↑β).

CONCLUSIONS. Crystalloid solutions are not able to improve microrheological parameters. HES 130/0.42 increases RBC's deformability and reduced RBC's aggregability. Gelofusin increases erythrocyte aggregation and no effect on deformability.

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NOREPINEPHRINE CAN MISLEAD THE PULSE PRESSURE VARIATION-BASED THERAPY IN TRAUMA PATIENTS

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INTRODUCTION. Trauma patients often require norepinephrine (NE) infusion and fluid challenge to keep normal blood pressure values. The reliability of dynamic predictors of fluid responsiveness during vasopressors therapy is under debate. We investigated the impact of norepinephrine (NE) infusion changes on pulse pressure variation (PPV) assessed with the MostCare system (Vytech Health, Laboratoires Pharmaceutiques Vygon, Ecouen, France) in intensive care unit patients. This device is a pulse contour method that provides cardiac output and fluid responsiveness variables and does not need any kind of calibration or preloaded data.

METHODS. 15 trauma patients (8 female, 7 male, mean age 53 ± 22) admitted to a 13-bed university hospital medico-surgical ICU were prospectively enrolled. Inclusion criteria were: mechanically ventilated patients (tidal volume >8 ml/kg and constant respiratory rate); invasive arterial blood pressure monitoring; NE infusion. PPV values were recorded continuously during three different haemodynamic states: at baseline (T1), 10 min after a 0.05 μg/kg/min NE increase (T2), 10 min after a further 0.05 μg/kg/min NE increase (T3), 10 min following the reduction of NE to T2 dosage (T2′) and 10 min after setting NE to baseline value (T1′). During the study neither fluid challenge nor other vasoactive/inotropic drug changes were done. ANOVA test was applied.

RESULTS. See data in Table 1. At T1 NE mean dosage was 0.12 μg/kg/min (range 0.05–0.2 μg/kg/min). The mean PPV was: at T1 10.69 ± 6.9%, at T2 8.78 ± 5.9%, at T3 7.77 ± 6.1%, at T2′ 8.73 ± 5.5%, at T1′ 12.07 ± 8.2% ($p < 0.05$).

TABLE

Variables	T1	T2	T3	T2′	T1′	ANOVA P
PPV (%)	10.69 ± 6.9	8.78 ± 5.9	7.77 ± 6.1	8.73 ± 5.5	12.07 ± 8.2	<0.05
Cardiac output (l/min)	4.98 ± 0.9	5.04 ± 0.8	4.98 ± 0.89	5.04 ± 0.9	4.96 ± 0.7	0.9
Mean arterial pressure (mmHg)	82.3 ± 9.1	86 ± 10.4	85.9 ± 8.8	83.4 ± 6.4	82.18 ± 9.7	<0.05
Heart rate	85 ± 22.4	83.5 ± 22.8	86.1 ± 21.7	87.3 ± 21.6	85.8 ± 22.9	0.6

CONCLUSIONS. Our findings demonstrated that PPV was significantly affected by changes in NE: the higher the NE dosage the lower the PPV. Changes in arterial tone due to NE infusion can impair PPV reliability in assessing fluid responsiveness in trauma patients.

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1002

AUTOMATIC CALCULATION OF RESPIRATORY VARIATIONS IN PULSE OXIMETRY PLETHYSMOGRAPHIC WAVEFORM AMPLITUDE TO PREDICT FLUID RESPONSIVENESS

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INTRODUCTION. In mechanically ventilated patients respiratory variation in the arterial pulse pressure (ΔPP) is a reliable predictor of fluid responsiveness[1]. Respiratory variation of pulse oximetry plethysmographic waveforms correlate to ΔPP[2] and can be calculated automatically in real time (Heart-Lung Index [HLI®] from Hamilton Medical). This prospective study evaluates the relationship between ΔPP and HLI® to predict fluid responsiveness.

METHODS. Mechanically ventilated patients were investigated; all connected to an Hamilton G5 ventilator and ventilated in Adaptive Support Ventilation (ASV), paralyzed and none had severe cardiac dysrhythmia. 15 were eligible for fluid expansion. ΔPP, HLI® (obtained from a finger probe pulse oximeter integrated to the ventilator) and Cardiac Index (CI from transthoracic echo-doppler), were obtained before and after fluid expansion (8 ml/kg of HEA over 20 min). CI-responders were defined by 15% increase from baseline.

RESULTS. 10 out of the 15 patients were CI-responders and had significantly higher HLI® before volume expansion (21% ± 6 vs. 9% ± 4, $p < 0.02$). Before fluid expansion HLI® was correlated with ΔPP ($r^2 = 0.68$, $p < 0.01$, Fig. 1). HLI and ΔPP were significantly correlated with change in IC induced by fluid expansion ($r^2 = 0.53$ and $r^2 = 0.73$, respectively).

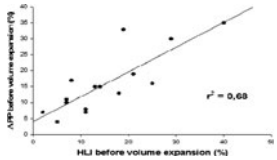

Figure 1

CONCLUSIONS. HLI® is an acceptable surrogate for ΔPP to predict fluid responsiveness.

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1003

ABILITY OF RESPIRATORY VARIATIONS OF THE DIAMETER (RVD) OF THE INFERIOR VENA CAVA (IVC) TO PREDICT FLUID RESPONSIVENESS IN PATIENTS WITH SPONTANEOUS BREATHING

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INTRODUCTION. RVD of the IVC is predictive of the response to a fluid challenge in ICU patients under controlled mechanical ventilation.

OBJECTIVES. The primary end point of this study was to evaluate the RVD of the IVC in ICU patients with spontaneous breathing.

METHODS. ICU patient with spontaneous breathing and signs of hypoperfusion (oliguria, mottles, serum lactate level >2 mmol/l) were eligible after the approval of the local Ethics Committee. We excluded patients with acute heart failure with pulmonary edema, moribund and arrhythmic patients. The trans thoracic echocardiographic (TTE) evaluation was done by 4 confirmed intensivists (level >2 in echocardiography). The aortic diameter measured at the LV outflow chamber and the TVI were measured. The vena cava inferior diameters at inspiration and at expiration were measured on the sub costal view. The RVD of the IVC was defined as the (maximal IVC diameter − minimal IVC diameter)/maximal IVC diameter. These measures were realized at T0, before fluid challenge, and after a fluid challenge of 500 ml of HES 6% (130.9/1) over 30 min (T30). Patients with an increase of TVI of more than 15% were considered as responders to the fluid challenge. The measures of TVI and of the RVD of the IVC were validated by an experimented intensivist and echographist (level 3) after blinding the patient' name and of the times of measurement. ROC curves were constructed, and the cut off was determined as the closest point of the ROC curve to the ideal point (sensibility = specificity = 1). The values are expressed as median and extremes.

RESULTS. 22 patients [14 male, age 64 (24–83)] were included. There were 13 responders (59%). The area under the ROC curve was 0.79 ± 0.10. The absolute values of RVD of the IVC are shown in Fig. 1. The best cut off was 40% (se = 46.2%, sp = 100%).

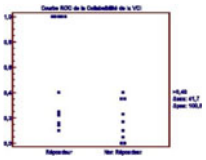

Fig. 1 ROC curve IVC collapsibility

CONCLUSIONS. The TTE assessment of the IVC can predict the response to a fluid challenge when the IVC collapses completely. In all other cases the effects of a fluid challenge are hard to predict.

1004

INCREASE IN AORTIC BLOOD FLOW AFTER THE INFUSION OF 100 ML COLLOID OVER ONE MINUTE CAN PREDICT FLUID RESPONSIVENESS: THE MINI-FLUID CHALLENGE STUDY

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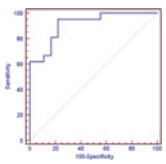
INTRODUCTION. Predicting fluid responsiveness remains a difficult question in hemodynamically unstable patients under mechanical ventilation with low tidal volume since usual indices like dynamic parameters or passive leg raising could be non available.

OBJECTIVES. Our objective was to test whether non invasive assessment by trans thoracic echocardiography of sub aortic velocity time index (VTI) variation after a low volume of fluid infusion (100 ml of hydroxy ethyl starch, HES) can predict fluid responsiveness.

METHODS. Sub aortic VTI was measured by transthoracic echocardiography before fluid infusion (baseline) in 39 sedated patients with acute circulatory failure and low tidal volume mechanical ventilation in whom volume expansion was planned. Then, VTI was recorded after 100 ml of fluid infusion over 1 min, and after an additional infusion of 400 ml of HES over 1 min. We measured the variation of VTI after 100 ml of fluid (ΔVTI_{100}) for each patient. Receiver operating characteristic (ROC) curves were generated for ΔVTI_{100} in all patients. When available, ROC curves were also generated for pulse pressure variation (PPV) and central venous pressure (CVP).

RESULTS. After 500 ml of volume expansion, SI increased ≥15% in 21 patients (54 %) defined as responders. Before fluid infusion, VTI was lower in Responders (14 [12–16] cm) than non responders (20 [12–16] cm) ($p = 0.02$). ΔVTI_{100} >10% predicted fluid responsiveness with a sensitivity and specificity of 90 and 78%, respectively. The area under the ROC curves (AUC) of ΔVTI_{100} was 0.92 [95% CI: 0.78–0.98]. In 29 patients, PPV and CVP were also available. In this subgroup of patients, AUC for ΔVTI_{100}, PPV and CVP were 0.90 [95% CI: 0.74–0.98, $P < 0.05$], 0.55 [95% CI: 0.35–0.73, NS], and 0.61 [95% CI: 0.41–0.79, NS], respectively.

CONCLUSIONS. In patients with low volume mechanical ventilation and acute circulatory failure, ΔVTI_{100} accurately predicts fluid responsiveness.



ROC curve for ΔVTI_{100}

1005

CLINICAL EVALUATION BETWEEN CARDIAC OUTPUT (CO), CARDIAC INDEX (CI), STROKE VOLUME (SV), SYSTEMIC VASCULAR RESISTANCE (SVR) MEASURED BY THE FLOTRAC/VIGILEOTM AND INTERMITTENT CO MONITORING USING A PULMONARY ARTERY CATHETER (PAC) WITH THE USE OF A CO-SET

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INTRODUCTION. Assessment of cardiac output (CO) by the FloTrac/VigileoTM (FTV) system offers a less invasive mean of determining the CO than the use of intermittent CO (ICO) monitoring using a pulmonary artery catheter (PAC) with the use of a CO-set.

OBJECTIVES. To compare CO, CI, SVR, SV between FTV and and ICO from PA catheter.

METHODS. In this study 194 patients were enrolled with unpreserved function of the left ventricle with circulatory support with vasoconstrictors and inotropes. In 82 patients (Group A) was used the FTV with the previous software version (0.79 ver.) and intermittent CO monitoring using a PAC with intermittent pulmonary artery thermodilution (ICO) with CO-set. In the rest 112 patients (Group B) was used the FTV with the updated software version (1.03 ver.) and intermittent CO monitoring using a PAC with ICO with CO-set. Cardiac output measurements were performed twice daily at predefined time points after hemodynamic stability was achieved. Transpulmonary thermodilution measurements were made under stable hemodynamic conditions. Three injections of iced NaCl 0.9% (10 ml, 4–68°C) were made using a closed cold injection delivery system and the mean value recorded. The measurements were free of interference from infusion boluses.

RESULTS. The comparison between the absolute differences, Percentage Difference and Lyn's concordance correlation coefficient in group A demonstrated overestimation of cardiac output, cardiac index, and stroke volume and underestimation of systemic vascular resistance by the FTV versus intermittent CO monitoring using a PAC with intermittent pulmonary artery thermodilution (ICO) with CO-set. The comparison in group B demonstrated underestimation of cardiac output, cardiac index, and stroke volume and overestimation of systemic vascular resistance by the FTV versus intermittent CO monitoring using a PAC with intermittent pulmonary artery thermodilution (ICO) with CO-set.

CONCLUSIONS. The previous software version of the FTV overestimated cardiac output, cardiac index, and stroke volume and underestimated systemic vascular resistance by 20% versus PAC. The updated software version of the FloTrac/Vigileo system underestimated cardiac output, cardiac index, and stroke volume and overestimated systemic vascular resistance by 10% versus PAC. The new software edition of the FTV system seems to be more accurate in estimating hemodynamic parameters in patients with sepsis.

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1006

THE USEFULNESS OF "SMALL VOLUME CHALLENGES" TO PREDICT VOLUME RESPONSIVENESS (VR)

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INTRODUCTION. Numerous variables including pressures (CVP, PAWP), volumes (GEDVI) and variabilities (SVV, PPV) have been suggested to predict volume responsiveness (VR). The final classification of a patient as "volume responsive" is usually made by a volume challenge (VC) with an infusion of a pre-defined amount of fluid over a certain time. Among many variations of VCs, the infusion of 7 ml crystalloid over 30 min is one of the most established. Despite superior predictive capabilities of SVV, PPV and GEDI compared to CVP and PAWP in a number of studies, they fail to predict VR in a substantial number of patients. Furthermore, the use of these parameters is limited due to femoral access of the CVC (GEDI; CVP) or the absence of controlled ventilation and/or sinus rhythm (SVV, PPV). Repeated "exploratory" VCs with 7 ml/kg might result in volume overload in some patients.

OBJECTIVES. Therefore, we investigated the usefulness of a "small VC" with 3.5 ml/kg crystalloid over 15 min compared to a standard VC with 7 ml/kg over 30 min.

METHODS. In 48 patients equipped with PiCCO hemodynamic monitoring we performed a 30 min VC with 7 ml/kg of crystalloid. During the VC transpulmonary thermodilution (TD) was performed at 0, 15 and 30 min to obtain TD-derived CI (CI_{td}). Additionally pulse contour CI (CI_{pc}) was recorded in intervals of 5 min.

RESULTS. n = 48; 26 male, 22 female; age 64 ± 11 years; APACHE-II 27.2 ± 8.5; the use of GEDI was limited due to femoral venous access in 9 VCs, the use of SVV due to spontaneous breathing and/or arrhythmia in 39 cases. In 13 cases there was an increase in CItd of ≥15% after 30 min. The increase of CI_{td} after 15 min significantly correlated to the increase of CI_{td} after 30 min ($r = 0.736$; $p < 0.001$). ROC-analysis demonstrated an area under curve (AUC) of 0.878 for the increase of CI_{td} after 15 min to predict an increase in CI_{td} of ≥15% after 30 min. Sensitivity, specificity and accuracy of an increase of ≥7.97% in CI_{td} after 15 min to predict an increase in CI_{td} of ≥15% after 30 min were 85, 90 and 91%. CI_{pc} after 15 min significantly correlated to the subsequent CI_{td} after 15 min ($r = 0.979$; $p < 0.001$). The change in CI_{pc} after 15 min compared to CI_{td}-baseline provided a ROC-AUC of 0.717 for the prediction of VR after 30 min. Sensitivity, specificity and accuracy of an increase in CI_{pc} of ≥5.61% after 15 min were 77, 77 and 84% to predict an increase in CI_{td} of ≥15% after 30 min. CI_{pc} 20, 25 and 30 min after the first TD (i.e. 5, 10 and 15 min after the second TD) provided ROC-AUCs of 0.864, 0.804 and 0.801 regarding VR after 30 min, respectively. By contrast, changes in CI_{pc} after 5 and 10 min were poorly correlated to VR after 30 min.

CONCLUSIONS. CI_{td} after a "small 15 min VC" accurately predicts VR after 30 min. Regarding several factors impeding the use of CVP, SVV and GEDI in a substantial number of patients, "small VC" seems to be a useful tool for hemodynamic assessment.

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NOREPINEPHRINE INCREASES CARDIAC PRELOAD AND REDUCES PRELOAD DEPENDENCY ASSESSED BY PASSIVE LEG RAISING IN SEPTIC SHOCK PATIENTS

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INTRODUCTION. During septic shock, norepinephrine (NE) improves the cardiovascular status by increasing the arterial tone through its arterial vasoconstriction. Through venous vasoconstriction, it could also increase the venous return, the cardiac preload and the cardiac index in case of preload dependency, but this has never been investigated in septic shock patients.

OBJECTIVES. To assess the effects of NE on cardiac preload, cardiac index and preload dependency during septic shock.

METHODS. We included 25 septic shock patients (62 ± 13 years old, SAPS II 53 ± 12, lactate 3.5 ± 2.1 mmol/L) with a positive passive leg raising (PLR) test (defined by an increase in cardiac index ≥10%) and a diastolic arterial pressure ≤ 40 mmHg. We performed a 1-min PLR at baseline (PLR1), immediately after increased the dose of NE (to 0.48 [0.36–0.71] µg/kg/min), performed a second 1-min PLR (PLR2) when the haemodynamic status was stabilized and eventually infused 500 mL saline.

RESULTS. Increasing the dose of NE significantly increased central venous pressure (+23 ± 12%), left ventricular end-diastolic area (+9±6%), E mitral wave (+19 ± 23%) and global end-diastolic volume (+9±6%). Simultaneously, cardiac index significantly increased by 11 ± 7%, suggesting that NE had recruited some cardiac preload reserve. PLR2 increased cardiac index to a lesser extent than PLR1 (13 ± 8 vs. +19 ± 6%, $p < 0.05$), suggesting that NE had decreased the degree of preload dependency. Volume infusion significantly increased cardiac index by 26 ± 15%. However, cardiac index increased by <15% in 4 patients (fluid unresponsive patients) while PLR1 was positive in these patients. In 3 out of these 4 patients, PLR2 was also negative i.e. PLR2 (after NE increase) predicted fluid responsiveness with a sensitivity of 95% and a specificity of 100%.

CONCLUSIONS. In septic patients with a positive PLR at baseline suggesting the presence of preload dependency, NE increased cardiac preload and cardiac index and reduced the degree of preload dependency. Finally, even after increasing NE, the PLR test kept its value as an indicator of fluid responsiveness.

1009

OBESE PATIENTS ON THE INTENSIVE CARE UNIT: IMPLICATIONS FOR NURSING

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INTRODUCTION. The prevalence of obesity, defined as a Body Mass Index (BMI) ≥30 kg/m^2, reaches epidemic proportions. It is not only a risk factor for health problems, but also exacerbates illness progression. Consequently, the number of obese patients on the Intensive Care Unit (ICU) has increased enormously. Caring for obese patients can be quite challenging due to the weight and size of this person. The extent of and specific problems associated to the care of obese ICU patients are unknown. The aim of this study is to identify and quantify problems nurses face in caring for obese patients on the ICU.

METHODS. This study was performed on the ICU at the Radboud University Nijmegen Medical Centre and contained two parts. In the first part a selection was made of 44 obese patients admitted between 2004 and 2009; these patients were matched with 44 normal weight patients (BMI 18.5–24.9 kg/m^2). Patients were matched on gender, age, length of ICU stay and APACHE-II score. All patient files were screened for the presence and intensity of problems in caring for these patients.

In the second part 25 nurses were asked in a survey to share their experiences in caring for obese patients. They were asked about the nature, frequency and intensity of the problems they faced.

RESULTS. In total, 94 problems were identified in the 88 screened patient files. Seventy-two problems (76.6%) occurred in care for obese patients and 23 (23.4%) in care for normal weight patients. In both groups, most of the problems were related to activities of daily living (ADL) such as (re)positioning in bed, transfers and personal care. Surprisingly, the intensity of the problems was similar in both groups. Most of the problems were moderate (hardly to solve by one person) or severe (only to solve with two persons or special equipment). Moderate problems occurred in 32.3% of normal weight patients and in 33.3% of obese patients; severe problems 29.0 and 31.9%, respectively. This result was also confirmed by the survey. The nurses qualified most of the problems they were asked about as moderate or severe, and the frequency of the experienced problems was much higher. From the files it appeared that in 31.8% of the obese patients nurses had ADL problems. Strikingly, in the survey nurses reported that they frequently (72.0%) or even always (28.0%) experienced ADL problems in obese patients.

CONCLUSIONS. Nurses reported and experienced more problems in daily care for obese ICU patients compared to normal weight ICU patients. Although the intensity of the problems with obese patients did not differ from normal weight patients, the frequency in which they occur was much higher. Differences between reported problems and the survey suggest an underestimation of problems that can be solved by performing a prospective study. Nevertheless, based on these results, and taking into account that obesity will increase in the future, we recommend anticipating to the needs of the nurses whenever possible.

Challenges in nursing: 1008–1020

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CARDIAC CHAIR POSITION IMPROVES VENTILATION AND OXYGENATION IN MECHANICAL VENTILATED OBESE ICU PATIENTS

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INTRODUCTION. Little is known about the physiological effects and beneficial mechanisms of lowering the legs (cardiac chair position) in ventilated obese patients. Objective effects of lowering the legs on the peripheral oxygen saturation (SpO_2), end tidal carbon dioxide (ET-CO_2) and the respiratory rate/tidal volume index (RR/Vt) were observed in ventilated obese patients who were on pressure support ventilation.

OBJECTIVES. To improve the peripheral oxygen saturation, end tidal carbon dioxide and the respiratory rate/tidal volume index in ventilated obese patients by lowering the legs.

METHODS. Ten obese patients (BMI > 30) were included for this pilot study. Patients were ventilated on pressure support mode with a Servo 300(A)® and Servo-i® ventilator (Maquet, Solna, Sweden). First, patients were placed in the 30° position with the legs horizontal (semi-recumbent position). Half an hour after stabilisation, end tidal CO_2, tidal volume, breathing frequency and oxygen saturation were measured. Thereafter legs were placed as down as possible (cardiac chair position). The body position was changed with a Total Care® bed (Hill-Rom, Batesville, USA). Values were compared using paired samples T test with SPSS 15.0. A p value <0.05 was considered significant.

RESULTS. Mean SpO_2 horizontal legs 96.9% ± SD 2.283 versus mean SpO_2 low legs 97.6% ± SD 2.366, mean ET-CO_2 horizontal legs 4.9% ± SD 1,484 versus mean ET-CO_2 low legs 4.69% ± SD 1,233 and a mean RR/Vt horizontal legs 28.66 ± SD 9.,374 versus mean RR/Vt low legs 27.2 ± SD 11.36. The SpO_2 and ET-CO_2 were significantly changed in cardiac chair position ($p < 0.05$). RR/Vt index did not show significant changes.

PAIRED SAMPLES TEST

	Paired differences		Sig. (2-tailed)
	Mean	Std. Deviation	
Pair 1 SpO_2 low-SpO_2 horizontal	,700	,949	,045
Pair 2 ET-CO_2 low-ET-CO_2 horizontal	−,22000	,30478	,048
Pair 3 RR/Vt low-RR/Vt horizontal	−1,46000	6,06908	,466

Low = lowering the legs (cardiac chair position) and horizontal = legs horizontal (semi-recumbent position)

CONCLUSIONS. We demonstrated an increase in SpO_2 and a decrease in ET-CO_2 when the legs of obese patients were lowered during pressure support ventilation. Relieve of abdominal pressure may play a role in this phenomenon. In this study obese patients were examined who were weaned from the ventilator. We believe, positional therapy in obese patients is very important. Just like the semi-recumbent position, lowering the legs is an easy, simple, effective and safe treatment in ICU patients. Due to the small number of patients additional work has to be done to confirm our observations.

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1010

STRICT PROTOCOL ADHERENCE IMPROVES NURSE-IMPLEMENTED SEDATION IN ACUTE SEPTIC SHOCK

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INTRODUCTION. ICU nurses are closely involved in sedation management of critically ill patients. However, providing adequate sedation may be challenging in specific conditions such as acute septic shock.

OBJECTIVES. We investigated whether a stringent protocol based on monitoring of the bispectral index (BIS™) combined with evaluation of the Richmond Agitation Sedation Scale (RASS) could optimize nurse-driven sedation during resuscitation of septic shock.

METHODS. Twelve patients with pneumonia-induced septic shock were studied. All were mechanically ventilated and received standard treatment for septic shock, including analgesic sedation with midazolam and fentanyl, starting at respectively 2 and 0.05 mg/h. Sedation in the control group (CG; n = 6) was adapted routinely on the basis of vital parameters and Ramsay Sedation Scale under supervision of nurses unaware that patients were enrolled in a study. Sedation in the protocol group (PG; n = 6) was considered adequate at BIS levels around 50 and RASS levels between 0 and −3. If BIS values exceeded 60 in the presence of RASS values above +1, midazolam was augmented by 1 mg hourly.

RESULTS. Both patient groups did not differ in gender, age, weight and APACHE II score. CG patients were all unarousable (no response to verbal or physical stimuli) during the study period. The sedation level in the PG group varied from mild to moderate (arousable to easily awakening on verbal stimulation). Mean BIS and RASS values were respectively 54 ± 2.5 and −3 ± 0.5. The PG needed less midazolam (3.3 ± 1.1 vs. 4.9 ± 1.0 mg/h; $p < 0.05$) and fentanyl (0.010 ± 0.006 vs. 0.21 ± 0.04 mg/h; $p < 0.001$) and had a shorter mean duration of sedation (60 ± 25 vs. 120 ± 45 h; $p < 0.05$). The PG also received no other sedative, analgesic, or muscle relaxant drugs. In contrast, three patients in the CG required supplemental propofol and four patients were curarized.

CONCLUSIONS. In patients with acute septic shock, a combined BIS/RASS nurse-driven sedation protocol significantly decreased dose and duration of sedation and diminished analgesia need. In the absence of protocolized orders, nurses intuitively aimed at inducing a more profound coma.

1011

A CLINICAL GUIDELINE: MOBILISATION OF THE OBESE ICU PATIENT

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INTRODUCTION. Worldwide the number of obese patients (BMI > 40) is increasing rapidly (1); this also includes patients admitted to the Intensive care units (ICU). This raises special demands on the staff, the surroundings and the equipment (2). Often the obese patient is not mobilised according to the clinical standard this causes complications to breathing, circulation and skin etc. Furthermore the length of stay in the ICU increases and the mortality rises.

OBJECTIVES. The aim of this study therefore was to make clinical guidelines and recommendations for mobilisation of the obese ICU patient based on evidence. This will increase the knowledge and importance of mobilisation between staff and on longer term improves the daily average number of mobilisations performed with these patients. A secondary aim is that increased knowledge on this topic will improve the interdisciplinary work between the different professions based on the same overall aim.

METHODS. A systematic review of the literature concerning mobilisation of the obese ICU patients was made in the year 2009–2010. The study is still work in progress analysing the literature to make guidelines and recommendations based on evidence. Furthermore evidence-based education of special trained staff in mobilisation has been conducted in January/February to improve their knowledge of the impacts mobilisation has on the respiration, circulation and skincare etc. The education was planned to aiming at a interdisciplinary audience.

RESULTS. The preliminary results shows that it is more difficult to care for and mobilise the obese ICU patient, because there is lack of space, non-availability of the correct equipment, too few available staff members and a significant negative attitudes among the staff towards the obese patient. Recommendations are made within airway, breathing, circulation, nutrition, pain, equipment and patient experience according to the procedure of mobilisation of the obese ICU patient. The recommendation was implemented in the already performed education and resulted in a changed attitude among the participant and improved the status of mobilisation in the daily prioritization. This knowledge was obtained in the evaluation-interview conducted approximately one month after the seminar.

CONCLUSIONS. According to the literature mobilisation of the obese ICU patient needs special attention towards a safe clinical practise based on evidence with focus on both the patient and the staff. Special attention towards this group of patient is created by performing evidence based research resulting in clinical guidelines that has to be implemented through theoretical and practical education on an interdisciplinary level.

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1012

SECONDARY TRAUMATIC STRESS AMONG ICU NURSES IN GREECE

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INTRODUCTION. Health outcomes and, in particular, patient health outcomes have become a driving force within health-care delinery[1]. Little is known about the effects nurses experience when caring for patients and their families who are experiencing suffering or trauma, especially day after day[2]. Nurses are constantly exposed to the pain and suffering of those in their care[3].

OBJECTIVES. The primary aim of this study was to investigate the risk of secondary traumatic stress/compassion fatigue (STS/CF—the trauma suffered by the helping professional) and burnout (BO—emotional exhaustion, depersonalization, and reduced sense of personal accomplishment), and the potential for compassion satisfaction (CS—the fulfillment from helping others and positive collegial relationships) among nurses working in ICU. An additional goal was to test the relationship of these three constructs to each other.

METHODS. The Professional Quality of Life Scale (ProQOL R-IV, STS/CF, BO and CS subscales)[4] and a demographic tool were distributed to ICU nurses (N = 335) in 22 Public Hospitals in Greece.

RESULTS. Findings revealed that 57.9% of ICU nurses (n = 194) are at the high level of risk for STS/CF and 56.1% (n = 188) are at the high level of risk for BO, while 61.5% of participants (n = 206) reported low potential for CS. A strong negative relationship was discovered between BO and CS ($r = -.394$, $p < .001$) and a strong positive relationship was discovered between BO and CF ($r = .569$, $p < .001$).

CONCLUSIONS. High prevalence of STS/CF in our sample indicates that potentially large numbers of ICU nurses may be experiencing the negative effects of secondary traumatic stress. The key implication for practice is to educate nurses about compassion fatigue and proactively manage it in order to prevent personal and professional costs of caring.

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THE IMPACT ON THE INCIDENCE OF VENTILATOR ASSOCIATED PNEUMONIA (VAP) USING CLOSED (CSS) VERSUS OPEN ENDOTRACHEAL SUCTION SYSTEMS (OSS) IN THE ICU

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INTRODUCTION. The incidence of pneumonia in Critical Care has been reported to 10–60% of which VAP accounts for approximately 80%. VAP increase ICU mortality, morbidity and thus increases costs and LOS. Earlier studies have shown a decreasing VAP incidence after prophylactic interventions bundles (1). The use of closed suction circuits has been suggested beneficial as a prophylactic measure (2).

OBJECTIVES. The aim of this study was to compare the incidence of VAP and the occurrence of desaturation during suction using either OSS or CSS. We also investigated contamination of the closed suction circuit and the occurrence of adverse events.

METHODS. CSS were a new product in our clinic. All staff underwent a user course supervised by the manufacturer of the closed circuit. After this, data were collected during four periods in 2009, 2 month CSS followed by 2 months OSS which was repeated twice. During the summer period CSS were used without any data collection and then followed by two periods of CSS and OSS. All mechanical ventilated patients were consecutively included. A culture of deep endotracheal aspirate and a blind microbiology brush was taken in association with the intubation, after 72 h and every Monday. After changing CSS and in case of extubation, the tip of the catheter was sent for culture. Demographic data were retrieved from the hospital database. Data were analyzed with descriptive methods.

RESULTS. The incidences of VAP were higher in the CSS group (Table 1). Both suction systems showed almost no desaturation during and after suctioning. Positive cultures were obtained in 55% of all the retrieved CSS catheters. The microbiological flora resembled the species found in the airway cultures. There were no inter patient contamination and neither did the bronchoscopy frequency differ between OSS and CSS patients. In the CSS group six adverse events were seen; three tube occlusion and three incidences with secretion clogging.

CONCLUSIONS. The use of a CSS did not prevent VAP, in our study. There were no benefit with CSS other than maybe to protect the staff and our finding of positive culture in 55% of the cases is in line with earlier studies.

INCIDENSES OF VAP

	OSS	CSS	TOTAL
VAP			22/126 17%
Early VAP	1/56 2%	10/70 14%	11/126 9%
Late VAP	4/56 7%	7/70 10%	11/126 9%

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MOBILISATION OF OBESE ICU PATIENTS; A CLINICAL STUDY

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INTRODUCTION. The number of obese patients is increasing worldwide (1); this is also the fact in Intensive care units (ICU). This raises special demands on the staff, the surroundings and the equipment (2). Since 2007 mobilisation of obese ICU patients has been a clinical study in our ICU, containing three studies until now.

OBJECTIVES. The three studies have had the following aims:
1. to investigate whether obese ICU patients (BMI > 40) are mobilised according to the clinical standard.
2. To investigate the healthcare professionals experiences of working with mobilisation of obese ICU patients and furthermore
3. to make practical use of staff member's innovative thinking and in that way improve the work with the mobilisation of obese ICU patients in their unit.

METHODS. 1. A retrospective observational study (conducted in year 2007–2008). Focus group interviews of the staff in two qualitative studies:
2. with focus on experiences (conducted in year 2009–2010) and
3. with focus on solutions, clinical guidelines and checklists within the themes conducted in study two (conducted in year 2010–2011).

RESULTS. 1. Seventeen patients with BMI > 40 were included. Two were mobilised according to the clinical standard. The average mobilisation was 2.87/day (range 0–6) for the remaining 15 patients. The average mobilisation during the whole stay for all 17 patients was 6.41/day.
2. Four focus group interviews with a total of 14 healthcare professionals working with mobilisation of obese ICU patients. The analysis of the interviews showed that it is more difficult to care for the obese patient, for reasons such as lack of space, non-availability of the correct equipment and available staff. Furthermore the attitude of the staff plays a significant role in the treatment and care of the obese when caregivers seem to be subjective in their treatment in a negative direction.
3. Study three is work in progress analysing data. Involving the staff through integration, debate and orientation is also an important part of the project in this phase.

CONCLUSIONS. Only two of 17 patients were mobilised according to the clinical standard. Space, equipment and available staff members are needed if the clinical standard for mobilisation of the obese ICU patients has to be met. Implementation of the results of study 3 will hopefully increase the mobilisation rate of the obese ICU patients and improve the physical working environment around this group of patients.

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DOES THE TIME OF BYPASS SURGERY AFFECT IN THE DEVELOPMENT OF DELIRIUM AFTER CARDIAC SURGERY?

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INTRODUCTION. Delirium is an acute deterioration of brain function characterized by fluctuating consciousness and the inability to sustain attention. Is a major problem and not uncommon after cardiac surgery. This table is associated with increased morbidity and mortality, prolonged stay and increased costs.

OBJECTIVES. To determine whether a relationship exists between the time of bypass surgery and the development of delirium in patients after cardiac surgery.

METHODS. Prospective descriptive study conducted in an intensive care unit after cardiac surgery (UCICC). The sample consisted of 40 patients undergoing cardiac surgery requiring a minimum of 72 h from January to December 2009. We conducted a data collection sheet including demographic and predisposing and precipitating factors of delirium. The RASS, Minimental and CAM-ICU scales were evaluated. Analysis of variables was performed using the statistical program SPSS.

RESULTS. 20% of patients had delirium, 60% were men. The average age of the group was 63.35 years. The predominant initial diagnosis was aortic stenosis (30%) and surgical procedure performed to repair and/or replacement of aortic valve replacement (32.5%). The time of cardiopulmonary bypass (CPB) has averaged 115.8 min with a standard deviation of 43.08 and aortic clamping time of 74.22 min and a standard deviation of 29.42. The average stay was 8.53 days. No statistically significant CPB and aortic clamping with the development of delirium.

CONCLUSIONS. Prevention of delirium can contribute to improved patient recovery while avoiding an increase in the stay and the final cost of treatment, so it is important to establish a care plan aimed at the detection and prevention.

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KEYWORDS: Delirium, critically ill, cardiac surgery.

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WHICH PATIENTS INTENSIVE CARE NURSES FIND DIFFICULT AND HOW THEY COPE

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OBJECTIVES. The aim of this study was to determine which intensive care patients the nurses defined as 'difficult' and their experiences in coping with such patients.

METHODS. The study was carried out as a qualitative design with 18 voluntary nurses employed in five intensive care units of a research and training hospital. The data were collected using demographic characteristics form and a semi-structured interview form. Interviews with nurses were made individually and face to face. The data were evaluated by using Colaizzi's phenomenological data analysis method.

RESULTS. As a result of data analysis into two categories and two themes were identified. The categories were (1) difficult patient definition of the nurses, (2) the effect of difficult patients on their care, and (3) how the nurses are affected and cope with difficult patients. The nurses listed their reasons for defining some persons as difficult as difficult physical care of the patients, and the difficulty in communicating due to dementia, agitation, Alzheimer's disease or the patient's personal characteristics. The nurses said that they found taking care of patients they found difficult physically and psychologically demanding. They used methods such as finding out the patient's problem and taking appropriate measures, increasing communication with the patient and providing explanations, trying to obtain spiritual satisfaction and transferring the patient's care to another nurse when communication problems were impossible to overcome.

CONCLUSIONS. Intensive care nurses have difficulty in caring for and communicating with some intensive care patients due to the characteristics of the disease, physical/psychological factors and personal characteristics. We found that nurses continued the care of these "difficult" patients by focusing on solving their problems, transferring the care to another nurse when necessary or by trying to obtain spiritual satisfaction.

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DIFFICULT PATIENT PERCEPTIONS AND COPING STRATEGIES OF NURSES

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OBJECTIVES. The aim of this study was to determine which patients the nurses defined as difficult and how often they encountered such patients.

METHODS. A total of 173 nurses (14 males) participated in the study. The mean age was 35.39 (22–52) years, employment duration was 14.05 (1–30) years and 57.2% worked as staff clinical nurses. The study was carried out in two parts. The first part was a qualitative study on the difficult patient phenomenon. A data collection form which contained demographic data and semi-structured questions was used. We asked the questions on the data collection form to 36 nurses working at various departments of a training and research hospital using the face to face interview technique and recorded their responses. A list of the types of patients the nurses considered 'difficult' was obtained at the end of the first section. A table was created by adding literature data to this list. The table was arranged like a scale and two sections were placed next to 39 difficult patient definitions. The first section had the degree of accepting such a patient as difficult and the second section the frequency of encountering such patients. A 5-item Likert scale was used for both sections.

RESULTS. The nurses categorized patients as difficult most commonly when they had communication problems or chronic pain while other common reasons were medical problems that were difficult to solve or frequent admissions with multiple problems. The most common 'difficult' patients were those that were bedridden, patient requiring constant care or dependant or nursing care and those with low socioeconomic, cultural or educational levels. The nurses stated that they used the following measures to cope with difficult patients: solving their problems quickly, acting in concert with the healthcare team, using positive communication techniques, dedicating time to the patient, and finally transferring the care of the patient to another nurse if it was not possible to solve the communication problems.

CONCLUSIONS. We found that nurses categorized some patients as 'difficult' due to the patient's characteristics or their own personal characteristics. However, nurses continued the care of these patients by trying to develop positive attitudes both as an individual and as a team. We recommend holding meetings to develop coping and communication techniques, participation of all the healthcare team in the interventions regarding difficult patients and improving the working conditions and hours of nurses to help nurses successfully tackle the difficult patient phenomenon.

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VALIDATION OF THE CAM-ICU AS PERFORMED BY BED-SIDE ICU NURSES: A MULTICENTRE STUDY

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INTRODUCTION. Delirium is a frequent disorder in the ICU associated with poor outcome. Several organizations, including the SCCM and the APA, therefore recommend standard screening for delirium to improve early diagnosis and treatment. The CAM-ICU is the most frequently used delirium detection tool in the The Netherlands. Numerous studies to validate the CAM-ICU always yielded excellent sensitivity and specificity, but were all performed by a limited number of research nurses.

OBJECTIVES. The diagnostic value of the CAM-ICU as administered by the bedside nurse in daily practice.

METHODS. Teams of three delirium experts visited ten ICU's in the The Netherlands in which the CAM-ICU was incorporated in daily practice, twice. These teams consisted of two consultants in either psychiatry, clinical geriatrics or neurology, and either a research-physician (MMJvE) or a research-nurse (MvdB). Based on cognitive testing, inspection of the files and DSM-IV criteria for delirium, the teams classified patients as awake and not delirious, or delirious or comatose. This classification served as gold standard to which the CAM-ICU as performed by the bed-side nurses was compared. A simple 2×2 table was used to calculate the sensitivity and specificity.

RESULTS. 15 delirium experts performed 333 assessments. 181 (54%) of these patients were assessable for delirium, 126 (38%) patients were excluded because the level of consciousness was too low, and 27 (8%) patients were non-assessable due to other reasons. Overall, we found a sensitivity of 47% (95% CI 35–58%) and a specificity of 98% (95% CI 92–99%). The strengths of this study include the large numbers, the multicentre design, the extensive evaluations by teams of various delirium experts and the independent assessments of delirium experts and bed-side nurses. A limitations is the time interval between the expert assessment and the administration of the CAM-ICU (mean 125 min; standard deviation 118 min). There were striking differences in implementation strategies of the CAM-ICU between the centres. Tables 1, 2.

TABLE 1 POPULATION CHARACTERISTICS OF THE PATIENT

Description	Result
Male gender (%)	63%
Age (mean; SD)	61.1; SD 14.7
APACHE II (mean; SD)	17.8; SD 7.2
Admitting department (%): Surgery/Medicine/Neurology or neurosurgery/Cardiology or cardiothoracic-surgery	35%/28%/13%/24%
Percentage of patients able to communicate verbally (%)	57%
Percentage of patients who received psychoactive medication between the expert assessment and the bed-side CAM-ICU (or vice-versa) (%)	25%

SD standard deviation, *APACHE II* acute physiology and chronic health evaluation II, *CAM-ICU* confusion assessment method for the intensive care unit

TABLE 2 DIAGNOSTIC PERFORMANCE OF THE CAM-ICU REL

	Expert +	Expert −	
CAM-ICU +	35	2	37
CAM-ICU −	40	104	144
	75	106	**181**

CAM-ICU confusion assessment method for the intensive care unit

CONCLUSIONS. The sensitivity of CAM-ICU as administered by the bedside nurse in daily practice seems to be lower than in the original validation studies, and may depend on the implementation strategy. In this study, half the delirious patients had a negative CAM-ICU.

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NURSING DETECTION OF EXPIRATORY PATIENT-VENTILATOR ASYNCHRONIES DURING MECHANICAL VENTILATION

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INTRODUCTION. Presence of expiratory ineffective efforts in mechanically ventilated patients is a common problem associated with increased duration of mechanical ventilation, length of stay and also a higher cost and mortality. Nowadays, identification and categorization of expiratory asynchronies can only be done at the bedside with the continuous observation of the ventilator interface. Nurses must be skilled to understand non appropriate situations of anomalous patient-ventilator interactions.

OBJECTIVES. We tested the hypothesis that after specific training nurses would acquire enough skills to detect expiratory efforts as intensive care expert physicians would do.

METHODS. *Training Phase*: Nurses were provided with selected bibliography on patient ventilator interaction and afterwards trained by intensivists with expertise on mechanical ventilation (2 h/day during 20 days) on airway pressure, flow and volume waveforms identification and eye interpretation of early and late ineffective expiratory efforts during expiration. *Validation phase*: Airflow and airway pressure waveforms were obtained from 8 different ICU mechanically ventilated patients using and acquisition and processing biomedical signal software (Better Care®). One thousand and seven breaths were randomly selected from a total of 2,608,800 breaths. Subsequently, selected breaths were blindly analyzed by 2 trained nurses and 3 intensivists to identify ineffective expiratory efforts. *Statistical analysis*: Nurses and intensivists performance were compared using the Kendall's rank correlation and Chi-square test. A p value <0.05 was considered statistically significant.

RESULTS. Nurses detection of expiratory asynchronies was significantly correlated with the intensivists performance. Kendall's rank correlation for Nurse 1: 85.3% ($p < 0.001$) and for Nurse 2: 83.5% ($p < 0.001$). Comparing performances in terms of a contingency table, the positive predictive values were equal to 97.2 and 98.4% respectively, and the negative predictive values were equal to 95.4 and 70.7% respectively, over a 26.9 prevalence of adverse events. Chi-square test of independence in the contingency tables was highly significant ($p < 0.001$ in both cases).

CONCLUSIONS. Nurses were able to identify early expiratory asynchronies after specific training as accurately as experts in patients receiving mechanical ventilation. These results suggest a new clinically important competence for nursing care to identify early patient-ventilator asynchronies.

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MANUAL HYPERINFLATION IN INTENSIVE CARE

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INTRODUCTION. Several publications indicate that manual hyperinflation is a widely used measure in the ICU, but more important is the fact that there is no uniformity in the implementation of this measure. This is also on my ward. In literature there are a number of reasons given to start manual hyperinflation: abolish mucus retension, improve oxygenation and removal of atelectasis. The positive effects are improved compliance, improved oxygenation and a decrease in the number of VAP's (Ventilator Associated Pneumonia). The negative effects are a decrease in cardiac output due to high peak pressures, an increased risk of baro-/volutrauma and the risk of giving too much tidal volumes. The risk of barotrauma increase with pressures above 40 cmH_2O. Other side effects include the development of a pneumothorax and increased ICP (intra cranial pressure).

OBJECTIVES. Creating more awareness of the procedure with lower peak pressures as a result.

METHODS. Through literature review, clinical courses and the introduction of a pressure gauge achieve greater uniformity and awareness of the procedure. We used a flow analyzer of IMT Medical, a laptop with Flowlab software version 4.1.1 and an artificial lung to demonstrate how much pressure and volume is generated during manual hyperinflation.

RESULTS. During the clinical course I showed what pressures are generated by manual hyperinflation according to the method that most of us use. This is with the thumb on the valve. Pressures up to 70 cmH_2O were recorded using the Flow Analyzer. After installing a pressure gauge, these pressures did not exceed 45 cmH_2O. In 1995, Clapham et al investigated the way in which staff of a neurosurgical ICU performed the hyperinflation procedure. There were large variations in relation to the administered Tv observed, the TV ranged from 30 to 127% over the drafts of which were given by the ventilator, and mean airway pressures ranged from 24 to 96 cmH_2O.

Redfern et al, in 2001, showed a number of physiotherapy students performing manual hyperinflation without using a pressure gauge. The average was more than 11 cmH_2O blown over the target maximum inspiratory pressure.

CONCLUSIONS. A pressure gauge improves the accuracy and decrease the variability of the inspiratory pressure. This promotes patient safety and use of appropriate technology on manual hyperinflation. Implementation requires training and education of ICU staff, because the effect of manual hyperinflation depends on the skill of the nurse and the preparation of guidance on manual hyperinflation.

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Pneumonia: 1021–1034

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OUTCOMES OF PATIENTS AGED OVER 80 YEARS ADMITTED TO A UK TEACHING HOSPITAL CRITICAL CARE FACILITY OVER A 5 YEAR PERIOD WITH COMMUNITY ACQUIRED PNEUMONIA (CAP)

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INTRODUCTION. The UK population aged >65 years is increasing. The greatest increase will be in people >85 years where CAP is an important cause of hospital admission [1]. Advancing age is a poor prognostic outcome marker from CAP [3], but little data directly considers the outcomes of this sub-set when admitted to critical care.

OBJECTIVES. (1) To gather baseline data on the outcome of patients >80 years admitted with CAP to our unit in the past 5 years. (2) To examine compliance with established CAP protocols. (3) To identify factors which may influence clinical decision-making.

METHODS. Retrospective chart analysis of all patients in the past 5 years >80 years with an admission diagnosis of CAP. CAP data collection was based on the British Thoracic Society (BTS) Guidelines for CAP [4], plus additional information specific to critical care from a patient data management system.

RESULTS. Preliminary results are reported. 105 patients were identified (0.8% of all critical care admissions). 68% were male (mean age 84 years) and 57% had 2 or more co-morbidities. 96% were admitted from their own home, 46% were self-caring. 68% were active (18%) or ex-smokers. CURB65 score was used in 43% of hospital admissions (mean = 3). 71% had radiological (CXR) confirmation of CAP and 61% were given antibiotics within 2 h of initial imaging. A causative pathogen was identified in only 39% of cases. 93% received level 2 care: in 75% of patients this was the documented limit of escalation. 64% had 2 or more organ failures on critical care admission, with 36% developing subsequent organ failures on critical care. 75% of survivors had unilateral CXR consolidation, versus 58% in non-survivors (NS). Mean length of hospital stay (LOS) was 15.4 days, median 16 days (1–49), compared to a mean LOS to discharge of survivors of 21.9 days, median 17.5 (9–49). In patient mortality was 43%. No patient leaving hospital had died 30 days post-discharge.

CONCLUSIONS. Compliance with BTS Guidelines could be improved. Unsurprisingly co-morbidities were frequent, but did not seem to affect outcome. Use of a pneumonia severity assessment tool was sub-optimal, however mean CURB-65 score didn't correlate with that recommended to prompt critical care assessment. Apart from functional status, we are unable currently to identify any factors in this age group which can be used to guide critical care admission decision making.

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ROLE OF MICROBIOLOGIC CULTURE RESULTS OF SPUTUM, ENDOTRACHEAL ASPIRATE PRIOR TO ONSET OF PNEUMONIA, BRONCHIAL WASHING AND BRONCHOALVEOLAR LAVAGE IN THE PATIENTS ADMITTED TO INTENSIVE CARE UNIT

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INTRODUCTION. Patients with ventilator-associated pneumonia (VAP) admitted to intensive care units have a high mortality rate. The routine microbiologic culture results obtained previously play limited role in selecting antimicrobials. Previously, some studied reported that the mini-bronchoalveolar lavage (mini-BAL) was a safe, effective technique and has a high concordance rate with conventional BAL in detecting the causative organisms of VAP.

OBJECTIVES. We compared the microorganism from sputum, endotracheal aspirate (ETA) and bronchial washing with mini-BAL in the patient with pneumonia in intensive care unit.

METHODS. We reviewed 31 patients with pneumonia admitted to intensive care unit. Every patient underwent fiberoptic bronchoscopy (FOB) to obtain washing and mini-BAL samples that obtained only few ml of BAL fluid to isolate microorganism. We reviewed clinical findings and microbiologic specimen results of prior sputum and ETA, including bronchial washing and mini-BAL fluid on the day of FOB. Microorganisms of the same genus, species and antibiotics susceptibility patterns were considered "identical".

RESULTS. A total of 33 microorganisms were cultured from 27 samples of mini-BAL. Those include 33.3% of methicillin-resistant *Staphylococcus aureus* (MRSA), 12.1% of carbapenem-resistant *Acinetobacter baumannii* (CRAB) and 12.1% of *Stenotrophomonas maltophilia* in order. A total of 71 microorganisms were cultured from 71 respiratory specimens prior to the mini-BAL. Those were 19.7% of MRSA, 13.8% of CRAB, 7% of Klebsiella pneumonia and 5.6% of *Stenotrophomonas maltophilia* in order. When 26 mini-BAL fluids with the 31 respiratory specimens prior to the mini-BAL were compared, only 14 (53.8%) respiratory specimens were identical. Previous respiratory specimens obtained within 72 h of day of FOB were not significantly different to that after 72 h ($p = 0.139$). In contrast, when we compared the 18 mini-BAL fluids with the bronchial washing fluids on the time of FOB, 14 (77.7%) bronchial washing fluids were identical.

CONCLUSIONS. Based on these data, the respiratory specimens obtained before onset of pneumonia often plays limited role for the selecting antimicrobials. However, respiratory sample on the time of pneumonia might be reliable in selecting appropriate antimicrobials.

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THE IMPACT OF COAGULATION PARAMETERS ON THE OUTCOMES OF PATIENTS WITH SEVERE COMMUNITY-ACQUIRED PNEUMONIA REQUIRING ICU ADMISSION

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INTRODUCTION. Numerous tools have been used to stratify the patients with severe community-acquired pneumonia (CAP). However, their ability in predicting outcomes has significant shortcomings. Coagulation abnormalities are frequent in patients with severe sepsis and they are associated with worse outcomes.

OBJECTIVES. The aim of this study is to investigate the predictive value of coagulation parameters in patients with severe CAP admitted to the ICU.

METHODS. This single center cohort study was performed between August 2005 and June 2007. D-dimer, antithrombin, ISTH score, clinical variables, SOFA, APACHE II and CURB-65 score were measured in the first 24 h of the ICU admission. Results are shown as median (25–75% interquartile range). The main outcome measure was hospital mortality.

RESULTS. Ninety patients with severe CAP admitted to the ICU were evaluated. D-dimer levels in non-survivors were higher than survivors [2,271 (955.8–3,831) vs. 1,234 (817–2,020) ng/dl respectively]. In the univariate analysis, D-dimer, ISTH score at day 3, SOFA and APACHE II scores were predictors of death. The discriminative of ability of D-dimer [AUROC = 0.75 (95% CI 0.64–0.83)] for hospital mortality was comparable to APACHE II and SOFA and better than C-reactive protein. Moreover, the addition of d-dimer to APACHE II or SOFA score increased the discriminative ability of both scores [AUROC = 0.82 (0.72–0.89) and 0.84 (0.75–0.91) respectively].

CONCLUSIONS. D-dimer levels are good predictors of outcome in severe CAP and may augment the predictive ability of scoring systems as APACHE II and SOFA.

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COMPLICATED PNEUMONIA IN PICU

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INTRODUCTION. Community-acquired pneumonia is a common infection in childhood, with a usually benign course. However it can evolve into complications including pleural effusion, empyema, lung abscess and necrosis. An increased number of complicated pneumonia cases has been reported in some studies, probably due to an increased use of better diagnosis methods, such as computed tomography. There is no consensus in the literature about the best treatment of these cases, including the surgical approach.

OBJECTIVES. To describe the complicated pneumonia cases observed in the PICU of secondary hospital in their epidemiology, etiology and surgical evolution, highlighting necrotizing pneumonia cases.

METHODS. Retrospective analysis of records of patients with clinical, laboratory and radiological findings of complicated pneumonia in the PICU of the University Hospital at Universidade de São Paulo, Brazil, during the period of January 2000 to December 2009. A statistical analysis comparing necrotizing and non-necrotizing pneumonia cases, and comparing survivors and non-survivors, was done using either chi-square or Fisher exact tests.

RESULTS. The study included 131 patients of 4137 admitted in PICU over the same period. All of them had radiographic images compatible with pleural effusion, 100 (76.3%) patients were diagnosed with empyema, 31 (23.6%) with necrotizing pneumonia and only four (0.3%) with abscess. The mean age was 40.1 ± 34.5 months and there were 43.5% of males. The median length of stay in hospital was 16 ± 15 days. The agent most commonly isolated was *S. pneumoniae* (58.1%) and secondly *S. aureus* (8.1%).The higher rate of positivity in cultures was in the pleural fluid (42/77 cases with an identified agent). In necrotizing pneumonias blood culture was more positive than in non-necrotizing pneumonias (35.4% × 16% p = 0.02, OR 2.88).The complication rate was 47.3%. Mechanical ventilation was used for 49.6% of the patients and 30.5% received vasoactive drugs. DIC was diagnosed in 9.1%. A CT scan was performed on 67.1% of the patients and the median pleural drainage time was 7 days. Thoracoscopy was performed in 15.2%, segmentectomy in 12.9%, lobectomy in 4.5% and decortication in 24.4%. Death was related with DIC (p < 0.001), use of vasoactive drugs (p = 0.03) and mechanical ventilation (p = 0.03) for all patients. There were no significant differences in mortality comparing necrotizing (3.2%) and non-necrotizing (6.1%) pneumonia (p = 0.58).

CONCLUSIONS. In our study the incidence of complicated pneumonia was 316/10,000 patients admitted in PICU. In necrotizing pneumonias the blood cultures were more positive than in non-necrotizing patients. Although the surgical approach in necrotizing pneumonia is controversial, it resulted in a insignificantly lower mortality rate, comparing with non-necrotizing pneumonias.

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THE PRESENCE OF BACTEREMIA ISN'T ASSOCIATED WITH POOR OUTCOMES IN PATIENTS WITH PNEUMOCOCCAL COMMUNITY-ACQUIRED PNEUMONIA

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INTRODUCTION. *Streptococcus pneumoniae* is the most common cause of community-acquired pneumonia (CAP). The influence of pneumococcal bacteremia on outcomes of patients remains controversial.

OBJECTIVES. To determine whether pneumococcal bacteremia increases the risk of poor outcomes in ICU patients with CAP.

METHODS. A retrospective cohort study of all pneumococcal CAP hospitalized in the medical ICU of Hospital A. Mami of Ariana (Tunisia) between January 1, 2000, and March 31, 2010. To investigate the effect of pneumococcal bacteremia on patient outcomes, we compared the complications, the prognosis and length of hospital stay of patients with pneumococcal CAP and bacteremia, and patients with pneumococcal CAP without bacteremia.

RESULTS. One hundred thirty-five patients were included, 35 (25.9%) had pneumococcal bacteremia CAP. Both groups were similar on demographic, clinical, biological and radiological characteristics. The septic shock at admission, is more frequent in patient with pneumococcal bacteremia compared to patients without bacteremia (42.9 vs. 21%, respectively; p = 0.012). The complications in ICU stay were comparable in two groups (37.1 vs. 32% respectively in bacteremic and non bacteremic group; p = 0.57). There was no statically difference in median length of hospital stay between no bacteremic and bacteremic group (10 vs. 6 days, respectively; p = 0.57). No difference in all-cause mortality (25.7 vs. 21% respectively in bacteremic and non bacteremic group; odds ratio [OR], 1.3; 95% CI, 0.53–3.19; p = 0.56) nor in CAP-related mortality (20 vs. 13% respectively in bacteremic and non bacteremic group; OR, 1.67; 95% CI, 0.61–4.61; p = 0.31) between the two groups.

CONCLUSIONS. The presence of pneumococcal bacteremia has not impact on morbidity and mortality of patients hospitalized for CAP.

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DIFFERENCES BETWEEN PRIMARY PANDEMIC INFLUENZA PNEUMONIA AND SEVERE COMMUNITY-ACQUIRED PNEUMONIA

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INTRODUCTION. Severe community-acquired pneumonia is associated with a high morbidity and mortality. Influenza A (H1N1)v pneumonia is know as the most severe expression of influenza infection.

OBJECTIVES. To describe clinical features of patients with severe pneumonia admitted in ICU and to compare clinical characteristics and outcome according microbiological etiology: Influenza A (H1N1)v pneumonia versus non viral severe community-acquired pneumonia.

METHODS. Descriptive study in a 17-beds medical-surgical ICU of a community hospital. Consecutive patients admitted in ICU from October 2009 to January 2010 with severe pneumonia were registered. Main variables of interest: age, APACHE II at admission, non invasive and invasive mechanical ventilation requirement, time of mechanical ventilation, ICU length of stay, radiological pattern, cultures result, procalcitonin and C-reactive protein levels, leukocytes count and mortality were collected. Patients were classified according the microbiological diagnosis.

RESULTS. During the time of study 24 patients were admitted in ICU with severe pneumonia. In 15 patients microbiological diagnosis was confirmed with infection by influenza virus A (H1N1)v and in 9 patients pneumonia was caused by other microorganism. In the group of influenza pneumonia non invasive mechanical ventilation was required in 20% and mechanical ventilation in 80%, in the other group non invasive mechanical ventilation was used in 44.4% and mechanical ventilation in 88.9%. Table 1 show the differences between groups.

CLINICAL CHARACTERISTICS OF PATIENTS

Severe pneumonia admitted in ICU	Community acquired pneumonia	Influenza A (H1N1)v pneumonia
Age	52.9 ± 15.1	43.7 ± 11.6
Apache II at admission	16.6 ± 6.9	12.4 ± 6.1
Time of mechanical ventilation (days)	11.6 ± 66	13 ± 7.8
ICU length of stay	13.9 ± 10.4	16.1 ± 10.7
Radiological infiltrate	Unilateral 77.8% Bilateral 22.2%	Unilateral 13.3% Bilateral 86.7%
C-reactive protein	34.7 ± 18.9	20.8 ± 16.1
Procalcitonin	14.1 ± 19.6	4.9 ± 15.8
Leukocytes count	17,182.2 ± 11,067	5,853 ± 2,776
Mortality	33.3%	13.3%

CONCLUSIONS. Pandemic influenza A pneumonia appears to be more in young people with a lower APACHE II score at admission in ICU. Biomarkers like C-reactive protein, procalcitonin and leukocytes count potentially assist in the discrimination between influenza A (H1N1)v pneumonia and pneumonia caused by other microorganisms.

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THE FCG RECEPTOR IIA-H/H131 GENOTYPE IS ASSOCIATED WITH BACTEREMIA IN PNEUMOCOCCAL COMMUNITY-ACQUIRED PNEUMONIA

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INTRODUCTION. The functional polymorphism rs1801274 in the FcgRIIA gene (FCGR2A) influences the recognition of two opsonins: the variant encoded by FCGR2A-H131 has a high affinity for IgG_2, whereas that encoded by FCGR2A-R131 binds preferentially to C reactive protein (CRP). Both opsonins are involved in the clearance of *Streptococcus pneumoniae*.

OBJECTIVES. We assessed the potential association of this polymorphism with the susceptibility to and the severity of community-acquired pneumonia (CAP) in a large group of adults.

METHODS. Multi-centre, prospective observational study. FCGR2A-H131R polymorphism was determined in a 1262 patients with CAP and 1224 controls. Severe sepsis was recorded in 366 patients.

RESULTS. No significant differences in genotype or allele frequencies were seen among patients with CAP or pneumococcal CAP (PCAP) and controls. Patients with bacteremic PCAP (B-PCAP) had significantly higher frequencies of FCGR2A-H/H131 genotypes than those with non-bacteremic PCAP ($p = 0.00016$, OR = 2.9, 95% CI 1.58–5.3). The differences remained significant when adjusting for PSI, hospital of origin and intensive care unit (ICU) admission ($p = 0.0012$, OR = 2.83, 95% CI 1.51–5.32). B-PCAP was associated with a significantly higher severity of the disease, evaluated as sepsis severity ($p = 0.000006587$, OR = 4.40, 95% CI 2.31–8.39), multiorgan dysfunction syndrome (0.000482794, OR = 3.29, 95% CI 1.69–6.41), ICU admission, acute renal failure, and acute respiratory distress syndrome.

CONCLUSIONS. Our results do not support a role of the FCGR2A-H131R polymorphism in the susceptibility to CAP or PCAP. However we provide insight that homozygousity for FCGR2A-H131 predisposes to B-PCAP, which was associated with higher severity in our study.

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SEVERE MIXED COMMUNITY ACQUIRED PNEUMONIA

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BACKGROUND. Community-acquired pneumonia (CAP) of mixed etiology has frequently been described in the literature, but its clinical significance remains unknown. The aim of this study was to describe the prevalence, clinical characteristics, and outcome of severe CAP of mixed etiology in ICU patients.

METHODS. A 5-year prospective study was conducted on consecutive patients with severe CAP admitted to ICU in whom an extensive microbiological investigation was performed.

RESULTS. 316 patients were included. A single pathogen was detected in 128 (40.5%) cases, while two or more pathogens in 38 (12.0%) cases. The most frequent pathogens' combinations were those of two bacteria (28.9%) and bacterium plus virus (21.1%). Compared with patients with monomicrobial pneumonia, patients with mixed pneumonia were older, had higher severity score (PSI) and were more likely to have previous chronic pulmonary disease (see Table 1 below). Moreover, mixed CAP patients showed similar clinical and analytical data at admission but increases in the frequency of respiratory distress and in length of stay and a trend to higher orotracheal intubation and mortality rates.

CONCLUSIONS. A mixed etiology was detected in 12% of cases with CAP requiring ICU hospitalization and was associated with older age and increased severity. Despite similar radiological features (n of involved lobes, pleural effusion) at admission, CAP with mixed etiology showed a trend to worse clinical course and outcomes than monomicrobial pneumonia.

MAIN CHARACTERISTICS

Characteristics	Mixed pneumonia (n = 38)	Monomicrobial (n = 128)	p
Age ≥65 years, %	61	46	0.018
Males, %	68	66	NS
Smokers, %	30	29	NS
Chronic pulmonary disease, %	57	39	0.049
C-Reactive protein, mg/dl	21 ± 13	26 ± 14	0.057
PSI high risk (V), %	55	31	0.020
Length of stay, days ± SD	24 ± 26	16 ± 14	0.024
Respiratory distress, n (%)	7 (18%)	6 (5%)	0.006
30-day mortality, n (%)	7 (18%)	12 (10%)	NS

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EPIDEMIOLOGY OF PULMONARY INFECTION OVER 5 YEARS IN A MIXED ITALIAN INTENSIVE CARE UNIT

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INTRODUCTION. Pneumonia is a relevant cause of admission to Intensive Care Units (ICU), and among the commonest infective complication during ICU stay. Antibiotics induce germ resistance and selection of multi resistant strains is common in ICU.

OBJECTIVES. To assess the incidence and aetiology of pneumonia in a mixed medical-surgical ICU, in order to develop local epidemiologically guided protocols to reduce antibiotic resistance selection in patients with pneumonia.

METHODS. Retrospective observational study on prospectively collected data in a mixed medical-surgical ICU of a secondary care Italian hospital. At our institution, epidemiological data on infections and data on antibiotic use are recorded since 1992; in 2005 a new electronic recording of ICU infections was introduced. Type of infection, germ characteristics, clinician diagnosis and antibiotic use were prospectively collected in an electronic database and retrospectively reviewed. Antibiotic exposure index was calculated as each antibiotic total amount administered divided by its defined daily dose times total days of admission.

RESULTS. Between 2005 and 2009 a total of 690 patients were admitted to our ICU. Pneumonia was the commonest infectious disease at admission (148 cases, 21% of patients), and the commonest infectious complication during ICU stay (38 new occurrences, 21% of total pneumonia patients). Table 1 shows major epidemiological findings in the study population.

TABLE 1 EPIDEMIOLOGICAL FINDINGS

	Overall (n = 690)	Pneumonia (n = 186)
Age (years)[a]	68.5 (± 14.5)	70.2 (± 12.7)
Sex (male)	397 (58%)	118 (63%)
SAPS II[a]	38.4 (± 16.2)	49.8 (± 12.5)
ICU LOS[b]	4.4 [1–106]	15.1 [2–104]
Medical patients	412 (60%)	171 (92%)
ICU mortality	149 (21%)	57 (31%)
Hospital mortality	179 (26%)	63 (36%)

[a]Mean (± SD)
[b]LOS = length of stay (days) as median [range]

The incidence of acquired pneumonia was remarkable: 9.7 cases every 1,000 days of mechanical ventilation. The most frequent isolated organisms were *S. aureus* (18 patients) and *P. aeruginosa* (12 patients). Methicillin-resistant *S. aureus* (MRSA) accounted for 61% of pneumonia caused by *S. aureus*, and its prevalence matched closely the exposure index to vancomycin. Such a high incidence of MRSA is consistent with other records in Mediterranean countries. Carbapenem-resistant *P. aeruginosa* was somewhat less of a problem (33% of pneumonia by *P. aeruginosa*), and was not apparently associated with antibiotic exposure, at least within the unit.

CONCLUSIONS. In our retrospective observational study we found a high incidence of pneumonia at our institution, as well as a high percentage of MRSA, the latter with strong relationship with exposure to vancomycin. New protocols for infection containment and antibiotic usage are urgently needed.

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COMMUNITY-ACQUIRED PNEUMONIA IN THE INTENSIVE CARE UNIT

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INTRODUCTION. Community-acquired pneumonia (CAP) is one of the most common infectious diseases, with important impact in mortality and morbidity worldwide. The majority of this admissions recover uneventfully with appropriate management. But between 5 and 10% of this patients are more severely ill, needing management on intensive care unit (ICU). From this group up to 58% die. This retrospective study describes the clinical picture, prognostic factors, treatment and outcomes of adult patients admitted to the medical-surgical ICU with CAP, during 2008 and 2009.

METHODS. Retrospective study including all patients with CAP admitted in ICU between January 2008 and December 2009. Data collected included demography, comorbidities, clinical presentation, diagnostic techniques, microbiological documentation, severity scores (APACHEII, SAPSII, SOFA, antibiotic regime and other variables related with ICU intervention.

RESULTS. In this period, 13.1% of the patients admitted in the ICU had CAP (87/663), mainly from emergency department, 65.5% male, with medium age of 58.3 ± 14.1 years old. Chronic respiratory diseases were the most frequent comorbidity found. The commonest symptoms were dyspnea (86.2%) and cough/expectoration (78.2%). On admission, mean APACHE II and SAPS II was 16.5 ± 5.6 and 45.2 ± 10.8 respectively; severe sepsis and septic shock were present in 96.5% and 97.7% were mechanical ventilated. At 24 h, SOFA were 7.5 ± 3.3. A multilobar involvement in 89.6% patients, a pO_2/FiO_2 <200 in 80.5 and 58.6% developed ARDS. The antibiotic regimen mostly used was ceftriaxone and azithromycin, infectious agent isolated in 26.4% of patients—17.2% had positive blood culture and 34.5% of them had done a bronchofibroscopy. The average length of stay in the ICU was 13.1 ± 11.1 days, with a mortality in the ICU of 13.7% and 76.6% were alive at 30 days of admission on hospital.

CONCLUSIONS. These results are in agreement with the literature, although with a lower mortality rate despite the severity scores. Nevertheless the small sample, this study allowed a better characterization of CAP in ICU.

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BEDSIDE MONITORING OF REGIONAL INHOMOGENEITY OF VENTILATION AND ALVEOLAR INFLAMMATION IN COMMUNITY-ACQUIRED PNEUMONIA

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INTRODUCTION. Community-acquired pneumonia (CAP) carries a high morbidity and mortality. A major problem is the insufficient monitoring of CAP by standard chest radiography, as the evaluation depends highly on the observer and the extent of pulmonary infiltration cannot be assessed properly (1).

OBJECTIVES. The aim of our study was to compare the process of inflammation in CAP measured by alveolar Nitric oxide (NO)-analysis (2) in exhaled breath and the extent of the inflammatory infiltration by electrical impedance tomography (EIT) (3) in spontaneously breathing patients.

METHODS. After approval of the local ethic committee and obtained written informed consent 24 patients with CAP were included in the study. All patients showed an acute pulmonary infiltration in chest X-ray, pulmonary symptoms (coughing, shortness of breath), positive findings in auscultation, leukocytosis, elevated CRP and a pneumonia severity index $\geq$4. NO analyses (Analyser CLD88sp, ECO MEDICS, Dürnten, Switzerland) were performed at t0 (up to 24 h after admission), t1 (2 days after admission) and t2 (4 days after admission. EIT measurements (EIT Evaluation KIT, Dräger Medical, Lübeck, Germany) were performed at t0 and t2 and inhomogeneity of ventilation was assessed by offline analysis. All measurements were made at beside in sitting position. Data were compared by t test and regression analysis.

RESULTS. There was no significant correlation between the alveolar NO concentration and the extent of inhomogeneity of the local infiltration measured by EIT. Also during the study the time course of the inhomogeneity index was not correlated with change in exhaled NO. The right/left distribution of the pulmonary infiltration in the chest X-ray and the EIT measurement showed a positive correlation ($p < 0.0001$; $r^2 = 0.69$).

CONCLUSIONS. Pulmonary regional infiltration in CAP measured by EIT can not predict the actual alveolar process of inflammation in the lung. Nevertheless the monitoring devices give additional information to better evaluate the time course of inflammation and the dimension of the respiratory dysfunction in diseased lung.

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CLINICAL FEATURES AND PROGNOSIS OF ORGANIZING PNEUMONIA PRESENTING AS ACUTE RESPIRATORY FAILURE IN ICU

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INTRODUCTION. Organizing pneumonia (OP) presenting as acute respiratory failure (ARF) is a relatively rare disease, and was only previously specifically reported in 2 small series [1,2], with mortality up to 90%. These studies were performed before the publication of international consensus classification of idiopathic interstitial pneumonias in 2001 [4].

OBJECTIVES. To compare clinical features and prognosis of patients with OP with those of patients presenting diffuse alveolar damage (DAD), during ARF.

METHODS. *Design:* Retrospective monocentric study in a university hospital conducted during an 11 yr-period.

Inclusion criteria:

1. patients with diagnosis of OP or DAD on open lung biopsy (OLB) during ICU stay,
2. mechanical ventilation for ARF. 38 patients were eligible: 9 with OP, 6 with exudative DAD, 13 with organizing DAD, and 10 with fibrosis post DAD.

Categorical variables were compared by chi-squared test, and continuous variables using ANOVA. Data are presented as median [IQR]. Statistical significance was set at $p < 0.05$.

RESULTS. At ICU admission, DAD subgroups were more frequently immunosuppressed, more severely hypoxemic, and less likely to receive exclusive NIV during ICU stay, as compared to OP patients. At the time of OLB, DAD patients were more severely hypoxemic than OP patients. PEEP level was significantly higher in exudative DAD patients, while tidal volumes were not different and amounted to 6 [5–7] ml/kg of PBW in all groups. DAD patients exhibited significantly higher global SOFA than OP patients, while respiratory SOFA was not different between groups. In broncho-alveolar lavage, the only significant difference was an increase in lymphocytes, as compared with DAD patients. 89 and 66% of OP and DAD patients received steroid treatment after OLB, respectively (NS). Time between respiratory symptoms onset and steroid treatment was significantly higher in organizing DAD patients, while time between ICU admission and steroid treatment onset was similar between groups. Initial steroid dose was 1.4 [1.0–2.5] mg/kg and was not different between groups. 56% of patients increased their PaO_2/FiO_2 above 50% with steroids, regardless their anatomopathologic group. Ventilator free days were significantly higher in OP patients at day 28 and 90. ICU (11 vs. 83%) and hospital mortality (44 vs. 86%) were significantly lower in OP patients, as compared to DAD. Survival of DAD subgroups was not statistically different at days 28 and 90, but significantly lower than OP patients (log rank test, $p = 0.03$ and 0.006). One patient relapsed after ICU discharge in both OP and DAD groups. Oxygen requirement was not different between groups at both ICU and hospital discharge.

CONCLUSIONS. Prognosis of OP patients presenting as respiratory failure and treated with steroids, is significantly better than DAD, and may be better than previously reported.

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HOW CAN WE PREDICT OUTCOME AT ICU ADMISSION IN PATIENTS WITH SEVERE COMMUNITY-ACQUIRED PNEUMONIA?

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INTRODUCTION. Severe community-acquired pneumonia (SCAP) may lead to death and long hospital stay.

OBJECTIVES. To determine variables associated with poor outcome at intensive care unit (ICU) admission in patients with SCAP.

METHODS. Prospective, single-center, observational cohort study in the Intensive Care Department of a University Hospital in Portugal. Besides demographic data, at ICU admission severity scores (SAPS2, SAPS3, PSI, PIRO-CAP, CURB-65, total SOFA) were calculated and leucocytes (WBC), C reactive protein, PaO_2/FiO_2 ratio, lactate, procalcitonin, D-Dimer, brain natriuretic peptide, cortisol, pH and platelets were measured. ICU, hospital and 28 day mortality were analyzed.

RESULTS. 43 patients were included, 63% male with a mean age 58. 39.5% of the cases were microbiologically documented (*S. pneumoniae*: 28%; H1N1 influenza; 11.6%) and 16% presented with secondary bacteremia. At ICU admission, mean scores were: SAPS2 51, SAPS3 73, PSI 148, CAP-PIRO 3.5, CURB-65 2.65, total SOFA 10. Median time for antibiotherapy and oxygenation was 170 (IQR 63–404) and 11 (IQR 6–45) min. Antibiotherapy was appropriate in 96% with a mean duration of 10 $\pm$ 4 days. ARDS developed in 20% and duration of MV was 11 days (IQR 6–22). Median ICU and hospital LOS were 12 (IQR 8–24) and 21.5 (IQR 14–38.5) days. 28 day, ICU and hospital were respectively 26, 28 and 37%. SAPS3 (81.3 vs. 70.4; $p = 0.025$), PSI (171.4 vs. 139.7; $p = 0.037$), PIRO-CAP (4 vs. 3; $p = 0.014$), WBC (28,156 vs. 12,000 $\times$ 10^3/l; $p = 0.003$), lactate (6.5 vs. 3.9 mmol/l; $p = 0.022$) and pH on admission (7.17 vs. 7.28; $p = 0.022$) were significantly higher in non-survivors than in survivors. Only PIRO-CAP was significantly higher in ICU non-survivors than survivors (4 vs. 3; $p = 0.003$). Regarding hospital mortality, in non-survivors, WBC (22,964 vs. 12,223 $\times$ 10^3/l; $p = 0.03$) and lactate (5.5 vs. 3.6; $p = 0.041$) were higher than in survivors. ROC curves showed that SAPS3 0.73 (95% CI 0.56–0.90; $p = 0.026$), PSI 0.712 (95% CI 0.535–0.888; $p = 0.038$), CAP-PIRO 0.746 (95%CI 0.572–0.919; $p = 0.016$), WBC 0.795 (95%CI 0.640–0.951; $p = 0.004$), lactate 0.733 (95% CI 0.552–0.914; $p = 0.022$) and pH 0.733 (95% CI 0.545–0.922; $p = 0.023$) were reasonable predictors of 28 day mortality. PIRO-CAP (AUC = 0.711 [95% CI 0.535–0.887]; $p = 0.034$) was the only predictor of ICU mortality. The best predictors of hospital mortality were WBC (AUC = 0.702 [95% CI 0.542–0.862]; $p = 0.030$) and lactate (AUC = 0.690 [95% CI 0.525–0.855]; $p = 0.041$).

CONCLUSIONS. In SCAP, SAPS3, PSI and pH on admission seem to predict 28-day mortality. CAP-PIRO performs well as 28-day and ICU mortality prediction tool in SCAP. WBC count and lactate provide potentially valuable prognostic information for 28-day and also in-hospital mortality.

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TREATMENT OF SEVERE COMMUNITY-ACQUIRED PNEUMONIA WITH NON INVASIVE VENTILATION

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INTRODUCTION. The use of noninvasive ventilation in the treatment of acute respiratory failure due to community acquired pneumonia (CAP) is a controversial issue (1), especially in patients with de novo acute respiratory failure (ARF), with a variable rate of success. Furthermore, there are well known risk factors for ventilatory failure of this modality in these patients

OBJECTIVES. The aim of this study is to analyze the effectiveness of NIV in the treatment of severe CAP and to identify risk factors for failure of the technique

METHODS. Prospective, observational study of all patients admitted to ICU with a diagnosis of severe CAP and treated with NIV. VNI success was defined as the avoidance of endotracheal intubation and survival in the ICU and at least 24 h on the medical ward with no signs or symptoms of respiratory failure. The variables are expressed as means $\pm$ standard deviation and percentages. Comparison between variables by Pearson's X2 test and Student T. The analysis of risk factors was made using logistic regression

RESULTS. We studied 184 patients with severe CAP with a mean age of 66 $\pm$ 16 years and 123 (66.8%) were male. SAPS II at admission was 44 $\pm$ 14. The PaO2/FiO2 at admission was 131 $\pm$ 35 and respiratory rate 36 $\pm$ 7. The BiPAP ventilatory method was used in 180 patients. The success of NIV was achieved in 116 (63.1%) patients and hospital mortality was 8.6% in those with success and 54.4% in those who NIV failed ($p < 0.001$). Among patients with successful NIV, "de novo" ARF is showed in 47.4% while in NIV failure patients ARF appears in 69.1% (p 0.004). In the multivariate analysis were associated variables associated with failure were SAPS II (OR: 1,078, 95% CI: 1022–1139), maximum SOFA during NIV (OR: 1,577, 95% CI:1.274–1 949), age (OR: 1,078, 95% CI: 1028–1131), respiratory rate after 1 h of NIV (OR: 0.876, 95% CI: 0.781–0.983), empyema (OR: 14,071, 95% CI: 1.447–136 855) and increased lung damage after 24 h after admission (OR: 35,672, 95% CI: 8.979–141 723).

CONCLUSIONS. Patients with severe community-acquired pneumonia and respiratory failure can be treated with NIV with a high rate of avoidance of endotracheal intubation. The presence of major complications at admission, and multiorgan failure, determine a higher failure rate of NIV

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Weaning: 1035–1048

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WEANING OUTCOME PREDICTION BY BEDSIDE ESTIMATION OF SPONTANEOUS INSPIRATORY EFFORT DURING MECHANICAL VENTILATION

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INTRODUCTION. The imbalance between muscular endurance and ventilatory workload during spontaneous breathing is an important determinant of ventilator dependence. Mean inspiratory pressure, a determinant of respiratory tension-time index, cannot be measured noninvasively. Work performed during spontaneous breathing can be estimated from peak inspiratory airway pressure (Ppeak) observed during controlled ventilation. For each tidal volume and inspiratory flow combination, Ppeak value depends on compliance and resistance, which are main determinants of respiratory workload during spontaneous breathing.

OBJECTIVES. We have assessed the predictive value of Ppeak/MIP index (MIP: maximum inspiratory pressure) over the success rate of a weaning trial.

METHODS. Sixty one weaning trials in patients receiving prolonged (>48 h) mechanical ventilation (MV). Ventilator settings in MV: Vt 10 ml/kg; respiratory rate (f) 12 b/min; I:E ratio 1:2; inspiratory pause 0.55 s; effective inspiratory time (Ti) 1.15 s; PEEP 0. Square inspiratory wave flow pattern (32–50 L/min). Measurements during MV: Ppeak, Cdyn. Measurements with pressure transducer and Fleishflow transducer at the beginning of the T piece weaning trial: f, Vt, P01, MIP at FRC, Vt/Ti, Ti/Ttot. Patients were extubated after 2 h when common extubation criteria were achieved. Predictive indexes calculated: f/Vt, P01/MIP, Ppeak/MIP. We compare weaning success vs. weaning failure. Statistical analysis: Mann-Whitney U test, area under ROC curve and diagnostic accuracy. Statistical significance: $p < 0.05$

RESULTS.

RESULTS 1

	Weaning success (n = 41)	Weaning failure (n = 20)	p value
Age	59.9 ± 13.9	63.4 ± 11.2	0.369
Male	32 (78%)	16 (80%)	0.571
APACHE II	18.1 ± 4.6	18.6 ± 5.8	0.814
Length of MV (days)	10.4 ± 7.3	9.7 ± 5.6	0.871
Cdyn (ml/cmH2O)	32.1 ± 5.5	27.8 ± 5.7	0.053
MIP (cmH2O)	33.7 ± 10.1	22.3 ± 13.2	<0.0001
Ppeak/MIP	0.72 ± 0.19	1.15 ± 0.19	<0.0001

RESULTS 2

f (bpm)	25 ± 5.8	33 ± 16.4	<0.0001
Vt (ml)	422 ± 103	378 ± 59	0.066
P01(cmH2O)	3 ± 1.2	4.1 ± 1.7	0.024
Vt/Ti (ml/s)	428 ± 111	474 ± 97	0.179
Ti/Ttot	0.407 ± 0.037	0.437 ± 0.040	0.007
f/Vt (bpm/ml)	63 ± 21	90 ± 25	<0.0001
P01/MIP	0.09 ± 0.05	0.18 ± 0.07	<0.0001

Reintubations: 4. Area under ROC curve: Ppeak/MIP: 0.946; P01/MIP: 0.849; f/Vt: 0.797. Predictive value of Ppeak/MIP <1 for weaning success: sensitivity 88%; specificity 85%; diagnostic accuracy: 87%.

CONCLUSIONS. Setting standard ventilator parameters during controlled mechanical ventilation, Ppeak/MIP index provides a bedside non invasive estimation of inspiratory spontaneous effort. A value of Ppeak/MIP index <1 predicts weaning success with a sensitivity of 88% and specificity of 85%. This bedside non invasive index could be added to common criteria used to recognize those patients able to start weaning.

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PREDICTORS OF FAILURE OF NON-INVASIVE VENTILATION AS A WEANING TOOL AFTER EXTUBATION

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INTRODUCTION. Non-invasive ventilation (NIV) is used as a weaning tool after extubation in patients with respiratory failure. However, limited data exist on the predictors of failure of NIV in such patients.

OBJECTIVES. To determine predictors of NIV failure in patients who were intubated for respiratory failure and extubated directly to NIV.

METHODS. This is a retrospective analysis of prospectively collected data from January 2008 to Dec 2009. Patients with respiratory failure were mechanically ventilated in a university hospital's medical intensive care unit (ICU) and subsequently extubated to NIV. Physiological and biochemical parameters, using arterial blood gas measurements, were collected at the end of the spontaneous breathing trial and 1 h after the application of NIV. Failure of NIV was defined as respiratory failure requiring re-intubation within 48 h.

RESULTS. Out of 175 patients, 78.9% were successfully extubated to NIV. Success rates were 70.6% in patients with chronic obstructive pulmonary disease (COPD) and 80.9% in other patients ($p = 0.24$). Patients who failed NIV were more tachypnoeic, acidaemic and hypercapnic pre-NIV, and more tachycardic, hypotensive, acidaemic, hypercapnic and hypoxaemic post-NIV (p all <0.05). On logistic regression analysis, three physiologic parameters predicted NIV failure: pre-NIV respiratory rate (OR 1.57, 95% CI 1.07–2.31 per 5 breaths increase), post-NIV heart rate (OR 1.28, 95% CI 1.08–1.52 per 5 beats increase) and post-NIV systolic blood pressure (OR 1.15, 95% CI 1.02–1.29 per 5 mmHg decrease).

CONCLUSIONS. Physiologic parameters, including the respiratory rate pre-NIV, and heart rate and systolic blood pressure post-NIV, independently predict NIV failure post-extubation. These parameters should be taken into account in the decision to extubate directly to NIV.

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INVESTIGATION OF CARDIORESPIRATORY COUPLING, HEART RATE AND BREATH-TO-BREATH VARIABILITY FOR WEANING OUTCOME ASSESSMENT IN MECHANICALLY VENTILATED PATIENTS

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INTRODUCTION. Discontinuation of mechanical ventilation in critically ill patients is a challenging task and involves a careful weighting of the benefits of early extubation and the risks of premature spontaneous breathing trial (SBT). Only a few studies have explored indices derived from both heart rate and breathing pattern variability analysis for the estimation of weaning readiness.

OBJECTIVES. To investigate heart rate (HR) and respiratory rate (RR) complexity in patients with weaning failure or success, using both linear and nonlinear techniques from signal processing theory.

METHODS. Forty-two surgical patients were enrolled in the study. There were 24 who passed and 18 who failed a weaning trial. Signals were analyzed for 10 min during two phases: 1. pressure support (PS) ventilation (15–20 cm H_2O) and 2. weaning trials with PS: 5 cm H_2O. Low and high frequency (LF, HF) components of HR signals, HR multiscale entropy (MSE), RR sample entropy, HR-RR cross-sample entropy between cardiorespiratory signals, Poincaré plots and $\alpha 1$ exponent were computed in all patients and during the two phases of PS.

RESULTS. Weaning failure patients exhibited significantly decreased RR sample entropy (0.84 ± 0.12 vs. 1.24 ± 0.16) and $\alpha 1$ exponent (0.75 ± 0.11 vs. 1.20 ± 0.21, $p < 0.001$ for both comparisons) and increased HR MSE (1.09 ± 0.29 vs. 0.76 ± 0.32) and HR-RR cross entropy (0.45 ± 0.26 vs. 0.21 ± 0.05, $p < 0.05$ for both comparisons) compared with weaning success subjects. Their changes were opposite between the two phases, except for MSE that increased between and within groups, demonstrating different curve profiles ($p < 0.001$). A1 exponent, HR MSE, RR and HR-RR cross sample entropies predicted successfully weaning outcome. Areas under the curve (AUC) were respectively: 0.891 (0.05), 0.68 (0.08), 0.879 (0.05) and 0.824 (0.08) ($p < 0.05$) and were found to be similar with those of rapid shallow breathing index [0.88 (0.07)].

CONCLUSIONS. We suggest that nonlinear analysis of cardiorespiratory dynamics has a prognostic impact upon weaning outcome in surgical patients.

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EFFECTS OF REMIFENTANIL ON RESPIRATORY DRIVE AND TIMING DURING PSV AND NAVA

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INTRODUCTION. Analgo-sedation is commonly used to improve patient comfort and tolerance. Benzodiazepines and opioids are the most used sedatives; remifentanil is particularly interesting for its pharmacokinetic characteristics.

OBJECTIVES. To evaluate the effects of increasing doses of remifentanil on respiratory drive and pattern in a group of critically ill patient with Acute Respiratory Failure ventilated in PSV and NAVA.

METHODS. 11 critically ill, mechanically ventilated (PSV mode) patients (Ramsay sedation score 1) were enrolled. After recording basal values, a remifentanil continuous infusion was started randomly administering different dosages (0.03, 0.05, 0.08, and 0.1 gamma/kg/min). At each dosage, the patients were ventilated in PSV and NAVA for 30' each. Before the study all patients were equipped with the EAdi cathether. We measured mechanical and neural respiratory patterns, inspiratory effort, gas exchange and patient-ventilator interaction.

RESULTS. Increasing doses of remifentanil, with both modes, did not reduce Peak EAdi; conversely, above 0.05 gamma/kg/min, Peak EAdi showed a trend toward an increase more evident during NAVA. Remifentanil above 0.08 gamma/kg/min significantly decreased RRneu and RRmecc with both modes ($p < 0.01$); at 0.1 gamma/kg/min two patients stopped the study for bradypnea. No significant difference was found in Timecc and Tineu with both modes; increasing doses of remifentanil significantly reduced Timecc/Ttot and Tineu/Ttot during NAVA ($p < 0.01$) but not during PSV.

CONCLUSIONS. This physiologic study shows that increasing doses of remifentanil do not reduce respiratory drive as assessed by Peak EAdi; conversely a significant effect on respiratory timing is observed as a decrease in RRmecc and RRneu both during PSV and NAVA. At low dosage (below 0.08 gamma/kg/min) remifentanil can be safely used for mechanically ventilated patients both during PSV and NAVA.

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THE REASONS FOR CONTINUING MECHANICAL VENTILATION AFTER PASSING A WEAN PROTOCOL

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INTRODUCTION. Prolonged mechanical ventilation is associated with increased health care costs, morbidity and mortality. To decrease the duration of mechanical ventilation we introduced a wean screen protocol based on the ABC-trial. This wean screen protocol includes.

1. Daily Spontaneous Awakening Trial (SAT)
2. Rapid Shallow Breathing Index (RSBI)
3. Spontaneous Breathing Trial (SBT)
4. MD enumerates reason to continue

Despite of passing the protocol the decision to extubate was postponed in some patients.

OBJECTIVES. To gain insight on the physicians reasons for continuing mechanical ventilation after passing the wean screen protocol.

METHODS. A wean screen protocol was introduced at a mixed medical (neuro-)surgical ICU of a teaching hospital in December 2009 to April 2010. Ventilation practitioners assessed ventilated patients and recorded the physicians reasons for continuing mechanical ventilation despite of passing the wean screen protocol.

RESULTS. 223 patients were ventilated in this period. 135 daily screens were performed, 111 screens were successful. Only 24 passed wean screens resulted in extubation. The rate of extubation was 22%. 78% screens did not lead to liberation from mechanical ventilation. The extubation rate does not correspond with the findings of the ABC trial with an extubation rate of 54%. Table 1 shows the physicians' reasons to continuing mechanical ventilation. It should be noted that all patients with an unsafe airway were patients with a Glasgow Coma Scale (GCS) of ≤ 8 [intracerebral haemorrhage (68%), cerebral infections (13%), post-CPR encephalopathy (13%) and severe brain injury (6%)].

TABLE 1

N = 87	n	%		n	%
Unsafe airway	47	54.0	MD thinks patient will get worse	3	3.4
Oversedated	9	10.3	Unstable, swollen airway	2	2.3
Patient too weak	9	10.3	Agitation/mental status	1	1.1
Imminent/awaiting procedure	8	9.2	Family issues	0	0
Fluid overload	4	4.6	MD refuses answer	0	0
Secretions	4	4.6	No reason above applies	0	0

CONCLUSIONS. First results of this trial suggest that a wean screen based on the ABC trial of Girard et al seems not to be applicable on neurosurgical patients due to frequently observed GCS ≤ 8. Additional work has to be performed to confirm our observations.

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DAILY WEANSCREEN IN MECHANICALLY VENTILATED PATIENTS

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INTRODUCTION. Delayed extubation is associated with prolonged ventilation, muscle-weakness and ventilation-associated complications (e.g. VAP). Therefore the duration of mechanical ventilation (MV) should be limited as much as possible. Several studies show positive results with their interventions. To decrease the time spend on ventilator we introduced a four interventions wean screen-protocol based on the ABC-trial and Robertson's work:

1. Daily Spontaneous Awakening Trial (SAT)
2. Rapid Shallow Breathing Index (RSBI)
3. Spontaneous Breathing Trial (SBT)
4. Consultation of MD to extubate or reason to continue

OBJECTIVES. To reduce the use of sedatives and to decrease the amounts of time spend on a ventilator (MV-duration) through daily assessment by a ventilation practitioner (R.N.) using a four-step-wean screen-protocol.

SETTING. A 20-bed mixed medical- (neuro-) surgical level III Intensive Care Unit of a teaching hospital in the The Netherlands.

METHODS. In 2009 the sedation goal was prescribed each day by the intensivist; nurses evaluated the Ramsay-score every 2 h and doses of sedatives were adapted accordingly.

From January to March 2010 we assessed all ventilated patients every day from Monday till Friday. The subsequent four steps of the wean screen protocol were carried out to promote extubation. The amount of sedatives per month was divided by the number of ventilated patients, resulting in an average dose of midazolam/propofol/morfine per patient. The time spend on ventilators was calculated and all data were compared with the same period in 2009. Data were analysed with the Mann-Whitney U test.

RESULTS. 160 and 163 patients were included in the 2009 and 2010 cohorts, respectively. We accomplished a reduction in the use of sedatives (-12% midazolam and -35% propofol) and morphine (-27%) (Table 1). The amount of time spend on ventilators decreased, albeit not significantly ($p = 0.902$). This was probably due to the VAP-ventilatorbundle (introduced last year), the heterogeneity of our cohort and the already short MV-duration.

TABLE 1

	Control group	Intervention group	Differences
Number of patients	160	163	
Periods of MV	185	177	
Median MV-duration (h)	40 (Q1 = 9, Q3 = 118)	33 (Q1 = 11, Q3 = 139)	(n.s.)
Average dose of propofol per patient (mg)	2844	1840	−35%
Average dose midazolam per patient (mg)	485	429	−12%
Average dose of morphine per patient (mg)	251	184	−27%

CONCLUSIONS. In our population a daily four-component-weans creen is an effective way to reduce sedative- and morphine-use but not the duration of mechanical ventilation.

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THE INDICATION FOR REMIFENTANIL SEDATION IN CRITICAL CARE PATIENTS IN A UK DISTRICT GENERAL HOSPITAL: A 5 YEAR RETROSPECTIVE CASE SERIES FOCUSSING ON ITS ROLE IN PATIENTS RECEIVING NON INVASIVE VENTILATION

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INTRODUCTION. Remifentanil is used as a sedative in critical care for intubated patients because of its unique pharmacokinetic properties. Its use in non-intubated patients is less well described.

OBJECTIVES. To report the indications for remifentanil sedation in a thirteen bed ICU in the UK in both intubated and non-intubated patients.

METHODS. A retrospective observational study of drug records and patient notes. Controlled drug records were analysed for a 5-year period up to October 2009. Number of days of remifentanil treatment and dose given were determined. The notes of these patients were analysed and age, reason for admission, type of ventilatory support received and main indication for the use of remifentanil sedation were recorded.

RESULTS. From 1/11/2004 to 31/10/2009, over 2,500 remifentanil prescriptions were analysed. Only 8 could not be linked to patient records. There were 3,259 admissions during this time, of whom 469 (14.4%) received remifentanil. The mean age was 60 years (range 11–92). The mean duration of remifentanil sedation was 2.9 days (median 2.0, range 1–40), with a mean dose of 4.9 mg/day (median 4 per day, range 1–28). The admitting diagnosis was medical in 329 (70.1%) patients and surgical in 140 (29.9%). Of the medical patients 191 (58.1%) were admitted with a primary lung condition. The main indications for remifentanil sedation were: as an adjunct to non invasive ventilation in 279 (59.5%), as part of a weaning plan for intubated patients in 80 (17.1%) and as sedation with face mask oxygen alone in 54 (11.5%). Other indications were: as primary sedation agent for elective overnight ventilation in post operative patients 50 (10.7%), as the first line agent in intubated patients 24 (5.1%), in patients with multiple organ failure in whom other agents were contraindicated 12 (2.6%) and as a second line agent in difficult to sedate patients 7 (1.5%). Six patients (1.3%) received remifentanil to allow accurate neurological assessment following a period of sedation. Of the patients receiving non-invasive respiratory support, 50 (21.3%), were deemed unsuitable for intubation; of these 22 (44.0%) survived to unit discharge.

CONCLUSIONS. Remifentanil is most frequently used for those patients unable to tolerate non invasive ventilation without sedation. Almost half of those in whom this was the limit of treatment survived to discharge. It was also used to facilitate weaning from mechanical ventilation in patients who have received longer acting agents and in a number of other challenging clinical scenarios where its' unique properties make it the preferred choice.

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NON-INVASIVE VENTILATION VIA HELMET IN WEANING PATIENTS WITH HYPOXEMIC ACUTE RESPIRATORY FAILURE

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INTRODUCTION. Mechanical ventilation is a life-saving intervention for patients with hypoxemic acute respiratory failure (ARF). Non-invasive ventilation (NIV) has been utilized in selected patients with hypoxemic ARF to avert endotracheal intubation, which is related to life-threatening complications. NIV has been also proposed to facilitate weaning and extubation in patients with hypercapnic ARF. So far, no controlled randomized study has investigated the potential role of NIV in weaning patients with hypoxemic ARF.

OBJECTIVES. We designed this pilot study to assess safety and feasibility of NIV to wean hypoxemic ARF patients. Twenty mechanically ventilated patients with hypoxemic ARF were randomized to receive early extubation followed by NIV application via helmet (Helmet group) or conventional weaning through the endotracheal tube (Tube group). Primary outcomes were the duration of invasive mechanical ventilation and the adherence to the study protocol. Secondary outcomes were protocol failure (i.e. need for re-intubation), ICU and hospital mortality, rate of tracheotomy, duration of continuous intravenous sedation, weaning time, and septic complications.

METHODS. Inclusion criteria were: (1) mechanical ventilation for more than 48 h; (2) partial pressure of arterial oxygen to fraction of inspired oxygen (PaO_2/FiO_2) ratio between 200 and 300 in pressure support (PS) with a total applied pressure (i.e. positive end-expiratory pressure (PEEP) + inspiratory PS) ≤ 25 cmH_2O; (3) $PaCO_2 \leq 50$ mmHg and pH ≥ 7.35; (4) Glasgow Coma Scale ≥ 10. The criteria for protocol failure were defined a priori. Data were analysed according to the intention-to-treat analysis.

RESULTS. The main findings are summarized in Table 1. Weaning through helmet by NIV application following early extubation was safe and feasible. Overall the adherence to the study design was 90%. In addition, in the helmet group, there was a significant reduction in the rate of tracheotomy and a trend toward a lower rate of protocol failure, and fewer days on invasive ventilation. There was no difference with respect to days of continuous sedation, ICU and hospital mortality, weaning time and septic complications.

TABLE 1

Variables	Helmet group	Tube group	P value
Invasive mechanical ventilation (days)	7.6 ± 6.0	15.0 ± 10.8	p = 0.08
Failure rate (%)	10	50	p = 0.05
Hospital mortality rate (%)	20	30	p = 0.99
ICU mortality rate (%)	10	30	p = 0.58
Tracheotomy rate (%)	0	40	p = 0.03
Continuous sedation (days)	10.7 ± 7.8	15.5 ± 11.1	p = 0.28
Weaning time (days)	4.0 ± 4.4	4.4 ± 6.7	p = 0.63
Septic complications (%)	30	50	p = 0.36

CONCLUSIONS. NIV application to wean patients with hypoxemic ARF is a safe technique in a well-experienced centre. A further randomized controlled multicentre study is deemed to ascertain potential clinical advantages of this technique.

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A UK DISTRICT GENERAL HOSPITAL EXPERIENCE WITH A COMBINED PROTOCOL OF DAILY SEDATION HOLDS, WEANING ATTEMPTS AND DELIRIUM SCREENING USING THE INTENSIVE CARE DELIRIUM SCREENING CHECKLIST (ICDSC)

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INTRODUCTION. Daily sedation holds and weaning attempts have been validated as a means of reducing ICU stay and improving outcomes (1). Delirium is a common occurence on the ICU and is associated with increased length of stay (LOS) and poor outcomes (2).

OBJECTIVES. We developed a combined daily sedation hold, delirium management, and weaning (SDW) protocol and implemented this to reduce ICU LOS and improve outcomes.

METHODS. A SDW protocol was implemented in 2009. We prospectively audited all patients from January to March 2010. Delirium was measured using the ICDSC. Data was analysed using Graphpad statistical software.

RESULTS. 109 consecutive patients were analysed. The incidence of delirium was 35% (38 pts). Of these, 63% (24) had risk factors for delirium. There was no difference in onset of delirium between sexes, age, type of admission, or severity of illness. However, in patients with delirium, duration of mechanical ventilation (MV) and ICU LOS were significantly longer and there was a trend towards increased hospital LOS (Table 1).

CHARACTERISTICS OF PATIENTS WITH/WITHOUT DELIRIUM

	Delirium (n = 38)	No delirium (n = 71)	P value
Mean age	60	62	0.60
Male/female	18/20	39/32	0.55
APACHE II	18	18	1.00
Medical/surgical	28/10	51/20	1.00
Mean ventilator days	5.9	2.3	0.014
Mean ICU length of stay (days)	9.29	4.86	0.004
ICU survival	30	51	0.50
Hospital survival	28	47	0.52
Hospital length of stay post ICU (days)	19.3	13.5	0.13

The duration of delirium was short (median 2 d IQR 1–4) and responded to non-pharmacological management in the majority of cases (Table 2).

METHODS OF TREATMENT FOR DELIRIUM

Method	Number (%)
Non-pharmacological	27 (72)
Clonidine	5 (13)
Haloperidol	5 (13)
Other	1 (2)

When compared to the same period prior to implementation of the protocol (2008), there was a trend towards reduction in duration of MV (5.72 vs. 3.58 days, P = 0.07) despite similar admission severity of illness (mean APACHE II 19 vs. 18).

CONCLUSIONS. 1. Delirium on the ICU is associated with significantly increased duration of MV, increased ICU LOS and a trend towards increased hospital LOS.
2. A combined protocol of daily sedation holds, weaning attempts, and delirium assessment and management may lead to a reduction in duration of mechanical ventilation.
3. In general, duration of delirium was short and responded to nonpharmacological treatment.

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1044

MEASURING THE LINEAR BEHAVIOR AMONG THE VARIABLES OF THE EQUATION OF MOTION FOR THE MECHANICAL VENTILATION DURING WEANING TO IDENTIFY DIFFERENCES BETWEEN THE MECHANICAL VENTILATION WITHDRAWAL OUTCOME

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INTRODUCTION. Determining the linear relationship among the variables of the Equation of Motion for the Mechanical Ventilation (EMMV), through a fixed period of time, could be used to assess the success or failure of the Mechanical Ventilation (MV) withdrawal.

METHODS. This is a prospective study effectuated at San José Tec de Monterrey University Hospital ICU. Data from 13 patients withdrawn from MV was collected automatically from an 840NPB® ventilator every 3 min. All patients were on MV more than 24 h. MV data from the last 12 h was used to perform the Time Series Analysis (TSA). The studied variables were selected according to the EMMV i.e. Inspiratory Pressure (Pi), Tidal Volume (Vt) and Inspiratory Time (Ti). The variables were analyzed in pairs so there were three Bivariate Time Series (BTS). Patients were classified as Group 1 (G1) if 48 h after the MV withdrawal respiratory support was not required; else patients were classified as Group 2 (G2). Once the BTS met the weakly stationary condition, the Fourier transform was calculated for each time series. Then, the TSA was performed to estimate the measures of linearity such as the Squared Coherence (K^2) and Angle of Phase (ø) for the three BTS. To estimate the statistical differences between the K^2 and ø from G1 and G2 an ANOVA was performed. If the ANOVA p value <0.05, Tukey-Kramer and LSD post hoc tests were conducted.

RESULTS. The Bivariate Time Series (BTS) producing K^2 and ø with statistical significance are Vt-Ti and Pi-Vt respectively. Furthermore, the frequency interval form 6 to 1 $(h)^{-1}$ for the referred BTS, present *post hoc* tests p values <0.05. Calculating the 95% Confidence Intervals for the mentioned frequency interval, evince the statistical difference between G1 and G2 (Table 1).

STATISTICS ON SQUARED COHERENCE AND ANGLE OF PHASE

Measure of Linearity	BTS variables	Mean ± SD		95% confidence interval	
K^2	Vt-Ti	0.807 ± 0.105[a]	0.658 ± 0.028[b,c]	0.752–0.862[a]	0.580–0.737[b]
ϕ	Pi-Vt	−0.129 ± 0.379[a]	0.584 ± 0.225[b,c]	−0.360–0.102[a]	0.257–0.911[b]

[a]G1 (n = 9); [b]G2(n = 4); [c]LSD and Tukey-Kramer post hoc tests p value <0.05 vs. G1

CONCLUSIONS. Measuring the linear dependence of variables through time by K^2 and ø may be used to determine non-linear behavior between the variables of the EMMV. Non-linear behavior during weaning perhaps indicates the dependency of, either the resistance or compliance of the respiratory system, on the ventilatory support (i.e. Pi). Accordingly, K^2 and ø, estimated at the frequency interval form 6 to 1 $(h)^{-1}$, can provide information concerning to the dynamics of the respiratory system that can be used as a complement to determine the suitability of the MV withdrawal.

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1045

TRANSITION FROM CMV TO APRV MAY FACILITATE THE WEANING PROCESS IN PATIENTS WITH SEVERE ARDS

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INTRODUCTION. Acute Respiratory Distress Syndrom (ARDS) is a common condition that is characterized by acute severe hypoxia that is not due to left atrial hypertension. Despite advances in our understanding of the pathophysiology and management of ARDS, it is still associated with a high mortality[1]. The principles of treating ARDS are providing good supportive care and maintaining oxygenation while diagnosing and treating the underlying cause[2].

OBJECTIVES. To study the potential superiority of APRV on CMV in a subgroup of patients with severe ARDS.

METHODS. Retrospective observational study on 39 patients severe ARDS who were admitted between July 2008 and January 2010 to Mafraq Hospital ICU in UAE. The diagnosis of ARDS was based on presence of bilateral infiltrates in CXR and P/F ratio of less than 200 in absence of evidence of elevated left atrial pressure. All patients were managed according to ARDSnet guidelines using low tidal volume CMV and IV steroids. Criteria for transition to Airway Pressure Release Ventilation (APRV) included failure to wean down FiO2 below 60% after 24 h, hemodynamic instability due to high PEEP, and failure to maintain plateau airway pressure below 30 cmH_2O. Initial settings of APRV were Ph 26, Pl 2, Th 5, and Tl 0.5 with titration of FiO_2 as required keeping PaO_2 more than 60 mmHg. We compared the outcome of CMV and APRV groups with special concern to the duration of mechanical ventilation, requirement for tracheostomy, and survival to ICU discharge.

RESULTS. Twenty four male and 15 females were included in the study with a mean age of 42 years (± 24). Fourteen out of them fulfilled the criteria and were shifted to APRV within 24 h of initiating mechanical ventilation. Ten out of 14 (70%) patients in the APRV arm survived to ICU discharge versus 16 out of 24 (67%) patients in CMV group (p 0.45). Survivors in APRV group spent significantly shorter periods of mechanical ventilation compared to survivors in CMV group (9.6 vs. 12.1 days p 0.03). While 8 out of 16 (50%) survivors in CMV required tracheostomy for prolonged intubation or recurrent lavage, only 2 out of 10 (20%) survivors in APRV group required tracheostomy tube placement (p 0.02).

CONCLUSIONS. We concluded that APRV can be effectively used as rescue measure of ventilation in patients with severe ARDS. Although our study does not show any mortality benefit of using APRV over CMV, there was a shorter ventilation days and ICU stay using APRV. We strongly recommend further studies to investigate the probability of using APRV as initial mode of ventilation in this subset of patients.

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AN ETHNOGRAPHIC INSIGHT INTO THE DYNAMICS OF THE DECISION ENVIRONMENT WHEN MANAGING A WEANING PATIENT

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INTRODUCTION. Weaning from mechanical ventilation is a common daily procedure when caring for critically ill patients, and a lifesaving practice on which nurses are taking an increasing role with the introduction of nurse-led protocols. The literature supports that nurse-led protocols facilitate weaning and increase nurses' input in decision-making. On the other hand, decision-making is a complex function affected by the nature of the task, the decision environment and the characteristics of the decision maker. Although the cognitive process of clinical decision-making has been investigated with many different methodologies, little is known about the decision environment and its impact on decisions' during the weaning process.

OBJECTIVES. This paper aims to address one of the factors of the clinical environment and its impact on the decisions when discontinuing mechanical ventilation.

METHODS. This paper is part of a large comparative ethnographic study looking at nurses' input during the weaning process of mechanically ventilated patients. Participant observation of critical care nurses took place in an 12-bedded ICU in Greece and an 18-bedded ICU in Scotland for 6 months each to examine nurses' involvement in the decisions made. In-depth semi-structured interviews with the nurses followed focusing on how nurses perceived their participation in the decisions made. Data from field notes and interview transcripts were analysed thematically using the Qualitative Data Analysis software NVivo, version 8.

RESULTS. Inter-personal and inter-professional relationships were considered revealing influences of nurses' input in decision-making. Clinicians' personality played a significant role in their involvement in decisions, whereas trust and appreciation, the sense of support and the sense of accountability were also considerable dynamics of inter-professional relationships and predisposed decision-making.

CONCLUSIONS. Clinical decision-making is a multi-dynamic process specifically in complex clinical long-term situations such as weaning. Aspects of the decision environment, such as the inter-professional relationships should be acknowledged when introducing methods to enhance nurses' role in teamwork and collaborative decision-making in order to improve the weaning process of ventilated patients and their outcome.

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COMPARISON OF PROPORTIONAL ASSIST VENTILATION PLUS WITH PRESSURE SUPPORT VENTILATION DURING WEANING FROM MECHANICAL VENTILATION: A PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION. Assisted ventilatory modes are often used for progressive withdrawal of mechanical ventilation (MV). Pressure Support Ventilation (PSV) is commonly used for this purpose. Proportional Assist Ventilation Plus (PAV+) has occasionally been used for the same goal.

OBJECTIVES. The objective of our study was to analyze the temporal trends and outcomes of two cohorts of patients ventilated with PSV and PAV+.

METHODS. A cohort of 16 consecutive patients who were ventilated with PAV+ and another cohort of 15 consecutive patients who were ventilated with PSV were compared. All patients had the same inclusion criteria (gas exchange, ventilatory mechanics, PEEP level, resolution/stabilization of the cause leading to invasive MV and appropriate level of consciousness). Both modes were adjusted to predefined clinical criteria (PSV to reach a respiratory rate about 25 bpm and PAV+ to reach a physiological inspiratory effort). All patients were ventilated with PB 840 machines. We analyzed: the number of patients successfully extubated, the number of patients who failed/intolerated the technique and needed to return to Assist Control Ventilation (ACV), the days under MV and the tracheostomy and reintubation (within 48 h) rates. Proportions were compared using χ^2 test. Continuous variables were compared with Mann Whitney test. $P < 0.05$ was considered significant.

RESULTS. PSV and PAV+ cohorts did not significantly differ in terms of baseline criteria (during ACV): age 69 ± 10 versus 61 ± 10 yr ($p = 0.14$), SAPS II 45 ± 19 versus 42 ± 14 ($p = 0.84$), PaO_2/FiO_2 242 ± 97 versus 192 ± 54 ($p = 0.13$), PEEP 5.7 ± 1.0 versus 6.6 ± 2.0 cmH_2O ($p = 0.21$), Vt 454 ± 52 versus 450 ± 65 ml ($p = 0.98$), Pplat 17.6 ± 4.4 vs. 20.5 ± 4.2 cmH_2O ($p = 0.054$), previous days under MV 4.4 ± 4.6 versus 5.1 ± 3.0 ($p = 0.28$). The ventilatory parameters within the first 30–60 min of PSV/PAV+ cohorts did not differ: PEEP 5.6 ± 1.0 versus 6.3 ± 2.1 cmH_2O ($p = 0.47$), Paw max-PEEP 13.2 ± 2.4 versus 11.5 ± 3.5 cmH_2O ($p = 0.09$), respiratory rate 21.2 ± 7.2 versus 25.5 ± 5.8 ($p = 0.07$), Vt 479 ± 143 vs. 472 ± 122 ml ($p = 0.89$), PaO_2/FiO_2 246 ± 86 versus 212 ± 71 ($p = 0.16$), $PaCO_2$ 41 ± 7.3 versus 38 ± 12 mmHg ($p = 0.08$). The number of patients successfully extubated was 8/15 in PSV and 11/16 in PAV+ ($p = 0.37$). The proportion of patients meeting failure criteria was 8/15 with PSV and 4/16 with PAV+ ($p = 0.10$). The number of days under MV was 6.1 ± 4.3 in PSV and 8.6 ± 4.1 in PAV+ ($p = 0.16$) for the patients who tolerated these modes, and it was 19.7 ± 8.7 during PSV and 20.0 ± 4.8 during PAV+ ($p = 0.93$) for the patients who did not tolerate the modes. Tracheostomy and reintubation were 3/15 and 1/15 in PSV and 2/16 and 1/16 in PAV+ ($p = 0.65$ and $p = 0.96$ respectively).

CONCLUSIONS. In the way they were used, both modes PSV and PAV+ , can be considered as clinically equivalent.

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VALIDATION OF AN AUTOMATIC CONTINUOUS SYSTEM TO DETECT EXPIRATORY ASYNCHRONIES DURING MECHANICAL VENTILATION

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INTRODUCTION. Presence of expiratory asynchronies (EA) (ineffective efforts, cough and continued contraction of inspiratory muscles) is a common problem associated with increased duration of mechanical ventilation, longer stay, higher costs and increased mortality. Because of the lack of systems that automatically detect and report EA, their identification is currently done by examining ventilator interface at the bedside or by applying dedicated algorithms in investigational conditions.

OBJECTIVES. Validate the accuracy of linear mathematical algorithms to automatically detect EA built in a new computerized system that grabs and process data from different bedside ICU monitors and mechanical ventilators.

METHODS. Observational and prospective study in a general ICU of 16 beds. Two beds were equipped with a software (Better Care®), a technological platform responsible for data acquisition and synchronization, processing, storing—as non static and processable DICOM objects—and also for integrating all this data with health information systems. By using the Better Care® platform, a total of 2,600,000 breaths from 8 consecutive adult patients were collected with at least 24 h of mechanical ventilation. *Algorithm #1*: The EA algorithm consisted in a mathematical analysis of the airflow and airway pressure waveform variations during expiration not followed by a mechanical breath. *Algorithm #2*: Designed to select 1,000 breaths out of the total number. This algorithm sorted and classified the breaths by the percentage of deviation from the expected expiratory curve. The result was 1,000 breaths covering most of the shapes the expiratory curve could have. Five expert attendant physicians independently analyzed the 1,000 selected breaths and classified them as EA or not. The EA algorithm processed the same 1,000 selected breaths and assigned a percentage to each one, according to the variation in the shape and direction of the expiratory airflow and airway pressure curves. The expert criterion against the EA algorithm scores was used to construct a logistic regression model. We calculated sensitivity, specificity, positive predictive value and negative predictive value. The predictive performance of EA algorithm was evaluated using ROC curves.

RESULTS. Optimal sensitivity and specificity were achieved by setting the cut-off point at a EA algorithm score of 42%. A variation in the shape and direction of the expiratory airflow and airway pressure curves >42% compared to the theoretical curve identified an EA with a sensitivity of 91.5%, specificity of 91.7%, a positive predictive power of 80.3% and a negative predictive power of 96.7%.

CONCLUSIONS. The EA algorithm built-in the Better Care® platform was able to detect expiratory asynchronies similar to expert attendant physicians in patients receiving mechanical ventilation.

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Hemodynamic monitoring: 1049–1060

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PARAMETERS OF DYNAMIC TISSUE O_2 SATURATION RESPONSE IN THE FINGER COMPARED WITH THENAR OF CRITICALLY ILL PATIENTS

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INTRODUCTION. Near-infrared spectroscopy (NIRS) in combination with a vascular occlusion test (VOT) has been proposed to assess and identify metabolic and microcirculatory alterations during sepsis and shock in critically ill patients. However, to automatize repeated measurements at the bedside, this technique can potentially cause discomfort to the patient. Vascular arterial occlusion performed in the finger may be a more attractive method to execute repeated measurements at the bedside because of more tolerability from the patient. We have previously showed in healthy volunteers that NIRS can be used on finger to assess the StO2 response to VOT and that 5 min was an adequate occlusion time to provide the best curve fit for NIRS dynamic variables[1].

OBJECTIVES. We aimed to investigate whether StO2 response to VOT obtained from the finger could predict conventional StO2 response measurements obtained from the thenar of critically ill patients.

METHODS. Parameters of StO2 response were measured with an InSpectra Spectrometer model 650 (Hutchinson Technology Inc.) equipped with a 15-mm or a 5-mm probe. The 15-mm probe was placed over the thenar eminence and the 5-mm probe was place over the ventral face of the middle finger. We performed in each patient a series of two vascular occlusion tests (VOT): one on the finger (5 min) followed by one on the arm (3 min). The measurements were obtained within 24 h of intensive care admission and every 24 h thereafter until day 3. VOT-derived StO2 traces were analyzed for baseline, ischemic (RdecStO2, %/min) and reperfusion (RincStO2, %/s) parameters.

RESULTS. We performed 63 paired of NIRS measurements in 25 critically ill patients (Age 62 ± 15; 16 M/9F). Although StO2 did not differ significantly between thenar and finger (76% ± 11 vs. 79% ± 12; $P = 0.31$), RincStO2 and RdecStO2 were statistically lower in the finger (1.5%/s ± 0.7 vs. 2.5%/s ± 0.8, $P = 0.001$; 3.1%/min ± 1.0 vs. 11%/min ± 3.3; $P = 0.001$). We performed bivariate linear model with correlated errors in which StO2 outcomes on thenar and on finger were treated as responses. The correlation was significant for StO2 and RincStO2, but not for RdecStO2 (Table 1). Furthermore, mixed model analysis showed that thenar-StO2 as dependent variable could be significantly predicted by finger-StO2 parameters with estimation coefficient (± SE) of 0.7 ± 0.06 ($P = 0.0001$), 0.9 ± 0.09 ($P = 0.0001$) and 0.98 ± 0.3 ($P = 0.0061$) for StO2, RincStO2 and RdecStO2, respectively.

CORRELATION OF STO2 RESPONSE: FINGER VS. THENAR

TABLE 1	StO2	RincStO2	RdecStO2
Day 1	0.84 (*P = 0.001*)	0.74 (*P = 0.006*)	0.17 (*P = 0.42*)
Day 2	0.80 (*P = 0.004*)	0.91 (*P = 0.01*)	0.35 (*P = 0.18*)
Day 3	0.88 (*P = 0.003*)	0.85 (*P = 0.001*)	0.54 (*P = 0.07*)

CONCLUSION. Near-Infrared spectroscopy can be used on finger to assess the StO2 response to VOT in critically ill patients. Our results showed that StO2 baseline and the reperfusion parameter RincStO2 from the finger were the best predictors for the StO2 response obtained from the thenar.

[1]*Intensive Care med* 2009;35:205 (A794).

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HUMAN VALIDATION OF A NEW TRANSPULMONARY THERMODILUTION METHOD TO ASSESS GLOBAL END-DIASTOLIC VOLUME AND EXTRAVASCULAR LUNG WATER

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INTRODUCTION. A new method has been developed to assess global end-diastolic volume (GEDV) and extravascular lung water (EVLW) from a transpulmonary thermodilution curve.

OBJECTIVES. Our goal was to assess the performance of this new method in critically ill patients.

METHODS. 18 critically ill patients (9 females, 9 males, mean age (± SD) 67 ± 11 years, mean body weight 76 ± 17 kg) were included in this multi-centre observational study. All patients were monitored with a central venous catheter and a thermistor-tipped femoral arterial catheter (5F VolumeView, Edwards Lifesciences, Irvine, CA). The femoral catheter was connected to the EV1000 monitor (Edwards) and used to measure cardiac output (COe), GEDVe and EVLWe applying the new method based on the equation: GEDVe = f (S2/S1) × COe × MTt, where S1 and S2 are respectively the maximum up- and down-slopes of the dilution curve, MTt the mean transit time and f a proprietary factor. Thermodilution curves were transferred to a computer and re-run through a PiCCO2 monitor (Pulsion Medical Systems, Munich, Germany) that was used to measure COp, GEDVp and EVLWp using the method based on the equation: GEDV = -COp × (MTt − DSt), where DSt is the exponential downslope time of the dilution curve. 136 paired measurements were available for comparison.

RESULTS. Overall, COp and COe ranged from 1.8 to 11.2 and from 2.2 to 12.0 l/min, respectively. COp and COe were closely correlated ($r^2 = 0.98$), mean bias (± SD) was 0.20 ± 0.28 l/min and %error was 9%. GEDVp and GEDVe ranged from 677 to 2217 and from 716 to 2326 ml. GEDVp and GEDVe were closely correlated ($r^2 = 0.94$), mean bias was 27 ± 88 ml and %error was 14%. EVLWp and EVLWe ranged from 238 to 2,153 and from 295 to 2,516 ml. EVLWp and EVLWe were closely correlated ($r^2 = 0.98$), mean bias was 41 ± 54 ml and %error was 17%.

CONCLUSIONS. In critically ill patients, and over a very wide range of values, the new transpulmonary thermodilution method is at least as reliable as the PiCCO method to assess cardiac output, cardiac preload and extravascular lung water.

REFERENCE(S). NA.

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TISSUE OXYGEN SATURATION (STO_2) IS AN EARLY, NON-INVASIVE PREDICTOR OF PATIENT OUTCOMES IN THE ICU

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INTRODUCTION. Mortality of critically ill patients in the intensive care department remains high despite advanced monitoring techniques employed to indicate problems in patients' health. Tissue oxygen saturation (StO_2) is a non-invasive, continuous, and real time indicator of tissue perfusion status which forecasts clinical outcomes in critically ill patients in several different settings, particularly in trauma (1). The current study tests the ability of a single measurement of StO_2 taken on admission to the medical intensive care unit to predict a patient's prognosis, and compares it with other currently used metrics of hemodynamic status.

METHODS. Thirty two subjects were enrolled in this observational clinical trial with varying diagnoses as is typical in this medical ICU. Parameters recorded at admission included age, mean arterial blood pressure (MAP), central venous oxygen saturation ($ScvO_2$), lactate, base excess, ejection fraction, SpO_2, temperature, and StO_2 (InSpectra StO_2 monitor, Hutchinson Technology Inc.). The APACHE II score was calculated. Patients were treated according to standard practice, and were monitored for survival at 60 days post admission. Comparisons between survivors and non-survivors were analyzed using the Mann-Whitney U test (2-tailed), and the discriminatory ability of the various parameters was analyzed by calculating receiver operating characteristic curves.

RESULTS. Mean patient age was 57 years (range 13 to 87) with 20 males out of 32 total subjects. Thirteen patients died (41%). Table 1 shows statistical comparisons between groups for StO_2, SpO_2, $ScvO_2$, and lactate. Only StO_2 and SpO_2 differed statistically between the survivors and non-survivors. There was no statistical difference between groups for APACHE II score, MAP, base excess, ejection fraction, or temperature.

CONCLUSION. The non-invasive parameters StO_2 and SpO_2 are significant indicators of survival in critically ill patients. Surprisingly, $ScvO_2$ showed no discrimination between survivors and non survivors.

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VOLUME- VERSUS PRESSURE-GUIDED HEMODYNAMIC MANAGEMENT IN THE CRITICALLY ILL SEPTIC AND NON-SEPTIC PATIENT: TRANSPULMONARY THERMODILUTION WITH PICCO^{TM} TECHNOLOGY VERSUS PULMONARY ARTERY CATHETER

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INTRODUCTION. Volumetric hemodynamic monitoring through transpulmonary thermodilution by PiCCO^{TM} (Pulsion Medical Systems AG, Germany) technology may result in better hemodynamic management and fewer days on the ventilator in critically ill patients than monitoring of filling pressures by a pulmonary artery catheter (PAC).

OBJECTIVES. A prospective randomized clinical trial performed in ICU's of an university and teaching hospital during a 2.5 year period, involving 120 septic and non-septic patients, randomized (after stratification) to hemodynamic monitoring, by PiCCO^{TM} or PAC with both techniques allowing cardiac output and central/mixed venous O_2 saturation monitoring.

METHODS. Hemodynamic management was guided by extravascular lung water index (EVLWI) and global end-diastolic volume index (GEDVI) in the PiCCO^{TM} group and by the pulmonary capillary wedge pressure (PCWP) in the PAC group for 3 consecutive days. Primary outcome measures were ventilator-free days (VFD), for which the study was powered, and lengths of stay in ICU and hospital. Secondary measures were the course of cardiorespiratory parameters, fluid and vasopressor requirements, lactate levels, organ functions and mortality.

RESULTS. In the study period, 72 septic and 48 non-septic patients were included. 60 patients received a PiCCO^{TM} and 60 a PAC catheter. Monitoring arms were comparable at baseline, although sepsis differed from non-sepsis in hemodynamics and severity of lung injury. Premorbidity was greater in non-septic patients. The fluid infusions and balances did not differ between monitoring arms, except at $t = 24$ h when the PiCCO^{TM} group had a more positive balance ($P = 0.044$). Cardiac index and central venous O_2 saturation increased more in the course of time in the PiCCO^{TM} than in the PAC group. The decrease in norepinephrine requirements strongly tended to favor the PiCCO^{TM} group ($P = 0.06$). The course of lactate levels and organ failure did not differ between monitoring arms. VFD did not differ among monitoring arms. PiCCO^{TM} monitoring was associated with relatively fewer mechanical ventilation and ICU days in sepsis but more in non-sepsis (after day 28). The changes in respiratory parameters, SOFA and number of catheter-related complications did not differ among the arms of the study. Overall, 19 patients (32%) died in the PiCCO^{TM} group before day 28 and 21 (35%) in the PAC group ($P = 0.85$).

CONCLUSION. Hemodynamic management guided by PiCCO^{TM} monitoring is safe and results in better tissue oxygenation than guidance by PAC, without inducing pulmonary overhydration, in septic and non-septic, critically ill patients. This was associated with fewer mechanical ventilation and ICU days in patients with sepsis but more days in patients with non-sepsis (after day 28), partly attributable to greater cardiovascular premorbidity in the latter. The major primary and secondary endpoints, VFD and mortality, were not affected.

GRANT ACKNOWLEDGMENT. Pulsion Medical Systems AG, Germany.

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PROGNOSTIC VALUE OF ENDOTHELIAL DYSFUNCTION ASSESSED BY BRACHIAL ARTERY ULTRASOUND IN SEVERE SEPTIC SHOCK

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INTRODUCTION. Non-invasive evaluation of endothelial function may be easily accomplished by ultrasound assessment of flow-mediated vasodilation (FMD) of the brachial artery, but this technique has not been fully explored in septic patients.

OBJECTIVES. This prospective study aims to investigate the role o FMD analysis on intra hospital prognosis of patients with severe sepsis and septic shock.

METHODS. Adult patients admitted to the Intensive Care Unit with a diagnosis of severe sepsis or septic shock (<24 h of duration) were consecutively included. FMD of the brachial artery was measured upon admission and after 24 and 72 h using a high-frequency linear transducer (7.5–10 MHz) according to internationally accepted protocols. A group of apparently health subjects paired for gender and age was used as controls for FMD analysis. Patients were followed up to discharge or death.

RESULTS. We studied 42 adult patients 9 mean age 51 ± 19 years, 26 females, 79% on vasopressors with sepsis predominantly of abdominal or respiratory etiology (75%). APACHE II risk score was 23 ± 7 and intra hospital mortality rate was 33%. FMD was similar in patients with or without use of vasopressors at baseline ($p = 0.56$). FMD in septic patients was significantly lower than in health controls (1.5 ± 7 vs. 6 ± 4%; $p < 0.001$). We observed that survivors depicted a gradual improvement on endothelial function, so that 72 h after sepsis onset FMD was significantly lower in nonsurvivors (−3.3 ± 10 vs. 5.2 ± 4%; $p < 0.05$; time-group interaction p value = 0.03).

CONCLUSIONS. Brachial FMD is altered in septic patients with hemodynamic instability and its improvement may be an early marker of favorable prognosis.

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RESPIRATORY VARIATIONS IN PULSE OXIMETRY PLETHYSMOGRAPHIC WAVEFORM AMPLITUDE CALCULATED AUTOMATICALLY AND CONTINUOUSLY

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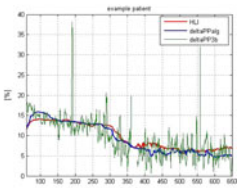
INTRODUCTION. Change in pulse pressure variation (dPP) and respiratory variation of the pulse oxymetry plethysmogram (POP) may predict the hemodynamic effect of PEEP in mechanically ventilated patients [1,2]. Reported comparisons [3,4] between POP variations (POPv) and CO or dPP are based on selection of 3–5 consecutive breaths (dPP3b) during a "stable" period of POP. Recently, a fully automatic ventilation mode (IntelliVent®, Hamilton Medical, Switzerland) that incorporates an automatic and continuous POPv calculation (HLI®) using a dedicated algorithm has been developed. The present study was designed to compare dPP3b, dPP calculated with the algorithm as HLI® (dPPalg) and HLI®.

METHODS. 11 sedated ICU patients ventilated with Hamilton Medical S1 ventilator (with integrated pulse oxymetry (PO)) were included (age = 66 ± 13 years, SAPS II = 54 ± 24, no arrhythmia, norepinephrine: 1.0 ± 1.2 mg/h in 6 patients, MAP = 74 ± 10 mmHg, Vt = 8.4 ± 0.6 mL/kg). Waveforms of PO from a finger sensor and of blood pressure from a radial catheter were recorded for 1–2 h. From the waveforms, breath by breath (using respiratory flow signal), without pre-selection of stable periods and using known formula [1] dPP3b (averaging 3 breaths without any filtering), dPPalg and HLI® were automatically obtained (Matlab®). dPP3b was compared to dPPalg (2600 pairs) using Mann-Whitney t test. 18287 pairs of HLI® and dPPalg values (see Fig. 1 below) were compared using linear regression and Bland-Altman method. A dPPalg threshold value of 13% was used to generate HLI® ROC curves.



Recordings form patient 3

RESULTS. dPP3b and dPPalg were significantly correlated ($r^2 = 0.99$, $p < 0.001$), but standard deviation of dPP3b were higher than the standard deviation of dPPalg (1.2 ± 0.4 vs. 0.2 ± 0.1%, $p < 0.001$). dPPalg and HLI® were correlated ($r^2 = 0.73$, $p < 0.001$), mean difference was 2 ± 4%. HLI® above 13% predicted dPPalg above 13% with a sensitivity of 95% and specificity of 82% (ROC: 0.96).

CONCLUSIONS. dPP3b should be interpreted with caution due to the high variance of this index. In real conditions and during long time monitoring dPPalg and HLI® are in acceptable agreement and HLI® may help estimating continuously the hemodynamic effects of ventilation.

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1055

TRANSTHORACIC ECHOCARDIOGRAPHY: A USEFUL TOOL IN PATIENTS WITH SEPTIC SHOCK

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INTRODUCTION. Transthoracic echocardiography (TTE) is supposed not to be useful in ventilated patients (Pt). Echocardiography is usually performed transesophageally in ventilated Pt and is thought to be independent of the examiner's skills. We want to demonstrate that TTE in ventilated Pt could be learned even by medical students with reasonable results and that TTE could add useful informations for interpretation of the hemodynamic status.

OBJECTIVES. In a prospective observational study 42 consecutive patients (pt) were enrolled in a 9-bed medical intensive care unit of a university hospital. Inclusion criteria was septic shock according to actual guidelines.

METHODS. Transthoracic echocardiography (Acuson CV70, Siemens, Germany) was performed by a medical student in each subject on day 1, day 7 and survival was reported on day 28. TTE-examination was reduced to an apical 4-chamber view for interpretation of left ventricular global function and calculation of left ventricular ejection fraction (EF) with the Simpson method and to a subcostal view in order to examine the diameter of the inferior caval vein (IVC) and to rule out pericardial effusion. Each examination was digitally recorded and was interpreted by an experienced cardiologist. Every single Pt was mechanically ventilated. Cardiac output (CO) was measured with the transpulmonary thermodilutional technique (PiCCO-Catheter, Pulsion, Germany). The insertion of the PiCCO-Catheter took place due to an individual physician's decision. CRP was measured as an parameter of inflammation.

RESULTS. 42 pt, mean age 71 years ± 7.22, 27 male (64%), 23 Pt with known coronary artery disease (55%), 2 Pt with known dilated cardiomyopathy (5%). Mean APACHE II-score 35.9 ± 6.8. 22 pt died within 28 days (52%). PiCCO-Catheter was inserted in 21 Pt (50%). TTE could be successfully performed in 38 Pt (91%). The following values are expressed as mean values ± SD, Student's t test, $p < 0.05$ denotes statistic significance. EF on day 1 43.6% ± 16.2, EF on day 7 42.9% ± 15.7, $p = 0.04$. IVC on day 1 20.3 mm ± 4.5, IVC on day 7 20.2 mm ± 4.5, p = ns. CO on day 1 5.5 l/min ± 3.4, CO on day 7 4.0 l/min ± 3.4, $p = 0.05$. CRP on day 1 19.82 mg/dl ± 10.4, CRP on day 7 9.91 mg/dl±, $p < 0.0001$. Pericardial effusion in no Pt.

CONCLUSIONS. In older Pt coronary artery disease is common and EF is at the start of septic shock severely diminished. EF decreased slightly in the early course of septic shock, may be as an expression of septic cardiomyopathy. The IVC diameter did not change and may not be useful as a predictor of preload in ventilated Pt. CO decreased over time as the hyperdynamic circulation in septic shock is getting normalised. TTE adds useful hemodynamic information and should be performed in each ventilated Pt. TTE could be performed in almost each ventilated Pt and is easily learned even by medical students.

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CENTRAL VENOUS OXYGEN SATURATION ($SCVO_2$): THE PHYSIOLOGIC TRANSFUSION TRIGGER?

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INTRODUCTION. In critically ill patients $ScvO_2 < 70\%$ and central venous-to-arterial carbon dioxide difference (CO_2-gap) >5 mmHg may reflect oxygen debt (1, 2), which can often be caused by anaemia. In current guidelines the transfusion trigger is haemoglobin (Hb) < 7 g/dl, but there is no recommendation for $ScvO_2$ (3).

OBJECTIVES. The aim of this retrospective study was to evaluate the change in $ScvO_2$ before and after transfusion and to reveal whether CO_2-gap reflects it.

METHODS. Over a 6 month period Hb, $ScvO_2$, CO_2-gap and O_2-extraction ratio (O_2ER) were recorded before and after transfusion. Data are presented as median [interquartile range], for statistical analysis Wilcoxon, Mann–Whitney tests and Pearson correlation were used as appropriate.

RESULTS. Out of 128 transfusion events the $ScvO_2$ was measured in 50 cases. After transfusion Hb increased significantly: 7.7 [7.1–8.2]–9.0 [7.9–9.7] g/dl, $p < 0.001$. The median $ScvO_2$ was 71 %, therefore two groups were created: "Low" ($ScvO_2 < 71$ %, n = 27); "High" ($ScvO_2 \geq 71\%$; n = 23). Hb increased significantly in both groups ($p < 0.001$), but $ScvO_2$ and O_2ER changed only in the Low-group (62 [57–64]–70 [65–72]%, $p < 0.001$; 37 [33–51]–28 [20–35]%, $p = 0.002$, respectively) and not in the High-group (77 [75–81]-80 [76–82]%, $p = 0.659$; 20 [15–24]–20 [15–22]%, $p = 0.156$, respectively). There was also a significant difference in CO_2-gap before transfusion (Low-group: 5.5 [4.5–9.0], High-group: 4.3 [2.2–5.7] mmHg, $p = 0.017$), which showed significant correlation with O_2ER only in the Low-group ($r^2 = 0.267$, $p = 0.035$).

CONCLUSIONS. In the High-group the low Hb levels did not cause oxygen debt, as after transfusion Hb increased significantly but $ScvO_2$ did not, and O_2ER and CO_2-gap were within the normal range. Our results give further support that not only the Hb level should serve as a transfusion trigger, but measures of oxygen debt such as $ScvO_2$ and CO_2-gap should also be considered, hence unnecessary transfusions could be avoided.

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1057

CONTINUOUS AND AUTOMATIC MEASUREMENT OF RESPIRATORY VARIATIONS OF THE PULSE OXYMETER PLETHYSMOGRAM (HLI®) IS CORRELATED WITH PEEP CHANGES DURING FULLY CLOSED LOOP VENTILATION

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INTRODUCTION. IntelliVent® is a fully closed loop ventilation designed to keep the patient within target ranges of EtCO2 and SpO2. The system includes an automatic adjustment of PEEP and FiO2 following the ARDSnetwork tables [1]. If required PEEP is changed by 1 cmH_2O every 6 min with a maximal possible value set by the user or depending on an automatic and continuous calculation of the respiratory variations of the plethysmogram from an integrated pulse oxymeter (HLI®), i.e. the higher the HLI® the lower the maximal PEEP allowed by the system. The present study was designed to estimate whether changes in PEEP are reflected in HLI® changes.

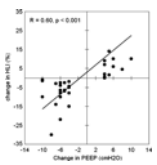
METHODS. In 17 sedated ICU patients ventilated for 120 min in fully closed loop ventilation with IntelliVent® (Hamilton Medical S1 ventilator), 34 episodes of significant changes in PEEP (≥ 4 cmH_2O) were selected and HLI® values within 5 min before and after PEEP changes were collected. Statistics were done using SigmaStats with $p < 0.05$ as significant.

RESULTS. Changes in PEEP and in HLI® are shown in the Table 1 below.

CHANGES IN PEEP AND IN HLI®

	PEEP before	PEEP after	HLI before	HLI after	P value
PEEP increase (n = 13)	8 ± 2 cmH_2O	14 ± 4 cmH_2O	10 ± 6%	23 ± 30%	$P < 0.001$
PEEP decrease (n = 21)	15 ± 3 cmH_2O	9 ± 4 cmH2O	17 ± 12%	9 ± 6%	$P < 0.001$

The correlation between change in PEEP and change in HLI® is shown on the Fig. 1.



Change in HLI versus change in PEEP

CONCLUSIONS. Based on these preliminary data changes in PEEP are reflected HLI® changes and may help estimating continuously the hemodynamic effects of ventilation.

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EPICARDIAL DISPLACEMENTS BY A 3-AXIS ACCELEROMETER SENSOR DETECT LEFT VENTRICULAR DYSFUNCTION DURING CORONARY ARTERY OCCLUSION

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INTRODUCTION. No accurate method for continuous monitoring of myocardial ischemia during cardiac surgery exists. Ischemia induces disturbances in cardiac wall motions.

OBJECTIVES. We have tested a 3 axis accelerometer sensor for detection of regional left ventricular ischemia.

METHODS. In 12 pigs a 3-axis accelerometer was sutured to the left ventricular (LV) apical region in left descending coronary artery (LAD) supply area Accelerometer x-axis measured longitudinal-, y-axis circumferential- and z-axis radial epicardial motions. Epicardial displacements were calculated from the acceleration signals and systolic displacements within 150 ms after peak R on ECG was measured. LAD was occluded for 60 s to induce regional LV dysfunction. Myocardial circumferential strain (shortening) measured by echocardiography in the LV apical anterior region was used to confirm ischemia. The ECG ST-segment in lead II was also monitored. Data are presented as mean ± SE.

RESULTS. Early systolic displacement at baseline was 11 ± 4 mm, 12 ± 2 mm and 3 ± 2 in circumferential, longitudinal and radial directions, respectively. LAD occlusion induced akinesia in circumferential (0 ± 3 mm, $P < 0.001$) and radial (0 ± 1 mm, $P = 0.01$) directions, whereas longitudinal displacement changed less to 10 ± 2 mm ($P = 0.280$). Ischemia was confirmed by echocardiography strain, showing lengthening in systole ($P < 0.001$). No significant changes were observer in the ECG ST-segment during coronary occlusion ($P = 0.341$).

CONCLUSIONS. Epicardially placed 3-axis accelerometers offer a possibility for continuous monitoring of left ventricular motions very similar to what can be periodically obtained by echocardiography. The technique detected LV dysfunction induced by coronary artery occlusion and may thereby improve continuous monitoring in cardiac surgery.

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PERIOPERATIVE TISSUE OXYGENATION(STO_2) IS RELATED TO LONG TERM SURGICAL OUTCOME

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INTRODUCTION. There is increasing evidence to suggest perioperative complications are predictive of long term survival and that reducing them may improve survival rates[1]. Goal directed therapy has been shown to reduce mortality and morbidity perioperatively, with those unable to increase oxygen delivery perioperatively having demonstrably worse outcomes. The advent of non invasive tissue oxygenation monitors using near infrared spectroscopy has allowed further study of oxygen flux during goal directed therapy.

OBJECTIVES. To observe changes in tissue oxygenation during an 8 h oxygen delivery targeted post surgical optimisation program and provide long term mortality followup of a surgical cohort of high risk patients.

METHODS. 40 patients undergoing high risk surgery and postoperative optimisation (targeting of oxygen delivery index of >600 ml/min/m^2) on the tensive care unit at a London teaching hospital were enrolled. Each patient underwent a protocolised haemodynamic optimisation protocol as per our standard unit policy for 8 h with consecutive recordings of tissue oxygenation at the thenar eminence using an inspectra 325 monitor. Additional variables relating to global and tissue perfusion were measured concurrently. Patients were followed up for survival status at 3.5 years using routinely available information held within our hospital records.

RESULTS. In hospital mortality was 17.5% (N = 7), whilst at 3.5 years this had increased to 50% (N = 20). There was no significant difference between APII scores 11 (4) versus 9.5 (4), Age 61.95 ± 16.23 versus 65.8 ± 16.35 or operation type for survivors and non-survivors at 3.5 years respectively. Significant differences between groups were found however for admission and mid optimisation protocol (4 h) HR and STO2 (see Table 1), But not for DO_2i, Lactae, or Base excess. results are shown as mean and sd or median and IQR where not normally distributed.

STO2 DIFFERENCES FOR SURVIVORS AND NON-SURVIVORS

Optimisation time point	Ovear all	Survivors	Non-Survivors	Significance (Mann–Whitney)
Admission	72.5 (29)	79.5 (29)	66.5 (29)	p = 0.009
4 h	69 (24)	75.5 (15)	58.5 (20)	p = 0.007
End of optimisation	79 (13)	79.5 (10)	77.5 (25)	p = 0.098(ns)

There were no significant differences in measured variables for 30 day mortality.

CONCLUSIONS. There appears to be a statistical and clinical difference in HR and tissue oxygenation between the long term survivors of high risk surgery who undergo monitored postoperative goal directed optimisation.

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GRANT ACKNOWLEDGMENT. Inspectra 325 monitor and probes were loaned by Hutchinson technology.

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CORRELATION OF THORACIC FLUID CONTENT DERIVED BY BIOREACTANCE TECHNOLOGY WITH PULMONARY ARTERY PRESSURE

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INTRODUCTION. Bioreactance, a new noninvasive technology for cardiac output monitoring, has shown to be accurate, precise and time responsive enough for clinical use.[1] It also allows assessing changes of thoracic fluid content(TFC).[2] However, the practical interest of the absolute value of TFC is actually limited by the absence of proven relationship with traditional hemodynamic variables.

OBJECTIVES. To optimize TFC absolute value for clinical use.

METHODS. We used the bioreactance validation database[1] to determine first the relationship between TFC and other hemodynamic variables coming from a pulmonary artery catherization (PAC). Then, we modeled PAC-related hemodynamic variables from TFC, demographic data (Age, Height, Weight, BSA, BMI) and bioreactance variables (TFC, Heart Rate, chest impedance, first time derivative of reactance, ventricle ejection time) using a multiple regression. Finally, we tested the best results on a second new data base.

RESULTS. Our data base included 32231 hemodynamic point in 119 post cardiac surgery patients. Although weak, the best relationship was found between TFC and systolic pulmonary artery pressure (PAPs: $R = 0.15$, $p < 0.001$). A multiple regression including demographic data and bioreactance variables allows to model an estimated PAPS that was acceptably related with PAPs: $R = 0.57$, $p < 0.0001$). When reported on the second data base (70 patients, 12254 points), the relationship between estimated PAPs and PAPs was still acceptably good: $R = 0.40$ $p < 0.0001$)

CONCLUSIONS. It seems possible to derive a standardized TFC that roughly correlates with PAPs. Further researches are needed to find better models and to determine if suitable for clinical use.

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GRANT ACKNOWLEDGMENT. Cheetah medical

Acute lung injury: Experimental studies: 1061–1074

1061

SIGNIFICANCE OF VEGF RECEPTORS IN THE ACUTE RESPIRATORY DISTRESS SYNDROME

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INTRODUCTION. Vascular endothelial growth factor (VEGF) is produced by many type of cells, including the alveolar ones. Its activity depends on the interaction with kinase receptors VEGF-R1 and -R2. Many studies showed that in normal lung tissue both VEGF and its receptors were immunohistochemically expressed by the alveolocytes, macrophages, epithelial and endothelial cells. Their exact role in pathogenesis of Acute Respiratory Distress Syndrome (ARDS) is not yet known.

OBJECTIVE. To investigate the expression of VEGF-A, VEGF-R1 and -R2 in the lung of ARDS patients.

METHODS. Lung specimens were obtained by bronchoscopic biopsy from 11 living ARDS patients in the early phase or by open biopsy in the proliferative phase during autopsy (50 patients). Patients with fibrosis were excluded. For the immunohistochemical study we used the following antibodies, provided by LabVision: VEGF-A—clone VG1 and polyclonal antibodies Flt-1/VEGFR1 and Flk-1/KDR/VEGFR2. A charge-coupled video camera connected to an optical microscope, was used to view the sections and to digitize images on a PC host computer, using a program of assisted quantification

RESULTS. For the specimens obtained from living ARDS patients, the early ARDS phase was characterized by both VEGF and VEGFR1 endothelial and alveolar expression: 9.5 (5.3–11.8) and 26.7 (9.5–38.6). Moving along the time frame, VEGF expression decreased in the lung tissue: 6.05 (4.4–9.2) ($p < 0.05$), while alveolocytes were still marked by VEGFR1, but to a lesser extent: 23.5 (15.7–36.2) ($p < 0.05$). For the specimens obtained from autopsy, in the proliferative phase the hyaline membranes strongly expressed VEGF, being negative for VECFR1. However, the alveolocytes in lung areas without hyaline membranes were positive for VEGFR1 but the number of alveolar cells positive for VEGFR1 was smaller. VEGFR2 marked only bronchial epithelium in both early and proliferative phase with no expression on alveolocytes or hyaline membranes.

CONCLUSIONS. Three steps in the pathogenesis of ARDS could be defined: decrease of VEGF expression in alveolocytes, damage of surfactant and hyaline membranes constitution and subsequent apoptosis of the alveolar cells in those areas. Persistence of VEGFR1 immunostain in alveolar cells outside hyaline membranes areas proved that only a part of these cells were destroyed during ARDS. The number of non-damaged alveolar cells seems to be decisive for survival.

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EVALUATION OF NONBRONCHOSCOPIC LAVAGE BY AIRWAY EXCHANGE CATHETER AS A DIAGNOSTIC INSTRUMENT FOR MONITORING CHANGES IN THE ALVEOLAR MILIEU

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INTRODUCTION. Bronchoscopic bronchoalveolar lavage (B-BAL) is today the gold standard for sampling of inflammatory markers in the distal airways. Nonbronchoscopic bronchoalveolar lavage (N-BAL) by ordinary suction catheter has been investigated as a more easily accessible method for alveolar sampling in the setting of acute respiratory distress syndrome (ARDS). The results, however, were disappointing, probably due to more proximal sampling by the N-BAL.

OBJECTIVES. To investigate wether N-BAL by a catheter with physical properties similar to those of the bronchoscope is comparable to B-BAL.

METHODS. B-BAL and N-BAL by Cook's airway exchange catheter was performed with 3 × 30 ml normal saline on opposite sides 15 min apart at nine different occasions on 5 anesthetized and intubated pigs. The volume of the recovered lavage was noted, after which the fluid was analyzed for albumin, total cell count, viability and differential cell count. Statistical analysis was performed using Wilcoxon's rank-sum test.

RESULTS. N-BAL yielded significantly higher albumin content than B-BAL (20.1 ± 8.7 vs. 11.7 ± 3.4 mg/L, $p = 0.027$). In all other measurements there were no significant differences between N-BAL and B-BAL (recovered volume 52.1 ± 19.2 vs. 67.9 ± 9.4 ml, total cell count 40.0 ± 28.4 vs. 40.7 ± 17.3 × 10^6 cells, viability 49.6 ± 20.4 vs. 62.6 ± 13.1% and percent macrophages 70.5 ± 15.5 vs. 77.1 ± 6.6%.

CONCLUSIONS. N-BAL by airway exchange catheter does not differ significantly in recovered volume and cell count when compared to B-BAL. N-BAL for alveolar sampling deserves further investigation.

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SERUM MARKERS OF COLLAGEN SYNTHESIS AND DEGRADATION IN ACUTE RESPIRATORY FAILURE WITH PROLONGED HOSPITALISATION

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INTRODUCTION. Collagens I and III are the most abundant proteins of extracellular matrix (ECM) produced by fibroblasts. During synthesis procollagen-derived propeptides are released into the circulation. Type I cross-linked collagen telopeptides (ICTP) are markers of collagen I degradation.

OBJECTIVES. We hypothesized that collagen synthesis and degradation are disturbed in acute respiratory failure.

METHODS. In the FINNALI-study we defined acute respiratory failure as need of non-invasive and/or invasive ventilatory support for more than 6 h (1). After informed consent we collected blood samples for serum procollagen propeptides I and III (PINP, PIIINP) and ICTP levels at study admission, day 2, 7 and 21. Patients with all four blood samples were included in this substudy. Multiple organ dysfunction (MOD) was defined as two or more individual organ SOFA scores of 3–4 at any day during the first week.

RESULTS. The study population comprised 68 of 958 FINNALI patients (1). The mean (SD, range) age was 60 years (15, 20–86) and the majority were male 74%. On admission the mean SAPSII score was 45 (15, 2–83). 16 patients (24%) developed MOD during the first 7 days. Over time PIIINP/PINP-ratio first increased and then decreased to baseline by day 21 while PINP/ICTP-ratio decreased and then decreased to baseline by day 21($P < 0.001$ and $P = 0.006$, respectively) (Fig. 1). There were no statistical differences in the ratios between patients with or without MOD.

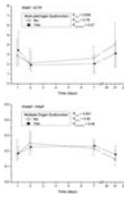

Figure 1 PIIINP/PINP and PINP/ICTP-ratios in patients with acute respiratory failure with or without MOD.

CONCLUSIONS. We found that in patients with acute respiratory failure the balance of collagen synthesis was towards degradation of type I collagen and production of collagen type III.

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ASSESSMENT OF HIGH MOBILITY GROUP BOX 1 (HMGB1) VALUES IN THE EARLY STAGE AFTER THE ONSET OF ALI/ARDS AND THE OUTCOME

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We investigated HMGB1 in the early stage after the onset of septic acute lung injury (ALI; 15 patients) [not acute respiratory distress syndrome (ARDS)]/ARDS (33 patients) during the 4-year period since April 2005 until March 2009. The overall 30-day mortality rate was 8.3%, 60-day mortality rate was 14.8%, and 90-day mortality was 18.8%. The HMGB1 value was 87.3 ± 43 ng/ml in the ARDS group, and significantly higher than the 53.8 ± 37.0 ng/ml in the ALI (not ARDS) group. The difference in HMGB1 values in the early stage between the group that died up to the by 30th day and the surviving group was not significant, but the HMGB1 values were significantly higher in the group that died until the 60th day and 90th day than in the survival group. It was concluded that differences in HMGB1 values in the early stage after the onset of ALI (not ARDS)/ARDS are useful as outcome determining factors after 30 days of onset. An inverse correlation was observed between the HMGB1 values and lung oxygenation, suggesting the possibility that HMBG1 is involved in the development of respiratory failure.

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SUPPRESSIVE EFFECTS OF SIVELESTAT SODIUM HYDRATE ON INTERLEUKIN 8 AND TNF-α PRODUCTIONS FROM LPS-STIMULATED GRANULOCYTES; ASSESSMENT BY THE WHOLE BLOOD CULTURE METHOD AND FLOW CYTOMETRY

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INTRODUCTION. Sivelestat sodium hydrate (sivelestat) is a selective polymorphonuclear leukocyte elastase (PMN-E) inhibitor and has also been shown to be effective for pulmonary disorders associated with SIRS in clinical patients. Blood levels of inflammatory cytokines have been shown to be decreased in patients treated with sivelestat. However, since patients with SIRS have already received other drugs, it remains indefinite whether or not sivelestat might suppress the production of cytokines. Moreover, it is difficult to clarify any cells releasing cytokines. In the experiment using cells isolated from the blood, intercellular mutual actions and cytokine networks were blocked and the experiment failed to faithfully reproduce the *in-vivo* condition.

OBJECTIVES. The possibility of sivelestat suppressing the production of cytokines from granulocytes and monocytes was assessed by intracellular cytokine staining using the whole blood culture method and flow cytometry to faithfully reproduce the in-vivo condition.

METHODS. Blood samples were collected from 9 healthy volunteers. A vehicle (control group), lipopolysaccharide (LPS; LPS group), or LPS + sivelestat (sivelestat group) was added to the whole blood, followed by the addition of a protein transport inhibitor in each group. After incubation, they were subjected to staining of the cytokines retained in the cells by the addition of an anti-interleukin 8 (IL-8) or anti-tumor necrosis factor α (TNF-α) antibody and analysis by flow cytometry. The data were analyzed by the Kolmogorov–Smirnov test. Values obtained [D/s(n)] result from the comparison of the fluorescence histograms of each sample with a control one.

RESULTS. Addition of sivelestat at low concentrations (1 and 10 μg/ml) significantly ($P < 0.01$) suppressed the production of IL-8 from granulocytes induced by a low concentration (1 ng/ml) of LPS. On the other hand, the granulocytic production of TNF-α induced by a high concentration of LPS (10 ng/ml) was significantly ($P < 0.01$) suppressed by treatment with sivelestat at high concentrations (10 and 100 μg/ml). With regard to the monocytic production of TNF-α and IL-8 induced by LPS, there was no significant suppression of either TNF-α or IL-8 production by sivelestat.

CONCLUSIONS. Sivelestat, a neutrophil elastase inhibitor, suppressed granulocytic production of IL-8 and TNF-α, suggesting the potential usefulness of sivelestat for the treatment of various morbid conditions involving IL-8 and TNF-α in their onset.

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PROGNOSTIC VALUE OF SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR (SUPAR) AND PLASMINOGEN ACTIVATOR INHIBITOR 1 (PAI-1) LEVELS IN CRITICALLY ILL PATIENTS WITH RESPIRATORY FAILURE

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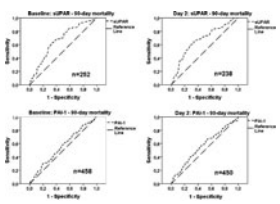
INTRODUCTION. Coagulation, fibrinolysis and extravascular fibrin deposition are the hallmarks of the pathogenesis of Acute Lung Injury (ALI). PAI-1 has a central role in antagonizing fibrinolysis by decreasing the plasminogen turnover to plasmin. PAI-1 has been suggested as a clinical severity marker of ALI. In previous studies it was associated with higher mortality and morbidity in the critically ill. UPAR is a cell surface receptor activating the serine protease uPA. Increased expression of UPAR is found in various stages, including inflammation, tissue remodelling and malignancies, indicating poor prognosis. PAI-1 antagonizes the proteolytic activities of uPA and plasmin.

OBJECTIVES. We sought to evaluate the prognostic value of sUPAR and PAI-1 for 90-day mortality of patients with Acute Respiratory Failure (ARF).

PATIENTS AND METHODS. The FINNALI-study patients needed invasive or non-invasive ventilation for more than 6 h (1). Blood samples were collected from patients at baseline and on day 2 after baseline. Healthy volunteers were also analyzed. Sera were frozen at −80°C until analyses. Concentrations of sUPAR and PAI-1 in blood serum were measured by enzyme linked immunosorbent assay (ELISA). Data are presented as median (IQR). The prognostic value of sUPAR and PAI-1 for 90-day mortality was determined with ROC analysis.

RESULTS. In the critically ill, sUPAR and PAI-1 were 12.7 (10.7–14.7) ng/ml and 2.33 (1.33–3.13) ng/ml vs. 0.6 (0.5–11.0, $n = 10$) ng/ml and 0.32 (0.31–0.43, $n = 9$) ng/ml in healthy volunteers, respectively. At baseline and day 2, the AUC:s for sUPAR were: 0.667 (95% CI 0.594–0.740, $p < 0.0001$, cut-off 13.3 ng/ml, sensitivity 0.50, specificity 0.73) and 0.670 (95% CI 0.591–0.748, $p < 0.0001$, 14.78 ng/ml, 0.50, 0.78). The corresponding AUC:s for baseline and day 2 PAI-1 were 0.556 (0.496–0.615, $p = 0.030$, cut-off 2.83 ng/ml, sensitivity 0.50, specificity 0.56) and 0.565 (0.503–0.627, $p = 0.036$, 2.19 ng/ml, 0.50, 0.60).



ROC analysis

CONCLUSIONS. SUPAR and PAI-1 concentrations are markedly increased in ARF. High serum concentrations of sUPAR at baseline and on day 2 have only moderate predictive value for 90 day mortality in patients with ARF. SUPAR was superior to PAI-1.

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SYSTEMIC ANTITHROMBIN MITIGATES VENTILATOR-INDUCED PULMONARY COAGULOPATHY

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INTRODUCTION. We have previously shown that injurious mechanical ventilation (MV) exaggerates pulmonary coagulopathy in *Streptococcus pneumoniae* pneumonia (1).

OBJECTIVES. We hypothesized that administration of plasma-derived human antithrombin (AT), a natural inhibitor of coagulation could diminish ventilator-induced pulmonary coagulopathy.

METHODS. *Streptococcus pneumoniae* pneumonia was induced in Male Sprague-Dawley rats. 48 h later the animals were connected to a ventilator with an injurious ventilation strategy (V_T 12 ml/kg; 0 PEEP) for 3 h with or without a systemic administration of plasma-derived human AT (250 IE/kg). Broncho alveolar lavage fluid (BALf) was collected and analyzed for markers of lung injury and coagulopathy.

RESULTS. Lung injury between the 2 groups was similar as measured by BALf protein levels no AT; 0.35 ± 0.1 mg/ml and with AT; 0.35 ± 0.07 mg/ml or total cell count no AT (1.7 ± 0.8 cells 10^6/ml) and treated with AT (1.9 ± 0.8 cells 10^6/ml). Systemic administration of plasma-derived human AT increased pulmonary levels of AT and reduced the level of TATc (fig). Fibrinolysis as assessed by plasminogen activator inhibitor-1 was not different between the 2 groups.

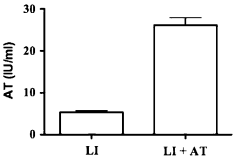

Figure 1

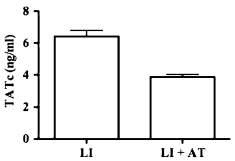

Figure 2

CONCLUSIONS. Administration of plasma-derived human AT in a *S. pneumoniae* pneumonia model mitigates ventilator-induced pulmonary coagulopathy, but not lung injury.

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GRANT ACKNOWLEDGMENT. CIHR

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TRANSCRIPTIONAL CHARACTERIZATION OF ACUTE LUNG INJURY IN MICE

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INTRODUCTION. Acute lung injury is a common disease in intensive care, associated to various septic or inflammatory diseases. Inflammation is part of the defense mechanisms of innate immunity, occurring after tissue injury.

OBJECTIVES. The aim of the project was to decipher the transcriptional changes occurring after the onset of an inflammatory injury by intravenous injection of oleic acid.

METHODS. Experimental study of the lung transcriptome after oleic acid injection. Thirty-six C57Bl/6 J mice, aged of 7 weeks, were sacrificed at 1H, 1H30, 3H, 4H, 18H and 24H after physiological serum or oleic acid injection (20 µL) in the caudal vein. Left and right lung were separated for mRNA extraction and pathological examination. Labelled cDNA were hybridized on cDNA nylon microarray (TAGC, Marseilles, France) and raw data were extracted from scanned images with BZScan2 software. Raw data were normalized with the quantile method, and supervised analysis was conducted with Significance Analysis of Microarray algorithm within the R statistical suite and Bioconductor libraries.

RESULTS. After the administration of oleic acid, the mice were tachypneic and prostrated. All survived during the 24 first hours. The pathological analysis of lung tissue revealed an early infiltration of the lung tissue by polynuclear cells, as well as a pulmonary edema. These alterations were not observed after 4H. The time course analysis of transcriptional lung data identified a thousand genes which expression is modulated after injury. Hierarchical clustering identified 3 major groups of genes. The first one (365 genes) is composed of genes transiently up-regulated between 1H and 3H after oleic acid injection. Th second group (366 genes) is composed of genes expressed between 1H30 and 4H. The third group (366 genes) is composed of genes expressed at the later time points (18H–24H). The functional annotation linked these signatures with keywords related to pro-inflammatory response, vascular endothelium modification and lipid metabolism, respectively. RT-PCR analysis of pro- (TNF, IL6) and anti-inflammatory (IL4, IL10) markers related the pro-inflammatory phase to the earlier time points (1H-1H30) and the anti-inflammatory phase to the late points (after 4H).

CONCLUSIONS. Oleic acid injection in mice induced a transient acute lung injury. This is confirmed by clinical, pathological and transcriptional modifications. The modulation of gene expression after the oleic acid injection revealed an early pro-inflammatory response, followed by an anti-inflammatory response and lipid metabolism modificiations. This model could now be used to describe the specific modulation occuring during pulmonary infection and critical injuries like acute respiratory distress syndrome.

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EFFECTS OF THE AMOUNT OF PARTIAL VENTILATORY SUPPORT DURING EXPERIMENTAL ACUTE LUNG INJURY IN RATS

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INTRODUCTION. Ventilator associated lung injury (VALI) is influenced by tidal volumes, airway pressure and cyclic opening of alveoli during mechanical ventilation. Preserved spontaneous breathing during partial ventilatory support may be protective, but it is not known whether the transpulmonary pressure generated by spontaneous breathing has the same effect on VALI as if generated by the ventilator.

OBJECTIVES. To determine whether hemodynamics, respirtory function and VALI are influenced by the amount of support provided by pressure support ventilation.

METHODS. After approval from the institutional animal care committee, acute lung injury was induced in 50 anesthetized SD rats by acid aspiration. Ten animals each were then ventilated with positive end-expiratory pressure 5 cmH2O in pressure control (PC), pressure-regulated assist control (AC) or pressure support mode with 100% (PS100), 60% (PS60) or 20% (PS20) pressure support of initial distending pressure needed to maintain tidal volume. PC animals were paralyzed. After 4 h animals were killed and VALI determined.

RESULTS. There were no differences in baseline characteristics. Acute lung injury was characterized by a decrease of the P/F ratio from 447 ± 75 to 235 ± 90 mmHg and of the dynamic compliance from 0.5 ± 0.2 to 0.28 ± 0.1 ml/cmH_2O. Table 1 depicts the measurements after 4 h of ventilation.

PARAMETERS AFTER 4 H OF VENTILATION

	PC	AC	PS100	PS60	PS20
Paw [cmH2O]	26 ± 7	25 ± 7	19 ± 7	15 ± 5	9 ± 3
VT/kg [ml]	8.4 ± 1.6	9.4 ± 2.0	10.7 ± 6.1	10.6 ± 4.2	8.6 ± 1.9
VE [ml/min]	318 ± 70	411 ± 117	320 ± 115	366 ± 122	330 ± 129
Cdyn [ml/cmH_2O]	0.4 ± 0.2	0.5 ± 0.2	0.9 ± 0.5	1.1 ± 0.6	2.1 ± 1.6
P/F [mmHg]	98 ± 50	118 ± 108	166 ± 126	106 ± 67	83 ± 64
Ptranspul [cmH_2O]	25 ± 7	27 ± 8	24 ± 9	23 ± 6	23 ± 9
MAP [mmHg]	47 ± 39	74 ± 44	80 ± 16	78 ± 26	72 ± 35
Wet-to-dry ratio	16 ± 17	13 ± 7	8 ± 5	8 ± 5	17 ± 17

CONCLUSIONS. Compared to controlled ventilation, preserved spontaneous breathing activity improved hemodynamic stability, respiratory function and lung edema clearance. The reduction in pressure support did not lead to reduced tidal volume, but transpulmonary pressure was preserved by muscular activity of the chest wall. No difference was observed between full or 60% of pressure support, but further reduction in pressure support resulted in increased wet-dry ratio.

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GRANT ACKNOWLEDGMENT. Supported by Dalhousie University, Halifax.

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THE EFFECT OF METABOLIC ACIDOSIS ON ENZYMATIC AND NON-ENZYMATIC NITRIC OXIDE PRODUCTION IN HYPOXIC AND HYPEROXIC LUNG REGIONS

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INTRODUCTION. In the severely ill intensive care patients metabolic acidosis and hypoxia often co-exist. Conflicting findings regarding the effect of acidosis on endogenous nitric oxide (NO) production and hypoxic pulmonary vasoconstriction (HPV) have been reported.

OBJECTIVES. We studied the effects of metabolic acidosis on enzymatic and non-enzymatic NO-production in hypoxic and hyperoxic lung regions in a pig model.

METHODS. Eighteen healthy anesthetized pigs were separately ventilated with hypoxic gas to the left lower lobe (LLL) and hyperoxic gas to the rest of the lung. Six pigs received HCl infusion (HCl group), six pigs received N^w-nitro-L-arginine methyl ester (L-NAME) and HCl (L-NAME + HCl group) and six pigs received buffered Ringer's solution (Control group). NO concentration in exhaled air (ENO), NO synthase (NOS) activity in lung tissue, and regional pulmonary blood flow were measured.

RESULTS. Metabolic acidosis, induced by infusion of HCl, decreased the relative perfusion to the hypoxic LLL (Q_{LLL}/Q_T) from 7 (±3) to 3 (±1)% in the HCl group ($p < 0.01$), and from 4 (±1) to 1 (±1)% in the L-NAME + HCl group ($p < 0.05$), without any measurable significant changes in ENO from hypoxic or hyperoxic lung regions There were no significant differences between the HCl and Control groups for Ca^{2+}-dependent or Ca^{2+}-independent NOS activity in hypoxic or hyperoxic lung regions.

CONCLUSIONS. Metabolic acidosis augmented the hypoxic pulmonary vasoconstriction, without any changes in pulmonary enzymatic or non-enzymatic NO-production. When acidosis was induced during ongoing NOS-blockade, the perfusion of hypoxic lung regions was almost abolished, indicating acidosis-induced pulmonary vasoconstriction was not NO dependent.

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BIOMARKERS OF ACUTE LUNG INJURY IN FRESH AND "WASTE" BLOOD SPECIMENS

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INTRODUCTION. Assessing and monitoring biomarkers in acute lung injury (ALI) may improve knowledge of its pathogenesis, early recognition, and management and predict remote organ injury and multiple organ failure.

OBJECTIVES. Early consents for research are difficult to obtain in patients with or at risk of ALI because of the emotional burden of the severity and sudden onset of the disease. However, study samples may be obtained from left-over clinical blood draws, which are readily available if processed adequately. The aim of this study was to compare fresh and "waste" blood samples prospectively in a series of consecutive critically ill patients. The hypothesis is that "waste" blood samples if appropriately processed provides accurate and reliable results comparable to the gold-standard, which is immediate collection and processing of fresh blood samples.

METHODS. Prospective study comparing biomarkers of epithelial injury (sRAGE) and inflammation (20 different cytokines/chemokines) in critically ill patients measured on fresh blood or waste blood, kept at 4 degrees Celsius for 24 h. An automated system performed a daily screening of adults in the ICU with an increased risk for ALI (lung injury prediction score, LIPS) within 12 h of admission and/or on recognition of the diagnosis of ALI, using the American-European Consensus Conference criteria. Risks factors for ALI include pneumonia, sepsis, pancreatitis, shock, aspiration, high risk surgery and high risk trauma. IRB approved the protocol and written consent was obtained from patients or their surrogates. Statistical measurements were performed using the Bland-Altman analysis for correlation between fresh and waste blood sample data.

RESULTS. Between May and December 2009, 30 patients were enrolled. One patient was excluded due to lack of sample. Samples were obtained either at one time point ($N = 25$) or two, on consecutive days ($N = 13$). Female/male patient ratio was 12/17. Seven of the 29 patients had ALI. Twenty two patients had risk for ALI with a median LIPS score of 4 (IQR 3.5–4.5). Sepsis was the most common risk factor, present in 23 patients. In-hospital mortality was 28% (8/29). The Bland-Altman plot (mean bias ± SE, limits of agreement) showed good correlation for IL-1ra (-9 ± 14.3 pg/ml, -38.3 to 20.4 pg/ml), IL-6 (0.9 ± 2.9 pg/ml, -5 to 6.8 pg/ml), IL-8 (-0.3 ± 0.3 pg/ml, -0.9 to 0.3 pg/ml), IL-12 (p40) (-0.2 ± 0.3 pg/ml, -0.7 to 0.4 pg/ml), MCP-1(-0.2 ± 2 pg/ml, -4.2 to 3.9 pg/ml) and sRAGE (-24 ± 53 pg/ml, -130 to 83 pg/ml) between fresh blood and "waste" blood samples.

CONCLUSIONS. In patients with ALI, properly stored blood, drawn for clinical purposes, can be processed within 24 h for research purposes. However, the stability of each biomarker of interest needs to be individually validated before using stored blood

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GRANT ACKNOWLEDGMENT. Small Grant Award of the Department of Medicine, Mayo Clinic, Rochester.

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SURFACTANT REPLACEMENT RESTORES LUNG FUNCTION IN A TWO HIT MODEL OF ACUTE LUNG INJURY

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INTRODUCTION. Pulmonary surfactant inactivation following acute lung injury might promote alveolar derecruitment and reduce the airspace available for ventilation, making the lung more prone to ventilation-induced lung injury (VILI).

OBJECTIVES. Our aim was to test the potential for a protective effect of exogenous surfactant treatment in a model of acid aspiration and VILI.

METHODS. 17 male C57/BL6 mice were anesthetized, mechanically ventilated (Vt 15 ml/kg; RR 130/min; PEEP 2 ± 0.2 cmH_2O; FiO_2 0.5) and immediately subjected to intrabronchial (right) instillation of 1.5 ml/kg HCl 0.1 M. Mechanical ventilation went on for 420 min. 180 min after the acid instillation, 9 mice were treated with exogenous surfactant (80 mg of phospholipids/ml) given as bolus of 1 ml/kg in the right bronchus (*surf* group). We measured oxygenation, lung compliance (measured every 60 min throughout the experiment), macrophage inflammatory protein (MIP) 2 in broncho-alveolar lavage (BAL) fluid.

RESULTS. PaO_2 at the end of the experiment was significantly higher in the *surf* than in control group (383 ± 163 vs. 198 ± 104 mmHg, $p < 0.05$). Although surfactant bolus caused a reduction in lung compliance measured 10 and 60 min after treatment, in the *surf* group compliance restored to $98 \pm 7\%$ of the post injury level, while it decreased in control group to $88 \pm 8\%$ ($p < 0.05$). There were no differences between groups in the dosage of MIP-2 in BAL neither in right or left lung.

CONCLUSIONS. Exogenous surfactant treatment improved lung function in a murine model of two hit lung injury.

GRANT ACKNOWLEDGMENT. The present study was partially supported by an unrestricted grant from Chiesi Farmaceutici, Parma, Italy

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ACTIVATING TRANSCRIPTION FACTOR 3 CONFERS PROTECTION AGAINST VENTILATOR INDUCED LUNG INJURY

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INTRODUCTION. Ventilator induced lung injury significantly contributes to the mortality in patients with acute respiratory distress syndrome, the most severe form of acute lung injury. Understanding the molecular basis for response to cyclic stretch and its derangement during high volume ventilation is of high priority.

OBJECTIVES. To identify specific molecular regulators involved in the development of ventilator induced lung injury.

METHODS. We undertook a comparative examination of cis-regulatory sequences involved in the coordinated expression of cyclic stretch responsive genes using microarray analysis. Analysis of stretched vs. non-stretched cells identified significant enrichment for genes containing binding sites for the transcription factor ATF3 (Activating Transcription Factor 3). To determine the role of ATF3 in vivo, we compared the response of ATF3 gene deficient mice to wild type litter mates in an in vivo model of ventilator induced lung injury.

RESULTS. ATF3 deficiency results in increased sensitivity to mechanical ventilation alone or in conjunction with inhaled lipopolysaccharide (10 mg/kg) as determined by assessment of lung and bronchoalveolar lavage cell infiltration and pro-inflammatory mediator release, pulmonary edema and indices of tissue injury. The expression of genes containing an ATF3 cis-regulatory region was significantly altered in gene deficient animals. ATF3 protein expression and nuclear translocation is increased after mechanical ventilation.

CONCLUSIONS. ATF3 deficiency confers increased sensitivity to mechanical ventilation alone or in combination with inhaled endotoxin. In our model, ATF3 acts to "counterbalance" cyclic stretch and high volume-induced inflammation, limiting its potential to cause additional lung injury and consequently protecting animals from injurious cyclic stretch.

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ALVEOLAR MACROPHAGES DEPLETION IMPROVES OXYGENATION IN EXPERIMENTAL ACID INDUCED LUNG INJURY

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INTRODUCTION. Alveolar macrophages play an important function in the inflammatory response during Acute Lung Injury. It is well known that, beyond a phagocytic activity, they can release different proinflammatory cytokines.

OBJECTIVES. Our aim was to evaluate the role of the alveolar macrophages in a murine model of ALI, by selective depletion of this type of cells from the air space achieved by clodronate administration.

METHODS. Mice were treated (it) with 100 µl of clodronate (*Clo*)- or PBS (*PBS*)-liposomes. After 24 h mice were anesthetized and ventilated (Vt 8–10 ml/kg, RR 140 min^{-1}, FiO_2 0.21); in order to induce lung injury 2 ml/kg of HCl (0.1 M) or air bolus (sham group) was instilled in the right bronchus. Mice were ventilated for 10 min, and extubated after awakening. 24 h after injury, animals were sacrificed and Broncho-Alveolar Lavage (BAL) and blood gas analysis ($FiO_2 = 0.21$) were performed.

RESULTS. 24 h after lung injury animals with alveolar macrophages depletion, showed a better oxygenation versus PBS-treated group. However, recruitment of neutrophils in BAL was not statistically different between clo_HCl and PBS_HCl group.

TABLE

	Clo_HCl (n = 10)	PBS_HCl (n = 9)	Clo_Sham (6)	PBS_Sham (6)
PaO2 (mmHg)	93 ± 4*	75 ± 5	146 ± 9	112 ± 5
PMN in BAL (× 103)	239 ± 39	342 ± 64	311 ± 39	123 ± 59
Peripheral leukocytes (/mm3)	680 ± 91	547 ± 70	572 ± 119	662 ± 112

Results expressed as mean ± SEM

* $p < 0.05$ versus *PBS_HCl.*

CONCLUSIONS. In a murine model of ALI we showed that a reduced number of alveolar macrophages (almost 80%) leads to a better oxygenation, although no difference in recruitment of neutrophils in BAL was observed.

ECMO for ARDS: 1075–1088

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OSELTAMIVIR CARBOXYLATE ACCUMULATION IN PATIENTS TREATED BY HAEMODIAFILTRATION AND EXTRACORPOREAL MEMBRANE OXYGENATION

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INTRODUCTION. The recommended dose of Oseltamivir (OT), neuraminidase inhibitor licensed for treatment of influenza A and B, is 75 mg twice a day during 5 days. This dose can be increased to 150 mg twice a day during 10 days in complicated infections but has to be reduced to 75 mg three-time a week in patient undergoing a curse of dialysis. Loss of antibacterial's concentration has already been reported in patients treated by Extracorporeal Membrane Oxygenation (ECMO), a rescue therapy for critically ill patients with medically refractory acute cardiopulmonary failure.

OBJECTIVES. To describe Oseltamivir carboxylate, the active form of OT, pharmacokinetics of 5 patients treated with various dosage of OT (75 mg or 150 mg bid), ECMO and haemodiafiltration or not.

METHODS. 3 patients received 150 mg bid, 2 of them underwent an haemodiafiltration. 2 patients received 75 mg bid one presented a moderate renal failure and none of them underwent an haemodiafiltration. In order to check OC blood levels, blood samples were taken before oseltamivir administration and 1, 2, 3, 4, 5, 6, 8, 10 and 12 h after. Oseltamivir carboxylate was quantified using an LC-MS/MS method.

RESULTS. High levels of OC were found in patients treated by 150 mg of OT bid. OC levels ranged from 2,507 to 4,551 ng/mL in these patients. Concentrations of OC were five- to tenfold higher than concentrations reported in healthy volunteers. Lesser levels were found in patients treated by 75 mg of OT bid. Nevertheless, the patient with the moderate renal failure seemed to accumulate OC (levels ranged from 906 to 1470 ng/mL) whereas concentrations reported in the patient with a normal renal clearance were below (152–349 ng/mL).

CONCLUSIONS. ECMO seemed not to have any influence on OC concentrations while renal insufficiency seemed to be the parameter leading to OC accumulation. As IC50 was very low and reached even with usual dosage, increasing OT dose to 150 mg bid appeared to be unnecessary.

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DAILY NURSING IN PATIENTS DURING VENOUS–VENOUS ECMO: OBSERVATIONAL STUDY

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INTRODUCTION. Daily nursing in critical care patients may alter vital parameters.

OBJECTIVES. Aim of our study was to evaluate the effect of nursing care on patients undergoing venous–venous ECMO for acute respiratory distress syndrome (ARDS).

METHODS. we recorded physiological and ECMO parameters (heart rate, arterial blood pressure, mixed venous saturation (SvO_2), arterial oxygen saturation (SpO_2), body temperature and extracorporeal blood flow (BF)) before and during daily nursing in 5 patients undergoing vv-ECMO for several days (each patient was followed on average for 4.6 days, 23 cases in total). Arterial blood gases were also collected before and after nursing care. Daily nursing was performed following defined steps (sponge bath, oral hygiene, change position of endotracheal tube, elevation with scooping stretcher for sheets replacement and back hygiene, dressing replacement) in agreement with a standard protocol in use in our department.

EVENTS OBSERVED DURING DAILY NURSING

Events	Numbers of events	Baseline mean ± SD (min-max)	Peak value mean ± SD (min-max)	Statistical significance
Hypertension (mmHg)	29	122 ± 20 (82–159)	162 ± 18 (128–191)	$p < 0.01$
Tachycardia (beats/min)	17	100 ± 15 (60–120)	117 ± 16 (84–140)	$p < 0.01$
↓ SvO2 (%)	19	83 ± 5 (74–92)	76 ± 9 (61–87)	$p < 0.01$
↓ SpO2 (%)	31	97 ± 3 (89–100)	88 ± 9 (68–97)	$p < 0.01$
↓ BF (L/min)	17	3.2 ± 1.06 (2–5.1)	2.4 ± 1.4 (0.44–4.7)	$p = 0.01$

RESULTS. (Expressed as mean ± standard deviation). All patients were affected by ARDS H1N1-related. Patients were sedated with propofol (182 ± 68 mg/h) or midazolam (7.9 ± 1.8 mg/h) plus an opioid drug (fentanyl 175 ± 45 mcg/h or remifentanil 0.2 ± 0.01 mcg/kg/min or sufentanil 0.32 ± 0.09 mcg/kg/min). Ramsey score before nursing was 5.4 ± 0.9. In 11 cases patients were paralysed. In Table 1 we summarized the adverse events observed during nursing care, divided into hypertensive or tachycardic episodes, blood oxygen desaturation, reduction in SvO_2 or reduction in BF. Forty-nine sedative bolus were administered during nursing (mean request for each patient: 2.1 ± 1.9), always after an episode of hypertension or tachycardia (most frequently during elevation with scooping stretcher and changing position of endotracheal tube). Although in 13 cases preventive bolus of sedation were administered before nursing, in 8 of those cases (61%), additional bolus were required. We found an inverse correlation between BF and the increase in heart rate, drop in arterial saturation and SvO2. Despite active warming, we observed a drop of 0.31 ± 0.15°C ($p < 0.01$) in body temperature.

CONCLUSIONS. Nursing care may have a significant impact on physiologic parameters of patients during vv-ECMO. Tachycardia, hypertension and reduction in oxygenation were commonly recorded and were not prevented by pre-nursing bolus of sedation but were attenuated in patients with higher BF.

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EFFECT OF PRONE POSITION ON INTRAABDOMINAL PRESSURE AND RENAL FUNCTION

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INTRODUCTION. Prone position has been used in cases of ARDS with refractory hypoxemia but some physiological effects are still unknown. Prone position could increase intraabdominal pressure (IAP) and could lead to acute renal failure (ARF). Acute kidney injury in ICU is associated with increased mortality.

OBJECTIVES. The aim of this study was to determine whether prone position could increase intraabdominal pressure and possibly promote ARF.

METHODS. We studied all adult ARDS patients who were ventilated using the protective strategy defined by ARDS Network criteria and who needed prone position to improve oxygenation. We collected respiratory data (ventilator parameters and gas exchange) and hemodynamic variables (heart rate, systolic, diastolic and mean arterial pressure). IAP was measured using the Abdo-Pressure™ bladder transducer following World Society of Acute Compartment Syndrome recommendations. Abdominal perfusion pressure was calculated as mean arterial pressure minus IAP. Main renal parameters were: filtration gradient (FG), creatinine clearance, fractional excretion of sodium (FENa) and urea (FEUrea). Patients were classified according to RIFLE score after each manoeuvre. All data were recorded in prone and in supine position at least once per day.

RESULTS. The study included 18 patients (14 male) admitted to a medical–surgical ICU over a one-year period. Their mean age was 47.3 ± 17.8 and length of ICU stay was 23 ± 18 days. All 18 patients had primary ARDS and 9 had received nephrotoxics. ICU mortality reached 50%. We recorded at least 3 manoeuvres per patient (A, B, C). Prone positioning improved $PaFiO_2$ ratio from 101.5 ± 5 to 150 ± 72 ($p = 0.027$). IAP showed a small increase from 6.1 ± 2.7 to 8.9 ± 2.9 mmHg (A; $p = 0.004$), from 8.4 ± 3.4 to 11.2 ± 3.7 mmHg (B; $p = 0.038$) and from 7.6 ± 1.3 to 9.9 ± 0.8 mmHg (C; $p = 0.001$). There were no statistically significant changes in hemodynamic parameters or abdominal perfusion pressure. Renal function parameters (FG, creatinine clearance, FENa and FEUrea) showed no modification after each prone positioning. In contrast, when patients were classified according to RIFLE score, we observed a trend towards worsening, though this was not statistically significant.

CONCLUSIONS. Prone positioning improved arterial oxygenation in primary ARDS patients and was associated with an increase in IAP. However, creatinine clearance and glomerular filtration remained unchanged.

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DIFFERENT MANAGEMENT STRATEGY OF PERCUTANEOUS EXTRACORPOREAL LIFE SUPPORT SYSTEM FOR REFRACTORY CARDIAC ARREST AND SHOCK; MEDICAL VERSUS SURGICAL PATIENTS

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INTRODUCTION. Percutaneous Extracorporeal life support system (p-ECLS) including ECMO becomes widely used in medical and surgical emergent situation, such as refractory cardiogenic shock, cardiac arrest and acute respiratory failure. Patients requires highly specialized intensive care and monitoring system.

OBJECTIVES. We reviewed our ECLS experience and tried to analyze the clinical outcomes, factors for survival and frequently faced problems during management for improving weaning and survival rate (medical vs. surgical patients).

METHODS. From January 2005 to December 2008, a total of 110 patients (mean age 64.5 ± 7.5, 71 male and 39 female) inevitably underwent p-ECLS in ICU. 48 (43.6%) patients were post-operative state of cardiac or vascular surgery(Group A; surgery group) and the other 62 (56.4%) patients equipped the p-ECLS because of sudden prolonged cardiac arrest, refractory cardiogenic shock, acute respiratory failure and other causes(Group B; medical group). 18 (16.4%) patients underwent veno–veno type p-ECLS. Veno-arterial p-ECLS was performed 92 (83.6%) patients. 7 (6.4%) patients underwent the p-ECLS more than 2 times during same hospitalized period. Combined Continuous Renal Replacement Therapy (CRRT), modified ultra-filteration, transesophageal or transthoracic echocardiography and Intra-aortic balloon pump (IABP) were actively used and specialized team approach was performed in every case. Mechanical ventilator was applied as minimal as possible and lung protective manner.

RESULTS. Mean ICU and hospital stay time of survivors was 16 ± 8.5 day and 75 ± 34.2 days, respectively. p-ECLS weaning rate and survival rate were 55.4%(61 pts) and 31.8%(35 pts), respectively. Mean p-ECLS time was 5.5 ± 4.3 days (1–28 days). There were no statistical differences between survivors and non-survivors in terms of insertion place (Angio room vs. ICU), preoperative diagnosis, gender. Survival rate was higher in medical disease group (Group B). Multivariate analysis showed the risk factors for mortality were different between the two groups in term of anticoagulation.

CONCLUSIONS. p-ECLS showed improved survival rate than conventional CPCR in our study. However, different management strategy in term of ACT control should be applied for improving clinical outcomes. Even though 31.8% of patients were survived, their hospital stay time was extremely long and quite a number of patients were dead even if they weaned from p-ECLS because of other morbidity. Thorough care should be warranted in ICU.

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LOW FLOW EXTRACORPOREAL MEMBRANE OXYGENATION (LF-ECMO) FOR ACUTE HYPOXEMIC RESPIRATORY FAILURE (AHRF): 10 YEARS CASE–SERIES ANALYSIS

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INTRODUCTION. in spite of the huge efforts spent over the last years, conventional treatment of acute hypoxemic respiratory failure (AHRF) is often inadequate and alternative procedures must be instituted. ICUs skillful in extracorporeal membrane oxygenation (ECMO), as recently shown [1], may improve survival of these patients. Since 1989 we developed a treatment algorithm for AHRF which encomprises: (1) low flow venous-venous ECMO (LF-ECMO) consisting in a relatively low initial blood flow (BF, 2–2.5 L/min) to maximize extracorporeal CO_2 removal while providing partial oxygenation (if needed, BF can be increased up to 4.5–5 l/min to keep arterial pO2 above 45 mmHg); (2) femoral-femoral percutaneous cannulation with 21–25 Fr cannulas to allow free movements of the neck and increase patient's tolerance; (3) early institution of spontaneous assisted ventilation (SB) and weaning from sedation and mechanical ventilation (MV) while on ECMO.

OBJECTIVES. to review our last 10 years LF-ECMO activity.

METHODS. study period was January 2000–2010. LF-ECMO entry criteria were: potentially reversible acute hypoxemic respiratory failure, LIS $\geq$3, no evidence of intracranial bleeding and no absolute contra-indications to heparinization. ECMO was performed with different type of heparin coated hollow-fiber artificial lungs.

RESULTS. we treated 31 patients (mean $\pm$ SD, 37 $\pm$ 18.5 years old, 68% males, BMI 27 $\pm$ 6, SOFA 7.5 $\pm$ 3, OI 38 $\pm$ 14). 48% of these patients were placed on ECMO at other hospitals and transported to our ICU by a dedicated ECMO team. Ventilation days before ECMO were 12 $\pm$ 16 (range 1–69). Before ECMO Vt/kg was 6 $\pm$ 1.5 and RR was 33 $\pm$ 12: after ECMO beginning Vt/kg was unchanged while RR decreased to 11 $\pm$ 4 ($p < 0.01$). ECMO was set at BF 2.5 $\pm$ 1 L/min, GF 3.3 $\pm$ 1.5 L/min, FiO2 0.98 $\pm$ 0.1. ECMO was performed for 26 $\pm$ 28 days (range 2–139). Switch to SB occurred after 7.5 $\pm$ 6 days while ICU length of stay was 41 $\pm$ 36 days (range 2–154). No differences on outcome were found for all the investigated variables. 18 patients (58%) survived the ICU: in this group 14 (77.2%) were weaned from ECMO while on SB. Before decannulation, clinical data were: FiO_2 0.48 $\pm$ 0.1, P/F 232 $\pm$ 54, Vt/Kg 7.3 $\pm$ 2.6, mean airway pressure 17 $\pm$ 4 cmH_2O, PEEP 12 $\pm$ 4 cmH_2O. OI was 8 $\pm$ 3, while SOFA was 3.5 $\pm$ 1.8.

CONCLUSIONS. Use of venous-venous femoral LF-ECMO approach allows effective application of protective ventilatory strategy, adequate gas exchange, early institution of SB and good patient's tolerance while still on ECMO. Outcome was comparable to that reported by other institutions employing a more conventional approach (maximized BF 4–5 l/min, bigger drainage cannulas).

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RESPIRATORY EFFECTS AND SAFETY OF AN INTERMITTENT STANDING POSITION DURING MECHANICAL VENTILATION

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INTRODUCTION. Ventilating patients with acute lung injury (ALI) in supine position potentially leads to an impaired pulmonary gas exchange. Prone position (PP) is an attractive means to improve ventilation-perfusion (V/Q) ratio [1,2] but has several contraindications and showed no improvement in survival so far [3]. Another therapeutical option is an upright position, which is easy to perform and has theoretical advantages over PP: the upward shift of the abdominal compartment is less pronounced, thus increasing thoracoabdominal compliance [2].[4] However, to date regimes of an upright position did not tilt patients more than 45° [4].[4]

OBJECTIVES. We hypothesised that a 60° standing position (SP) during mechanical ventilation may improve respiratory function. Furthermore, we aimed to determine the feasibility of a SP for 2 h during mechanical ventilation.

METHODS. We studied 30 adult patients, receiving mechanical ventilation for more than 48 h in the intensive care unit of an university hospital. After recording baseline data, patients were placed in a 60° SP with the body entirely straight. Further data sets were recorded during 2 h in SP, and after patients position was readjusted to supine position.

RESULTS. Functional residual capacity (FRC) increased immediately after reaching SP ($p < 0.001$) and remained elevated after repositioning to supine position. PaO_2/FiO_2 ratio and compliance decreased initially during SP, but increased ($p < 0.05$) after patients were retransferred to supine position. Haemodynamic variables remained stable under a moderate increase of doses of catecholamines during the study period.

CONCLUSIONS. Changes in respiratory function during SP are probably explained by a downward shift of the diaphragm due to gravitational forces[2] leading to an increased FRC but not altering V/Q ratio as demonstrated by the paO_2/FiO_2 ratio. After reaching the initial supine position the opening of the lung proved by the elevated FRC is the predominant effect now associated with an increase in oxygenation as reflected by the paO_2/FiO_2 ratio due to an optimised V/Q ratio. Our results are confirmed in a subgroup analysis for 9 patients meeting ALI criteria. Ventilating patients in SP may be a new therapeutical approach to improve respiratory function in patients with ALI.

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EFFECT OF INTRAVENOUS N-ACETYLCYSTEINE IN ACUTE RESPIRATORY DISTRESS SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION. Oxidative stress plays an important role in the development of acute respiratory distress syndrome (ARDS) (1). There are several clinical trials investigating the efficacy of the free radical scavenger N-acetylcysteine (NAC) in ARDS, but its advantage remains uncertain.

OBJECTIVES. Critically appraise and summarize all randomized clinical trials involving intravenous NAC administration in adult patients suffering from ARDS.

METHODS. We included trials involving participants with ARDS according to the American-European Consensus Conference Criteria (2) regardless of the underlying cause, and where one of the groups was treated with intravenous N-acetylcysteine in bolus intravenous doses or as continuous infusion, or combination of the two, and the other group was given placebo or standard treatment. The following databases were searched: Cochrane Central Register of Clinical Trials (CENTRAL) (The Cochrane Library); MEDLINE (January 1950 to March 2010); EMBASE (January 1980 to March 2010); CINAHL (1982 to March 2010); the NHS Trusts Clinical Trials Register and Current Controlled Trials (http://www.controlled-trials.com); LILAC; KoreaMED; MEDCARIB; INDMED; PANTELEIMON; Ingenta; ISI Web of Knowledge and the National Trials Register to identify all relevant randomized controlled trials available for review.

RESULTS. 15 fully published studies (including 583 patients) met the study inclusion criteria. 12 out of the 15 studies reported mortality. Using the longest reported follow-up data mortality was similar in the NAC group: 97/244 (37.75%) and in the placebo group: 92/258 (35.65%) (RR 1.12 95% CI 0.90–1.40). Neither had NAC any significant effect on length of stay or duration of mechanical ventilation. Excluding those studies with high risk of bias, did not affect risk of mortality (RR 1.25, 95% CI 0.99 to 1.59 Analysis 1.4).Early NAC treatment did not affect outcome, however late administration of NAC (after 24 h of initial presentation of symptoms) was associated with increased mortality (RR 1.38, 95% CI 1.05 to 1.81, 285 patients, 7 trials).

CONCLUSIONS. The main finding of this meta-analysis is that intravenous NAC is ineffective in reducing mortality, length of stay or duration of mechanical ventilation in ARDS. We also found that late administration of NAC may be associated with adverse outcome. The mechanism of this potentially deleterious effect remains unclear, but dosing and timing of NAC appear to be critical issues.

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SAFETY OF COMBINED USE OF VENO-VENOUS EXTRACORPOREAL MEMBRANE OXYGENATION AND RECOMBINANT HUMAN ACTIVATED PROTEIN C (RAPC) FOR ACUTE RESPIRATORY DISTRESS SYNDROME AND SEPTIC SHOCK

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INTRODUCTION. Septic shock in patients with Acute Respiratory Distress Syndrome (ARDS) is associated with high mortality rate. Patients with septic shock and severe ARDS may benefit from administration of recombinant human activated protein C (rAPC). Recently, the CESAR study underlines the potential benefits of Extracorporeal Membrane Oxygenation (ECMO) use in patients with ARDS.

OBJECTIVES. However, it is known that rAPC administration can increase the risk of bleeding, primarily during concomitant anticoagulant administration. Here we show our experience of two ARDS-patients with septic shock treated with veno-venous ECMO and rAPC.

METHODS. Between January and February 2010, 2 patients have been treated with combined use of ECMO and rAPC (Xigris®, Eli Lilly, US) at the Intensive Care Unit of Emergency Department of a tertiary referral centre for ARDS (Careggi Teaching Hospital, Florence, IT). Veno-venous ECMO positioning was achieved percutaneously trough Seldinger technique and ECMO high-flow technique (up to 6 l/min) was initially established according to patient's requirement. ECMO device is a Rotaflow Maquet Centrifugal Pump with a Quadrox-D oxygenator (Maquet, Rastatt, Germany) and biocoated circuits. rAPC administration was started within 24 h after onset of sepsis and dosage regimen was performed at 24 μg/kg of body weight per hour as a continuous infusion over a period of 96 h. Heparin infusion was set at a maximum of 15 UI/kg/day, as recommended by Producer. Coagulation status was bedside controlled by bedside activated partial thromboplastin time (aPTT) with Hemocron (Hemochron Jr. Sign. plus, ITC Europe, Milan, IT) every 2 h, and heparin infusion titrated according to maintain aPTT between 50 and 60 s.

RESULTS. Demographic and clinical characteristics of patients are represented in Table 1.

TABLE 1 PATIENTS CLINICAL FEATURES

	Patient 1	Patient 2
Age (years)/sex	45/M	41/M
SAPS II at admission	47	60
Septic shock etiology	MRSA pneumonia	Bacterial pneumonia, not isolated germ
ECMO duration (h)	432	360
IABP	No	Yes
Days on ventilator	48	46
ICU LOS (days)	83	62
ICU outcome	Discharged	Discharged

ECMO was positioned after 49 h after rAPC initiation in patient 1, whereas rAPC initiation succeeded ECMO start after 16 h in patient 2. Total ECMO hours were 396, days on ventilator were 47 and both were discharged from our ICU after 72.5 days. During combined treatment, local bleeding from ECMO cannulae insertion site was observed in one case: blood loss was easily controlled with local care and no red blood cells transfusions were needed.

CONCLUSIONS. In our case series, the use of ECMO and APC resulted feasible and safe. A strict bedside control of coagulation status permitted to titrate heparin infusion avoiding hemorrhages.

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DO OR DO NOT EXTUBATE A PATIENT ON EXTRACORPOREAL LIFE SUPPORT

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INTRODUCTION. Extracorporeal life support (ECLS) is increasingly used for adults with cardiovascular or respiratory collapse. Patients on ECLS typically remain intubated and sedated. We report a patient with circulatory failure who was extubated while on full ECLS.

OBJECTIVE. To evaluate if extubation during ECLS is harmful or beneficial.

CASE. A 28-year-old woman was admitted to our intensive care unit (ICU) after removal of a left ventricular assist device. This device was implanted as bridge to recovery for postpartum cardiomyopathy and ventricular function seemed to have recovered sufficiently. However, shortly after ICU admittance she developed massive left and right ventricular failure. Therefore a centrally cannulated veno-arterial ECLS (Maquet Permanent Life Support) was implanted as a bridge to transplant. Four days later she was extubated while on full ECLS support, in order to reduce the risk of ventilator associated pneumonia. While on ECLS, the patient was mobilized, practiced with an ergometer and chatted with her family. Three days later the patient underwent cardiac transplantation. The postoperative period was characterized by temporary pulmonary failure, due to the combination of lung edema and atelectasis. Eventually she made a full recovery.

DISCUSSION. ECLS provides a valuable means as bridge to transplantation, bridge to bridge or bridge to recovery. With the increasing use of ECLS for circulatory failure, debate about the necessity of mechanical ventilation during this treatment ensues. ECLS is usually applied under deep sedation and controlled mechanical ventilation. Discontinuation of sedation possibly prevents intensive care acquired weakness. Extubation during ECLS may provide better pulmonary perfusion due to negative intra-thoracic pressure. Furthermore, the awake and extubated patient is able to mobilize and exercise which may reduce the risk of atelectasis and ventilator associated pneumonia. Our patient however developed pulmonary edema and atelectasis after discontinuation of ECLS. The edema was probably a consequence of reperfusion injury, due to severely decreased pulmonary flow while on ECLS. An absent ventilatory drive while on ECLS may have led to hypoventilation while the patient was extubated, resulting in atelectasis. An extensive Medline search resulted in one other case report describing an extubated patient on ECLS.[1] Intermittent non-invasive positive pressure ventilation was used to prevent atelectasis, but the patient developed pneumonia after 30 days of ECLS. Our patient was successfully extubated while on ECLS. However, we conclude that there is insufficient evidence to recommend or oppose extubation of patients on ECLS for circulatory failure.

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EXTRACORPOREAL OXYGENATION (ECMO) RESCUE IN THE TREATMENT OF SEVERE ARDS WITH A REFRACTORY HYPOXEMIA

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INTRODUCTION. Severe ARDS and refractory hypoxemia were defined with a PaO2/fraction of inspired oxygen (FiO2) ratio of $\leq$100, or uncompensated hypercapnea with a pH of $<$7.20 despite receiving optimal conventional treatment. The ECMO can be used as a rescue treatment in these case.

OBJECTIVES. Evaluation of severe ARDS treated with extracorporeal oxygenation (ECMO). All these ARDS were due to bacterial pneumonia or H1N1 influenza.

METHODS. Over the last year (December 2009–January 2010), the recourse to extracorporeal oxygenation (ECMO) was used in ten patients with severe ARDS and severe hypoxemia. Two groups were defined: bacterial pneumonia with ARDS (BP group, n = 5), and H1N1 influenza with ARDS (H1N1 group, n = 5). All ECMOs were implanted at the bedside to facilitate intra-hospital or inter-hospital transfer, because of severe hypoxemia or hemodynamic instability making impossible patient mobilization before ECMO.

RESULTS. All patients in the ARDS BP group were male. There was three female and two male in the ARDS H1N1 group. The median [range] age was 54 years old [18–57] (BP) versus 21 [28–45] (H1N1), p = 0.11. The most common associated comorbidity in the group H1N1 was obesity (30 kg/m^2 [25–41] vs. 26 [17–30], p = 0.07). The time between the onset of respiratory symptoms and implantation of ECMO were longer in the BP group (12 days [6–36] vs. 1 [1–13], p = 0.06). When comparing BP and H1N1 groups, duration of ECMO (14 days [6–30] vs. 20 [10–41], p = 0.84), duration of mechanical ventilation (66 days [36–77] vs. 42 [15–75], p = 0.4), ICU length of stay (77 days [38–92] vs. 48 [21–94], p = 0.6) and duration of hospitalisation (91 days [38–112] vs. 56 [29–113], p = 0.46) were similar. In the BP group, 60% survived to hospital discharge (1 patient died on ECMO, 1 patient died after discharge from ICU). All patients of the H1N1 group survived to hospitalization. All survivors of both groups were in good health condition upon leaving the hospital.

CONCLUSIONS. Given these good results, and despite long periods of mechanical ventilation, ICU duration and hospital length of stay, the standard respiratory ECMO support should be discussed again in the algorithm treatment of ARDS with refractory hypoxemia.

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INTER HOSPITAL TRANSPORTATION ON EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO): THE EXPERIENCE OF THE ECMO CENTRE KAROLINSKA, SWEDEN

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INTRODUCTION. For patients suffering from the most severe respiratory or circulatory failure ECMO can be a lifesaving procedure. ECMO is only provided by specialized centres and therefore the patients often need to be transferred for treatment, sometimes over long distances. Conventional transportation may be associated with fatal complications like cerebral hypoxia or death. An ECMO transportation service was therefore established in 1996.

OBJECTIVES. To update and reevaluate our recently published experiences from transportation of patients on ECMO and their outcome.

METHODS. Data of all patients who were transported on ECMO since this service was started in 1996 were retrospectively analysed.

RESULTS. Between 1987 and December 2009 547 patients (226 neonatal, 135 paediatric, 186 adult) were treated with ECMO at the ECMO Centre Karolinska. Since 1996 we performed 272 transports on ECMO. 220 patients (86 neonates, 41 paediatrics, 93 adults) were transported to Karolinska on a total of 236 occasions (5 neonates and 11 adults twice). Another 36 patients were directly transported from the referring hospital to another ECMO unit due to unavailability of beds at our department. The transports were performed either with ambulance (91), helicopter (34) or fixed wing air craft (147). One patient died during the transport because of circulatory arrest. No other obvious medical complication occurred. 55 transports were international. Survival of transported patients to discharge from our unit was 91% in the neonatal, 76% in the paediatric and 67% in the adult population.

CONCLUSIONS. During the last 15 years we transported 256 patients on ECMO. When performed by an experienced team the transportation of patients on ECMO is a safe procedure. It decreases, in our opinion, the likelihood for fatal complications compared to conventional transports in this subgroup of severly sick patients. Therefore ECMO centres should provide a dedicated transportation service.

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EXTRACORPORAL MEMBRANE OXYGENATION WITH A TARGET-PTT OF 35 SEC

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INTRODUCTION. In patients with acute lung injury and severe hypoxemia the Extra-Corporporal Membrane Oxygenation (ECMO) can be used as rescue therapy. Despite the use of extracorporeal circuits with heparin coating, manufacturers still suggest therapeutic anticoagulation (AC) e.g. with Heparin achieving a target-PTT of 50–60 s to avoid thrombosis. This target-PTT can be associated with adverse effects such as bleeding or intracranial hemorrhage.

OBJECTIVES. We hypothesized, that ECMO-therapy with heparin-coated circuits can be safely used at low-dose AC with a target-PTT of 35 s.

METHODS. In this retrospective study, we examined 47 patients from 01/2003 until October 2009 treated with ECMO (rotation pump: Bio-Pump, Medtronic, Minneapolis, MN, USA and since 2007 Levitronix® CentriMag®, Waltham, Massachusetts, USA and Jostra-Maquet, Qadrox Oxygenator with Bioline™ coating, Rastatt, Germany). Analyzes included coagulation samples, transfusion requirements, change of ECMO circuit during treatment and adverse effects like bleeding or thrombosis.

RESULTS. Data sets of 44 patients of 47 consecutive patients treated with ECMO were complete and included into analyses. We had no clinical or radiological evidence for thrombosis or clotting within ECMO-circuit with a target-PTT of 35 s. One patient with systemic aspergillosis died because of intracranial hemorrhage. One ECMO circuit had to be replaced due to insufficient oxygenator function after 10 days. Further data are presented in Tables 1 and 2.

TABLE 1

	Median	Range	Standard value
Heparin (IE/h)	400	1,600	
aPTT (s)	37.1	79.8	25–36
D-dimer-FSP (µg/ml)	4.6	26.3	0–0.49
Fibrinogen (mg/dl)	326	820	177–376
AT-Activity (%)	74	102	85–130
red blood cell (units per day)	1	24	

TABLE 2

	Median	Range
Patient on ECMO (h)	146.5	541
Age (years)	42.5	68
ICU-Mortality	38%	N = 18
ECMO-Mode	Veno-venous: 40	Veno-arterial: 7
Days on ICU	27	70

CONCLUSIONS. In this retrospective analysis of 44 patients who underwent ECMO-treatment, AC with low-dose heparin (target-PTT of 35 s) was safe and without any observation of macroscopic thrombosis or clotting within the circuit. Transfusion requirements and intracranial hemorrhage were low as compared with previous reports [1,2]. Therefore our data suggest that it is possible and safe using ECMO-therapy with low-dose Heparin.

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GRANT ACKNOWLEDGMENT. Levitronix® Waltham, Massachusetts, USA.

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A TEAM FOR INTER-HOSPITAL ECMO IMPLANTATION AND TRANSPORT OF PATIENTS WITH SEVERE RESPIRATORY FAILURE

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INTRODUCTION. In response to H1N1 pandemy, Italy and Lombardy created a national and a regional ICU network, respectively, for treatment of ARDS patients. Our hospital Policlinico San Matteo of Pavia participated with a team for inter-hospital ECMO implantation and subsequent patient transport.

OBJECTIVES. Description of the Pavia ECMO team and activity analysis.

METHODS. Our team is composed by a cardiac surgeon, two intensivists, a perfusionist, an ICU nurse, two emergency rescue technicians and a driver. All necessary aids for implantation and intensive care are ranged in three trolleys and three transport bags. Equipments are firmly mounted on a two-level steel bridge connected to a spinal board. A portable ultrasonograph is also available. The ECMO team was alerted by the national call center. Each mission used two ambulances, and in one case the ambulances were embarked on a Hercules C130 J.

RESULTS. From 31 October to 31 December 2009, four patients were implanted and transported, three suffering from H1N1 influenza (including a 190-kg body weight patient) and one from acute mitral valve rupture. All patients, already mechanically ventilated with maximal support, had veno-venous ECMO implanted by femoro-femoral percutaneous cannulation. The median mission duration was of 7.25 h (range 6–17 h). All patients were transported to our ICU, where the median ECMO duration was of 8 days (range 6–10 days). No major managing issue occurred during the ECMO missions, and patient hospital survival was of 100%.

CONCLUSIONS. A multispecialist team with good knowledge of ECMO can provide an effective support in severe respiratory failure, with ECMO implantation in peripheral hospitals and subsequent patient transport, thus realizing a fast and safe continuum between phone call activation and admittance to the reference center.

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RIGHT VENTRICULAR FAILURE IN PATIENTS ON V-V ECMO FOR SEVERE ARDS: IS CONVERSION TO V–A ECMO BENEFICIAL?

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INTRODUCTION. When patients with sever respiratory failure are treated with V-V ECMO the right heart sometimes fails. This is a serious complication with a high mortality. In our unit these patients have been converted to V-A ECMO, although it is not fully agreed upon in the ECMO community due to previously depressing results.

OBJECTIVES. To evaluate the results of conversion to V–A from V–V ECMO in case of right heart failure.

METHODS. Retrospective analyses of all patients with severe respiratory failure, treated between 1987 and 2009 at the Karolinska ECMO centre. Patients who were converted to V–A ECMO due to right ventricular failure were evaluated.

RESULTS. A total of 214 patients (78 adults, 57 peadiatric, 79 neonatal) were treated on V-V ECMO for severe respiratory failure. Of them 50 (33 adults, 9 peadiatric, 8 neonatal) needed conversion to V-A ECMO due to right ventricular heart failure demonstrated clinically by multiorgan failure and verified by ECHO cardiography. The survival after conversion to V-A ECMO was 10/33 (30%) in the adult age group, 7/9 (78%) in the peadiatric age group and 2/8 (25%) among the neonates.

CONCLUSIONS. Given the high risk of fatality if not treated, conversion to V-A from V-V ECMO should be considered when the right ventricle fails. Patients on V-V ECMO with right ventricle heart failure have very bad prognosis. It is concluded from the present results that conversion to V–A ECMO can save some of these patients.

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RELATION OF TRICUSPID ANNULAR DISPLACEMENT AND TISSUE DOPPLER IMAGING VELOCITIES WITH PULMONARY HYPERTENSION AND LENGTH OF THE WEANING PROCESS IN MECHANICALLY VENTILATED PATIENTS WITH ACUTE HEART FAILURE

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INTRODUCTION. Recently, numerous studies have documented that tricuspid annular plane systolic excursion (TAPSE) is linearly related to right ejection fraction in different clinical scenarios. Moreover, tissue Doppler imaging (TDI) techniques that measure velocities of cardiac tissue have been studied for the assessment of left ventricular diastolic function in the Intensive Care Unit (ICU), whereas only a limited number of researchers have investigated their diagnostic accuracy on right ventricular (RV) dysfunction, in different clinical settings.

OBJECTIVES. To test whether TAPSE and right ventricular systolic (Sm) and diastolic (Em and Am) tissue Doppler imaging velocities are related with pulmonary artery systolic pressure (PASP) and length of the weaning process in mechanically ventilated patients with acute heart failure (AHF).

METHODS. RV fractional area change (RVFAC), left ventricular ejection fraction (LVEF), PASP, TAPSE, Sm, Em, Am RV TDI velocities, early diastolic mitral E wave and E′ maximal TDI velocities of the mitral annulus at the lateral wall were obtained at admission by Doppler echocardiography in a cohort of 32 patients with AHF, presented with pulmonary oedema, who required positive-pressure ventilation for more than 48 h in the Intensive Care Unit (ICU). Echo-derived measures were compared between patients with and without pulmonary hypertension, whereas their association with duration of mechanical ventilation and length of the weaning process was tested with multivariate linear and logistic regression analysis.

RESULTS. Patients with pulmonary hypertension (PASP $\geq$35 mmHg, n = 22) had de-creased TAPSE (15.69 $\pm$ 1.73 vs. 21.96 $\pm$ 1.92 mm), Sm (9.40 $\pm$ 1.21 vs. 12.96 $\pm$ 1.35 cm/s) and Em/Am ratio (1.54 $\pm$ 0.96 vs. 3.04 $\pm$ 0.29, $p < 0.001$ for all comparisons) and increased E/E′ ratio (10.8 $\pm$ 1.21 vs. 7.6 $\pm$ 0.54, $p < 0.001$) compared with subjects with normal PASP (n = 10). These variables were negatively associated with duration of mechanical ventilation ($R^2 = 0.55$, beta slope = −0.89 for TAPSE, $R^2 = 0.52$, beta = −0.57 for Sm, $R^2 = 0.45$, beta = −0.27 for Em/Am, $p < 0.001$) and were proven to successfully discriminate patients with (n = 12) and without (n = 20) prolonged weaning (>7 days of weaning after the first spontaneous breathing trial failure, $p < 0.001$ for all comparisons).

CONCLUSIONS. We suggest that in critically ill patients with AHF presented with pulmonary oedema, low TAPSE and RV TDI velocities upon admission are associated with pulmonary hypertension and prolonged length of the weaning process.

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CEREBRAL HEMODYNAMICS IN THE EARLY POSTOPERATIVE COURSE OF CARDIAC SURGERY. ROLE OF TRANSCRANIAL DOPPLER

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INTRODUCTION. Neurologic complications (NC) represent the second commonest cause of postoperative morbidity and mortality after cardiovascular surgery (CVS). Precise pathogenesis is often uncertain. Transcranial Doppler ultrasonography (TCD) is an easy, reproducible and non-invasive tool to evaluate middle cerebral artery (MCA) blood flow and might be useful in the neurological monitoring of patients undergoing CVS.

OBJECTIVES. The aim of the study was to study changes in cerebral blood flow (CBF), as determined by TCD, during the early postoperative course of CVS and to correlate such changes with post-operative NC.

METHODS. We studied 72 patients undergoing extracorporeal circulation CVS (coronary by-pass, valve replacement or both) between March 2007 and March 2008. CBF was assessed by measuring bilateral MCA flow velocities by TCD before and 10, 24 and 48 h after CVS. Changes $\geq$20% between consecutive TCD results were considered significant. Demographic and clinical variables, co morbidities, Euroscore, SOFA, type and duration of surgery and type and severity of NC were also recorded. Patients were assigned to 3 groups according to CBF changes from baseline: A) Changes $\leq$20%; B) CBF increases $\geq$20%, C) CBF decreases $\geq$20%. NC were classified as major (stroke, TIA and coma) and minor (delirium, encephalopathy, transient cognitive impairment). We used descriptive statistics and inference by X_2, ANOVA and Pearson's correlation.

RESULTS. Of the 72 patients, 20 were excluded (2 early post-operative death and 18 due to technical difficulties or incomplete TCD recordings). Of 52 evaluable patients, 17 (33%) had no CBF changes (group A), 12 (22%) had increases $\geq$20% (group B) and 23 (45%) had decreases $\geq$20% after CVS (group C). A positive correlation was found between CBF changes and duration of circulatory arrest ($p < 0.02$), maximum SOFA score ($p < 0.001$), respiratory dysfunction ($p < 0.016$) and duration of mechanical ventilation ($p < 0.001$). Neurological complications occurred in 16 patients (31%), of which 4 (25%) were major and 12 were minor (75%). 11 patients had a hyperemic response persisting >24 h, of whom 2 had major (TIA) and 4 minor NC.

CONCLUSIONS. Most CVS patients have CBF changes in the first hours post surgery. Bilateral symmetric CBF decreases are transient and do not seem to correlate with NC incidence. In contrast, bilateral increase CBF $\geq$20%, are associated with NC in $\sim$ 50% of cases. There is a positive correlation between circulatory arrest time and worst SOFA at entry and significant changes in CBF. Variations in CBF, rather than absolute values, seem to reflect cerebral hemodynamic events with potential clinical relevance.

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B-TYPE NATRIURETIC PEPTIDE IS AN INDEPENDENT PREDICTOR OF MORTALITY IN NON-CARDIAC CRITICALLY ILL PATIENTS

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OBJECTIVES. To determine if plasma concentrations of B-type natriuretic peptide (BNP) on admission predict mortality in non cardiologic ICU patients.

METHODS. We performed a prospective study in a medical-surgical ICU of an university hospital. Patients admitted due to heart failure, acute coronary syndrome and cardiac surgery were excluded. Plasma BNP concentrations, demographic data, SAPS II and APACHE II, SOFA, laboratory data, and physiological variables were collected at admission.

RESULTS. We included 55 patients (26 women) with a mean age of 57.1 ± 18.7 years, SAPS II 46.6 ± 16.1, APACHE II 17.2 ± 8, SOFA 6.9 ± 3. Patients who died (n = 13) had higher plasma concentrations of BNP 304 pg/mL [interquartile range (IQR) 113–1490] vs. 115 pg/mL (IQR 21–353) $p = 0.02$, SAPS II 56 ± 13 versus 36 ± 14 $p < 0.001$; APACHE II 25 ± 9 versus 15 ± 6 $p < 0.001$; and SOFA 9 ± 3 versus 6 ± 3 $p = 0.02$. No significant differences regarding age, gender and other physiological variables collected at admission were shown. The area under the ROC curve for predicting mortality in ICU was 0.74 for BNP (95% CI 0.58–0.9, $p = 0.016$). The cutoff of BNP on admission that best predicted mortality in ICU was 231 pg/mL with a sensitivity of 73% and a specificity of 58%. The multivariate analysis revealed that APACHE II [odds ratio (OR) 1.21, $p = 0.007$] and BNP (OR 1.01, $p = 0.005$) were independent predictors of mortality in ICU.

CONCLUSIONS. In non-cardiac ICU patients plasma BNP concentrations are frequently elevated and are independent predictors of mortality in ICU.

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INTRAARTERIAL LOCAL THROMBOLYSIS IMPROVES RIGHT VENTRICULAR DYSFUNCTION AFTER PULMONARY EMBOLISM

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OBJECTIVE. Management of pulmonary embolism (PE) with right ventricular (RV) dysfunction and haemodynamic stability is controversial. The aim of our study is to evaluate the effectiveness of local thrombolysis (LT) in a group of these patients and its impact on RV function.

METHOD. Prospective study. Inclusion criteria: (1) haemodynamic stability (systolic arterial pressure >90 mmHg); (2) PE proven by helical CTA; (3) RV dysfunction defined by at least one of the following echocardiographic (ECO) parameters: subjective alteration of right ventricular contractility, RV diameter in the four chamber view >40 mm, tricuspid annular plane systolic excursion (TAPSE) <15 mm and/or systolic pulmonary artery pressure >30 mmHg. All patients underwent angiography (ANG) and pulmonary artery catheterization with measurement of pulmonary pressures (PAP).LT was performed with urokinase (UK) (bolus of 100,000–200,000 UI plus a 100,000 UI/h infusion) or tPA (10 mg bolus plus a 40 mg infusion in 4 h).Both treatments were associated to an unfractioned heparin infusion (goal TTPA: 1.5 to 2 times control values).ICU monitoring after LT.ECO and ANG follow ups were done in all patients. Statistical method: Paired t test. Results are shown as mean difference between initial and final values with a confidence interval (CI) of 95%.

RESULTS. Twenty one patients. Thirteen males. Age 55 ± 20 years. Initial symptom: dyspnea (90%).Systolic arterial pressure (SAP) on arrival: 131 ± 26 mmHg, heart rate (HR): 108 ± 21 bpm. Median Troponin I on admission: 0.3 µg/mL (range 0.05 to 6.8); median proBNP on admission: 2004 pg/mL (range 68 to 13310).All patients had thrombus occupying the main pulmonary artery in the CTA.ECO: 28% had severe RV dysfunction, 44% moderate, 17% mild and 11% had a normal function; RV diameter 46 ± 7 mm; TAPSE 15 ± 2 mm. ANG: systolic PAP: 48 ± 12 mmHg; diastolic PAP: 25 ± 9 mmHg; mean PAP 35 ± 8 mmHg. Twenty patients received UK, one received tPA. Mean time of LT 53 h (range 4–84).Mean decrease of HR after LT: 28 bpm [IC95 (19–37), $p < 0.001$].Control ANG: nineteen patients had radiological improvement (85%), four of them had a complete resolution. Mean reduction of PAP after LT: systolic PAP: 16 mmHg [95 CI (10–22), $p < 0.001$]; diastolic PAP: 10 mmHg [95 CI (7–13), $p < 0.001$] and mean PAP: 13 mmHg [95 CI (10–15), $p < 0.001$].Control ECO (1–7 days after LT): 24% had mild RV dysfunction, the rest of them had a normal contractility of the RV; mean reduction of RV diameter: 9.7 mm [IC95 (6–13), $p < 0.001$]; mean rise of TAPSE: 8.5 mm [95 CI (5–11), $p < 0.001$].Complications: LT was associated with a decrease in the levels of fibrinogen and platelets, the lowest levels achieved were 120 mg/dL and 73,000 cel/mm^3 respectively. Seven patients had mild haematomas at the puncture site. One had hematuria that resolved after stopping the treatment. All patients survived.

CONCLUSION. LT in this group of patients improved RV function rapidly and was associated with mild complications.

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NIRS GUIDED HEMODYNAMIC THERAPY IN CARDIAC SURGERY PATIENTS:THE NIGHT STUDY

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INTRODUCTION. The sole monitoring of macrohemodynamic variables is not always sufficient in the early detection of tissue hypoperfusion, especially in cardiac surgical patients that frequently present with microcirculatory derangements. Near infrared spectroscopy (NIRS) is an easily applicable non invasive technique that has been used to provide an estimate of tissue oxygenation at the bed side.

OBJECTIVE. The aim of our study was to evaluate the effect on outcome of guiding hemodynamic therapy and specifically inotrope titration in cardiac surgical patients postoperatively with NIRS.

METHODS. Patients operated on with cardiopulmonary bypass were assigned, after stratified randomization (gender, Euroscore-cutoff of 6), to an Intervention (IG) and a Control Group (CG). Postoperatively, following cardiac Intensive Care (cICU) admission, after initial resuscitation according to cICU protocol, StO_2 (%) was measured in patients of the IG in 3 muscle sites: thenar, masseter and deltoid. If it was less than 80% in 2/3 sites, dobutamine was administered in incremental doses (2.5 µg/kg/min), with the StO_2(%) measured every half hour. The interventional period began upon cICU admission and lasted for 6 h, after which both groups were treated according to cICU protocol. Primary outcome measured was the oxygen consumption rate at the end of the 6 h intervention period as assessed with NIRS vascular occlusion technique.

RESULTS. 18 patients were included in the study (8 in the intervention group and 10 in the control group). The 2 groups did not differ statistically significantly regarding age, Euroscore, and macrohemodynamic variables postoperatively (with the exception of CVP). Microcirculatory parameters upon admission to the cICU also did not differ, excluding masseter StO_2(%). The oxygen consumption rate and the reperfusion rate increased in the 6 h study period in both groups, without differing statistically significantly between the groups at any time point (CG oxygen consumption rate 20.1 ± 12.4 upon cICU admission and 32.8 ± 15.5 6 h later, IG 15.4 ± 6.6 and 19.7 ± 7.7 respectively) (CG reperfusion rate 297 ± 210 upon cICU admission and 592 ± 254 6 h later and IG 201 ± 119 and 304 ± 163 respectively). As far as outcome parameters were concerned, the 2 groups did not differ statistically significantly in the total hours and total dose of vasopressors ± inotropes received, in the hours of mechanical ventilation, in the duration of cICU or hospital stay, and in SOFA scores the days following the operation.

CONCLUSION. NIRS guided titration of inotropes did not lead to a greater improvement in the microcirculation 6 h postoperatively, or to a better outcome. The limited power of the study prevents definite conclusions on the role of NIRS in hemodynamic therapy in cardiac surgery patients.

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PREVALENCE OF PULMONARY EMBOLISM IN INTENSIVE CARE UNIT

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INTRODUCTION. Pulmonary embolism (PE) is frequent and associated with high mortality. PE prevalence is well known in general population but not in critically ill patients. Post mortem studies have shown that PE is frequently underdiagnosed in the intensive care unit (ICU), probably because PE symptoms are nonspecific and confounding in patients requiring mechanical ventilation (MV).

OBJECTIVES. To estimate the prevalence of pulmonary embolism among MV patients in ICU and its association to deep vein thrombosis (DVT).

METHODS. In a monocentric prospective observational study, we included all the patients requiring mechanical ventilation with no previously diagnosed PE, who underwent a thoracoabdominal CT contrast scanner for any medical reason. We used a modified protocol for PE diagnosis with a 64-multidetector row CT scan read by two independent radiologists. The association with a DVT was explored by performing venous compression ultrasound of four limbs.

RESULTS. We included 81 patients; mean age 53 ± 14 years old, SAPS II 53, 40% males. CT scan was performed after 8.8 ± 4.5 days of mechanical ventilation (MV).PE was diagnosed in 12 (14.8%) patients; mean age: 54 ± 17; 91% males. The mean duration of MV before PE diagnosis was 11.9 ± 6.6 days. PE was unilateral in 91.6%; lobar in 33.3%, segmental in 33.3%, subsegmental in 16.7% and both lobar and segmental in 16.7%. PE occurred despite preventive or curative anticoagulation in 58.3% and 33.3% of cases respectively. PE was not suspected in 9 (75%) patients before diagnosis and was associated with a DVT of the lower limbs in 7 (58.3%) cases. In the patients without PE, 9 (13%) DVT were diagnosed. DVT, with or without PE, was associated with the presence of a central venous catheter (CVC) at diagnosis or within the 10 previous days in 11 (73.3%). Seven (46.6%) DVT were found in the upper limbs and 8 (53.3%) in the lower limbs. All the cases of PE with a DVT (6) were lower limbs DVT and 4 (66.7%) of them were associated with a CVC.

CONCLUSIONS. Pulmonary embolism is frequently undiagnosed in ICU patients and occurred despite the use of thromboprophylaxis or curative anticoagulant treatment. Risk factors and outcome are being studied in a larger population.

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INTRAABDOMINAL HYPERTENSION IMPAIRS LEFT VENTRICULAR RELAXATION: AN ANIMAL STUDY

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INTRODUCTION. Intraabdominal hypertension is a frequent, life-threatening situation in the ICU. Despite a high number of publications, the haemodynamic impairment due to intraabdominal hypertension (IAH) is still not well understood.

OBJECTIVES. The aim of this animal study was to evaluate the effect of intraabdominal hypertension on left ventricular diastolic function.

METHODS. After approval by an institutional animal care committee, 7 rabbits were anesthetised before mechanical ventilation. An intraperitoneal infusion of 1.5% glycine solution was used to increase intraabdominal pressure to 20 mmHg. The right common carotid artery was catheterised in the neck in order to introduce a Millar Mikro-Tip catheter (Millar Instruments inc., Houston, USA) into the left ventricle. Heart rate, arterial pressure, central venous pressure, oesophageal pressure and intraabdominal pressure were measured. The τ time constant of relaxation which is considered as best index of relaxation was calculated using the derivative method (1). All haemodynamic measurements were registered at baseline and after inducing intraabdominal hypertension. Data are presented as mean (IQR) and were compared using a Wilcoxon rank sum test.

RESULTS. Heart rate (from 202 ± 100 to 166 ± 100 beat/min, $p = 0.6$), mean arterial pressure (from 60 ± 29 to 50 ± 34 mmHg, $p = 0.20$) and dP/dt max (from 3,590 ± 255 to 2,111 ± 197 mmHg/s, $p = 0.14$) were not significantly modified by intraabdominal hypertension. However, the τ time constant of relaxation increased significantly (from 16 ± 3 to 43 ± 18 ms; $p = 0.05$).

CONCLUSIONS. In this animal model, intraabdominal hypertension impairs left ventricular relaxation.

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THENAR TISSUE OXYGENATION POSTOPERATIVELY CORRELATES WITH HOSPITAL LENGTH OF STAY IN CARDIAC SURGICAL PATIENTS

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INTRODUCTION. Cardiac surgery, especially under cardiopulmonary bypass (CBP), induces changes in microvascular perfusion and compromises peripheral tissue oxygenation. These changes in the condition of the microcirculation have been related to the degree of organ dysfunction and thus patient outcome ie hospital length of stay. Near infrared spectroscopy (NIRS) is an easily applicable non invasive technique that has been used to provide an estimate of tissue oxygenation at the bed side.

OBJECTIVES. The aim of our observational study was to examine whether impaired tissue oxygenation as assessed with NIRS immediately postoperatively correlates with hospital length of stay.

METHODS. Patients undergoing a planned cardiac surgical procedure on CPB were included in the study. Patients' thenar tissue oxygenation (StO_2%) was assessed with NIRS postoperatively in the cardiac Intensive Care Unit (cICU).

RESULTS. 22 patients undergoing cardiac surgery on CPB (13 male/9 female) (age: 64 ± 14 years, EuroSCORE: 5.7 ± 3; mean ± SD) were enrolled in the study. Patients length of stay was 8.5 (3–26); median(range). The haemodynamic parameters of our patients upon admission to the cICU were: MAP 84 ± 12 mmHg, CVP 9 ± 4 mmHg, PCWP 12 ± 4 mmHg, MPAP 24 ± 5 mmHg, CI 2.6 ± 1.1 L/min/m2, SVR 1407 ± 501 dyne x s/cm5, PVR 239 ± 106 dyne x s/cm5, HR 97 ± 15 bpm, Hb 11.7 ± 1.7 g/dl, lactate 2.8 ± 1.8 mg/dl; (all variables expressed as mean ± SD). Upon admission to the cICU all patients were mechanical ventilated, under vasopressor ± inotrope support and their central temperature was 36.9 ± 0.68; mean ± SD. The thenar StO_2% was 80 ± 11; mean ± SD. Thenar StO_2% correlated statistically significantly with hospital length of stay ($r = 0.53$, $P = 0.11$).

DISCUSSION. Tissue oxygenation as assessed with NIRS reflects the balance between regional oxygen delivery in relation to oxygen utilization. An elevated StO_2 in the presence of normal macrohemodynamics may reflect impaired oxygen consumption and thus an impaired microcirculation.

CONCLUSION. Patients with impaired tissue oxygenation immediately postoperatively have a longer hospital length of stay. Further studies are needed to confirm these results and to investigate the potential benefit from incorporating this information regarding tissue oxygenation in the treatment algorithm.

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PROPOFOL VERSUS ETOMIDATE AS A HYPNOTIC AGENT FOR IMPLANTATION OF CARDIAC RESYNCHRONIZATION/DEFIBRILLATION DEVICES

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INTRODUCTION. Implantation of cardiac resynchronization/defibrillation device systems (CRT-Ds) is an established option in patients who are at risk of sudden cardiac death due to advanced heart failure and complicating cardiac arrhythmia. When transvenous route is established, it is implanted in sedated patients under local anesthesia. However, since the defibrillation threshold testing is unpleasant and painful, deep sedation is desirable.

OBJECTIVES. The goal of this study was to compare two different sedative agents for implantation of CRT-Ds related to incidence of adverse events and patient's satisfaction.

METHODS. The study included forty-two, ASA III-IV patients, undergoing transvenous implantation of CRT-Ds under local infiltrative anesthesia with 20 to 30 mL of 1% lidocaine. Intraoperative sedation was established with intermittent boluses of midazolam (1–5 mg) to achieve desirable level of sedation. Before the induction of ventricular fibrillation in order to test the defibrillator function of the CRT-D device, patients received an additional bolus of either propofol (1.5–2.5 mg kg^{-1}, P group, $n = 20$) or etomidate (0.1–0.25 mg·kg^{-1}, E group, $n = 22$) targeting BIS values in the range 50–60. The incidence of apnea, hypotension, nausea, myoclonus, pain at injection site, allergic reactions as well as patient's satisfaction with anesthesia described as feel of well being were registered and compared between groups.

RESULTS. In 23 subjects (56%) no complications were recorded. Myoclonus was registered in 5 patients from E group (23%) and in none from P group ($p < 0.05$). No patients receiving etomidate reported pain at injection site compared to 4 patients (20%) receiving propofol ($p < 0.05$). There was no significant difference in incidence of apnea between two groups (15 vs. 9%, $p = 0.30$). Two patients in P group (10%) and 1 in E group (4.5%) became hypotensive after delivering the hypnotic agent ($p = 0.36$). Also, there was no statistically significant difference between groups considering the frequency of nausea (0% vs.9%, $p = 0.26$). All the patients whom propofol had been delivered (100%) reported feel of well being and only four of them filed the same after etomidate (18%) ($p < 0.01$). No allergic reactions and major adverse events were registered.

CONCLUSIONS. Implantation of CRT-Ds and its testing can be successfully performed with administration of both propofol and etomidate as a safe procedure with low per operative morbidity and shorter complication rates. Still, treating with propofol tends to be more satisfactory for the patients.

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COMPARATIVE EFFECTS OF ESMOLOL AND LANDIOLOL, ULTRA-SHORT-ACTING BETA-BLOCKER, ON CARDIAC FUNCTION, ION CHANNELS, AND CORONARY ARTERIES IN GUINEA-PIG

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INTRODUCTION. Ultra-short-acting β_1 selective adrenergic antagonists are now widely used to control tachycardia and tachyarrhythmia perioperatively. Among them, landiolol, a new ultra-short-acting β_1-blocker, has been reported to exert a more potent negative chronotropic effect with little effect on blood pressure than esmolol (1). However, detailed mechanisms underlying different cardiovascular actions are still unknown.

OBJECTIVES. In this study we evaluated direct effects of landiolol on cardiac performance and single cell electrophysiology in comparison to those of esmolol.

METHODS. The present study composed of two parts. The first part of the study used isolated guinea-pig hearts which were perfused in the Langendorff mode at constant flow with oxygenated Tyrode solution at 37°C. The coronary perfusion pressure (CPP) was continuously monitored throughout the experiment, and intrinsic heart rate (HR) and isovolumetric left ventricular contraction were measured with a thin saline-filled balloon inserted into the left ventricle. The second part of the study was to measure action potentials and ionic currents in ventricular myocytes isolated enzymatically from guinea-pig hearts. Comparison of data was conducted by repeated-measure ANOVA with post hoc test (Bonferroni's correction).

RESULTS. Both HR and systolic left ventricular pressure (sLVP) increased slightly with up to 3 μM esmolol (not significant), then decreased at the concentration of over 3 μM esmolol (HR: 0 vs. 30 μM, $P < 0.05$, and sLVP: 3 vs. 30 μM and 10 vs. 30 μM, $P < 0.05$). CPP increased in a concentration-dependent manner (CPP: 3 vs. 30 μM, $P < 0.05$). On the other hand, landiolol decreased HR dose-dependently (HR: 0 vs. 30, 0 vs. 100, 10 vs. 100, 30 vs. 100 μM, $P < 0.01$, and 10 vs. 30 μM, $P < 0.05$), while neither sLVP nor CPP were affected by landiolol. Application of esmolol (3–100 μM) shortened action potential duration (APD) in a concentration-dependent manner. Among various ionic currents examined, the inward rectifier K^+ current (I_{K1}) was inhibited by esmolol in a concentration-dependent manner. The L-type Ca^{2+} current (I_{CaL}) and outward current (I_{Ks} and I_{Kr}) were hardly affected at concentrations of <30 μM, but increasing the concentration up to 100 μM inhibited the currents slightly. On the other hand, landiolol had little effects on both action potential and various ionic currents (I_{K1}, I_{CaL}, I_{Kr}, I_{Ks}).

CONCLUSIONS. Esmolol had a more potent negative inotropic effect than landiolol. This effect is, at least in part, derived from shortening of APD. In addition, increase of the coronary resistance would facilitate the negative chronotropic action of esmolol *in vivo*.

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EFFECTS OF N-METHYL ACETAZOLAMIDE ON HYPOXIC PULMONARY VASOCONSTRICTION (HPV) IN CONSCIOUS DOGS

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INTRODUCTION. The carbonic anhydrase (CA) inhibitor acetazolamide (ACZ) reduces HPV in isolated lungs, intact animals and in humans[1]. The efficacy against HPV is not due to CA inhibition, since selective inhibition of either intracellular or extracellular CA by other potent but structurally different CA-inhibiting sulfonamides does not reduce HPV[2]. As compared to ACZ, n-methyl acetazolamide (NMA), possesses a simple uncharged additional methyl group at the sulfonamide moiety of ACZ, thereby lacking any CA inhibitory property. In isolated pulmonary artery smooth muscles, ACZ and NMA block hypoxia-mediated intracellular calcium increase. We hypothesized that NMA would effectively reduce HPV in conscious spontaneously breathing dogs without the systemic side effects of CA inhibition.

OBJECTIVES. To test the effects of NMA on hypoxic pulmonary vasoconstriction in conscious dogs.

METHODS. Five female Beagle dogs were kept under standardized environmental conditions. Each dog was studied twice in randomized order. Protocol 1: NMA (10 mg/kg bolus, followed by 10 mg/kg/h continuously). Protocol 2: Controls, without NMA. During all experiments dogs breathed spontaneously via a ventilator circuit. First hour: Normoxia ($F_iO_2 = 0.21$); followed by 2 h of hypoxia ($F_iO_2 = 0.1$). Arterial oxygen tension (P_aO_2), mean pulmonary artery pressure (MPAP), pulmonary vascular resistance (PVR) were determined at the end of each experimental hour. Data are given as means ± SEM; * $p < 0.05$ vs. normoxia; † $p < 0.05$ vs. Controls (GLM ANOVA).

RESULTS. During hypoxia P_aO_2 was 36 ± 1 mmHg in Controls and 38 ± 1 mmHg with NMA. In Controls, MPAP increased by 7 ± 1 mmHg and PVR increased by 182 ± 20 dyn s cm^{-5} after 2 h of hypoxia (* $p < 0.05$). With NMA, MPAP increased by 3 ± 1 mmHg and PVR by 74 ± 40 dyn s cm^{-5} during hypoxia († $p < 0.05$).

CONCLUSIONS. NMA moderates HPV in the conscious spontaneously breathing beagle, but not to the same degree as ACZ. As compared to ACZ, the additional methyl-group in NMA may impair its capability in vivo to act on a non-CA ACZ-sensitive cellular receptor or channel or that both, CA-dependent and CA-independent actions of ACZ yield a greater effect.

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A MULTICENTER TRIAL ON PATENT FORAMEN OVALE (PFO) DETECTION: TRANSCRANIAL DOPPLER (TCD) VERSUS TRANSESOPHAGEAL ECHO (TEE): TCD BETTER THAN TEE?

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INTRODUCTION. TEE with bubble test is considered as the "gold standard" method to detect a PFO with right to left shunt. TCD is a non-invasive method which has been shown to be as accurate as TEE for PFO detection.

OBJECTIVES. We conducted a multicenter trial to estimate the prevalence of PFO, the influence of the size of the heart chambers on the prevalence of PFO and the accuracy of TCD as a non invasive method for PFO detection in mechanically ventilated ICU patients.

METHODS. One hundred ICU patients (74 M and 26 F) under mechanical ventilation who needed a TEE study for hemodynamic assessment were included in the study. In each patient, the presence of a PFO was detected by TEE and TCD. Three bubble tests with agitated Haemacel® were performed by each method, with TEE probe at 60° and 90° rotation and with TCD the gate of pulse wave Doppler (PWD) at the M_1 segment of the middle cerebral artery (MCA). Patients without temporal acoustic window to perform TCD were excluded from the study. The size of PFO was classified as grade I, II and III according to the number of microbubbles passing from the right to the left atrium and the number of HITS (High Intensity Transient Signals) detected with PWD in the MCA (Grade I: <6 microbubbles or HITS, Grage II: >6 and <25 and grade III: more than 25 microbubbles or HITS). For each patient included in the study we measured and correlated the presence of PFO with the tidal volume (V_t), the plateau pressure (P_{plat}), the compliance of the respiratory system (C_{rs}) and the size of the right (RV) and left (LV) ventricle.

RESULTS. Mean P_aO_2/FiO_2 was 198 (min 50, max 350), mean C_{rs} was 39 ml/cmH_2O (min 11, max 72), mean V_t was 574 ml (min 260, max 980) and mean P_{plat} was 22 cmH_2O (min 14, max 37). The prevalence of PFO detected with TEE was 28% and with TCD 48%. There was no PFO detected with TEE and missed by TCD. TCD was more sensitive than TEE in detecting PFO of grade I (7 with TEE, 17 with TCD) and II (6 with TEE, 16 with TCD), while for grade III the two techniques had equal sensitivity (15 with TEE, 15 with TCD). No correlation was found between P_{plat}, C_{rs}, V_t and the presence of PFO. On the contrary, a strong correlation was found between RV dilatation and the presence of PFO ($p < 0.001$).

CONCLUSIONS. The prevalence of PFO detected by TCD is very high in mechanically ventilated ICU patients and this may have important clinical implications. TCD is more sensitive than TEE in detecting a small PFO. The presence of RV dilatation increases the prevalence of PFO.

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A MULTICENTER TRIAL ON THE PREVALENCE OF PATENT FORAMEN OVALE (PFO) IN ALI/ARDS PATIENTS

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INTRODUCTION. The prevalence of PFO in autopsy studies has been found as high as 26%. Contrast transesophageal echocardiography (c-TEE) is the "gold standard method" to detect a PFO. However, FO may open or close according to the interatrial pressure gradient. ARDS and mechanical ventilation (MV) may both stretch the pulmonary vasculature and right ventricle (RV) and thus reverse the interatrial pressure gradient, leading to an increased prevalence of PFO. Moreover, the sensitivity of PFO detection depends on the site of the injection of the contrast agent.

OBJECTIVES. The aim of our study was to identify in mechanically ventilated patients for ALI/ARDS the prevalence of PFO and to evaluate the factors that may influence the prevalence of PFO.

METHODS. Two groups of MV patients, one with ALI/ARDS and one without respiratory failure (RF), were enrolled in the study. All patients underwent a TEE study for hemodynamic assessment. In each patient three consecutive bubble tests with agitated Haemacel® were performed at 60^0 and 90^0 rotation of the TEE probe. The bubble test was performed through a central line in the inferior or superior vena cava (IVC, SVC). A PFO was diagnosed by the presence of microbubbles in the left atrium within five cardiac cycles following the injection. Furthermore, in ALI/ARDS patients in whom a PFO was not detected at baseline MV, three consecutive bubble tests during recruitment maneuver at 45 cmH_2O for 20 s were performed. The compliance of the respiratory system (C_{rs}), blood gas exchange and the ventilatory settings (P_{plat}, V_t) were recorded in both groups.

RESULTS. We studied 95 ALI/ARDS (44/51) patients and 76 patients without RF. A statistical significant difference ($p < 0.01$) was found between the prevalence of PFO in the ALI/ARDS group [36/95, 38%], compared to the control group [15/76, 20%]. Seven additional FO opened during recruitment (45%). PaO_2/FiO_2, C_{rs} and P_{plat} were statistically different between the ALI/ARDS and control group: 131 versus 296, 35 ml/cmH_2O versus 49 ml/cmH_2O, 28 versus 20 cmH_2O, respectively. The presence of RV dilatation was a strong predictor for the FO opening ($p < 0.01$); on the contrary, no statistical significant difference was found between the site of injection (SVC vs. IVC), the C_{rs}, V_t, and P_{plat} and the presence or absence of a PFO.

CONCLUSIONS. A high prevalence of PFO was found in ALI/ARDS patients. RV dilatation seems to be the reason of this high prevalence. RV dilation may be due to the lower C_{rs} and higher P_{plat} of the ARDS patients.

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DYNAMIC ASSESSMENT OF ARTERIAL ELASTANCE TO PREDICT ARTERIAL PRESSURE RESPONSE TO VOLUME LOADING IN PRELOAD-DEPENDENT PATIENTS

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INTRODUCTION. The clinical evaluation of arterial tone is mainly based on the calculation of total systemic vascular resistance (TSVR). However, given the pulsatile nature of arterial flow, this parameter provides an inadequate assessment of vascular tone. Another approach proposed would take account of changes in pulse pressure and blood flow, relationship known as arterial elastance (Ea). So, for a given stroke volume, the blood pressure generated in the circulatory system will depend on Ea (1).

OBJECTIVES. To assess the ability of the dynamic arterial elastance (Ea_{dyn}), defined as the relationship between pulse pressure variation (PPV) and stroke volume variation (VVS), to predict the hemodynamic response in mean arterial pressure (MAP) to a increase in stroke volume (SV) in hypotensive preload-dependent patients with acute circulatory failure.

METHODS. We performed a prospective clinical study in a 17-bed multidisciplinary intensive care unit, including 21 patients with controlled mechanical ventilation and monitored with the Vigileo® monitor, for whom the decision to give fluids was taken due to the presence of circulatory, including arterial hypotension (MAP ≤ 65 mmHg or systolic arterial pressure <90 mmHg), and preserved preload-responsiveness condition, defined as SVV ≥10%. Dynamic arterial elastance (VPP/VVS ratio), arterial pulse pressure to SV ratio, MAP/SV ratio, TSVR and MAP were compared to predict a MAP increase ≥15% after volume expansion (MAP-responders).

RESULTS. At baseline, only Ea_{dyn} was significantly different between MAP-responders and nonresponders. VE-induced increase in MAP was strongly correlated with baseline Ea_{dyn} ($r^2 = 0.82$, $P < 0.0001$) and changes in Ea_{dyn} after VE ($r^2 = 0.77$; $P < 0.0001$). The only predictor of MAP increase was Ea_{dyn} (AUC 0.98 ± 0.03; 95% C.I.: 0.8–1). A baseline Ea_{dyn} value >0.89 predicted an increase ≥15% in MAP after fluid administration with a sensitivity of 92.9% (95% C.I.: 66.1–99.8%) and a specificity of 100% (95% C.I.: 59–100%).

CONCLUSIONS. Dynamic assessment of arterial elastance by PVV to SVV ratio during controlled mechanical ventilation could be used to predict mean arterial pressure increase after volume loading in hypotensive preload-dependent patients.

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FOUR SEVERITY SCORING SYSTEM COMPARISON IN SEVERE SEPTIC PATIENTS

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INTRODUCTION. Severe sepsis is one of the major reasons for intensive care unit (ICU) admission and leading causes of mortality. Some of these score systems have been customized for patients such as APACHE II, APACHE III, SASP II and MODS. This study is to assess the validity of mortality prediction systems in severe septic patients.

OBJECTIVES. The aim of this study was to compare and evaluate four severity scoring systems in intensive care unit (ICU), including APACHE II, APACHE III, SASP II and MODS in severe septic patient**.**

METHODS. Fifty-six severe septic patients were divided into two groups. One was survival group and the other was non-survival group. Besides general data, the continuous surveillance of APACHE II, APACHE III, SASP II and MODS were recorded by 1st, 3rd and 7th day.

RESULTS. Compared with survival group, MODS was significant difference in non-survival group only in 1st day (7.9 ± 3.1 vs. 10.1 ± 2.9, $P < 0.05$) but APACHE II, APACHE III and SASP II were significant difference through 1st, 3rd and 7th day($P < 0.05$). In seven-day comparison, P value of APACHE III in non-survival group was the minimum ($P = 0.000$) and P value of MODS was the maximum ($P = 0.008$). In optimal survival evaluation, it seemed that APACHE III was the best (APACHE III > APACHE II = SASPII > MODS).

CONCLUSIONS. In order to evaluate the critical condition and prognosis of severe septic patients, APACHE III was the best and APACHE II and SASP II were followed and MODS was the worst.

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THE IMPORTANCE OF EARLY RECOGNITION AND TIMELY MANAGEMENT OF SEVERE SEPSIS IN THE EMERGENCY DEPARTMENT

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INTRODUCTION. Severe sepsis has a mortality of 28–50%, increasing by 8% for every hour it is left untreated. The college of Emergency Medicine (CEM) set out standards for the management of severe sepsis in 2009. These standards consist of 8 interventions that must be completed before the patient leaves the Emergency Department (ED): Administration of antibiotics and intravenous (IV) fluids must be completed in all cases. Oxygen, measurement of urine output, serum lactate, observations, blood cultures and senior ED or intensive care (ICU) review must occur in 95% of patients.

OBJECTIVES. To assess compliance with the CEM standards for management of severe sepsis across three ED sites in the West Midlands.

METHODS. Data was collected retrospectively over 3 months. Patients presenting to the ED within this period were assessed for likelihood of severe sepsis by the diagnostic code given to each patient upon leaving the ED. Data was analysed using a scanned copy of the ED clerking. Patients' notes were assessed for SIRS criteria and signs of new infection. If these criteria were met, and organ dysfunction was present, they were included in the audit.

RESULTS. 255 patients with severe sepsis were identified. Of these 17% were documented as septic by ED staff. The CEM standards of care were received in 41% of patients with a documented diagnosis of severe sepsis in the ED, and 23% of patients overall. 89% of patients received the 'treatment' aspects of care: Oxygen, IV antibiotics (with blood culture) and IV fluids. 71% of severely septic patients had no documented consideration of ICU referral.

CONCLUSIONS. Early recognition of severe sepsis in the ED led to greater performance in meeting the CEM standards. Although 100% of patients received observations and 89% received the treatment interventions, we performed poorly in meeting the remaining CEM standards. The trust has developed a severe sepsis proforma which incorporates the CEM standards to accurately record the completion of each intervention. A sepsis course for staff has been launched trust wide, and a formal referral process to ICU for all severely septic patients is being implemented.

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FEVER AND ANTIPYRETIC IN CRITICALLY-ILL EVALUATION (FACE) STUDY

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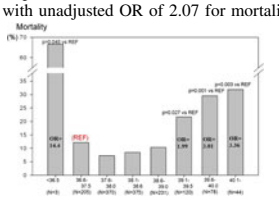
INTRODUCTION. The association of fever and antipyretic use and outcome in critically-ill patients is not well known and there is no prospective multicenter study.

OBJECTIVES. To observe association of body temperature (BT) and antipyretic use with mortality in the critically-ill.

METHODS. A prospective multi-national, multi-center observational study. Consecutive patients whose ICU stay were expected to be more than 48 h were recruited from 15 centers in Japan and 10 centers in Korea. Patient's BT was prospectively recorded every 4 h until patient's death, discharge from the ICU or up to 28 days. Information including patient's clinical characteristics at admission, presence of infection, and use of steroids, extracorporeal circuit, and antipyretics were recorded.

RESULTS. A total of 1,426 patients were included in the study with 58,501 measurements of BT and 4,940 incidents of antipyretic use. Median age was 66 (54, 74) years old, with APACHE II score of 17 (12, 22). In all, 691 (48.5%) patients had evidence of infection. Relationship between maximum BT and 28 day mortality showed a U-shaped curve, with maximum BT of <36.5°C and >39.0°C having significantly higher mortality compared to reference temperature (36.6–37.5°C). Antipyretic methods used were external cooling in 78.6%, acetaminophen in 11.6%, NSAID in 8.6% and others in 1.3% of time. Use of any antipyretic use, external cooling, any medication, and acetaminophen was significantly higher in patients non-survivors compared to survivors. In those with infectious fever, use of any medication was associated with unadjusted OR of 2.07 for mortality ($p < 0.001$).



Relationship between maximum BT and mortality

CONCLUSIONS. Both extremes of BT and antipyretic use were associated with poor outcome in these critically-ill patients.

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CLINICAL PREDICTORS OF DISEASE SEVERITY IN PATIENTS WITH INFECTION SUSPICION IN THE EMERGENCY DEPARTMENT

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OBJECTIVES. To analyze the ability of several clinical variables and biomarkers to predict disease severity in patients with suspicious of infection in the emergency department (ED).

METHODS. Prospective observational study. Population: all adult patients admitted in the ED with blood culture withdrawal with bacterial infection suspicion. Place: University hospital of 624 beds, with around 25,000 medical emergencies assisted yearly. Study duration: from March 1st to April 30 th 2009. Variables: Age, gender, comorbidities according to Charlson index, presence of leukocyte count above 15×109/L, presence of neutrophil band cells, presence of neutropenia, level of C reactive protein, procalcitonin (PCT), proadrenomedullin (ProADM), neopterin and final diagnose. Disease severity events were defined as: admission to the Intensive Care Unit (ICU) or death within the first 7 days after admission. Data was analyzed by statistical package SPSS 14.0 for Windows.

RESULTS. Blood cultures were obtained from 457 patients. 45 of them weren't included due to not enough data. Mean age 69 years (54–78), being 60.4% male. The most frequent diagnose was community acquired pneumonia: 87 (21.1%). Blood cultures were positive in 53 (12.8%) being the most frequently isolated microorganism E. coli: 18 (33.3%). 34 cases (8.2%) fulfilled severity criteria: 21 (5%) deaths, 14 (3.3%) admission in the ICU. In 47% of them an infection was proved and in other 26.4% was considered likely infection. Distribution of the variables in the univariate and multivariate analysis is shown in Table 1. The multivariate analysis showed as independent variables associated with severity: gender, PCT and proADM. The diagnostic yield of the biomarkers predicting severity is shown in Table 2. PCT and proADM show high negative predictive value.

TABLE 1 DISTRIBUTION OF VARIABLES. DISEASE SEVERITY

	NO severity N = 378, n (%)	Severity N = 34, n (%)	Univariate analysis (p)	Multivariate analysis OR (CI 95%)
Gender (female)	155 (41)	8 (23.5)	0.046	0.3 (0.13–0.75)
Charlson 0/1–2/3–4/> 5	56 (14.8)/213 (56.3)/ 63 (6.7)/46 (12.2)	3 (8.8)/19 (5.9)/ 2 (5.9)/10 (29.4)	0.019	NS
Leukocite >15 × 10^9/ml	86 (22.8)	13 (38.2)	0.043	NS
Neutrophil band cells	124 (32.8)	17 (50)	0.043	NS
Bacteremia	39 (10.3)	14 (41.2)	0.000	NS
CRP >126.5 (mg/L)	105 (27.8)	19 (55.9)	0.001	NS
PCT >1 (ng/mL)	73 (19.3)	21 (61.8)	0.000	3.6 (1.5–8.7)
proADM >1.94 (nmol/L)	66 (17.5)	21 (61.8)	0.000	4.6 (1.9–11.0)
Neopterin >32.5 (nmol/L)	122 (32.3)	22 (64.7)	0.000	NS

TABLE 2 DIAGNOSTIC YIELD OF SEVERITY PREDICTIVE VARIABLES

	Sensitivity	Specificity	PPV	NPV
PCT <1 (ng/mL)	61.8 (43.6–77.3)	80.7 (76.3–85.5)	22.3 (14.7–32.3)	95.9 (92.9–97.7)
ProADM >1.94 (nmol/L)	61.8 (43.6–77.3)	82.5 (78.2–86.1)	24.1 (15.9–34.7)	96.0 (93.1–97.8)

CONCLUSIONS. In patients with suspicious of infection in the emergency room, PCT and proADM make possible to define a group with low severity.

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FREQUENCY OF *STAPHYLOCOCCUS AUREUS* (SA) NASAL CARRIAGE BY RAPID SCREENING IN ANESTHESIOLOGISTS AND INTENSIVISTS

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INTRODUCTION. The incidence of SA nasal carriage among health care workers is poorly known. New techniques for rapid detection by PCR are now available.

OBJECTIVES. The objective of this study was to evaluate the proportion of SA carriage in medical healthy volunteers at the Conference of the French Society of Anesthesiology and Intensive Care Medicine in 2009 (SFAR).

METHODS. Anonymous nasal screening of SA in volunteers has been proposed in a booth during the congress. An anonymous questionnaire was completed containing demographic data, professional practice and epidemiological knowledge on MRSA (methicillin-resistant SA). A double nasal swab was performed and the analysis made in real time by the test Xpert MRSA/SA (Cepheid) with GenXpert system (Cepheid). The results were given back to volunteers anonymously within an hour. Two groups were formed based on the presence or absence of SA. Resistance to methicillin was evaluated for positive patients.

RESULTS. 289 screening tests were performed. The population was predominantly male (70.2%), mean age 48 $\pm$ 10 years, working in university hospitals (44%), in general hospitals (34%) and private hospitals (22%). 32% of volunteers were screened positive for SA, including 8% of MRSA. The group of volunteers SA + versus the SA − group, was more frequently male (87 vs. 69%, $p = 0.001$), working in ICU (38 vs. 28%, $p = 0.1$). There was no difference regarding the type of structure and number of beds. 93% of practitioners are in regular contact with MRSA, but only 17% know its prevalence within their hospital. Only 59% are screening patients at risk and 14% had the result available of this test in less than 24 h. Only 43% of practitioners perform the isolation of patients with MRSA. 80% of practitioners change their protocol of antibiotic prophylaxis if the screening test result is positive.

CONCLUSIONS. One third of medical volunteers, mostly male anesthetists working in ICU, is positive for a screening for nasal SA. The proportion of MRSA is very low, but the question of targeted nasal decontamination is asked. Medical knowledge about the management of MRSA is still very weak.

1108

TOWARD AN OPERATIVE DIAGNOSIS IN SEPSIS: A LATENT CLASS APPROACH

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INTRODUCTION. Three potential biomarkers have shown a regular presence in systemic infections: C-reactive protein (CRP), Procalcitonin (PCT), and D-dimer (DD); the latter as an unspecific signal of coagulation activation. So far, however, no large prospective studies support any of them as a single independent criterion for sepsis. Furthermore, the lack of a reference test has hampered the assessment of the accuracy of biomarkers to diagnose sepsis.

OBJECTIVES. To estimate the operative characteristics of CRP, PCT and DD as diagnostic tests for sepsis in patients admitted to hospital care with a presumptive infection as main diagnosis.

METHODS. Prospective study conducted between August 2007 and February 2009. Patients were enrolled if they were hospitalized in the emergency room (ER) with at least one of the following as admission diagnosis: any type of infection, fever of unknown origin, delirium of unknown origin or acute hypotension not explained by other syndromes. Serum levels of CRP, PCT and DD were determined within 24 h of admission. The patients were classified as no infection or sepsis by an expert consensus committee, blinded to the results of the index tests, on the basis of all the daily clinical and microbiological data collected during the first seven days of hospitalization. Additionally, a latent class analysis (LCA) with random effects was used to estimate the likelihood of belong to the latent cluster "sepsis" in the study population

RESULTS. Among 765 recruited participants CRP was measured from 748, PCT from 747 and DD from 744 patients. The main admission diagnosis in 505 sepsis patients (66%), according to the expert consensus, was community-acquired pneumonia (23%), followed by urinary tract infection (17%) and soft tissue infection (16%). Severe sepsis defined by a SOFA score ≥ 2 in any domain was recorded in 337 patients (67%). A microbiological diagnosis was confirmed in 221 (44%) sepsis patients. The LCA with a PCT cutoff point of 2 ng/ml (AUC = 0.95, LR + = 10.6, LR − = 0.09) identified a cluster of patients with higher mortality (17 vs. 9%), higher rate of positive blood cultures (39 vs. 12%) and higher values of lactate, SOFA and APACHE II scores. The areas under the curve (AUCs) for each biomarker compared to consensus expert are shown in the Table.

AUCS ACCORDING TO DIFFERENT GOLD STANDARD

	CRP	DD	PCT
Sepsis	0.71	0.55	0.70
Severe Sepsis (SOFA ≥ 2)	0.52	0.56	0.67
Severe Sepsis (SOFA ≥ 3)	0.52	0.59	0.76

CONCLUSIONS. In this cohort of ER patients suspected of having any infection; CRP, DD and PCT were not significantly able to discriminate, according to a consensus diagnosis, sepsis from no sepsis patients. Using LCA, however, a cutoff point for PCT higher than the usually recommended seems able to confirm and to discard those more acutely ill patients.

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HOW USEFUL IS BLOOD CULTURE IN A GENERAL CRITICAL CARE UNIT?

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INTRODUCTION. Blood culture is a common technique for the investigation of suspected infection in critical care. In a US whole-hospital study 14.4% of cultures were positive cultures, of which nearly half were regarded as contaminants (1). While blood culture results take time, treatment for bloodstream infection should be provided swiftly, usually before results are available (2). Prior treatment with antimicrobials increases the chances of false negative results. Haste, poor technique and alteration in commensal flora may increase the chances of falsely identifying pathogens.

OBJECTIVES. We have investigated the utility of blood culture tests in our general critical care unit over 1 year in terms of results yielded and actions prompted.

METHODS. The indication for blood culture was clinician's discretion. All critical care sourced blood cultures for the period Oct 2008 to Sept 2009 were reviewed from the microbiology laboratory database. Blood culture specimens were collected in BacT/ALERT® bottles (Biomerieux, Durham, NC, USA 27704). Notes review was made of the positive blood culture episodes to determine actions after the results were known. Consideration was given to the source of the blood sample: clean stab versus from an intravascular device. Categoric data was analysed using the Chi-squared test and P value of 0.05 was accepted as significant.

RESULTS. 423 samples were taken from 196 patients. 320 were from a new venous stab and 93 were from arterial or central venous catheters (10 sources were unclear). 60 of the specimens grew at least one organism (14.2%). 21 non-skin-commensal organisms were grown in 19 specimens, 4.5% of specimens. 41 samples grew skin commensals only (9.7%). Of the 46 positive blood cultures obtained from new venous stab, 12 grew at least one non-skin-commensal organism, 34 grew only skin commensal organisms with 9 of these (representing 8 episodes) having a matching central line tip culture. The pattern of organisms isolated from intravascular line samples and new venous stab was similar.

CONCLUSIONS. The frequency of positive blood cultures in this UK critical care sample is comparable to that in other studies. The pick up rate for pathogens was low in this population. The growth of skin commensal organisms was frequent, suggesting contamination, although line colonisation/infection accompanied a quarter of clean stab skin-commensal positive cultures. Overall, positive results had little impact on clinical decision making.

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FAILURE TO RECOGNISE PATIENTS WITH SEPSIS IN THE EMERGENCY DEPARTMENT

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INTRODUCTION. Patients with (severe) sepsis and septic shock have a high mortality rate varying from 22 to 75%. In order to treat sepsis adequately, it is necessary that sepsis is recognized as early as possible.

OBJECTIVES. We hypothesized that in the emergency department of our hospital many patients with sepsis are not recognized as such.

METHODS. In a retrospective design, patients of an age of 18 years and older who were admitted to the emergency department during a period of 3 months between January–April 2008 and diagnosed as having an infection were included. The diagnose infection was made on admission by the emergency department nurse. The included patients were either classified as having sepsis or not having sepsis, according to the SIRS criteria.

RESULTS. During the study period, 354 patients of 18 years and older admitted to the emergency department were diagnosed as having an infection. Of these 354 patients, only 15 patients (4.2%) were recognised and treated as having sepsis while 162 patients (45.8%) should have been. Patients on admission recognised and treated as having sepsis, who also were found to have sepsis in retrospect analysis ($n = 11$), were the patients with severe sepsis or septic shock. Of the patients having sepsis in retrospect, 5 of 162 (3%) died during their hospital stay without being recognized as having sepsis. Of the patients recognized as having sepsis 1 of 11 (9.1%) died.

CONCLUSIONS. Sepsis is under diagnosed in the emergency department of our hospital. In patients with sepsis not recognised as such, mortality is low.

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INVASIVE PROCEDURES IN A CRITICAL CARE UNIT. SURVEILLANCE AND MONITORING OF MEDICAL INDICATION IN A TERTIARY UNIVERSITY HOSPITAL. LOCAL IMPROVEMENT PROGRAM IN NOSOCOMIAL INFECTIONS. APRIL TO DECEMBER 2009

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INTRODUCTION. In the Critical Care Unit (CCU) of the Hospital Clínico Universidad de Chile (HCUCH), the problem of nosocomial infections is an important goal inside the Local Quality Programme. Protocols and standards have emerged aimed at maximizing surveillance, monitoring and control of risk factors for nosocomial infections. These strategies generate the need to monitor our CCU baseline. Compliance with medical indication of certain invasive procedures such as central venous access (CVC) and urinary catheter stay (CUP), are factors to evaluate in these protocols, to reduce the risks of infection associated.

OBJECTIVES. Assessing compliance with medical indications for invasive procedures type CUP and CVC, based on local recommendations of the Committee of Nosocomial Infections (CIIH) of HCUCH and international Society of Health Epidemiology of America and the Infectious Diseases Society of America (SHEA/IDSA).

METHODS. We monitored two specific procedures required by the guidelines of CIIH-HCUCH, indications of CVC and CUP. The guidelines are based on standard recommendations of the Manual of CIIH-HCUCH and international recommendations SHEA/IDSA. The period was from April to December 2009. It took the total UPC which has 12 beds in the Intensive Care Unit (ICU), 15 beds in the Medical Middle-Care Unit (MMCU) and 28 beds in the Surgical Middle-Care Unit (SMCU). The implementation of guidelines was conducted by medical resident during 1 month, with shift monthly the medical resident. The data collected were managed in database, with expression in medians, and percentages.

RESULTS. In our CCU had 4340 admissions in period April-December 2009. The ICU admissions were 484, 867 were in MMCU and 2989 in SMCU. We applied a total of 1853 supervision's patterns, covering the CCU in its entirety. 53.4% (990 patterns) was invaded at the time of supervision. 699 patterns were performed in the ICU (37.7%), 640 patterns in MMCU (34.5%), and 739 patterns in SMCU (39.9%). The distribution pattern of CVC was 954 (51.5%) and 899 patterns CUP (48.5%). In 19.2% of CUP patterns (92 patterns) and 10.4% of CVC guidelines (53 guidelines), showed no medical indication of invasion at the time of supervision. Indications not mentioned by CIIH, monitoring in oncological abdominal surgery (33%), spinal trauma surgery (25%) and skin protection in the management of pressure ulcers (18%) were the most representative CUP. The CVC for renal replacement therapy (50%) were not included in local recommendations.

CONCLUSIONS. There was a 19.2% of CUP guidelines and 10.4% of CVC guidelines in the period monitored, without a medical indication of invasion, which implies an important responsibility of the treating team. The supervision of medical indications for invasive procedures is an important process under surveillance and especially prevention of intrahospitalary infections.

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VARIABLES ASSOCIATED WITH DEATH OF SEPTIC PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT

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OBJECTIVES. To determine the variables associated with the prognosis of critically ill septic patients on admissions to the ICU.

METHODS. This retrospective study was carried out in a polyvalent ICU of a secondary hospital from January 1, 2006, to December 31, 2009. All patients meeting criteria for sepsis on admission to the ICU. The following variables were recorded: gender, age, chronic organ insufficiencies (liver, renal, pulmonary, cardiovascular, and inmunosuppression), comorbidities (alcoholism, smoking habit, diabetes mellitus, non-core malignancy, and previous surgery or sepsis), previous antibiotic therapy, nosocomial infection, bacteraemia, culture of focus, site of infection, appropriateness of empirical antibiotics and failure of organs on admission by SOFA scale and during the clinical course. The statistical analysis was performance with SPSS 11.5.1. The association between the variables and death was accomplished using Student's t test for parametric continuous variables, and Chi-square test for categorical variables. Survival analysis by log-rank and Cox regression multivariate analysis was made to identify the independent factors associated with mortality.

RESULTS. One hundred and forty nine patients were included at ICU admission. Sepsis was present in 22 patients (14.8%), severe sepsis in 33 (22.1%), and septic shock in 95 (63.8%). The mean age was 66 years and 61.1% were male. The mortality rate was 39%. Regarding surviving patients, SOFA score who died was greater 11 (SD 8.2), $p = 0.01$. The mean age of the patients who died was greater, 70.1 years (SD 10.6), than in surviving ones, 63.9 years (SD 15.3), $p = 0.031$. Factors associated with mortality in the ICU, were the gender (47.3% in male regarding 27.6% in woman, $p = 0.017$), non-core malignancy (58.3%, $p = 0.04$), septic shock (53%, $p = 0.001$), respiratory failure (59%, $p = 0.001$) and cardiovascular failure (47%, $p = 0.02$).In multivariate analysis, strong predictors of mortality were the gender male (HR 1,844; CI 95%, 1,027–3,308), the age (HR 1,035; CI 95%, 1,010–1,062), APACHE I (HR 1,037; CI 95%, 1,009–1,065), septic shock (HR 2,612; CI 95%, 1,216–5,609) and inadequate empirical antibiotic therapy (HR 2,459; CI 95% 1,159–5,218).

CONCLUSIONS. The prognosis of sepsis in males and older patients is worse. Regarding comorbidities, non-core malignancy was associated with mortality rate. Septic shock, greater SOFA score, respiratory failure and cardiovascular failure implies a higher mortality rate. The adequate empirical antibiotic was associated with a reduction in this rate.

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PANDEMIC INFLUENZA H1N1: HOW DID WE DEAL WITH IT!

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INTRODUCTION. Recently we faced 2009 pandemic influenza A H1N1v strain. In severe cases, prompt initiation of effective antiviral treatment, appropriate oxygenation and ventilation support are critical for survival.

OBJECTIVES. To describe characteristics, treatment and outcomes of critically ill patients with 2009 influenza A (H1N1) infection admitted to an Intensive Care Department, in a University Hospital in Portugal.

METHODS. Prospective, single center, observational cohort study of all patients with H1N1 infection from August 2009 to January 2010 admitted to an ICU. We collected data on demographic and clinical characteristics of the patients and on treatments and outcomes.

RESULTS. 36 patients were included, mainly man (53%) with a mean age of 45 years (44.9 ± 14.5). 22% were healthy subjects. Most prevalent co-morbidities were: obesity (33.3%), chronic pulmonary disease (33.3%) and diabetes mellitus (25%). Symptoms started 4.76 ± 3.3 days before ICU admission and the most frequent were: cough (80.6%), dyspnea (77.8%) and fever (66.7%). Median time for ICU admission was 1,268 min (IQR 185–2,549). Mean total SOFA, SAPSII and SAPS III score on ICU admission were 9.71 ± 3.73, 42.5 ± 19.1 and 62.3 ± 15.7, respectively. Primary viral pneumonia (77.8%) was the most frequent manifestation of influenza. Septic shock (27.8%) and bacterial pneumonia (25%) were the clinical conditions more frequently associated. Antiviral therapy (oseltamivir) was started 404.5 min (30–1,465) after hospital admission with a mean duration of 11.2 ± 4.7 days. 94% of the pts received concomitant antibacterial treatment, mainly a macrolide (83.3%). Most of the patients were severely hypoxemic [PaO_2/FiO_2 ratio 101.5 (62–479)] and 80.6% underwent mechanical ventilation with a median duration of 15 days (4–94). Lung rescue therapies included neuromuscular blockade (36.1% of patients), prone positioning ventilation (33.3%), inhaled nitric oxide (19.4%), extracorporeal membrane oxygenation (8.3%) and high-frequency oscillatory ventilation (2.8%). Vasopressors and steroids were use in 52.8 and 63.9% of the pts respectively. Renal replacement therapy was started in 19%. ARDS (44.4%) and nosocomial infection (44.4%) were the most frequent complications. ICU and global hospital mortality were, respectively, 25 and 36.1%. Median ICU and hospital LOS were 16 and 22 days respectively.

CONCLUSIONS. H1N1 infection was associated with significant morbidity and mortality. It occurred mainly in young pts with co-morbidities and was associated with severe hypoxemia, a trigger for prolonged mechanical ventilation and frequent use of lung rescue therapies. A significant delay in hospital admission and start of antiviral therapy should also be noted.

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PREDICTIVE MODEL ASSESSMENT OF POSITIVE BLOOD CULTURES IN CRITICALLY ILL PATIENTS

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OBJECTIVES. To search for independent predictors of bloodstream infection in Intensive Care Unit (ICU) patients. To analyze the clinical and epidemiological characteristics of patients who were taken samples for blood cultures (BC) in ICU. Evaluation of current indications for blood cultures, antibiotic treatments (ABT).

METHODS. Prospective observational study of adult patients consecutively admitted to an ICU who were taken BC from March to November 2009. Demographics, clinical data and laboratory tests at the time of collection of the BC were collected, as well as the BC indication and ABT. ABT was classified as adequate in terms of susceptibility received. Qualitative variables are expressed as percentage and quantitative variables as mean and standard deviation. logistic regression was performed of multivariate analysis. We considered statistically significant a p value <.05.

RESULTS. 336 BC were included of 194 patients. Mean age 59.6 ± 17.1. ICU stay 10.4 ± 11.6 days (hospital 29.6 ± 26.3d). Hospital mortality rate 32.5%. Patients were medical (63.6%), surgical (32%). BC indications: fever peak (60.7%), severe sepsis/septic shock (24.7%). The most commonly used ABT were cefotaxime and imipenem. Source of infection: abdominal (37.5%), respiratory (31.2%). Results of BC: 79 positive (23.5%), 257 negative (76.5%). The most commonly isolated microorganisms were *E. coli*, *S. aureus*, *P. aeruginosa* and *S. pneumoniae*. Appropriate empirical treatment: 84.8% of cases with positive BC. The factors that maintain independent association with outcome were CRP ($p < .001$, OR 1.005; 1.002–1.008) and SOFA ($p = .006$, OR = 1.138; 1.037–1.248).

UNIVARIATE ANALYSIS

	Hemocultive		
	Negative (N = 146)	Positive (N = 48)	P
Male/female (%)	67.8/32.2	52.1/47.9	.049
APACHE II	15 (10;20)	21 (10;25)	.024
SOFA	5 (3;7)	8 (4;12)	<.001
Cardiac frequency, bpm	98 (84;115)	112 (100;120)	.047
Leukocytes (×1,000)	12.6 (8.2;18.8)	16.5 (8.8;26.3)	.047
Lactate	1.8 (1.15;2.75)	2.15 (1.50;3.10)	.002
CRP	188 (113;270)	286 (270;376)	<.001
Before CRP	199 (62;273)	225 (114;355)	.016

CONCLUSIONS. In our sample, the levels of CRP and the SOFA value at the time of the BC were independently associated with the presence of bloodstream infection, defined as the presence of positive blood culture. The most common indications were the presence of persistent fever/fever peak and severe sepsis/septic shock. We got a 23.5% of positive BC, with *E. coli, S. aureus, P. aeruginosa* and *S. pneumoniae* as the most commonly isolated microorganisms. Cefotaxime and imipenem were the most commonly used ABT.

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1115

AN AUDIT OF TIME TO FIRST DOSE ANTIBIOTIC IN SUSPECTED SEPSIS

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INTRODUCTION. Sepsis is a leading cause of death worldwide. Delays in prompt antibiotic therapy in severe sepsis contributes to 10–15% increase in mortality rates. [1]International standards recommend administration of broad spectrum antibiotics within 3 h of presentation in patients with sepsis. [2]

OBJECTIVES. To assess the length of time from admission to administration of first dose antibiotic in patients with suspected sepsis, in an acute medical setting. We hypothesised that the following could contribute to a delay in antibiotic administration

1. admission method; emergency department versus community,
2. route of administration; oral vs. intravenous,
3. prescription method; immediate (once only) vs. regular prescriptions), and
4. source of infection.

METHODS. Prospective study over two-week periods in an acute medical unit: cycle one (May 2009) and cycle two (December 2009). Inclusion criteria included all adult patients prescribed antibiotic therapy in suspected sepsis with documented source of infection.

RESULTS. Cycle one ($n = 51$) mean time from admission to administration of first dose antibiotic was 5:33 ± 4:53 h. The method of prescription was statistically significant ($p = 0.002$, unpaired t test), with 'once only' prescriptions administered up to 2.4 times quicker than regular prescriptions. Recommendations from cycle one lead to the prescription of first dose antibiotic on the 'once only' section of the drug chart being incorporated into antibiotic guidelines.

Cycle two ($n = 63$) mean time from admission to administration of first dose antibiotic was 4.04 ± 3.42 h. There was not a statistically significant uptake of intervention by clinical staff. No hypothesised factors were identified to be significant contributors to the time delay, including prescription method ($p = 0.902$).

Admission to administration time difference between cycles was 1.26 h, with a mean reduction of 1.04 h between clinician assessment and prescription time in cycle two.

CONCLUSIONS. We identified delays against the standard after both cycles of the audit. We demonstrated that the method of prescription should be taken into consideration when prescribing antibiotics in patients with suspected sepsis. There are a multitude of factors that could contribute to a reduction in the clinician assessment to prescription time, which may be investigated in further audits.

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1116

PNEUMOCOCCAL DISEASE IN CRITICALLY ILL ADULTS IN THE 7-VALENT VACCINE ERA

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INTRODUCTION. In Spain, 7-valent conjugated pneumococcal vaccine (PCV7) was introduced in 2001. Several studies have shown a decrease in the pneumococcal disease (PD) in children. The effect on adults is still not well known.

OBJECTIVE. to determine if there is a change in the incidence, complications and severity of the PD after the introduction of the 7-valent conjugated vaccine.

METHODS. Observational study of patients with PD admitted to an Intensive Care Unit of a teaching hospital. The period of the study was from January 2000 until December 2009. Epidemiological data, clinical course, complications and mortality rate were obtained from hospital's records. Statistical tests: Chi-square, Fisher test, Student's t, U Mann–Whitney and logistic regression analysis.

RESULTS. 163 patients from the 8,548 total admissions at ICU during that period of time were studied. 62% were men, mean age 54.54 (16.85–82.90) years. Diagnose was performed by 2 or more methods in 47.9%, blood cultures in 20.5%, urinary antigen testing in 12.2%, pleural fluid in 1.3%, sputum in 9% and cerebrospinal fluid in 7.1%. APACHE-III at admittance was 67 (12–188). Comorbidities were present in 77.3% of the patients. The cause of admittance was meningitis in 23.9% and pneumonia in 74.2%. Patients affected with meningitis were older ($p = 0.004$) than those affected with pneumonia. During these years, the PD has shown a statistically significant increase ($p = 0.0043$) in the number of patients admitted and the in cases of pneumonia while the number of pneumococcal meningitis remained stable. Pleural effusion was developed by 21.2% of the patients. Mechanical ventilation was necessary in 59.7% of patients with pneumonia and 73.7% in patients affected with meningitis. Worst GCS at UCI in patients with meningitis was 7 (3–15). ICU length of stay was 8 (1–109) days. Mortality rate in patients with meningitis and pneumonia was 28.2 and 22.7% respectively (NS). The respiratory (38.4 vs. 1.7% $p < 0.001$) and renal failures (38.9 vs. 11.6% $p < 0.0001$) were significantly associated with a higher mortality. Neurological sequelae after meningitis were observed in 58.1% of the patients. The main risk factors associated with mortality were age (OR 1,071 95% CI: 1,017–1,127), solid neoplasia (OR 6,307 CI 95%: 1,022–38,904) and chronic hepatopathy (OR 3,211 95% CI: 1,144–9,014). HIV infection was shown as the most important independent risk factor for mortality (OR 38,44 95% CI: 5,596–264,02).

CONCLUSIONS. The incidence of PD in our ICU has significantly increased after the introduction of PCV7 in our area. Patients have a high proportion of comorbidities. PD was associated with a high rate of complications. Patients with HIV infection have the worst outcome.

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Using PK/PD properties: 1117–1123

1117

INFUSION TIME OF PIPERACILLIN/TAZOBACTAM AND OPTIMAL CLINICAL OUTCOMES IN *PSEUDOMONA AERUGINOSA* INFECTIONS IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Severe infections in ICU patients due to *P. aeruginosa* are related to higher morbi-mortality. Timely and adequate antibiotic treatment is fully justified according to resistance data. The minimum inhibitory concentration (MIC) becomes a surrogate of the pharmacodynamics (PD) of the combining infecting bacteria and drug. As pathogens become more resistant, treatment failure using standard dosing regimens increases. The pharmacokinetic (PK) profile in ICU patients is too variable to optimize therapeutic outcome by using the standard dosages. Monte Carlo simulations facilitate to theoretically forecast the probability of PK/PD target attainment. Regarding β-lactams, the PK/PD index that best correlates with clinical and bacteriological efficacy is the time for which the free serum drug concentration exceeds the MIC: $fT^{SS} > _{MIC}$. In order to optimize it, continuous or extended IV infusions have been proposed.

OBJECTIVES. This analysis evaluates, by means of Monte Carlo simulations, the appropriateness of several piperacillin/tazobactam (PT) extended IV infusions (EI) and continuous infusions (CI), in ICU patients with *P. aeruginosa* infections.

METHODS. For each dose regimen (EI and CI), 5000 PK profiles were simulated based on previous population PK data and creatinine clearance (CLcr): 80 mL/min, 40 mL/min and 20 mL/min. A wide range of MICs was studied: 1–32 mg/L, according to the CLSI cut-off for *P. aeruginosa* to PT. The likelihood of target attainment: $fT^{SS} > _{MIC}$ >70% (PP_{70}) was calculated for each EI while keeping the interdose interval of 6 or 8 h. A PP_{70} value >90% was considered satisfactory. Regarding CI, $fT^{SS} > _{MIC} = 100\%$ (PP_{100}) and the percentage of patients with free-PT concentrations (fC^{SS}) higher than the MIC ×1 or 4 were determined.

RESULTS. Results from simulations show that, in patients with CLcr: 80 mL/min, a dosage of PT of 4 g IV for 30 min/8 h is expected to reach the goal ($PP_{70} > 90\%$) only for MIC values ≤ 1 mg/L. For higher MICs, PP_{70} was clearly inadequate. The probability of attaining PP_{70} for a given MIC rises as long as the infusion time increases (i.e.: MIC = 4 mg/L; PP_{70}%: 74, 79, 81, 95, 98; EI(h): 0.5, 1, 2, 3, 4, respectively). Conversely, the length of infusion seems to have less impact on PP_{70} in patients with moderate and severe renal impairment. PP_{70} clearly remains above 90% whilst Clcr = 40 mL/min and MIC ≤ 4 mg/mL. Regarding CI, all regimens achieve full PP_{100}, although not all of them optimize the ratio fC^{SS}/MIC ≥4. For example, if MIC = 4 mg/L and CLcr = 80 mL/min, a loading dose of 2 g followed by CI of 4, 6, 8, 10 or 12 g of PT showed full PP_{100}, while fC^{SS}/MIC ≥4 was only achieved in 64, 73, 94, 99 and 100% of patients, respectively. These results improve when renal impairment is present.

CONCLUSIONS. PT administered either as a continuous or extended infusion (3 h) might increase the likelihood of microbiological eradication and clinical outcome in ICU patients and high MICs for *P. aeruginosa*.

REFERENCE(S). None.

1118

CARBAPENEM PHARMACODYNAMICS (PD) AGAINST *PSEUDOMONAS* AND *ACINETOBACTER* ISOLATED FROM INTENSIVE CARE UNITS (ICU) IN EUROPEAN HOSPITALS: RESULTS FROM THE 2009 PASSPORT PROGRAM

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INTRODUCTION. The treatment of *Pseudomonas aeruginosa* (PSA) and *Acinetobacter baumannii* (AB) remains problematic in many ICUs. With few novel antibiotics in development, surveillance of contemporary isolates coupled with PD modeling will aid optimal dosing of currently available carbapenems. Prolonged infusion is a popular administration method for optimizing PD of the carbapenems while retaining room temperature stability.

OBJECTIVES. The aim of this PASSPORT (Probability of target attainment of Antibacterial agents Studied for Susceptibility and Pharmacodynamic Optimization in Regional Trials) study was to determine the probability of obtaining bactericidal PD exposures for various carbapenem dosing regimens against PSA and AB collected in European ICUs.

METHODS. Monte Carlo simulation, based on population pharmacokinetics, modelled 5,000 patients receiving doripenem, imipenem, and meropenem dosages as standard and prolonged infusions against 1,018 PSA and 179 AB collected from ICUs in Europe ($n = 80$ centers from 16 countries) during 2009. Susceptibility was calculated using EUCAST (European Committee on Antimicrobial Susceptibility Testing) breakpoints. Bactericidal targets were free T > MIC for 40% of the dosing interval. The cumulative fraction of response (CFR) was the percentage of simulated patients achieving this exposure against each population.

RESULTS. Susceptibility and CFR results are provided in the table.

SUSCEPTIBILITY AND CFR RESULTS

Carbapenem Regimen (infusion duration)	CFR (%)	
	PSA (n = 1018)	AB (n = 179)
Doripenem susceptibility	57.2	41.3
0.5 g q8 h (1 h)	69.2	48.0
1 g qSh (1 h)	76.7	53.7
2 g q8 h (1 h)	83.3	61.6
0.5 g q8 h (4 h)	79.0	56.4
1 g q8 h (4 h)	85.5	60.7
2 g q8 h (4 h)	91.0	68.9
Imipenem susceptibility	56.9	46.9
0.5 g q8 h (0.5 h)	44.9	42.8
0.5 g q6 h (0.5 h)	51.6	47.2
1 g q8 h (0.5 h)	51.9	46.9
0.5 g q8 h (3 h)	56.4	50.3
0.5 g q6 h (3 h)	58.5	51.5
1 g q8 h (3 h)	60.9	52.4
Meropenem susceptibility	58.3	46.4
0.5 g q8 h (0.5 h)	58.0	44.6
0.5 g q6 h (0.5 h)	62.4	48.8
1 g q8 h (0.5 h)	65.2	51.2
2 g q8 h (0.5 h)	71.9	56.7
0.5 g q8 h (3 h)	64.9	51.7
1 g q8 h (3 h)	71.4	56.9
2 g q8 h (3 h)	78.1	61.9

CONCLUSIONS. Despite high levels of resistance among PSA and AB from these ICUs, CFR for most carbapenem dosing regimens were above the reported susceptibility. Doripenem provided greater CFR than meropenem, which was superior to imipenem against these isolates. While higher doses combined with prolonged infusions significantly improved CFR against PSA, alternative therapeutic strategies will be required to address these highly resistant AB.

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1119

PREVENTING ADVERSE DRUG EVENTS: POTENTIAL DRUG INTERACTIONS INVOLVING ANTIMICROBIALS IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Drug interactions are common, and the effects of these interactions can range from innocuous to deadly. Critically ill patients often receive a variety of potent drugs, including antimicrobials, making this population extremely susceptible to drug-drug interactions. Therefore, physicians must be familiar not only with the antimicrobial drugs capable of producing adverse drug events, but also their potential drug-drug interactions. There are scarce data about the incidence of these types of drug interactions and the how frequently it might cause adverse events.

OBJECTIVES. The purpose of this study is to evaluate the incidence of potential drug interactions involving antimicrobials and the possibility to cause adverse events.

METHODS. The clinical pharmacist has prospectively analyzed ICU prescriptions between January 2009 and December 2009 with the purpose to identify potential drug-drug interactions involving antimicrobials. The screening was done with the relief from a software (Epocrates Rx® drug reference). The interactions detected were classified in eight groups according to the affected system (neurological, cardiovascular, gastrointestinal, renal, endocrine, hematological, musculoskeletal and others) and through the type of interaction (pharmacokinetic, pharmacodynamic and others). We have identified the most common potential effects, the medications involved and have observed the incidence of adverse drug events.

RESULTS. The ICU admitted 347 patients during the study period. We have analyzed 661 physician orders with 8209 prescribed items. We have identified 871 antimicrobial drug interactions (71 different interactions) which compound 20% of the total drug interactions (n = 4349). The cardiovascular system and the pharmacokinetic interaction were the most potentially affected (38%; 42%). The most common medications involved were: fluconazole (24%), clarithromycin (23%), levofloxacin (12%); linezolid (11%). The clinical pharmacist has made an intervention regarding medication safety in 3% (n = 27) and the acceptance rate by the medical ICU staff was 74%. We have not been able to identify any adverse drug event caused by drug interaction even with our active search and the spontaneous reports. However, sub notification must be taken into consideration.

CONCLUSIONS. Clinicians should be aware of potential drug-drug interactions when making therapy selections for critically ill patients. Antimicrobial drugs are susceptible to interact with other drugs, which may increase the risk of adverse drug events. The clinical pharmacist interventions may improve clinical outcomes by optimizing medication use, monitoring potentially preventable adverse drug events and promoting information about this important issue to the ICU multi-professional team.

1120

PERI-OPERATIVE PLASMA CEFAZOLIN LEVELS FOR ANTIBIOTIC PROPHYLAXIS DURING CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS (CPB)

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INTRODUCTION. Cefazolin is one of the most frequently administered antimicrobial agent for prophylaxis in "clean" surgery. Its broad spectrum against Gram + micro-organisms and its pharmacological characteristics make it an easy-to-use choice to prevent infections caused by Staphylococcus aureus and coagulase-negative stapylococci.

OBJECTIVES. The aim of this study is the evaluation of the plasma concentrations of cefazolin administered as a prophylactic antimicrobial agent during cardiac surgery with CPB. Adequate cefazolin plasma levels can maintain a tissue concentration high enough to prevent the risk of developing post-operative infections.

METHODS. After obtaining Ethical Committee approval and personal written consent, two groups of patients were enrolled in this prospective study. The first group, 12 patients, received cefazolin, 2 g, 30–60 min before skin incision and 1 g adjunctive dose after 4 h. Then, three 2 g doses were administered every 8 h. In the second group of 12 patients the adjunctive 1 g cefazolin dose was given at the beginning of the CPB. Blood samples were collected immediately before the first dose and every hour for the whole time of surgery, and, only in the second group, after surgery, at 12th, 18th and 24th hour. Plasma cefazolin concentration was determined with a biological radial diffusion assay.

RESULTS. Plasma cefazolin was constantly higher than the MIC90 of the most involved micro-organisms (according to CLSI). In the first group, cefazolin concentration suddenly decreased after starting CPB. The 1 g adjunctive dose immediately restored it. The earlier administration of this dose in the second group prevented this sudden fall. Plasma cefazolin was maintained at effective inhibitory levels for the whole time of surgery in all patients (>32 mcg/ml). During the postoperative period cefazolin decreased slowly, but inhibitory plasma levels were always maintained. The rate of cefazolin clearance was found equal to the creatinine clearance in all patients.

Perioperative plasma cefazolin concentration

CONCLUSIONS. The administration of cefazolin 2 g every 8 h can guarantee effective inhibitory plasma concentrations during surgery and during the first 24 h after surgery. CPB causes a sudden fall in cefazolin plasma levels. This can be avoided administering an adjunctive 1 g dose immediately before starting CPB.

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VANCOMYCIN DOSE REGIMEN ADJUSTMENT IN BURN PATIENTS ACCORDING TO TOTAL BURN SURFACE AREA

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INTRODUCTION. Adequate antibiotic therapy during infections is essential for a successful outcome in burn patients.

OBJECTIVES. Vancomycin dose regimen was adjusted based on trough plasma levels in burn patients that were distributed according to the extension total burn surface area (TBSA); also pharmacokinetics changes were compared.

METHODS. Twenty seven adult burn patients of both sexes, requiring antimicrobial therapy with vancomycin for the control of sepsis were investigated. Pharmacotherapeutic follow up was performed in a serial of periods (112 observations) for all patients investigated by collection of blood samples, 1 mL each from the venous catheter as follows: 1st blood sample collection, 2 h after the beginning of drug 1 h infusion and a 2nd sample blood collection at the trough, immediately before the next dose. If necessary, additional sample blood collections were performed based on the laboratorial data for patients any time, for dose adjustment purpose and optimization of drug therapy. Vancomycin plasma concentrations were determined by high-performance liquid chromatography. Plasma curve decay was plotted, and pharmacokinetics was analyzed by one-compartment open model against the reference data reported.

RESULTS. Burn patients receiving the empiric dose regimen showed trough plasma level lower than the minimum effective concentration, consequently dose adjustment was required. Vancomycin adjusted dose regimen showed statistical significance differences according to TBSA ($p < 0.05$) as follows for daily dose normalized to body weight and expressed by mean ± SD: 25.5 ± 11.9 mg/kg/day were required for patients with TBSA below 20%, 32.0 ± 6.4 mg/kg/day for TBSA 20–40% and 34.8 ± 12.2 mg/kg/day were required for TBSA above 40%. Relevant changes on pharmacokinetics were observed by drug plasma clearance increased according the increase of TBSA ($p < 0.05$), while the apparent volume of distribution and also the biological half-life remained unchanged. Additionally, a weak correlation was observed between vancomycin plasma clearance and creatinine clearance ($R^2 = 0.36$; $p = 0.0004$), probably due to the contribution of the extra-renal clearance on total drug elimination.

CONCLUSIONS. On the basis of data obtained in the present study and to prevent therapeutic failure and also to reduce the risk of bacterial resistance, dose adjustment in burn patients is recommendable based on vancomycin plasma monitoring and also on the extension of total burn surface area.

1122

IS VANCOMYCIN DOSING APPROPRIATE IN OBESE PATIENTS OF A MEDICAL ICU?

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INTRODUCTION. The importance of early antibiotic therapy has been recently demonstrated. Regarding a rapidly increasing number of obese patients, appropriate drug dosage in these patients is an important challenge of critical care since it has been shown that not only early start of antibiotics but also correct target concentrations decrease mortality. Vancomycin is administered according to body weight (BW). Nevertheless, little is known about the percentage of obese patients achieving pre-defined target serum levels within 24 h after initiation of vancomycin therapy compared to patients with normal BW.

OBJECTIVES. Therefore, it was the aim of our study to analyze the appropriateness of serum vancomycin levels in patients with a BW between 40 and 150 kg.

METHODS. Over a period of January 2007 to February 2010 vancomycin therapy was initiated in 90 patients of a medical ICU. Vancomycin dosage was standardized with an initial bolus of 1 g i.v. for patients with a BW of <70 kg and 1.25 g i.v. in case of BW ≥70 kg. The target serum concentration was 15–25 mg/L. The first serum vancomycin level was determined within ≤ 24 h. Primary endpoint: comparison of the percentage of initial vancomycin levels within the pre-defined target concentration.

RESULTS. Patients characteristics: n = 90, 34 female, 56 male, mean age 61.5 ± 14.1 years, APACHE II Score 24.7 ± 8.3, height 1.71 ± 0.09 m, BW 79.0 ± 21.9 kg, BMI 26.8 ± 6.6 kg/sqm, serum level of vancomycin within 24 h 19.2 ± 8.9 mg/L. "First serum vancomycin level outside target rage" was *univariately* associated with height ($r = 0.267$, $p = 0.011$) and BW ($r = 0.257$, $p = 0.015$) but neither with BMI ($r = 0.176$, $p = 0.099$) nor with age ($r = 0.083$, $p = 0.439$). ROC analyses of these parameters (BW, height and BMI) regarding the prediction of "first serum vancomycin level outside target rage" found the highest ROC-area under curve for BW (ROC-AUC: 0.660). The cut off value with the highest sum of sensitivity and specificity was 80.5 kg. The distribution of vancomycin serum levels classified as lowered (<15 mg/L), normal (15–25 mg/L) and elevated (>25 mg/L) was 44%:21%:35% in patients with BW > 80.5 kg and 26%:74%:0% in patients with BW < 80.5 kg. The percentage of measurements within the target range was significant lower in patients with BW > 80.5 kg (9/43; 21%) compared to patients with BW < 80.5 kg (35/47; 74%; $p < 0.001$).

Additionally, *multivariate* analysis ($R = 0.55$) confirmed that "BW > 80.5 kg" was *independently* associated with "serum vancomycin level outside of target" ($p < 0.001$), whereas BMI, height and age were not significantly associated.

CONCLUSIONS. BW > 85 kg has a significant impact on vancomycin levels outside the target range. Within 24 h, target vancomycin serum concentrations were achieved in 21% of patients with BW > 80.5 kg compared to 74% of patients with a BW < 80.5 kg ($p < 0.001$). Future studies should develop dosage standards providing more appropriate early vancomycin levels in obese patients.

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VANCOMYCIN DELIVERED BY CONTINUOUS INFUSION DOES NOT WORSEN RENAL FUNCTION WHEN COMPARED WITH INTERMITTENT DOSING IN CARDIAC CRITICALLY ILL PATIENTS

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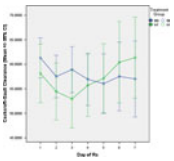
INTRODUCTION. Vancomycin is almost entirely excreted by the glomerulus and may be responsible for nephrotoxicity [1]. However, there is a lack of definitive evidence linking concentrations to either outcome or toxicity [2]. Few reports exist comparing intermittent dosing and continuous infusion. Ingram [3] suggested that whilst associated with a slower deterioration in renal function, there was no difference in the prevalence of nephrotoxicity. Similarly, Hutschala [4] demonstrated worsening creatinine in 149 patients following cardiac surgery with both intermittent and continuous infusion but infusion tended to be less nephrotoxic despite receiving higher doses. We wish also to report our experiences with vancomycin infusion in critically ill cardiac patients.

METHODS. We examined retrospective data from 2,512 patients treated with vancomycin. We perform adjusted and un-adjusted analysis using SOFA on the day of starting vancomycin and total dose received. Unlike APACHE, SOFA provides 'sickness' data throughout a patients ICU stay. Renal function was calculated using the Cockcroft-Gault Equation which although an unreliable estimate of creatinine clearance in the critically ill, allows normalisation of creatinine results across sex and weight.

RESULTS. There were 1,637 (65.2%) patients treated with BD vancomycin and 875 (34.2%) with infusion. Both unadjusted and adjusted analyses suggest that there is no difference in serum creatinine between BD and infusion (OR 1.88 95% CI −5.15 to 8.13 p = 0.599).



Renal function and day of treatment

CONCLUSIONS. There is no difference in renal function between intermittent dosing and continuous infusion in Cardiac Critically Ill.

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H1N1 infection in the ICU 2: 1124–1137

1124

OBESITY AS A RISK FACTOR ASSOCIATED WITH DEATH DUE TO 2009 PANDEMIC INFLUENZA A (H1N1)

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INTRODUCTION. Since April 2009, pandemic influenza A (H1N1) has spread worldwide. A high number of obese patients has been reported among severely ill.

OBJECTIVES. The aim of the present study was to determine whether obesity is a risk factor associated with death due to pandemic influenza A (H1N1).

METHODS. A retrospective cohort study of 64 adult patients, with complicated or severe forms of pandemic influenza A (H1N1), admitted to High Dependency Unit and Intensive Care Unit of The Institute for Pulmonary Diseases of Vojvodina, Serbia, between November 2009 and February 2010, excluding pregnant women because obesity definitions are not applicable to them. We defined categories of relative weight by body mass index (BMI, kg/m^2).

RESULTS. There were 61 patients, 32 male (n = 32, 52.5%), mean age 46 years (SD = ±12). Twenty nine patients were obese (BMI ≥ 30) (n = 29, 47.5%), among them 3 were morbidly obese (BMI ≥ 40) (n = 3, 4.9%). There was no difference in number of patients requiring mechanical ventilation (12/29 vs. 9/32, p = 0.41) and hospital length of stay between obese and patients with normal weight (13 vs. 11 days, p = 0.49). Death was associated with obesity (8/29 vs. 3/32, p = 0.03). Four of eleven patients who died had only obesity as an underlying condition.

CONCLUSIONS. Our observations support that obesity is a risk factor associated with death due to 2009 pandemic Influenza A H1N1 infection.

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1125

SEVERITY OF 2009 PANDEMIC INFLUENZA A (H1N1)V INFECTION IN PREGNANT AND NON PREGNANT WOMEN IN SPAIN

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INTRODUCTION. Pregnancy is a risk factor for critical illness due to 2009 (H1N1)v infection. Early data suggested pregnant women are at increased risk of hospitalization and death.

OBJECTIVES. To describe the severity of 2009 Influenza (H1N1)v illness among pregnant women and to study the relationship of pregnancy with mortality and primary pneumonia among women admitted in Spanish intensive care units (ICU).

METHODS. Prospective, observational, multi-center study conducted in 148 Spanish ICUs. We reviewed demographic and clinical data from GETGAG/SEMICYUC database reported from April 23–December 31, 2009. We included women of childbearing age (15–44 year) with confirmed (H1N1)v infection admitted in ICUs. Pregnant women (P) were compared with non-pregnant women (NP). To calculate ICU admission and mortality rates we used the 2009 census data and the number of pregnant women calculated as the annual number of births in Spain multiplied by 9/12 plus the estimated number of abortions (15/1000 women) multiplied by 2/12.

RESULTS. The number of women of reproductive age admitted in ICUs was 134, 50 (21.4%) of them pregnant. The number of deaths was 7 in P, and 22 in NP women. ICU admission and mortality rate estimates were, respectively, 6.3 times higher (CI 95%: 4.5–8.7) and 7.4 times higher (CI 95%: 2.7–17.9) for P than for NP women. Among ICU admitted women, there were not statistically significant differences between P and NP in severity of illness, APACHE, SOFA score, chest X-rays infiltrates, requirement of inotropes, need of mechanical ventilation, steroid and oseltamivir therapy. The age average, however, was slightly lower in P (31 vs. 33; p = 0.005) and obesity was less frequent than in NP (14 vs. 41%, p = 0.001). Viral pneumonia was more frequent in P women than in NP (94 vs. 75%, p < 0.01) with an OR (adjusted for asthma, time from onset influenza symptoms to hospital admission and obesity) of 4.9 (95% CI: 1.4–17.2), but bacterial co-infection was more frequent in NP (10 vs. 0%, p = 0.016). The frequency of viral pneumonia was higher in P than in NP women. Among ICU admitted women, the overall mortality was 13%, without statistically significant differences between P (14%) and NP (12%, p = 0.86). Compared to survivors, the patients who died had more APACHE II (means: 16.5 vs. 10.5; p = 0.002), SOFA (means: 8.4 vs. 4.3; p = 0.001), higher frequency of obesity (55 vs. 32%, p = 0.013) and shock (72 vs. 36%, p < 0.001). In the multivariate analysis the risk of dying was associated with obesity (OR = 3.7; 95% CI: 1.4–9.9) and time from onset influenza symptoms to hospital admission (OR per day = 0.72; 95% CI: 0.53–0.99). Pregnancy did not appear to be associated with mortality.

CONCLUSIONS. There is a higher risk of ICU admission and mortality associated with pregnancy in women. Among those admitted in ICUs, pregnancy is significantly associated with developing primary pneumonia but not with higher mortality.

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ACUTE RENAL FAILURE IN CRITICALLY ILL PATIENTS WITH INFLUENZA A (H1N1) VIRAL PNEUMONIA

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OBJECTIVE. To describe the incidence, risk factors and impact on mortality of acute kidney injury (AKI) in patients with 2009 influenza A (H1N1) viral pneumonia requiring mechanical ventilation.

METHODS. AKI was defined as risk, injury or failure, according to the RIFLE classification. Early and late AKI were defined as AKI occurring on ICU day 2 or before, or after ICU day 2, respectively. Demographic data and information on organ dysfunction was collected daily.

RESULTS. Of 110 patients, AKI developed in 52 patients (47%), and 21 (40% of patients with AKI) needed renal replacement therapy. Early and late AKI was found in 37 (34%), and 15 (14%) patients, respectively. Patients with AKI, as compared with patients without AKI had a higher APACHE II score and ICU mortality (69 vs. 40%, p < 0.01) and presented on admission a more marked respiratory, hematological, renal, and liver dysfunction. When we considered the time of presentation of AKI, early but not lake AKI presented on admission a higher APACHE II score, and a more marked organ dysfunction. ICU mortality was higher in late versus early AKI (93 vs. 60%, p < 0.001). Adjusted odds ratio for mortality for early and late AKI were, respectively, 1.2 (95% confidence interval 0.7–1.8) and 14.1 (95% confidence interval 1.6–122.7).

CONCLUSIONS. AKI is a frequent complication in 2009 influenza A (H1N1) viral pneumonia. AKI developing after 2 days in the ICU appears to be associated with different risk factors than early AKI, and is associated with a higher mortality rate.

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BACTERIAL CO-INFECTION IN CRITICALLY ILL PATIENTS INFECTED WITH PANDEMIC (H1N1)V INFLUENZA A INFECTION

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INTRODUCTION AND OBJECTIVES. Pandemic (H1N1)v Influenza A infection has led to a global increase in severe respiratory illness. Little is known about mortality in critically ill patients infected with pandemic H1N1 and bacterial co-infection.

METHODS. Prospective, observational, multi-center study conducted in 148 Spanish intensive care units (ICU).

RESULTS. The pandemic H1N1 group was composed of 645 confirmed by RT-PCR patients admitted in ICU with pandemic H1N1 with severe respiratory syndrome Bacterial co-infection occurred in 113 (17.5%) of patients. *S. pneumoniae* 61 (54%), Aspergillus sp. 10 (8.8%) and *P. aeruginosa* 9 (8%) were the pathogens more frequently isolated. Patients with bacterial co-infection were older (47.58 ± 15.7 vs. 43.8 ± 14.2 years, $p < 0.05$) and presented a higher score on the APACHE II (16.1 ± 7.3 vs. 13.3 ± 7.1, $p < 0.05$) and SOFA score (7.0 ± 3.8 vs. 5.2 ± 3.5, $p < 0.05$) at admission. No differences in comorbidities were observed. Patients who had bacterial co-infection required vasopressor (25.4 vs. 11.4%, $p < 0.05$) and invasive mechanical ventilation (19.8 vs. 13.5%, $p < 0.05$) more frequently who those who did not present. Bacterial co-infection was associated with increased death (26.2 vs. 15.5%; OR = 1.94; 95% CI, 1.21–3.09). Through Kaplan–Meier survival analysis, patients who developed a bacterial co-infection were at significantly increased risk of ICU mortality compared with no co-infection (Log rank 0.02); however a Cox regression analysis adjusted by severity (HR = 1.1 95% CI 0.73–1.87, p = 0.49) did not identify that bacterial co-infection is associated with worse outcome.

CONCLUSIONS. Bacterial lung co-infections are occurring among patients with Pandemic (H1N1)v Influenza A infection and seems not to be an independent risk factor for ICU mortality.

GRANT ACKNOWLEDGMENT. This study has been supported in part by SEMICYUC (Sociedad Española de Medicina Intensiva, Criticos y Unidades Coronarias).

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PULMONARY VERSUS NON PULMONARY PRESENTATION IN SEVERE PANDEMIC INFLUENZA A (H1N1)V

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INTRODUCTION. H1N1 Influenza A can present in a number of different ways. The initial presentation can be classified either as pulmonary or non pulmonary.

OBJECTIVES. To assess the differences in either an initial pulmonary or non pulmonary presentation.

METHODS. Prospective, observational, multi-center study conducted in intensive care (ICU). We reviewed demographic and clinical data for all Pandemic H1N1 Influenza A infections reported in the ESICM H1N1 registry.

RESULTS. 512 patients were screened from the registry. 330 patients with completed data entry for pulmonary and non pulmonary with outcomes were identified and analysed. All patients had either suspected, probable or confirmed pandemic H1N1 Influenza A infection and were being cared for in an ICU. 53% of the patients were male with a median age of 43 (IQR 32–55) years. The admission mean SAPS3 score was 54 ± 16 and the APACHE II score was 21 ± 9. 33% of the patients subsequently received non invasive ventilation and 72% received invasive mechanical ventilation. The ICU mortality rate was 30%. The Hospital mortality was 32%. 77% of patients presented with a pulmonary presentation. 73% of these were admitted with ARDS and/or bacterial pneumonia and 22% with an acute bronchospastic exacerbation. 23% of patients were admitted to the ICU with a non pulmonary presentation. The main reasons for admission in these patients were: cardiovascular instability (33%), altered level of consciousness (20%), renal failure (11%) and acute coronary syndromes (5%). Patients with a pulmonary presentation were older, had a increased history of asthma or COPD and were more likely to be ventilated. They had a higher mortality rate in the ICU. Non pulmonary presentations were more likely to suffer from chronic renal impairment. Table 1.

TABLE 1

		Pulmonary (77%)	Non pulmonary (23%)	p
Patient characteristics	Age	45 (35–55)	37 (26–47)	<0.0001
	Chronic Renal Impairment	6%	13%	0.04
	Asthma	13%	3%	0.013
	COPD	17%	1%	0.02
ICU admission	Apache II	22.04 (±8.81)	18.80 (±8.99)	0.011
	SAPS3	55.49 (±16.00)	44.78 (±11.90)	<0.001
ICU outcome	Invasive Mechanical Ventilation	80%	47%	<0.0001
	ICU Mortality	34%	17%	0.005

CONCLUSIONS. Pulmonary presentations of H1N1 were associated with an increased severity of illness and a higher mortality.

GRANT ACKNOWLEDGEMENT. This study was supported by ESICM.

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PIRO-CAP IN PANDEMIC INFLUENZA A (H1N1)V: RESULTS OF THE ESICM INFLUENZA A (H1N1)V REGISTRY

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OBJECTIVES. Prospective, multicentre, observational cohort study in patients admitted to ICUs of 33 Countries. A specific data collection document was designed and data were collected through a web-based eCRF (European Society of Intensive Care Medicine Influenza A (H1N1)v Registry).

METHODS. Prospective, multicentre, observational cohort study in patients admitted to ICUs of 33 Countries. A specific data collection document was designed and data were collected through a web-based eCRF (European Society of Intensive Care Medicine Influenza A (H1N1)v Registry).

RESULTS. After exclusion of all patients with unknown ICU outcome, a total of 512 episodes of pandemic Influenza A (H1N1)v infections in critical care setting were analyzed, from which 287 had complete data on the variables needed to access PIRO-CAP. Median age was 42 [IQR 30–55] years; 53.9% were male. The median APACHE II score was 20 [IQR 15–28] and the median admission SOFA score was 8 [IQR 6–10]. The top five recruiting countries were Norway, Spain, Portugal, Italy and UK. ICU-mortality was 26.4% with a corresponding hospital mortality of 28.5%. Overall, in this population, PIRO-CAP was 3.19 ± 3.00 points (median 3.00, IQ range 2.00–4.00), significantly lower in survivors (2.88 ± 1.56) than in non-survivors (3.88 ± 1.34), $p < 0.001$ by the Mann–Whitney U test. However, the relationship between the increase in the score and the corresponding increase in ICU mortality was not smooth (0 points: 15.0% ICU mortality, 1 point: 7.4%; 2 points: 10.2%; 3 points 31.0%; 4 points 41.7%; 5 points: 51.0%; ≥6 points 53.3%) and the discrimination, as evaluated by the area under the Receiver Operating Characteristics Curve (aROC) was 0.692 (95% confidence interval 0.632–0.753).

CONCLUSIONS. in this cohort, despite being related to mortality, the accuracy of PIRO-CAP was not enough to support its widespread use.

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H1N1 CHALLENGES IN INTENSIVE CARE

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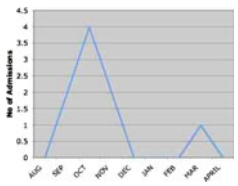
INTRODUCTION. In June 2009 a pandemic of human H1N1 influenza was declared by the WHO[1]. The Adelaide and Meath hospital is a major Dublin teaching hospital with a 9-bed intensive care unit with 2 isolation cubicles and an occupancy >100% for the past 4 years. A Critical Care Influenza Pandemic Contingency plan was made in preparation for this outbreak. The surge presented a significant challenge to our already overloaded system.

OBJECTIVES. We report our experiences with the pandemic including patient profiles, clinical course and workload on intensive care services in our hospital.

METHODS. We retrospectively reviewed all patients admitted to our ICU who were confirmed H1N1 positive by PCR. We have treated a total of 9 cases since our first admission on 3rd September 2009.

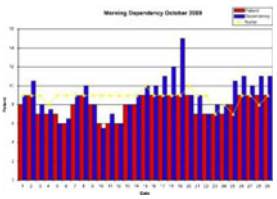


H1N1 waves

RESULTS.

PATIENTS' CLINICAL COURSE	
Median Age	54
Mortality	22%
Median ICU Length of Stay	11 days
Median Hospital Stay	21.5 days
CVVHDF	3 patients
Tracheostomy	2 patients
Median ventilated days	7.5 (range 1–25)
ECMO Evaluation	1

5 of the patients had APACHEII scores of 20 or greater. The maximum number of H1N1 cases was 3 at any one time. This necessitated creation of an improvised isolation area with divider thus preventing activation of surge plan phase 3 which would have led to cancellation of all elective surgery. Workload was significant as was apparent from nursing dependency scores at a time when staff illness had increased



Nursing dependency Scores

CONCLUSIONS. The group of H1N1 patients admitted had high severity of illness scores, significant percentage mortality and a prolonged length of stay. The outbreak posed a strain on capacity and staffing of intensive care services especially with respect to isolation room facilities.

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MR. H1N1 VS. MR. *ST. PNEUMONIAE*: HOW DIFFERENT ARE THEY… OR NOT?

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INTRODUCTION. Severe community-acquired pneumonia (SCAP) is a major cause for ICU admission. Recently we faced the novel swine-origin influenza (H1N1) virus global pandemic. Primary viral pneumonia is recognized as the most severe manifestation of influenza.

OBJECTIVES. To find out the differences between H1N1 and *St. pneumoniae* (SP) SCAP.

METHODS. Prospective, single center, observational cohort study of patients with SCAP admitted to the ICU of a Central University Hospital in Portugal between December 2008 and March 2010. Patients were included if all laboratory parameters could be measured in the first 12 h after diagnosis. Besides demographic data, at ICU admission, severity scores (SAPS2, SAPS3, PSI, CAP-PIRO, CURB-65, total SOFA) were calculated and leukocytes, C reactive protein (CRP), PaO2/FiO2 ratio, lactate, procalcitonin (PCT), D-Dimer, Brain Natriuretic Peptide (BNP), cortisol, pH and platelets were measured. Antimicrobial therapy, organ support and outcome (mortality and length of stay (LOS)) were also analyzed.

RESULTS. 25 patients (pts), mainly man (60%), were included (11 SP vs. 14 H1N1) with a mean age of 54 years. At least one co-morbidity was present in 88% of the cases. No differences were found between the two groups regarding age, gender, previous use of statins and co-morbidities. At ICU admission, pts with pneumococcal SCAP had a significantly higher CURB-65 (3.18 ± 0.98 vs. 1.86 ± 1.16; $p = 0.006$), PSI (163.6 ± 41.88 vs. 120 ± 41.7; $p = 0.016$), SAPS3 (76.9 ± 13.2 vs. 61.9 ± 16.0; $p = 0.025$) and total SOFA (11.45 ± 1.86 vs. 7.7 ± 2.4; $p < 0.001$) score while SAPS2 and CAP-PIRO were similar in both groups. Timing for oxygenation was similar in both groups but appropriate antimicrobial therapy was started significantly later in pts with H1N1 SCAP (215 (IQR 61–430) vs. 503.5 (IQR 231.5–1350) min; $p = 0.033$). A longer duration of antimicrobial therapy was observed in pts with H1N1 SCAP (9 ± 1.94 vs. 12 ± 3.55 days; $p = 0.014$). PCT (51.74 (IQR 14.5–101.7) vs. 0.43 (IQR 0.34–0.66) ng/ml; $p = 0.018$), lactate (5.46 (IQR 4.14–9.02) vs. 1.46 (IQR 0.89–2.86) mmol/l; $p < 0.001$) and BNP [803.2 (IQR 414–2,840.9) vs. 142.4 (IQR 22.9–805.1) pg/ml; $p = 0.036$] serum levels were significantly higher in SP group, while no differences were found regarding the other laboratory parameters studied. No differences were observed regarding duration of mechanical ventilation, need for vasopressors or renal replacement therapy and steroids use. Mortality (ICU, hospital and 28 days) and LOS (ICU and hospital) were similar in both groups.

CONCLUSIONS. At ICU admission, SP was associated with a significantly higher CURB-65, PSI, SAPS3 and SOFA scores. H1N1 SCAP is associated not only with a longer delay in starting appropriate empirical antimicrobial treatment but also with its longer duration. PCT, lactate and BNP could be helpful tools to distinguish between these two pathogens at ICU admission. No differences were found regarding outcome.

REFERENCE(S). None

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CURB-65 IN PANDEMIC INFLUENZA A (H1N1)V: RESULTS OF THE ESICM INFLUENZA A (H1N1)V REGISTRY

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INTRODUCTION. Recently we faced 2009 pandemic influenza A H1N1v strain. However, in this case, the accuracy and discriminatory power of the different severity-of-illness scores is unknown.

OBJECTIVES. To evaluate the accuracy of CURB-65 [1] in patients admitted to the Intensive Care Unit due to pandemic influenza A (H1N1)v.

METHODS. Prospective, multicentre, observational cohort study in patients admitted to ICUs of 33 countries. A specific data collection document was designed and data were collected through a web-based eCRF (European Society of Intensive Care Medicine Influenza A (H1N1)v Registry).

RESULTS. After exclusion of all patients with unknown ICU outcome, a total of 512 episodes of pandemic Influenza A (H1N1)v infections in critical care setting were analyzed, from which 318 had complete data on the variables needed to assess CURB-65. Median age was 43.5 [IQR 32–55] years; 53% were male. Median APACHE II and SAPSIII scores were respectively, 20 [IQR 15–28] and 51.5 [IQR 43–65]. The top five recruiting countries were Norway, Spain, Portugal, Italy and UK. ICU and hospital mortality were 31.1 and 36.8% respectively. Overall, in this population, CURB-65 was 1.78 ± 1.16 points (median 2.00, IQ range 1.00–2.00) and it was significantly related not only with ICU survival (survivors 1.53 ± 1.08 vs. non-survivors 2.33 ± 1.14; $p < 0.001$) but also with hospital survival (survivors 1.45 ± 1.01 vs. non-survivors 2.32 ± 1.17; $p < 0.001$).Although there was a smooth relationship between an increasing score and ICU mortality (0 points: 11.9% ICU mortality, 1 point: 18.9%; 2 points: 33%; 3 points 48.8%; ≥ 4 points 66.7%), the discrimination, as evaluated by the area under the Receiver Operating Characteristics Curve (aROC) was only 0.694 (95% confidence interval 0.631–0.756). In patients ($n = 137$) that according to the initial manuscript were eligible for outpatient treatment (CURB-65 ≤ 1), an important mortality rate was observed (23.2%) despite all of them being cared for in an ICU. Risk factors for ICU mortality in this group of patients were: chemotherapy (relative risk 3.96 (CI 95% 1.74–9.01; $p = 0.033$) and rhabdomyolysis (relative risk 3.04 (CI 95% 1.47–6.29; $p = 0.01$).

CONCLUSIONS. In this cohort, despite being significantly related to mortality, the accuracy of CURB-65 was not enough to support its widespread use, especially as triage instrument. Patients with low risk of death but with rhabdomyolysis or on chemotherapy should probably receive more aggressive treatment while in the ICU.

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PSI IN PANDEMIC INFLUENZA A (H1N1)V: RESULTS OF THE ESICM INFLUENZA A (H1N1)V REGISTRY

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INTRODUCTION. The recent pandemic influenza A (H1N1)v brought new challenges to intensive care since it was associated with high morbidity and mortality. In this case, the accuracy and discriminatory power of the different severity scores is unknown.

OBJECTIVES. To evaluate the accuracy of Pneumonia Severity Index (PSI) (1) in patients admitted to the Intensive Care Unit (ICU) due to pandemic influenza A.

METHODS. Prospective, multicentre, observational cohort study in patients admitted to ICUs of 33 countries. A specific data collection document was designed and data were collected through a web-based eCRF (European Society of Intensive Care Medicine Influenza A (H1N1)v Registry).

RESULTS. After exclusion of all patients with unknown ICU outcome, a total of 512 episodes of pandemic Influenza A (H1N1)v infections in critical care setting were analyzed, from which 317 had complete data on the variables needed to assess PSI. Median age was 43 [IQR 32–55] years; 53% were male. Median APACHE II score was 20 [IQR 15–28] and median SAPS III score was 51 [IQR 43–64.5]. ICU and hospital mortality were 30.9 and 36.6% respectively. Overall, in this population, PSI was 104.49 ± 44.48 points (median 100, IQ range 69–136), and it was significantly related to ICU (survivors 93.45 ± 41.71 vs. non-survivors 129.16 ± 40.56; $p < 0.001$) and to hospital (survivors 89.74 ± 39.16 vs. non-survivors 129.02 ± 42.93; $p < 0.001$) outcome. The relationship between the increase in the PSI class and the corresponding increase in ICU mortality was smooth (class I and II: 7.2% ICU mortality, class III: 19.6%; class IV: 38.1%; class V: 50.5%). The discriminatory power of the PSI score, as evaluated by the area under the Receiver Operating Characteristics Curve (aROC), was reasonable (0.734 [95% confidence interval 0.678–0.790]). According to PSI score 129 patients were candidate for outpatient treatment (PSI classes I, II and III); however, despite the fact that they have been admitted and cared for in an ICU, mortality rate was high (11.6%). Risk factors for ICU mortality in this group of patients were: concomitant septic shock (relative risk 3.13(CI 95% 1.24–7.87; $p = 0.021$) or acute coronary syndrome (relative risk 6.41 (CI 95% 2.48–16.60; $p = 0.036$).

CONCLUSIONS. In this cohort, PSI score performed reasonably as an ICU and hospital outcome prediction tool and helped to classify patients with increasing risk of death. However, it should be used with caution as a triage instrument as demonstrated by a significant mortality rate in patients considered not meeting even the criteria for hospital admission. Septic shock and acute coronary syndrome significantly increase ICU mortality in patients with low risk of death calculated by PSI score.

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CLINICAL CHARACTERISTICS IN A COHORT OF CRITICALLY ILL PATIENTS INFECTED WITH PANDEMIC INFLUENZA A (H1N1)V: THE ESICM H1N1 REGISTRY

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INTRODUCTION. The recent pandemic influenza A (H1N1)v represents a new challenges to intensive care since it is associated with high morbidity and mortality (1). Data on clinical characteristics and outcomes are important to improve our knowledge and to design strategies to manage these patients.

OBJECTIVES. To describe the clinical characteristics and outcomes of critically ill patients infected with pandemic Influenza A (H1N1)v from the European Society of Intensive Care Medicine (ESICM) Registry.

METHODS. Prospective, multicentre, observational cohort study in patients admitted to ICU in 33 Countries. A specific data collection document was designed and data were collected through a web-based electronic CRF (ESICM(H1N1)v Registry).

RESULTS. After exclusion of all patients with unknown ICU outcome, a total of 512 episodes of pandemic Influenza A(H1N1)v infections admitted to ICU were analyzed from ESICM Registry. The median age was 42 [IQR 30–55] years; 53.9% were male. The median APACHE II score was 20 [IQR 15–28] and the median admission SOFA score was 8 [IQR 6–10]. The top five recruiting countries were Norway, Spain, Portugal, Italy and UK. The most frequent comorbidities were obesity (BMI > 35) (22.2%), hypertension (21.1%), COPD (17.8%) and diabetes mellitus (13.5%). There were 26 pregnant women in this analysis (5.1%). At presentation, the most common symptoms were dyspnoea (61.5%), fever (60.0%) and cough (58.0%). The most common presentation was primary viral pneumonia in 293 patients (57.2%). Bacterial pneumonia was present in 30.3% of patients and asthma/COPD exacerbation in 64 patients (12.5%). Invasive mechanical ventilation(MV) was used in 407 patients (79.5%), prone positioning in 93 (18.2%), ECMO was used in 60 (11.7%), inhaled nitric oxide in 60 (11.7%) and high-frequency oscillatory ventilation in 11 (2.1%) patients. At admission, vasopressors were used in 162 patients (31.6%), acute renal failure was present in 68 (13.3%) with renal replacement therapy used in 38 (7.4%), patients. The Oseltamivir dose distribution was bimodal with two peaks at 150 and 300 mg/day. No correlation of dose with outcomes was found. ICU-mortality was 26.4% with corresponding hospital mortality of 28.5%. Corticosteroids were used in 218 patients (42.6%), but no association with outcomes was found. ICU mortality was associated with organ dysfunction at admission [shock with vasopressors (OR = 4.17 95% CI 2.75–6.31), need for MV (OR = 13.29 95% CI 5.84–30.22) and renal replacement therapy (OR = 3.09 95% CI 1.59–5.98)]. Higher SOFA score at admission was associated with worse outcomes.

CONCLUSIONS. Severity of disease and not comorbidities was the main determinant of high mortality in patients infected with pandemic Influenza A (H1N1)v infections in critical care setting.

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CLINICAL CHARACTERISTICS IN A COHORT OF CRITICALLY ILL PATIENTS INFECTED WITH PANDEMIC INFLUENZA A (H1N1)V RECEIVING EXTRACORPOREAL MEMBRANE OXIGENATION (ECMO) THE ESICM H1N1 REGISTRY

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INTRODUCTION. Use of Extracorporeal Membrane Oxygenation for Influenza A(H1N1)v Acute Respiratory Distress Syndrome is suggested as a therapy in refractory hypoxemic patients (1).

OBJECTIVES. To describe the clinical characteristics and outcomes of critically ill patients infected with pandemic Influenza A (H1N1)v that received ECMO therapy during the stay in the Intensive Care Unit (ICU).

METHODS. Prospective, multicentre, observational cohort study in patients admitted to ICU in 33 Countries. A specific data collection document was designed and data were collected through a web-based electronic CRF (ESICM Influenza A (H1N1)v Registry).

RESULTS. After exclusion of all patients with unknown ICU outcome, a total of 512 episodes of pandemic Influenza A (H1N1)v infections admitted to participating ICUs were analyzed, from which 60 patients receive ECMO therapy during the ICU stay. The median age was 38 [IQR 30–48] years; 61.7% were male. The median APACHE II score was 22 [IQR 16–28] and the median admission SOFA score was 9 [IQR 8–11]. The median CAP PIRO score was 4 [IQR 3–5]. CURB-65 distribution was 0—18%, 1—28.2%, 2—41.0% 3 or more—12.8%. The most common comorbidities were obesity (BMI > 35) (12.5%), COPD (10.0%), asthma (10.0%), and diabetes mellitus (8.3%). There were 4 pregnant women in this analysis (6.7%). Most common presentation was primary viral pneumonia in 51 patients (85.0%). Bacterial pneumonia was present at ICU admission in 8 patients (13.3%) and asthma/COPD exacerbation in only 1 (1.6%). At admission, vasopressors were used in 25 patients (41.7%), acute renal failure was present in 7 (11.7%) and renal replacement therapy was required in 5 (8.3%). Median PO2 at admission was 60 [IQR 48–80] and median arterial pH was 7.33 [IQR 7.20–7.42]. No significant differences were found on age, arterial pH, APACHE II score, CAP PIRO or PSI score when comparing patients receiving or not ECMO. There was significant difference on mean PO2/FiO2 at admission of patients receiving ECMO (90.4 SD 73.1 mmHg) comparing to patients that did not receive ECMO (116.0 SD 97.1 mmHg) ($p < 0.05$). Corticosteroids were used in 23 patients (38.3%), but no association with outcomes was found. ICU-mortality was 28.3%. No difference on ICU mortality was found when comparing patients who receive and not receive ECMO (28.3 vs. 26.1%, $p = 0.41$). ICU mortality in ECMO patients was associated with PO2/FiO2 ratio <100 mmHg (OR = 3.30 95% CI 1.05–10.32).

CONCLUSIONS. The presence of a lower PO2/FiO2 ratio at admission was associated with the use of ECMO therapy in pandemic (H1N1)v patients. In addition, a PO2/FiO2 <100 mmHg at start of the therapy was the only variable associated with worse outcomes in patients receiving ECMO therapy.

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INFLUENZA A (H1N1) FLU IN CRITICALLY ILL: CLINICAL STUDY OF 12 CASES AND EVOLUTION

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INTRODUCTION. Influenza A (H1N1) flu is an infection with significant morbidity and mortality among middle age adults. Often need to be admitted in ICU.

OBJECTIVES. To describe the clinical features and the evolution of a group of patients infected by the Influenza virus subtype H1N1 and admitted to an ICU.

METHODS. Observational and prospective study done in patients diagnosed with H1N1 flu that required ICU admission. The infection was confirmed by PCR performed in nasopharyngeal swabs and/or endotracheal aspirates.

RESULTS. During the Influenza A (H1N1) flu outbreak in Spain a total of 124 patients were admitted to our hospital with H1N1 flu confirmed infection. Of them, 12 (10%) were admitted in ICU. Eight were women (67%) and the mean age was 39.9 years (range 22–52). Seven patients (58%) had previous clinical conditions of importance such as: diabetes (2), COPD (1) cardiopathy (1), inmunodepression (1), encephalopathy (1) and neoplasia (1). Other factors of importance were: obesity (1), smoking habit (3) and pregnancy (2). The mean time of symptoms before admission was 4.3 days (range 1–8). Eight patients developed a complicated pneumonia, with a *S. pneumoniae* isolation in one case. The reason for UCI admission was: acute respiratory failure (83%) and/or shock (75%). Eight patients (67%) required intubation and mechanical ventilation (mean time of ventilation 12.8 days, range 2–30) and two, non invasive mechanical ventilation. Six patients developed ARDS (one had a mediastinal emphysema secondary to barotrauma) and required further therapies to guarantee oxygenation such as continuous neuromuscular blockage and/or prone position. All had positive PCR's after 7 days of treatment. All received antibiotics and eleven were treated with Oseltamivir during a mean time of 13 days (range 10–14). One of them was treated with Zanamivir due to a treatment failure.

CONCLUSIONS. Middle age patients with previous pathologies and other risk factors such as obesity, smoking habit and pregnancy that suffer from Influenza virus subtype H1N1 flu require more frequently ICU admission. Respiratory failure and shock are the principal reasons for it and they usually need intubation, prolonged mechanical ventilation and other strategies in order to fight ARDS.

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BACTERIAL PNEUMONIA COMPLICATING INFLUENZA A (H1N1)V VIRAL PNEUMONIA: RESULTS OF THE ESICM INFLUENZA A (H1N1)V REGISTRY

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OBJECTIVES. To compare patients admitted in the Intensive Care Unit (ICU) due to pandemic Influenza A (H1N1)v virus with bacterial pneumonia with those with primary viral pneumonia some of them with whizzing as major clinical sign.

METHODS. Prospective, multicentre, observational cohort study in patients admitted to ICUs of 33 Countries. Data were collected through a web-based eCRF (European Society of Intensive Care Medicine Influenza A (H1N1)v Registry).

RESULTS. A total of 512 episodes of pandemic Influenza A (H1N1)v infections in critical care setting were analyzed: 169 with bacterial pneumonia (94 males and 73 females) and 343 with wheezing or viral pneumonia (182 males and 161 females). The mean age was 45 (± 17) years in patients with bacterial pneumonia and 40 (± 17) in patients viral pneumonia. The mean APACHE II score was 25 (± 9) and 20 (± 9), with a corresponding probability of death of 37 (± 25)% and 24 (± 21)%.

Comorbidities were common, but without significant differences between the two groups (only exceptions pregnancy—more prevalent in patients without bacterial pneumonia—and dialysis dependence—more prevalent in patients with bacterial pneumonia). At ICU admission shock and acute renal failure were more common in patients with bacterial pneumonia. In patients without pneumonia; Severe hypoxia and ARDS did not presented significant differences between groups. Invasive mechanical ventilation was used more frequently in bacterial pneumonia (133 patients, 84.2% vs. 229 patients, 74.1%, $p = 0.02$), as well as non-invasive ventilation (61 patients, 40.7% vs. 128, 44.3%, p = NS). On the other side, ECMO was used in only 10 patients (7.9%) vs. 50 patients (18.5%), $p < 0.015$. We were not able to demonstrate significant differences in the use of prone position, vasopressors, renal replacement therapies, corticosteroids, and anti-vital drugs between both groups. IV antimicrobial therapy was used more frequently in patients with bacterial pneumonia (144 patients, 100% vs. 264, 94.6%, $p = 0.009$).

PNEUMONIA SEVERITY SCORES

Pneumonia Severity Scores	Bacterial pneumonia	Non-bacterial pneumonia	p
PIRO-CAP	3.6 ± 1.5	2.9 ± 1.5	<0.001
CURB-65	2.1 ± 1.2	1.6 ± 1.1	NS
PSI	115.6 ± 44.7	98.5 ± 43.3	NS

Mortality was similar in both groups: at ICU discharge (26.0 vs. 26.5%), at 28 days (33.9 vs. 26.2%) and at hospital discharge (43.8 vs. 35.6%).

CONCLUSIONS. Both presentation forms behaved similarly in terms of clinical picture and complications present at ICU admission. However, in patients with bacterial pneumonia at ICU admission it seems to exist a greater severity of illness, as very well captured by CAP-PIRO system. We have not been able to show significant differences in mortality between both groups.

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ICU nutrition 2: 1138–1151

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ISOCALORIC ARTIFICIAL NUTRITION RIGHT FROM THE BEGINNING CAUSES NO INCREASE OF NUTRITIONAL RELATED SIDE EFFECTS IN CRITICALLY ILL MEDICAL PATIENTS

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AIMS. Evaluation if an isocaloric beginning of artificial nutrition in critically ill medical patients is associated with increased nutritional related side effects compared to a hypocaloric start.

METHODS. 110 critically ill medical patients with an expected need for artificial nutrition of >5 days were included into this prospective, randomized clinical study. Artificial nutrition was started either isocalorically right from the beginning (group A; n = 55) or hypocalorically (50% of the energy demands) followed by a stepwise increase over the next 2 days (day 2: 75%); day 3: 100%) (group B; n = 55). Nutrition related side-effects were defined as the occurrence of hyperglycemia, hyperlactatemia, hypertriacylglycerolemia, upper digestive intolerance, cholestasis, or diarrhea as well as disturbances of serum electrolytes and were assessed on a daily basis.

RESULTS. Patients were randomized to receive either an artificial nutrition started isocalorically (group A) or hypocalorically followed by a stepwise increase (group B). Of the 150 patients, 100 patients completed the study (group A: n = 55; group B: n = 55). The calculated, cumulative energy requirements of patients of group A and B were 9,058 ± 1,236 and 9,125 ± 1,569 kcal, respectively (p = ns). Patients of group A received 76 ± 17% and patients of group B 69 ± 12% of the calculated energy requirements ($p < 0.01$). The incidence of nutritional related side effects was not different comparing both groups, except for hypophosphatemia, which was more pronounced in group A. Additionally, exogenous phosphate needs were higher in patients of group A. The number of interruptions of the artificial nutrition did not differ between groups.

CONCLUSIONS. An isocaloric start of artificial nutrition provided more energy during the first 5 days of their ICU stay than a hypocaloric beginning. There was no difference in the number of interruptions and in the incidence of nutritional related side effects, except hypophosphatemia suggesting the presence of refeeding syndrome.

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EFFECTS OF ENTERAL AND/OR PARENTERAL GLUTAMINE ON INTESTINAL MUCOSA AND ON LEVELS OF BLOOD GLUTAMINE, TNF-*A*, IL-10 IN THE EXPERIMENTAL SEPSIS MODEL

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In studies carried on to demonstrate positive effects of glutamine (Gln) that has innumerable biological features, the main point of discussion isn't whether Gln has positive effects in sepsis but rather the effect difference between different administration routes. Only enteral (en.) or parenteral (pn.) administration was analyzed in this respect and no studies on combined administration were performed. The primary endpoint in this study was to analyze the effects of administration of en. and pn. Gln together or separately on intestinal mucosa + immune system in the experimental sepsis model. For this purpose villus atrophy, bacterial growth in blood and tissue, levels of blood Gln, TNFα and IL10 were examined. The secondary endpoint was to evaluate the different administration models in terms of cost.

METHODS. Wistar, adult female rats were used. They were fed standard. Sepsis was developed in 4 groups (all rats) by injection of intraperitoneal(ip.) 1 mL (5×10^7 CFU/mL) *E. coli*. Grup C (n = 12):en./pn. isotonic saline (1 mL/day; 2 mL/d); Grup E (en., n = 10):en. Gln (0.5 g $kg^{-1}day^{-1}$) + pn. saline (2 mL/d); Grup P (pn., n = 11):pn. Gln (0.4 g kg^{-1} day^{-1} Gln) + en. saline (1 mL/d); Group EP (en. + pn., n = 11):pn. Gln (0.3 g $kg^{-1}day^{-1}$) Ala-Gln = 0.2 g kg^{-1} day^{-1} Gln) + en. Gln (0.3 g kg^{-1} day^{-1}); were administered. Feeding of rats began 4 h (h) after administration of ip *E. coli*. Blood Gln (with spectrophotometer), TNFα and IL10 concentrations(with ELISA) were examined at the start (baseline levels) and at 24–96 h after the experiment started. Samples of tissue from mesenteric lymph node, liver, lung, blood and small intestine were collected. Ala–Gln = 0.27 g kg.

RESULTS. Rates of reproduction of the strain administered were found lower for Group EP than Group C ($p < 0.05$). Rates of villus atrophy in ileum of Group EP, P and E were lower than Group C ($p < 0.05$).Plasma Gln levels were found lower in groups EP and P at 24 h, and higher at 96 h than other groups ($p < 0.05$). When plasma Gln levels at 96 h were compared with their baseline levels, significant increases were detected in Groups EP and P and significant decreases were detected in Groups C and E ($p < 0.01$). Serum TNFα and IL10 levels were found lower for Groups EP and P at 24 and 96 h when compared between groups ($p < 0.05$). When Serum TNFα and IL10 levels at 96 h were compared with their baseline levels, more distinctive increases were detected in Groups C and E than other groups ($p < 0.01$). Significant positive correlation was determined between TNFα and IL10 levels at 24 h ($p < 0.01$) and 96 h ($p < 0.01$). Cost of simultaneous administration of en. and pn. Gln was higher than en. administration but close to pn. administration at these doses.

PLASMA GLN (MMOL/L)

Group	n	Baseline Level	24 h	96 h
C	(n = 12)	0.714 ± 0.029	0.865* ± 0.037	0.483* ± 0.046
E	(n = 10)	0.708 ± 0.021	0.796* ± 0.019	0.599* ± 0.01
P	(n = 11)	0.707 ± 0.022	0.725* ± 0.029	0.748* ± 0.051
EP	(n = 11)	0.712 ± 0.016	0.730* ± 0.011	0.779* ± 0.018

* $p < 0.01$: within groups at day times

CONCLUSION. We determined that the combined administration of en. and pn. is the most effective method of administration of Gln in sepsis for its trophic effect on intestinal mucosa, immunomodulatory effect and cause of reduction in reproduction of tissue and blood cultures with cost close to pn. administration's.

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EARLY ENTERAL NUTRITION REDUCES MORTALITY IN TRAUMA PATIENTS REQUIRING INTENSIVE CARE: A META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

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INTRODUCTION. Recently published clinical practice guidelines recommend initiating enteral nutrition (EN) in the trauma patient 'as early as feasible' [1]. Although the provision of early EN has been demonstrated to have important benefits in other patient populations, there have been no meta-analyses published with a primary focus on the trauma patient [2].

OBJECTIVES. To determine whether the provision of early standard EN, provided within 24 h of injury, confers treatment benefits to adult trauma patients who require intensive care.

METHODS. Medline and EMBASE were searched. Hand citation review of retrieved guidelines and systematic reviews was undertaken and academic and industry experts were contacted. Only methodologically sound randomised controlled trials (RCTs) were eligible for inclusion in the primary analysis. The primary analysis was conducted on clinically meaningful patient oriented outcomes, which included mortality, functional status and quality of life. Secondary analyses considered vomiting/regurgitation, pneumonia, bacteremia, sepsis and multiple organ dysfunction syndrome. Meta-analysis was conducted using the Peto analytic method, which is known to minimize bias in the presence of sparse events. The impact of heterogeneity was assessed using the I^2 metric.

RESULTS. 4,217 unique abstracts were identified, resulting in the retrieval of 701 papers for detailed eligibility review. Four RCTs were identified to be on topic however one RCT reported excessive loss to follow-up such that an intention to treat analysis could not be conducted. Analysis based on the three methodologically sound RCTs demonstrated the provision of early EN was associated with a significant reduction in mortality (OR = 0.20, 95% confidence interval 0.04 to 0.91, $I^2 = 0$). No other outcomes could be pooled. Sensitivity analysis including all four on-topic RCTs (OR = 0.26, P = 0.04, $I^2 = 0$), and a simulation analysis conducted using a different analytical method. ($OR_{Exact} = 0.14$, 95% CI 0.01 to 0.97), confirmed the presence of a mortality reduction.

CONCLUSIONS. Although the detection of a statistically significant reduction in mortality is promising, overall trial size was small. The results of this meta-analysis should be confirmed by the conduct of a large multi-center trial.

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SEVERE GASTROINTESTINAL COMPLICATIONS IN PATIENTS WITH MALIGNANCIES

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INTRODUCTION. The digestive tract represents a unique challenge in patients treated for hematological malignancies and cancer. However, no study has focused on cancer patients with digestive-tract related acute organ dysfunction.

OBJECTIVES. To describe clinical, radiographic, and pathological factors associated with severe gastrointestinal complications in patients with malignancies.

METHODS. Cancer patients admitted to the Intensive Care Unit (ICU) with any acute gastrointestinal complication over a 10-years period. A multivariate Cox proportional hazards regression model was used to analyze the association between clinical, pathologic factors and overall survival.

RESULTS. Ninety-four patients aged 52 [40–61] were included in this analysis. Hematological malignancy affected 76 (80.8%) patients and solid cancer 18 (19.1%) patients. Forty-five (47.8%) patients were neutropenic. Median SAPSII was 51 [40–62]. Median body temperature was 38.6°C [38.0–39.6]. Abdominal cramp was the most common symptom (65.9%), followed by acute diarrhoea (51.1%), abdominal distension (47.8%), vomiting (30.8%), haemorrhage (28.7%), acute digestive tract occlusion (23.4%), oral mucositis (20.2%) and peritoneal irritation (18%). Neutropenic enterocolitis was the most frequent diagnosis (21.5%), followed by *Clostridium difficile*-related colitis (15.1%), perforated peritonitis (12.7%), digestive haemorrhage (9.7%), and graft-versus-host disease (7.5%). Thirty-six (38.2%) patients were diagnosed with digestive-related septic shock. Thirty-six (38.2%) patients were receiving mechanical ventilation and 40 (42.5%) did require vasopressors. Abdominal surgery was performed in 19 (20.2%) patients. The overall mortality rate was 29.8%. Multivariate analysis showed that admission for digestive haemorrhage (OR: 4.57 [1.40–14.97], p = 0.01), history of radiotherapy (OR: 6.75 [1.51–30.19]), and time before admission in the intensive care unit (OR: 1.02/day [1.00–1.50], p = 0.04) were significant adverse prognostic factors for hospital survival. Hospital mortality was not significantly different in neutropenic vs. non neutropenic patients or in surgical vs. medical patients.

CONCLUSIONS. Severe gastrointestinal complications justifying ICU admission are common in the management of onco-hematological malignancy patients. History of radiotherapy, admission for acute bleeding and delayed admission to ICU are poor prognostic factors.

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INTERIM RESULTS ON THE VALIDATION OF A NOVEL METHOD FOR MEASURING GASTRIC RESIDUAL VOLUME AND INTRA-ABDOMINAL PRESSURE IN MECHANICALLY VENTILATED CRITICALLY ILL PATIENTS

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INTRODUCTION. Gastric residual volume (GRV) is measured in a variety of ways, most often, the nasogastric tube is disconnected and the GRV is aspirated via a 60 cc syringe. Nurses experience this procedure as unpleasant and cumbersome. Intra-abdominal pressure (IAP) has traditionally been estimated via bladder pressure (IBP).

OBJECTIVES. This study looks at the validation of a novel method combining measurement of GRV and estimation of IAP via intragastric pressure (IGP).

METHODS. In total 135 paired IAP and 146 paired GRV measurements were performed in 37 mechanically ventilated ICU patients. IAP was estimated by the height of the urine column via the bladder (i.e. IBP) using the FoleyManometer (Holtech Medical, Charlottenlund, Denmark) and via the stomach (i.e. IGP) with the new device (Gastro PV, Holtech Medical, Charlottenlund, Denmark). The GRV was measured with the new device (GRV_{proto}) and via the classic method ($GRV_{classic}$). Male to female ratio was 4:3, age 62.8 ± 17.4 (range 22–86), BMI 26.3 ± 6.3 (16.6–42.3), APACHE-II score 21.1 ± 4.5 (11–31), SAPS-II score 50.4 ± 12.1 (17–83), and SOFA score 9.3 ± 3.1 (3–17). The number of measurements in each patient was 4 ± 1. Statistical analysis was done with SPSS 13™ software, values are expressed as mean ± SD or median (range).

RESULTS. The mean IBP was 10.7 ± 4.1 and mean IGP was 11.6 ± 4.1. Correlation between the IBP and IGP was significant however moderate (R2 = 0.51). Analysis according to Bland and Altman showed a bias and precision of 0.8 and 2.7 mmHg respectively, however the limits of agreement (LA) were large and ranged from −4.5 to 6.1 mmHg. The median GRV_{proto} was 80 mL (0–1,050) and median $GRV_{classic}$ was also 80 mL (0–1,250). Correlation between the 2 methods was excellent (R2 = 0.89). Analysis according to Bland and Altman showed a bias and precision of −0.8 and 52.3 mL respectively and the limits of agreement (LA) ranged from −103 to 102 mmHg. The median drainage time and return times were 5 min (0.5–15) and 2.5 min (0–21) for GRV_{proto} compared to 2 min (0.1–10) and 1 min (0–8) for $GRV_{classic.}$ A preliminary cost effectiveness analysis shows that the price of measuring GRV with the classic method ranges from 3.84€ to 24.18€ per day, depending on the GRV size. Price of measuring GRV with the gastro PV system is independent of GRV size and is estimated at 9.49€ per day. The gastro PV system if priced at 8.5€ could become cost effective at GRV of 100 cc and more.

CONCLUSIONS. The interim results of an ongoing multicentre pilot study show that the gastro PV is a good alternative to the standard method for measuring GRV. Because the nurse can perform other tasks during drainage and return of the GRV, and the fact that the system remains closed during measurement, this could be a major step forward in standardisation of GRV measurement. Furthermore it allows screening for intra-abdominal hypertension via IGP estimation.

ACKNOWLEDGMENT. The gastro PV devices were provided by Holtech Medical, free of charge.

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TRANSNASAL PLACEMENT OF AN ENTERAL FEEDING TUBE, USING A NEW EXTRALONG JEJUNOSCOPE IN INTENSIVE CARE PATIENTS

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INTRODUCTION. The importance of early enteral feeding of the critically ill patient has been well documented. It is the more physiological approach, which is associated with lower rates of infectious complications. Early enteral nutrition within 24 h is recommended by the ESPEN Guidelines on Enteral Nutrition. A recent meta-analysis revealed that mortality and the incidence of pneumonia were significantly reduced in patients with enteral nutrition within 24 h. Parenteral nutrition may be associated with higher mortality.

OBJECTIVES. Evaluation of a new technique for the placement of postpyloric feeding tubes by intensive care physicians.

METHODS. Prospective cohort study in 27 critically ill patients subjected to transnasal endoscopy and intubation of the pylorus. Attending intensive care physicians were trained in the handling of the new endoscope for transnasal gastroenteroscopy for 2 days. A jejunal feeding tube was advanced via the instrument channel and the correct position assessed by contrast radiography. Primary outcome measure was successful postpyloric placement of the tube. Secondary outcome measures were time needed for the placement, complications like bleeding and formation of loops and the score of the placement difficulty graded from 1 (easy) to 4 (difficult). Data are given as mean values and standard deviation.

RESULTS. Out of 34 attempted jejunal tube placements, 28 tubes (82%) were placed correctly in the jejunum. The duration of the procedure was 28 ± 12 min. The difficulty of the tube placement was judged as follows: grade 1: 17 patients, grade 2: 8 patients, grade 3: 7 patients, grade 4: 2 patients. In 3 cases, the tube position was incorrect, and in another 3 cases, the procedure had to be aborted. Only in one patient, bleeding occurred that required no further treatment.

CONCLUSIONS. Fast and reliable transnasal insertion of postpyloric feeding tubes can be accomplished by trained intensive care physicians at the bedside using the presented procedure. This new technique may facilitate early initiation of enteral feeding in intensive care patients.

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REDUCED RENAL ARGININE DE NOVO SYNTHESIS AND NOT REDUCED CITRULLINE PRODUCTION IN THE GUT IS RESPONSIBLE FOR REDUCED ARGININE AVAILABILITY DURING MALNUTRITION AND ENDOTOXEMIA

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INTRODUCTION. A well-nourished condition before prolonged endotoxemia results in a better ability to adapt to endotoxin-induced metabolic deterioration of arginine-nitric oxide metabolism than does reduced caloric intake before endotoxemia (1). The role of individual organs in the arginine-citrulline metabolism during malnutrition and sepsis is unknown and may be key to direct future interventions.

OBJECTIVES. To study the effects of reduced caloric intake and endotoxemia on the citrulline-arginine metabolism in the gut-liver-kidney axis.

METHODS. Organ arginine-nitric oxide metabolism was measured by using a primed-constant stable-isotope infusion of [15N2]arginine and [13C-2H2]citrulline during 4 conditions; a 7-day reduced caloric intake feed regimen (STARV; n = 9), normal control feed regimen (CO; n = 9), endotoxemia alone (CE) and reduced caloric intake and endotoxemia (RE) in. Catheters for blood sampling were placed in the abdominal aorta, which, in combination with the catheters in the portal, hepatic and renal veins, served for metabolic measurements across the portal-drained viscera, liver and the kidneys, respectively.

RESULTS. Interestingly, RE animals had similar citrulline appearance from the gut (331 ± 36 nmol/kg/min) compared to control and animals during CE, but higher in endotoxemia alone (102 ± 14, $P < 0.01$). This was related to a significantly higher NO production from the gut in the RE group (1,644 ± 153 vs. 720 ± 41, $P < 0.01$). In the kidney arginine appearance from citrulline decreased significantly during RE compared the control animals (3 ± 7 vs. 224 ± 30 nmol/kg/min, $P < 0.01$). In contrast, the liver disposed more arginine in the RE group compared to the other conditions, while NO production was not higher.

CONCLUSIONS. Despite reduced caloric intake prior to endotoxemia, the gut remains capable of increasing release of citrulline, although the capability of the kidney for the *de novo* production of arginine is severely compromised. Metabolic control of the citrulline-arginine metabolism in the gut-liver-kidney axis should focus on increasing *de novo* arginine production from citrulline.

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TRANSIT OF NUTRIENT THROUGH THE SMALL INTESTINE IN THE CRITICALLY ILL

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INTRODUCTION. Although it is a major determinant of nutrient absorption, the rate of small intestinal (SI) transit in critically ill patients has hitherto not been assessed.

OBJECTIVES. The aim of this study was to measure duodeno-caecal transit times of enteral feed in this patient group using a scintigraphic technique.

METHODS. A prospective observational study was performed in 16 mechanically ventilated critically ill patients (12 M, age 49 ± 17 yr, BMI 25 ± 5 kg/m^2, ICU admission day 5 ± 3, APACHE II on study 20 ± 7; mean ± SD) and 6 healthy subjects (3 M, age 24 ± 9 year, BMI 24 ± 45 kg/m^2). After a 6 h fast a 100 ml enteral feed (Ensure 1 kcal/min), labelled with 20 MBq ^{99m}Tc-sulphur colloid, was infused into the distal duodenum over 6 min. Dynamic anterior scintigraphic images were recorded in 3 min frames for 240 min and the time of first appearance of activity in the caecum was recorded by two blinded operators (KJ, AR). Data were assessed using Mann Whitney U test and are presented as median (IQR).

RESULTS. Caecal arrival times were not significantly different between patients [72 (22–240) min] and healthy subjects [115 (42–141) min; $P = 0.64$]. However, two distinct patterns of transit were observed in the patients. In 7 patients caecal arrival was rapid (<lower IQR for healthy cohort) whilst in 6 it was markedly delayed (>upper IQR for healthy cohort).

CONCLUSIONS. Small intestinal transit in critically ill patients appears highly variable with up to 75% of patients having either relatively rapid or delayed caecal arrival of enteral nutrition. Both of these scenarios may influence nutrient absorption and warrant further investigation. However, more subjects are required to form firm conclusions.

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CLINICAL IMPACT OF ERYTHROMYCIN PRESCRIPTION AS A PROKINETIC AGENT: AN OBSERVATIONAL COHORT STUDY CONDUCTED IN 160 CRITICALLY ILL PATIENTS VENTILATED FOR MORE THAN 5 DAYS

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INTRODUCTION. Erythromycin, a macrolide antibiotic is widely used as a prokinetic agent in intensive care unit (ICU) despite the lack of data supporting its prolonged effectiveness in enteral nutrition (EN) intolerant critically ill patients.

OBJECTIVES. To evaluate impact on clinical outcome of erythromycin prescription as prokinetic agent in ICU.

METHODS. All patients consecutively admitted from January 2008 through December 2009 mechanically ventilated for more than 5 days and receiving EN were included in an observational cohort study. EN intolerance was defined clinically as a 8-hourly gastric residual volume (GRV) ≥150 mL or vomiting. Successful EN was defined as a GRV <150 mL with a feeding rate ≥40 mL/h. Erythromycin prescription was left to practician appreciation.

RESULTS. A total of 160 patients were included; 74 (47%) patients experienced EN intolerance. Among them, 36 (48%) received erythromycin. Patients treated with erythromycin had same age (61 ± 14 vs. 63 ± 16), SAPS II (50 ± 18 vs. 51 ± 16) and SOFA score (7.8 ± 4.0 vs. 6.4 ± 3.0) than patients not treated with erythromycin. But they showed higher GRV before the start of enteral nutrition (32 ± 47 vs. 13 ± 29 mL, $p = 0.04$), more frequent persistent ileus (>7 days) (67 vs. 34%, $p = 0.014$), and longer sedation (15 ± 8 vs. 11 ± 7 days, $p = 0.03$). From day 1 to day 7 following EN intolerance, mean maximal GRV was significantly reduced (79 ± 68 vs. 47 ± 63 mL, $p = 0.02$) and mean EN volume significantly increased (871 ± 426 vs. 1,130 ± 432 mL, $p = 0.01$) only in patients treated with erythromycin. Proportion of successful EN was similar with or without erythromycin, except on day 7. Successful EN was then less frequent with erythromycin (54 vs. 80%, $p = 0.03$) due to more frequent recurrences of EN intolerance (53 vs. 30%, $p = 0.06$). Mortality in ICU (47 vs. 41%), incidence of pneumonia (28 vs. 31%), emergence of multidrug-resistant bacteria (39 vs. 24%) were similar with or without erythromycin. No serious adverse effects were reported with erythromycin.

CONCLUSIONS. Erythromycin induced significant reduction of GRV and increase of EN volume in case of EN intolerance. But no significant impact on clinical outcome was observed. Treatment with erythromycin was well tolerated.

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IS ENTERAL NUTRITION ASSOCIATED WITH DIARRHOEA IN THE INTENSIVE CARE UNIT?

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INTRODUCTION. Diarrhoea occurs commonly and the reported incidence varies between 2 and 95% in the Intensive Care Unit (ICU). Many physicians associate diarrhoea with enteral nutrition (EN) even if this association is not proved.

OBJECTIVES. This study aims at evaluating the relationship between diarrhoea and EN in ICU patients.

METHODS. During 1 month, the days with and without diarrhoea (≥ 3 liquid stools/day) and the characteristics of nutritional support of all patients staying in our ICU were recorded. Patients staying <24 h or presenting an intestinal stomy were excluded. We compared, between days with and without diarrhoea, total energy coverage and energy coverage by EN as % of needs, EN energy intake and EN volume for each patient. Needs were estimated as 25–30 kcal/kg body weight for women and men, respectively. The relationship between antibiotics, laxative treatment and diarrhoea was also analysed. Results are presented as mean ± SD. Comparisons were made by Mann–Whitney test. The risk of diarrhoea with EN was calculated by odds ratio and confidence intervals (CI).

RESULTS. The study included 1133 days of hospitalisation of 171 patients (60 ± 16 years, BMI 26 ± 5 kg/m^2, SOFA score at admission 6 ± 6). EN was present in 85 days of diarrhoea and 581 days without diarrhoea.

TABLE

	N	Total energy coverage (% of needs)	EN energy coverage (% of needs)	EN energy intake (kcal/day)	EN volume (mL/24 h)
Days with diarrhoea	101	71 ± 37*	65 ± 42*	1,353 ± 777*	42 ± 24*
Days without diarrhoea	1032	49 ± 42	42 ± 43	834 ± 886	25 ± 27

* $p < 0.05$

Odds ratio for developing diarrhoea under EN was 4.1 (95% CI 2.38–7.13, $p < 0.001$). Among the 85 diarrhoea days on EN, 11 occurred under laxatives and 67 under antibiotic treatment.

CONCLUSIONS. In the ICU, EN energy coverage as well as energy and volume intake were higher in days with diarrhoea than in days without diarrhoea. Although this study cannot identify a cause-response relationship between EN and diarrhoea, there is a higher risk of diarrhoea with EN than without EN.

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EPIDEMIOLOGY OF DIARRHOEA IN THE INTENSIVE CARE UNIT (ICU): A 3.5 MONTH RETROSPECTIVE STUDY

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INTRODUCTION. Diarrhoea is frequent in the ICU and associated with delayed enteral nutrition (EN) and underfeeding. The epidemiology of diarrhoea in the ICU is not well known.

OBJECTIVES. We aim at describing diarrhoea prevalence and epidemiology in ICU patients.

METHODS. ICU patients presenting at least 1 day (d) of diarrhoea (≥ 3 liquid stools/d) over a 3.5 month period were identified. The prevalence and duration of diarrhoea, and its time of onset from admission, were determined. The main characteristics of patients with diarrhoea were collected: age, gender, SOFA score at admission, length of stay (LOS), type of nutritional support, drug administration (antibiotics, laxatives, prokinetics, probiotics, anti-diarrhoeal drugs). Results are presented as mean ± SD.

RESULTS. During the study period, 89 out of 873 (10.2%) admitted patients reported diarrhoea (age 60 ± 16 years, sex ratio 54/35, SOFA 5 ± 4), corresponding to 198 diarrhoea days. Diarrhoea lasted between 1 and 4 d (1 d, n = 41; 2 d, n = 30; 3 and 4 d, n = 5, each) in 91% of patients, and more than 5 days in 8% (n = 9). Most diarrhoea (71%) occurred in the first week of ICU stay: <3 days, n = 39; 4–7 days, n = 24; 7–10 days, n = 10; >10 days, n = 16). The mean LOS of patients with diarrhoea was longer than the mean ICU LOS of the study period (10.9 vs. 7.2 d). Among 198 diarrhoea days, 53% occurred on EN, 5% on parenteral nutrition (PN) and 8% on combined EN + PN. Antibiotic treatment was associated with 156 (79%) diarrhoea days, including 83 (80%) of the 104 EN-associated diarrhoea days. Laxatives, prokinetics, probiotics and anti-diarrhoeal drugs were reported in, respectively, 32, 4, 0 and 2% of diarrhoea days.

CONCLUSIONS. The prevalence of diarrhoea was 10.2% in the ICU. Even though diarrhoea duration is short, it may be associated with a longer LOS. EN and antibiotic therapy may be associated with diarrhoea in ICU. The relationship between EN and the risk of diarrhoea is presented in a prospective study submitted for ESICM 2010.

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DEFINING THE PREFERRED ROUTE FOR THE CITRULLINE GENERATION TEST IN ICU PATIENTS

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INTRODUCTION. Determining the small bowel function is of great concern in ICU patients, because a malfunctioning small bowel may predispose to malnutrition and may increase the risk of SIRS. A recently developed test, the Citrulline Generation Test (CGT), measures the enterocytes' capability to convert glutamine into citrulline. The production of citrulline exclusively takes place in functioning enterocytes, therefore this conversion represents small bowel function.

OBJECTIVES. We aimed to define the CGT reference values in 16 'stable' ICU-patients to assess small bowel function. Secondly, we wanted to compare four different CGT methods; enteral and iv administration of Dipeptiven and measurement of citrulline in both arterial and venous samples.

METHODS. We performed the CGT on 16 stable ICU-patients, defined as having respiratory failure but not dependent on vasopressors. They had a normal renal function and were able to tolerate enteral nutrition.

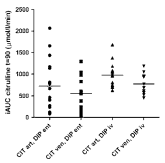
A 5 h fast was followed by administration of 20 g of glutamine-alanine (Dipeptiven®) either intravenously or enterally, randomly determined. The next day the same test was performed by using the other route. After each administration of Dipeptiven, citrulline levels, both arterial and venous, were measured at fixed time points using reverse-phase high performance liquid chromatography (HPLC).

RESULTS. Nine females and 7 males were admitted to the ICU with either a medical (11) or a surgical (5) diagnosis. They had a mean (± SD) age and BMI of 60.9 ± 10 years and 26.7 ± 7, kg/m^2 respectively. Their median APACHE II score was 24.5 (IQR = 19.5–26.8). On the day the CGT was performed their median SOFA score was 4.0 (IQR = 3.0–4.8).

IAUC CITRULLINE T = 90

Route of Dipeptiven	Intravenous				Enteral			
Sample	Arterial		Venous		Arterial		Venous	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
iAUC citrulline T = 90 (μmol/L/min)[a]	977.0	739.8–1084	769.3	576.6–949.5	723.8	264.8–1162	556.1	192.3–1006

[a] iAUC T = 90 is defined as the increment of the area under the curve of citrulline at t = 90 min



iAUC citrulline t = 90

CIT art and CIT ven refer to the sample from which citrulline was measured (arterial/venous)

DIP ent and DIP iv refer to the route of administration of Dipeptiven (enteral/intravenous)

CONCLUSIONS. The maximal citrulline response was observed after the intravenous administration of Dipeptiven and sampling of arterial blood. Therefore, arterial sampling for citrulline after intravenous administration of Dipeptiven appears to be the preferred way to perform the CGT.

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ELECTROMAGNETIC SENSOR GUIDED NASOJEJUNAL TUBE PLACEMENT IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Early post-pyloric feeding has been shown to improve clinical outcomes [1]. Commonly used methods for placing a nasojejunal tube (NJT) are blind, endoscopic or fluoroscopic placement. The later two methods are relatively invasive, expensive and can cause delay to feeding, whereas blind placement is often unsuccessful. Electromagnetic sensor guided NJT insertion is a bedside technique able to confirm successful placement without the need for abdominal X-ray. The system incorporates a liquid crystal display and a receiver unit. The receiver is placed over the patient's xiphoid process and picks up the signal from an electromagnetic transmitter located at the tip of the feeding tube. The screen provides a visual aid to enable the operators to trace the route of the tube tip and identify its' location according to anatomical markers.

OBJECTIVES. We were interested to determine the suitability of electromagnetic sensor guided NJT insertion especially in relation to success rate and procedure time.

METHODS. Fifty patients were referred for electromagnetic NJT insertion on units at the Leeds Teaching Hospitals. Insertion time was measured from oesophageal visualisation until post-pyloric placement. Various positional manoeuvres were employed along with administration of sedatives, prokinetics and air insufflation when applicable. All insertions were carried out by experienced investigators. All NJT insertions were confirmed by abdominal X-ray. Data collection included patient demographics, hospitalisation and procedural information.

RESULTS. Forty male and 10 female patients, mean age 40 (range 1–81 years), BMI mean 25 (14–33), had attempted electromagnetic NJT placement. Patients had been hospitalised for a median of 12 days (1–180). Indication for NJT insertion was either large aspirate and/or reflux (86%). Seventy six percent of patients had an artificial airway and 50% of patients were receiving sedation. Forty six percent of patients received metoclopramide and 58% air insufflation. Thirty six percent of patients were moved into either left or right lateral position. Successful post-pyloric placement was achieved in 90% of patients confirmed by additional abdominal X-ray. Procedural time varied from 2 to 180 min (mean 23). Two of the placement failures were due to patient intolerance.

CONCLUSIONS. Bedside electromagnetic guided NJT placement technique is an acceptable method of placing post pyloric feeding tubes with a high success rate.

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1151

PRIMARY AND SECONDARY GASTROINTESTINAL FAILURE HAS DIFFERENT INCIDENCE AND IMPACT ON ICU OUTCOME

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INTRODUCTION. For rough evaluation of the gastrointestinal (GI) function in clinical setting, the Gastrointestinal failure (GIF) score has been suggested (1). The GIF score defines GI failure as the occurrence of feeding intolerance (FI) and intra-abdominal hypertension (IAH) simultaneously.

OBJECTIVES. To compare the outcome of patients with primary vs. secondary GIF.

METHODS. All consecutive, mechanically ventilated (MV) patients treated for at least 24 h during January 2008 to December 2009 in two ICUs were studied. GIF was defined as GIF score equal or above 3 points according to the GIF score (1). 3 points = FI and IAH simultaneously; 4 points = abdominal compartment syndrome (ACS). FI was defined as the need to stop enteral feeding for any clinical reason (vomiting, high gastric residuals, bowel distension etc). IAH was defined as mean intra-abdominal pressure (IAP) $\geq$12 mmHg on any day. ACS was defined as IAP > 20 mmHg with the new onset organ failure. When GIF developed in a patient with primary pathology in abdomino-pelvic region it was classified as primary GIF, when occurred without previous pathology in abdomino-pelvic region it was taken as secondary.

RESULTS. We studied 418 patients with mean (SD) APACHE II score 16.4 (8.3) and SOFA score 7.4 (3.6) points on admission day. ICU mortality of the study patients was 11.2%. FI occurred in 237 (56.7%) and IAH in 118 (28.2%) patients during their ICU stay. GIF developed in 68 (16.3%) patients. The syndrome was of primary origin in 45 (66.2%) and secondary in 23 (33.8%) cases. ACS developed in 4 (1.0%) patients with no mortality. The most common underlying pathology in primary GIF was acute pancreatitis in 12/45 patients, followed by different intestinal pathologies (perforation, hemorrhage, ileus) in 16/45 patients in total. Secondary GIF developed most often in patients with sepsis (12/23) and cardiovascular insufficiency (5/23). Patients with GIF had longer duration of MV and ICU stay compared to patients without GIF (16.3 vs. 6.4 and 18.0 vs. 8.5 days, both p values <0.001), but ICU mortality was not different (16.2% vs. 10.3% p = 0.160). ICU mortality was 4/45 (8.9%) in primary and 7/23 (30.4%) in secondary GIF (p = 0.036). MV and ICU periods were similar in these two groups.

CONCLUSIONS. Patients with GIF have significantly longer ICU stay and MV duration, but not higher ICU mortality. Secondary GIF occurs less often than primary and is associated with higher ICU mortality.

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Fluid and temperature management: 1152–1165

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OCTAPLASLG®: IMPROVEMENT OF BIOCHEMICAL QUALITY AND PATHOGEN SAFETY

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INTRODUCTION. Due to four possible transmissions of variant Creutzfeldt-Jakob Disease (vCJD) through non-leukocyte depleted red blood cell concentrates in the UK, all manufacturers of plasma-derived biopharmaceuticals are requested to perform appropriate prion safety evaluations of their product portfolio. To further improve the safety margin of the solvent/detergent (S/D) treated plasma Octaplas®, a novel prion protein removal technology was incorporated into the manufacturing process, changing the product name to OctaplasLG®. The removal of the pathogenic prion proteins (PrP^{Sc}) was achieved by a chromatographic step, utilising an affinity ligand gel selected for prion protein binding (developed by Pathogen Removal and Diagnostic Technologies Inc., USA).

OBJECTIVES. In this study the biochemical quality and prion safety of the pharmaceutically licensed plasma OctaplasLG® was evaluated. The prion reduction factor achieved by Western blot was confirmed by animal studies.

METHODS. Eighteen consecutive batches of OctaplasLG® (Octapharma PPGmbH, Vienna, Austria) were tested on global coagulation parameters, fibrinogen levels, activities of coagulation factors and protease inhibitors, activation markers, as well as von Willebrand factor multimers. In parallel studies, plasma pool was spiked with exogenous spike material, derived from brains of hamsters infected with hamster-adapted scrapie 263 K, and a down-scale of the OctaplasLG® manufacturing process was performed. The PrP^{Sc} reduction factor for the resin was investigated in both Western blot and hamster bioassay studies.

RESULTS. A reduction factor of $\geq 3.1 \log_{10}$ PrP^{Sc} was found for this process step by Western blotting. The outcome of the hamster bioassay confirmed that the high level of removal PrP^{Sc} seen during OctaplasLG® manufacturing was equivalent to a removal of infectivity ($3.0 \log_{10}$). In OctaplasLG®, a parallel reduction of the S/D virus inactivation step led to significantly higher activities of plasmin inhibitor.

CONCLUSIONS. Our studies demonstrated that the same amounts of PrP^{Sc} and prion infectivity bind rapidly and with a very high affinity to the chromatography resin. OctaplasLG® has the same clinical safety and efficacy profile compared to that demonstrated by Octaplas® over the last 18 years, except for the increased safety margin in terms of prion disease transmission and the possible effect of a significantly increased plasmin inhibitor activity.

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UNIPLAS®: UNIVERSALLY APPLICABLE COAGULATION ACTIVE PLASMA WITH IMPROVED PATHOGEN SAFETY

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INTRODUCTION. Uniplas® is a second generation solvent/detergent (S/D) treated, coagulation active plasma for infusion produced with an implemented prion removal step. It was developed as an alternative to the blood group specific S/D plasma products, OctaplasLG® and Octaplas®, in order to obtain an universally applicable (i.e. blood group independent) plasma that can be used without taking into account the blood group of the recipient. Due to an initially controlled, optimal mixing of plasma of different blood groups prior to S/D treatment, in Uniplas®, the blood group specific antibodies (anti-A and anti-B of both IgM and IgG type) are neutralised and/or removed by free A and/or B substances and red blood cells (RBCs) to a clinical acceptable level with very limited or no complement activation.

OBJECTIVES. In this study an extensive biochemical characterisation of the first Uniplas® validation batches was performed.

METHODS. Three batches of Uniplas® were produced by OctapharmaPPGmbH (Vienna) under production conditions in 2008–2009. Uniplas® batches were tested on all important coagulation factors, protease inhibitors, activation markers, ADAMTS13 and factor H levels, as well as von Willebrand factor multimers. In addition, anti-A and anti-B titres of IgM- and IgG-type were investigated. Finally, complement activation products, as well as key components of the complement system, were measured.

RESULTS. In Uniplas® batches, all coagulation factor activities were higher than 0.7 IU/ml and all protease inhibitor activities, including protein S and plasmin inhibitor, were higher than 0.5 IU/ml. Uniplas® contained standardised levels of ADAMTS13 and factor H, within the normal ranges for single-donor fresh-frozen plasma. There was no activation of FVII obtained during manufacturing, thrombin-antithrombin (TAT)-complex, prothrombin fragments (F1 + 2) and D-dimer levels were within the normal ranges. Anti-A and anti-B titres were within the Uniplas® specification, i.e. anti-A IgM and anti-B IgM <1:8 as well as anti-A IgG and anti-B IgG <1:32, respectively. Uniplas® did not contain an increased amount of immune complexes and the manufacturing of Uniplas® associated with more complement activation than the one seen for OctaplasLG®.

CONCLUSIONS. The present study confirmed that Uniplas® displays the same high quality and clinical efficacy as the S/D treated blood group specific plasma OctaplasLG®, but with the additional advantage in being a blood group independent universally applicable plasma.

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INCIDENCE AND PROGNOSIS OF INTRA-ABDOMINAL HYPERTENSION AND ABDOMINAL COMPARTMENT SYNDROME IN SEVERELY BURNED PATIENTS

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INTRODUCTION. Burn pts are at high risk for secondary intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) due to capillary leak and massive fluid resuscitation (1–3).

OBJECTIVES. To examine the incidence and prognosis of IAH/ACS in mechanically ventilated (MV) burn pts.

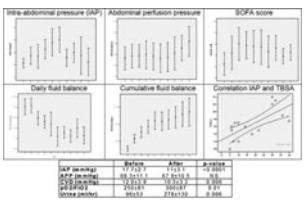
METHODS. Prospective observational study (April 2007–December 2009). The lowest (IAPlow) and highest IAP (IAPhigh), lowest abdominal perfusion pressure (APP = MAP-IAP) were recorded on each day together with SOFA score, capillary leak index (CLI = CRP/albumin), daily and cumulative fluid balance (FB). PiCCO parameters were obtained in 21 pts. Mean and maximal IAP during stay were calculated. Primary endpoint was ICU mortality.

RESULTS. 55 pts were studied. Age 43.1 ± 25.9 years, weight 68.6 ± 28.2 kg, BMI 24.5 ± 6.3. SAPSII 43.4 ± 15.1, SOFA 6.4 ± 3.4. TBSA burned was 25.2 ± 24.7%, 33 pts also had inhalation injury. IAPlow 7.2 ± 2.7, IAPhigh 9.9 ± 3 and APPlow 50.5 ± 9.4 mmHg on admission. IAPmean 9.7 ± 3.2 and IAPmax 15.7 ± 5.2 during stay. ICU stay was 24.8 ± 28.6. Mortality was 29.1%. IAH, defined as sustained IAP $\geq$12 mmHg was present in 41 (74.5%) and 11 (20%) had ACS. Pts with ACS had higher TBSA burned (39.6 ± 26.4 vs. 21.7 ± 23.6%, p = 0.03), higher cumulative FB (11.4 ± 15.8 L vs. 4.3 ± 3.6 L, p = 0.08) and higher mortality (81.8 vs. 13.6%, p < 0.0001). TBSA burned correlated well with IAPmean (R = 0.34, p = 0.01). In univariate analysis, SAPS II, APACHE II, %TBSA burned, % 3rd degree burns, IAP (low, high, mean, max), CLI, EVLWi (mean, max), PEEP, Pplat, total fluid intake, daily and cumulative FB were significantly higher in nonsurvivors (and remained higher during the 1st week) while APPlow and albumin were significantly lower (Table).

OUTCOME PREDICTORS AND EFFECT OF DECOMPRESSION

	Survivors (n = 40)	Nonsurvivors (n = 16)	p value		Before decompression	After decompression	p value
IAP max (mmHg)	15 ± 4.3	19.5 ± 4.1	0.0009	IAP (mmHg)	17.8 ± 3.4	11.1 ± 3.5	<0.0001
APP low (mmHg)	53 ± 8.8	43.2 ± 7.1	0.0007	APP (mmHg)	62.3 ± 13.8	69.1 ± 12.7	NS
%TBSA	16.3 ± 15.2	47.3 ± 30.2	<0.0001	CVP (mmHg)	16.6 ± 5.5	12.8 ± 4.3	0.005
%3rd degree	5.2 ± 9.6	30.1 ± 36.4	0.0002	P/F ratio	251 ± 110	303.2 ± 114.2	0.01
Fluid balance (mL)	3,337 ± 2,570	8,963 ± 13,524	0.014	Urine output (mL/hr)	83.3 ± 75.3	208.4 ± 148.6	0.0003

Most pts received more fluids than calculated by Parkland formula (7 ± 7.5 ml/kg × %TBSA). Interestingly, nonsurvivors received less (3.9 ± 4.1 vs. 8.3 ± 8.2 ml/kg × %TBSA). Gastric decompression, ascites drainage and the implementation of a stool protocol with rectal enemas (18 interventions in 12 pts) was able to remove 2.2 ± 1.3 L of body fluids and this was related to a significant decrease in IAP and CVP and an improvement in oxygenation and urine output (Table)



Evolution in burn patients

CONCLUSIONS. Based on our preliminary results we conclude that IAH and ACS are more prevalent in MV burn pts compared to other groups of critically ill pts. The %TBSA burned correlates with mean IAP. The combination of high CLI, positive (daily and cumulative) FB, high IAP, high EVLWi and low APP correlate with poor outcome. Non surgical interventions can lower IAP, CVP thereby improving endorgan function.

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CUMULATIVE FLUID BALANCE IS A PREDICTOR OF SICU SURVIVAL

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INTRODUCTION. The impact of cumulative fluid balance on SICU survival is not well defined.

OBJECTIVES. This is to investigate the possible impact of cumulative fluid balance on SICU survival.

METHODS. Our prospective observational study includes 219 SICU patients admitted after major abdominal procedures because of primary surgical pathology of intraabdominal structures—172 (79%), or abdominal traumas—47 (21%). During their SICU stay patients may receive various combinations of crystalloids (Plasmalite, Ringer's solution, normal saline, 4% potassium chloride, and (or) colloids (6% hydroxyethyl starch, 4% succinated gelatin, 5% albumin).

Daily fluid balance was calculated as a difference between fluid intake (oral and intravenous) and output (dieresis, discharge from drainaging tubes, nasogastric tub, and insensible loses). Insensible loses were assessed as 10 ml/kg/day in patients with mean daily temperature $\leq 37^{\circ}$, in case of $t > 37^{\circ}$ insensible loses were increased by 13% for each Celsius higher 37°. Each defecation was estimated to add 100 ml fluid lose. Cumulative fluid balance was defined as the sum of daily balances. The main end point of the study was patient's death in SICU.

RESULTS. The overall SICU mortality was 77 (35.3%), and the mortality was significantly higher in patients with positive cumulative fluid balance during the SICU stay $X^2 = 4.85$; $p = 0.028$. The odds ratio for positive cumulative balance in binary logistic regression model was 8.24 (95% CI 2.57–26.39); $p < 0.001$. The probability of death was directly proportional to fluid balance.

CONCLUSIONS. Positive cumulative fluid balance is an independent predictor of all cause mortality with odds ratio 8.24 (95% CI 2.57–26.39); $p < 0.001$.

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INDUCED HYPOTHERMIA: A RISK FACTOR FOR PROPOFOL INFUSION SYNDROME?

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INTRODUCTION. Propofol is commonly used to provide continuous sedation in critically ill patients in the intensive care unit (ICU). Propofol infusion syndrome (PRIS) is a rare but potentially fatal complication that has been described in children[1] and adults. It is characterised by the development of metabolic acidosis, lipaemia, rhabdomyolysis and myocardial failure. Risk factors include high-dose propofol, traumatic brain injury (TBI)[2], critical illness and the use of corticosteroids and catecholamines.

METHODS. In this paper we report the clinical course of two patients admitted to ICU with TBI who developed features suggestive of PRIS. Both patients received prolonged infusions of propofol (average daily dose of 4 mg/kg/h) and required active cooling for management of intracranial pressure (ICP).

RESULTS. Case 1: A 23 year old man with severe TBI was initially sedated with propofol and fentanyl. Midazolam was added in view of raised ICP and he was actively cooled to 34–35°C. On day 5 he developed infero-lateral T wave inversion on the ECG. 2 days later he developed widespread ST segment elevation (Brugada-like ECG pattern) with a raised troponin; the propofol infusion was stopped. The ECG improved although there was persistent T wave inversion. On day 12 he became cardiovascularly unstable with increasing vasopressor requirements finally resulting in cardiac arrest. A post mortem study revealed the presence of normal coronary arteries. Case 2: A 21 year old man with severe TBI was sedated with increasing doses of propofol and fentanyl for raised ICP. Midazolam was added on day 2 and he was actively cooled to 34°C. On day 4 the patient developed a mild lactic acidosis and 3 days later he developed infero-lateral ST segment elevation on the ECG followed rapidly by cardiac arrest and death.

CONCLUSIONS. PRIS is a difficult condition to diagnose and routine monitoring of the adverse effects of high-dose propofol remains sub-optimal. Hypothermia has been reported to alter propofol pharmacokinetics[3] and we propose that active cooling may increase the risk of developing PRIS. This may be particularly relevant in patients with TBI who are on high doses of propofol to control ICP in addition to concomitantly administered catecholamines to maintain cerebral perfusion pressure. We recommend that further research is required in this area in view of the increasing use of induced hypothermia in ICU.

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FLUID RESUSCITATION IN BURNT PATIENTS MANAGED INITIALLY IN EITHER A SPECIALIST OR NON-SPECIALIST CENTRE

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INTRODUCTION. Adequate fluid resuscitation in the first 24 h after severe burn injury is vital; however the best formulae, volumes and type of fluids remain controversial. There is no ideal formula; adequate resuscitation should be tailored to the patient's response and physiological parameters.

OBJECTIVES. To compare differences in fluid resuscitation based on direct or indirect admissions to the London Burns Unit.

METHODS. 67 admissions to the burns unit with >20% burned surface area (%BSA) were identified over 5 years. 16 were excluded from analysis due to palliation or death within the first 8 h. 12 sets of notes were randomly selected for analysis of fluid balance in the first 24 h period of fluid resuscitation after the burn injury.

RESULTS. Mean (SD) time from burn injury to arrival at the Burns Unit was lower for patients transferred direct to the burns hospital rather than via another hospital (117.9 ± 75.27 vs. 372.5 ± 255.7 min $p = 0.032$). Mean (SD) error in burn size estimation was lower for patients initially treated by burns specialists versus non-burns specialists (4 ± 3.6 vs. $10.6 \pm 4.3\%$, $p = 0.016$). All patients were resuscitated according to the Parkland formula calculated at one of 2, 3 or 4 ml/kg/%BSA. The mean (SD) actual fluid volume differed from the target by 30.06% (±40.43%); the lower the calculated fluid target, the greater the error between actual and planned resuscitation volumes; there was no difference in accuracy of fluid resuscitation at 24 h between patients initially managed by burns specialists versus non-burns specialists (44.14 ± 49.04 vs. $10.34 \pm 7.70\%$ respectively, $p = 0.163$).

CONCLUSIONS. Burned patients transferred directly to specialist Burns care receive a faster and more accurate assessment of their burn injury. Despite this, we found no difference in fluid targeting errors at 24 h, though this may reflect corrective fluid management on arrival at the specialist centre.

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STATIC VERSUS DYNAMIC ECHOCARDIOGRAPHY VARIABLES AS PREDICTORS OF RESPONSE TO VOLUME IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Echocardiography is an useful and minimally invasive tool that allows to know the heart filling pressures, also it has proven highly accurate in predicting the response to volume in critically ill patients.

OBJECTIVES. We try to determinate the response to fluid infusion by static variables as CVP or LAP, comparing with the variation of IVC.

METHODS. An observational prospective study with 18 patients undergoing coronary cardiac surgery (7 patients were excluded by a no presenting a good echo views), in the postoperative period under mechanical ventilation (Vt 8 ml/kg, FiO2 50%, PEEP 3). We performed an echocardiography if the patient presented hypotension, just before the habitual fluid load protocol were started (500 ml HES 6% in 30–45 min). We collected data before and after the infusion, and determine the responsiveness to volume if the cardiac output increased more than 10%. Data in the report included invasive CVP and LAP, and echo measures, ratio E/e', diameter and variations of inferior vena cava (IVC) and variations of stroke volume by echocardiography (ØLVOT x VTI LVOT) and with Vigileo® system.

RESULTS. The correlation between low values of CVP/LAP and volume response was poor, the relationship between CVP below 6 mmHg with increased cardiac output had a correlation (Pearson correlation −0.06) with a significance (2-tailed) 0.981, and the relationship between LAP <4 mmHg and an increase in cardiac output had a correlation (Pearson correlation 0.229) with a significance of (2-tailed) 0.362. The measurement of the variation of the inferior vena cava, led us to calculated a cutoff point more sensitive to determine which patients were responders to volume. Through the ROC curves (sensitivity/specificity), with the area under the curve of 82.5% (SE = 11.2%) and with a confidence interval of 95% (p significance of 0.002), resulted in a 12% variations of IVC with a sensibility of 100% and specificity of 42% (Younden's index of 42.9%). The same calculation, based on Kraemer's quality indices (QI) gave us a 13% of variation in IVC, with a w = 0.2 specificity rather than sensitivity (QI 0.58), and with a w = 0.8 sensitivity rather than specificity (QI 0.61)

CONCLUSIONS. • Studies with transthoracic echo may present artifacts in postoperative patients because poor window

- The static variables are not good predictors of response to volume, despite a good cardiac function
- The variation of the inferior vena cava into figures of 12–13% can very reliably predict the response to volume

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POSTOPERATIVE HYPOTHERMIA: SIMPLY TREATED OR MISUNDERSTOOD PATHOPHYSIOLOGY?

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INTRODUCTION. Hypothermia in surgical patients has detrimental multisystem effects leading to impaired immunity with increased risk of infection, poor metabolic regulation, glycaemic control and coagulation disorders. Inadvertent perioperative hypothermia, defined as core temperature <36°C, is a common but easily preventable complication. Risk factors as described by Flores-Maldonado et al

1. were used in the guidelines put forward by National Institute of Clinical Excellence
2. for inadvertent perioperative hypothermia.

OBJECTIVES. To ascertain whether postoperative hypothermia is linked to high or low risk surgical patients.

METHODS. We conducted a prospective systematic analysis looking at the incidence of postoperative hypothermia in adults who underwent general anaesthesia. Children age <18, pregnant women and patients undergoing regional anaesthesia were excluded from the survey. Patients were categorised according to their risk factors as described by the NICE guidelines ASA grade II to V, major or intermediate surgery. Preventative measures and management of hypothermia such as forced air warmers were recorded. Core temperature was measured on arrival to the recovery area using Welch Allyn Sure Temp Plus.

RESULTS. A total of eighty patients were assessed. 68 (84%) patients were deemed high risk having ASA II or greater and undergoing intermediate or major surgery. Postoperative hypothermia occurred on 14 (17.5%) of which 4 (28%) were low risk classified as ASA I and having had minor surgery. A forced air warmer was used intraoperatively in 8 of the 14 patients found to be hypothermic and in 1 of the 4 low risk patients.

CONCLUSIONS. Hypothermia is a frequent occurrence in high risk surgical patients with potentially adverse consequences. It is also a problem in what is classified by the NICE guidelines as low risk patients. Simple measures can be effectively introduced to prevent the complication of hypothermia. Although our practice did not strictly adhere to NICE guidelines our analysis highlighted that risk factors for hypothermia may need reassessing for quality improvement. Warming measures such as forced air blankets, fluid warmers and greater ambient temperatures should be considered in all patients undergoing surgery.

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A PILOT STUDY: SURVEY OF DOCTORS' KNOWLEDGE ON PERIOPERATIVE FLUID MANAGEMENT

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INTRODUCTION: As highlighted in the UK's National Confidential Enquiry into Patient Outcome and Death (NCEPOD) in 1999, suboptimal fluid management can cause serious morbidity and mortality in perioperative patients.[1] Up to 54% of patients can develop complications such as fluid overload, electrolyte derangement and dysrhythmias.[2] Intravenous fluid prescriptions should be tailored to each patient—the rate and type of fluid prescribed should be correlated with the patient's co-morbidities, surgical procedure, examination findings, fluid balance charts and serum biochemistry. Appropriate monitoring should also be undertaken.[3]

OBJECTIVES. To identify the current level of doctors' knowledge on perioperative fluid management.

METHODS. The survey was conducted at George Eliot Hospital, Nuneaton, UK in May 2009. Questionnaires consisting of ten multiple-choice questions on basic sciences and clinical scenarios were devised by a consultant anaesthetist. These were personally distributed to doctors of all grades working in anaesthetics and the surgical specialties. Doctors were asked to complete the questionnaire within 5 min. Of the 66 questionnaires distributed, 52 were completed.

RESULTS. The mean questionnaire score varied between specialties from 87% in the anaesthetics department to 64% for doctors in surgical specialties. The mean score of registrars and FY1 doctors in surgical specialties was found to be 72 and 65% respectively. The overall mean score was 74%. Of all doctors surveyed, the daily maintenance water requirement was known by only 52%, 62% knew the daily maintenance sodium requirement and 75% knew that of potassium. The electrolyte contents of 0.9% sodium chloride and Hartmann's Solution was answered correctly by 65% and 63% respectively.

CONCLUSIONS. There is a significant deficiency in doctors' knowledge on perioperative fluid management. More emphasis on optimal perioperative fluid management is required in undergraduate and postgraduate training. Increased awareness of the British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients would aid training. Based on this survey, a regional online survey of junior doctors is planned to further identify gaps in perioperative fluid management training. Optimal fluid management could also help to reduce prolonged hospital stay which can result from fluid-related complications.

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DYNAMIC ECHOCARDIOGRAPHIC PARAMETERS AS PREDICTORS OF VOLUME RESPONSIVENESS AFTER LAPAROTOMY SURGERY

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INTRODUCTION. Dynamic echocardiographic parameters (respiratory changes of inferior vena cava diameter and aortic blood flow) have not yet been evaluated as predictors of volume responsiveness in patients after laparotomy surgery.

OBJECTIVES. To evaluate dynamic echocardiographic parameters as predictors of volume responsiveness in surgical patients.

METHODS. 25 patients were included in the study after laparotomy surgery performed on the same day (4 breathing spontaneously and 21 mechanically ventilated in volume controlled mode with tidal volume of 10 ml/kg). A fluid challenge was performed in spontaneously breathing patients by passive leg raising and infusing saline (7 ml/kg). Echocardiographic analysis of respiratory changes of inferior vena cava diameter (ΔDIVC) and aortic blood flow (ΔABF) was performed in all patients. A threshold of 18% for ΔDIVC was used for classifying patients as volume responders or non-responders. Age, sex, gender, BMI, CVP, IAP, MAP, left ventricular ejection fraction, left ventricular systolic and diastolic area, and stroke volume in all patients, as well as ITBVI, CI, PPV and SVV in 16 patients were measured.

RESULTS. A positive correlation with ΔDIVC was established for ITBVI ($r = 0.49$, $p = 0.05$), IAP ($r = 0.47$, $p = 0.01$) and EF ($r = 0.38$, $p = 0.05$). A positive correlation with ΔABF was not established for any variable measured. 16 patients (64%) were classified as volume responders and 9 (36%) as non-responders. Responders had overall higher IAP than non-responders (13.45 ± 4.99 mmHg vs. 9.82 ± 3.33 mmHg respectively, $p = 0.04$).

CONCLUSIONS. Respiratory changes of IVC diameter showed positive correlation with ITBVI. So, conclusions about ITBVI could be indirectly made from ΔDIVC values in patients who are not being invasively monitored. PPV and SVV did not show positive correlation with ITBVI. Surprisingly, we confirmed a positive correlation between ΔDIVC and IAP. We detected 9 patients with high IAP, while all the volume responders had overall higher IAP. Although further investigations are needed to establish how longer duration of high IAP may influence ΔDIVC, it seems that ΔDIVC is a good parameter of volume responsiveness during first 24 h after laparotomy surgery. Unlike from other studies, we could not establish a positive correlation between ΔABF and any variable measured. These studies were performed in hypovolemic septic patients, so this could be the reason for such different results. More studies are needed in a larger set of patients undergoing laparotomy surgery to evaluate ΔABF.

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STROKE VOLUME VARIATION VERSUS OXYGEN DELILVERY FOR GUIDANCE OF EARLY GOAL DIRECTED THERAPY

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INTRODUCTION. Fluid optimization after major cardiac surgery was shown to improve patients postoperative outcome significantly. Several hemodynamic parameters were proposed for the guidance of therapy but never compared in a head to head trial.

OBJECTIVES. In this prospective randomized trial patients scheduled for elective cardiac surgery underwent early goal directed fluid therapy guided either by stroke volume variation (SVV) or by oxygen delivery index (DO2i). We hypothesized that while SVV is easier to obtain it will not be inferior to DO2i in outcome parameters.

METHODS. Following ethics committee approval and signing of a written informed consent, 84 patients were randomized in two groups to undergo either fluid optimization guided by Do2i or SVV in the first 8 postoperative hours in the ICU following elective cardiac surgery (CABG). Following a standardized EGT protocol the parameters were collected by using hemodynamic monitoring based on a pulse contour analysis and a transpulmonary lithium dilution (Lidco Plus, Lidco,UK). We compared amount and type of volume infused, need and amount of inotropic or vasopressor substances, time spent on ventilator, LOS in the ICU and postoperative complications. Statistics were evaluated by using a T Test for unpaired samples.

RESULTS. Data are shown in Table 1.

TABLE 1

Mean ± SD	LOS hosp (d)	TVent (h) ($p = 0.04$)	LOS ICU (h)	Complications (n) ($p = 0.004$)
SVV	13.15 ± 8.37	8.56 ± 2.2	48.8 ± 37.7	0.38 ± 0.73
DO2i	14.03 ± 11.98	10.03 ± 13.9	79.6 ± 129.1	0.76 ± 1.3

Compared to the DO2i group fluid optimization using SVV showed reduced ventilator times ($p = 0.043$) and less complications ($p = 0.004$) in the first 80 days after surgery. No differences between the groups were detected concerning the type and amount of volume infused, need for inotropes or vasopressors or the LOS in hospital

CONCLUSIONS. While SVV is less invasive, cheaper and easier to be obtained than DO2 outcome was at least not inferior and even showed improvements in postoperative cardiac surgery patients.

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DOES IT MATTER WHICH TYPE OF FLUID WE RUN THROUGH A GIVING SET BEFORE OR AFTER TRANSFUSION OF BLOOD? COMPATIBILITY OF BLOOD WITH DIFFERENT INTRAVENOUS FLUIDS

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INTRODUCTION. Over the years, there have been concerns over incompatibility of transfused blood with various intravenous fluids during blood transfusion, especially related to increased levels of haemolysis. It is often impractical, particularly in an emergency situation, to flush through a giving set with a so-called "safe" fluid prior to and after delivering blood. We wanted to investigate whether this is actually necessary and whether the usual fluids used in the perioperative period really do cause any demonstrable alteration in the composition of transfused blood.

OBJECTIVES. The purpose of this study was to expose packed red cells to a variety of different intravenous fluids commonly used during the perioperative period and to measure a number of parameters in the blood following their contact with each different fluid, including a blood film to examine for clumping of cells or haemolysis.

METHODS. A unit of A positive blood was passed through blood giving sets which were primed with various intravenous fluids. After adequate mixing of blood with fluids, samples were collected for full blood count, urea and electrolytes and blood films. One millilitre of mixed blood was taken in each bottle at a time. The intravenous fluids used in this study were Normal saline, Hartmann's solution, 5% Dextrose, 10% Dextrose, starch and gelatin.

RESULTS. There was no significant rise in blood parameters suggestive of haemolysis. The potassium and LDH levels were not significantly different with various fluids. The haemoglobin and haematocrit levels were also comparable to one another.

CONCLUSIONS. There was no demonstrable changes in blood parameters suggestive of haemolysis, nor were there any change in electrolyte values. This suggests that all of the fluids investigated during this study would be suitable to be used via the same giving set before and after the transfusion of pack red cells.

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COMPLIANCE WITH THE NATIONAL GUIDELINES IN AVOIDING INADVERTENT PERI-OPERATIVE HYPOTHERMIA IN ADULT SURGICAL PATIENTS

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INTRODUCTION. Several studies have established the adverse effects of peri-operative hypothermia. Recently, the National Institute for Health and Clinical Excellence (NICE) has issued guidelines on the management of inadvertent perioperative hypothermia in adults in the UK.

OBJECTIVES. To assess the compliance with the national guidelines in avoiding inadvertent peri-operative hypothermia in an acute district general hospital in England.

METHODS. We prospectively studied our local practice on maintaining normothermia in 165 consecutive adult surgical patients {61 men, mean age 57.4 years, 112 patients with ASA grade 2 (67.7%), 60 emergency surgical patients (36.4%), 49 patients with significant cardiac disease 29.7%}. We used a questionnaire that was filled pre-operatively by anesthetic nurses, intra-operatively by anesthesiologists, and post-operatively by recovery nurses. Patients were recruited from the following surgical subspecialties: General surgery (34%), Gynecology (24%), Trauma (22%), Breast surgery (9%) and Orthopedics (7%). Day surgery patients were excluded. Peri-operative hypothermia was defined as temperature <36°C as per the NICE guidelines.

RESULTS. Less than half of our patients (47.9%, n = 79) had their temperature measured preoperatively, on whom incidence of hypothermia was 25.3% (n = 20). Only one of these patients was warmed prior to induction. Patients requiring emergency surgery and those with ASA Grade 2 had increased incidence of preoperative hypothermia (30.8% and 28.6% respectively, $p < 0.05$). Based on NICE guidelines, 164 patients needed intraoperative forced air warming but only 64 (38.8%) patients received it. Intraoperative temperature measurement was made on 111 patients, of whom 28.8% (n = 32) were hypothermic. Incidence of intraoperative hypothermia was high in surgical procedures lasting longer than 30 min ($p < 0.05$) but was not affected by the use of regional anesthetic techniques. 161 patients had their temperature measured on arrival to recovery of whom 46 (26.6%) were hypothermic. 38 patients (23.6%) had their temperature measured every 15 min (NICE recommendation) and the mean time interval for temperature measurement in recovery was 26 min. 10 patients were still hypothermic on leaving recovery.

CONCLUSIONS. Majority of our surgical patients did not receive adequate perioperative care on maintaining normothermia. Consequently, the incidence of hypothermia was significant pre-, intra- and post-operatively. We are currently analyzing the data to investigate the effect of hypothermia on duration of recovery stay, length of hospitalization and mortality in our patients.

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IMPORTANCE OF CARDIAC OUTPUT MEASUREMENTS IN THE FLUID AFTER CARDIAC SURGERY STUDY (FACS)

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INTRODUCTION. We completed a double-blind randomized trial in patients undergoing cardiac surgery in which we compared fluid resuscitation with a hydroxyethyl starch (HES, 10% 250 MW pentastarch) and saline. Use of HES resulted in markedly less use of catecholamines the morning after surgery. An underlying design principle was that assessment of cardiac index (CI) is essential for a proper fluid protocol. In this analysis we examine that supposition.

METHODS. All subjects had pulmonary artery catheters. Patients were consented preoperatively, but randomized post operatively to receive up to 4 blinded 250 ml boluses for predefined hemodynamic targets; CI <2.2 L/min/m^2, blood pressure (BP) set by admitting team, CVP <3 mmHg, or urine output <20 mL/h. Hemodynamic measurements were made before and after each bolus. After the 4 study boluses, only saline was used.

RESULTS. 237 patients received fluids, 119 HES and 118 saline. There were 727 study boluses, 348 HES and 379 saline. Of these, 99 boluses (14%) could not be assessed for this hemodynamic analysis (but were still used for the primary outcome) because of protocol violation or missing data. Of the rest, 235 (37%) of boluses were given for a low CI; in 33 BP and 11 CVP were also low so that CI was the only trigger in 30%. A low BP was a trigger in 290 (46%). Low CVP was the trigger in 95 (15%). Only 50 HES and 65 saline patients required the maximum allowed 4 blinded boluses. At the 4th bolus, low CI was the trigger for 8 (16%) of HES but 20 (31%) of saline patients. There were 511 that could be evaluated for hemodynamic response based on four possible outcomes of CVP and CI.

CVP CI OUTCOMES

	Saline (n = 258) (%)	HES (n = 253 %)
CVP-no, CI-no	108 (42)	59 (23)*
CVP-yes, CI-no	48 (19)	50 (20)
CVP-no, CI-yes	62 (24)	59 (23)
CVP-yes, CI-yes	40 (16)	85 (36)*

* $p < 0.05$

In saline, only 40%, and even in HES 60%, of challenges increased cardiac output which meant that by the protocol further fluids were not used. The average change in CI was greater in HES (0.35 L/min/m^2) than saline (0.17) as were the changes in CVP (1.6 and 1.0 mmHg respectively).

CONCLUSION. Measurements of flow were important for determining the use of fluids as well as a guide to when to stop using fluids. This led to significantly overall less use of fluid in the HES group and less use of catecholamines in HES versus saline patients. (ClinicalTrial.gov identifier NCT00337805).

Liver diseases: 1166–1177

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VOLUME ASSESSMENT IN PATIENTS DURING MAJOR LIVER RESECTIONS: A COMPARISON OF GLOBAL END-DIASTOLIC VOLUME, CENTRAL VENOUS PRESSURE AND THEIR CORRELATION TO CARDIAC INDEX AND EXTRAVASCULAR LUNG WATER INDEX

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INTRODUCTION. Blood loss during liver resection constitutes the primary determinant of the postoperative outcome. Various techniques of vascular control and maintenance of a low central vein pressure (CVP) have been used in order to prevent intraoperative blood loss and postoperative complications. Several studies suggest that global end-diastolic volume (GEDI) might be superior to central venous pressure (CVP) with regard to preload assessment.

OBJECTIVES. The aim of our study was to evaluate the predictive value of CVP with regard to GEDI, and to correlate these parameters to cardiac index (CI).

METHODS. Design: Prospective study. **Setting**: Surgical intensive care unit, university hospital. **Patients and interventions**: 108 hemodynamic measurements using the PiCCO (Pulsion Medical System, Germany) were performed in 26 patients during major liver resection.

RESULTS. Mean CVP (8.35 ± 3.4 mmHg; normal 1–9 mmHg) was normal, whereas mean GEDI (620.03 ± 155.84 mL/m^2; normal 650–800 mL/m^2) was decreased. Thirty-one CVP measurements were elevated despite simultaneous GEDI levels indicating a normal or decreased preload. Sensitivity, specificity, positive predictive value, and negative predictive value of CVP with regard to volume depletion (GEDI < 650 mL/m^2) were 6.15 (0–12.77, CI 95%), 100 (98.86–100, CI 95%), 41, 9 (31.99–51.82, CI 95%) respectively. CVP did not correlate to GEDI ($r = 0.113$; $p = 0.249$), CI ($r = 0.228$, $p = 0.196$) and EVLWI (extravascular lung water index) ($r = -0.066$, $p = 0.503$). GEDI significantly correlated to CI ($r = -0.284$, $p < 0.01$) and VVS ($r = -0.413$, $p < 0.001$).

CONCLUSIONS. Volume depletion according to GEDI was found in more than half the patients. The predictive values of CVP with regard to volume depletion were low GEDI and its changes significantly correlated to CI and its changes, which was not observed for CVP. Therefore, GEDI appears to be more appropriate for volume management during mayor liver resections.

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METABOLIC STABILITY DURING CITRATE CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT) IN CRITICALLY ILL PATIENTS WITH IMPAIRED LIVER FUNCTION

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INTRODUCTION. Regional anticoagulation with citrate is an effective and established anticoagulation strategy during CRRT in critically ill patients, especially in surgical patients with a high risk of bleeding and in case of a heparin-induced thrombocytopenia (1). However, citrate CRRT could be associated with major metabolic derangements such as metabolic alkalosis, hypocalcemia, hypernatremia and citrate toxicity.

OBJECTIVES. The aim of our study was to investigate efficacy, safety and metabolic stability during citrate CRRT in critically ill patients with acute kidney injury.

METHODS. The retrospective study was performed in a mixed surgical and trauma ICU in a university hospital. Patient charts were reviewed for demographic data, the period and dosage of citrate CRRT and metabolic parameters. Reasons of admission, comorbidities and severity of illness were also evaluated. Citrate CRRT was performed using commercially available equipment and fluid solutions (Multifiltrate® with integrated Ci–Ca®-system; Fresenius Medical Care; Germany). To maintain stable metabolic and haemodynamic conditions we used an internal standard protocol for citrate CRRT. Statistical analysis was performed using descriptive methods (mean, median and standard deviation) and a Mann-Whitney U test where appropriate. $P < 0.05$ was regarded as statistically significant.

RESULTS. 50 consecutive patients treated with citrate CRRT from April 2008 through December 2009 were evaluated (Table 1; data are given as total numbers or mean ± standard deviation). During citrate CRRT the following metabolic values were observed (Table 2; data are given as total numbers or median (25th quartile; 75th quartile); */°statistically significant [$p < 0.0001$]):

TABLE 1

Number of patients (male/female)	50 (36/14)
Mean age (years)	68 ± 11
SAPS II	43 ± 12
Mean serum creatinine before CRRT (μmol/l)	338 ± 132
Number of patients with cirrhosis of the liver	5 (10%)

TABLE 2

pH	7.42 (7.38; 7.46)
Base excess (mmol/l)	1.00 (−0.90; 3.20)
Bicarbonate (mmol/l)	25.2 (23.2; 27.2)
Arterial CO2 partial pressure (mmHg)	39.8 (35.7; 44.7)
Number of patients with metabolic alkalosis	7 (14%)
Serum sodium (mmol/l)	138 (136; 140)
Total serum calcium in patients with impaired liver function (mmol/l)	2.23* (2.19; 2.31)
Total serum calcium in patients with normal liver function (mmol/l)	2.15* (2.03; 2.24)
Ratio total serum calcium/ionized calcium in patients with impaired liver function	1.97° (1.87; 2.04)
Ratio total serum calcium/ionized calcium in patients with normal liver function	1.82° (1.74; 1.91)

CONCLUSIONS. Although minor metabolic imbalances were observed, none led to a termination of citrate CRRT and all of them could be managed by adjustments of blood flow and dialysate rates according to a preset protocol. Our findings suggest citrate CRRT to be a safe and effective strategy for CRRT even in patients with hepatic dysfunction. Nevertheless, metabolic parameters need to be monitored regularly to avoid severe metabolic derangements.

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TREATMENT OF HYPERAMMONAEMIC ACUTE OR CHRONIC LIVER FAILURE USING CONTINUOUS VENO-VENOUS HAEMOFILTRATION: DOSE RESPONSE EFFECT ON AMMONIA CLEARANCE

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INTRODUCTION. The liver is central to ammonia metabolism, being the main site of urea cycle enzyme pathways. In acute liver failure (ALF) and decompensated chronic liver disease (CLD) ammonia dysmetabolism results in hyperammonaemia, thought to be of central importance in the pathogenesis of hepatic encephalopathy and, in ALF cerebral oedema [1]. Continuous renal replacement therapy (CRRT), commonly used in critically ill patients may be an effective method of clearing ammonia. Little is known of the efficacy such techniques have on ammonia clearance.

OBJECTIVES. To quantify the clearance of ammonia using an Aquarius haemofilter (AHF) using different renal replacement doses and techniques.

METHODS. Patients with a circulating ammonia level >100 μmol/l due to commence CRRT were enrolled. The AHF was programmed to run in either pre-or post-dilution modes at a blood flow rate of 200 ms/min using a 1.2 or 1.9 m^2 filter depending on the CRRT ultrafiltration (UF) dose, which included 35, 60 or 90 ml/kg/h (adjusted for ideal body weight). 2 ml of blood and effluent fluid were collected, on ice into lithium/heparin and serum separation tubes, from pre and post filter access points and effluent tubing to calculate urea and ammonia clearance using the Cordoba formula [2]. Delta whole body ammonia clearance was determined by measuring arterial ammonia at 0 and 60 min. Ammonia measurements were performed using a Pocketchem® Blood Ammonia bedside testing machine.

RESULTS. 20 patients (9 ALF and 11 CLD) were recruited (mean age 45 years, SD (14), with mean arterial ammonia 123 μmol/l, SD (49). 60 min whole-body ammonia clearance was −12 μmol/l, $p = 0.016$, Paired t test). Ammonia and urea clearance were correlated ($R = 0.748$, $p = 0.020$); UF rate correlated negatively with filtrate ammonia ($R = -0.496$, $p = 0.007$) and positively with ammonia clearance ($R = 0.515$, $p = 0.005$). Filter ammonia clearance was not dependent on filter size for the standard blood flow rate. Pre or post dilution modes did not affect ammonia clearance ($p = 0.100$, Student's t test). A constant filter size and blood flow rate achieved ammonia clearance of 39 ml/min/m^2 for 35 ml/kg/h, 60 ml/min/m^2 for 60 ml/kg/h and 52 ml/min/m^2 for 90 ml/kg/h ($p = 0.008$, One way ANOVA).

CONCLUSIONS. 60 ml/kg/h based on ideal body weight appears to be the optimum dose of CRRT for ammonia clearance when using a blood flow rate 200 ml/min and a 1.2 m^2 filter. Filter and delta whole body ammonia clearance may be increased further using the combination of a higher dose (90 ml/kg/h) with a larger filter size and higher blood flow rates.

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ORAL NUTRITIONAL SUPPLEMENTS AS AN EFFECTIVE STRATEGY FOR CALORIE DELIVERY ON INTENSIVE CARE

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INTRODUCTION. Malnutrition is common in intensive care following the catabolic state induced by critical illness. Patients who progress from enteral nutrition back to oral feeding are usually in an energy deficit. ESPEN guidelines recommend increasing calorie delivery during the recovery period to cover this anabolic phase. Oral nutritional supplements (ONS) are widely used to facilitate calorie delivery within the hospital setting however the effectiveness of this strategy is dependent on patient compliance with the products. Compliance among the elderly ward-based population has been considered[(1)] however that of intensive care patients has not been reported.

OBJECTIVES. To evaluate compliance to ONS in a mixed medical and surgical adult intensive care unit (ICU) in a District General Hospital.

METHODS. Prospective observational study was conducted over a 2 month period with data compiled from fluid chart analysis and discussions with nursing staff. All adult ICU patients prescribed, or offered without prescription, an ONS were included until the point they were discharged to the ward. The supplements studied, Resource® Energy, 2.0 Fibre, Fruit and Dessert (Nestlé Nutrition), were selected based on their availability within the trust. Patients were offered a choice of flavour.

RESULTS. Data was collected and analysed for 51 patient days. A total of 122 supplements were prescribed. Of the prescribed supplements, 42.6% were offered to patients and 26.6% consumed. 20% were offered the same at nursing discretion based on clinical need and 39.8% were consumed. Resource® Energy was the most frequently prescribed and offered product (76.2 and 59.2% respectively). Most common flavours selected by patients were strawberry and vanilla. Resource 2.0 fibre was better tolerated (91.7%) than Resource Energy, Resource Fruit and Resource dessert (73.9, 70.8 and 50.0% respectively). Across all products the best tolerated flavours were apricot, chocolate and coffee (100%). The highest calorie supplement, Resource® 2.0 fibre, resulted in the best compliance in both tested flavours.

CONCLUSIONS. Compliance with ONS demonstrated here is higher than previous studies[(1)] partly attributable to one-on-one nursing of ICU patients enabling active encouragement with feeding. Nursing staff discretion had better uptake than routine prescription of ONS. However, difficulties with ONS still remain. Interestingly in our study the highest calorie density supplement was tolerated the best and thus giving the most benefit to the patient. Despite the difficulties associated with ONS uptake we would recommend its regular use on ICU with a drive towards the highest calorie supplements being offered.

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LIVING WITH CIRRHOSIS: LIMITATIONS, CHALLENGES AND PERCEPTIONS

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INTRODUCTION. Cirrhosis is a chronic disease and the patient's quality of life is affected in a negative way due to the problems like ascites, jaundice, nutrition deficiency, fatigue, activity intolerance, itching, pain, insomnia, anxiety, hopelessness, work loss and depression.

OBJECTIVES. The aim of this study is to examine the changes in patient's lives that diagnosed with cirrhosis of the liver disease owing to the symptoms they experienced.

METHODS. This research is a qualitative study that has been carried out with 13 inpatients diagnosed with liver cirrhosis in the gastroenterology clinic of a teaching and research hospital. Average age of patients was 54 (ranging 39–70). Descriptive characteristics form and semi-structured interview form were used in the data collection. Interviews with patients have been performed individually and face to face. The data were evaluated by using Colaizzi's phenomenological data analysis method.

RESULTS. As a result of the data analysis, three categories and six themes were identified. Categories include: (i) problems of symptoms related to the physical limitations (ii) psychosocial issues. Patients suffer mostly from fatigue and malaise (12 Patients), while those in the later stages suffer from, additionally, physical ailments caused by acid. Inability to sleep due to anxiety and increase in tendency to sleep in advanced stages have been identified after being diagnosed. The majority of patients were identified to have undergone an anxiety besides having a fatal disease due to concern for the future, being forced to quit the job and being affected by the experiences of the patients in advanced stages. It also has been discovered that the patients had experienced social isolation because of fatigue and weakness in particular.

CONCLUSIONS. As the result of this study it has been determined that patients with cirrhosis have mainly problems of fatigue, weakness, sleep disorders, anxiety and associated problems.

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EFFECTS OF TRANSJUGULAR PORTO-SYSTEMIC STENT-SHUNT (TIPS) ON HEMODYNAMIC PARAMETERS AND HEPATIC AND RENAL FUNCTION: A PROSPECTIVE TRIAL

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INTRODUCTION. The transjugular porto-systemic stent-shunt (TIPS) is an established non-surgical treatment for complications of liver cirrhosis (recurrent variceal bleeding, refractory ascites, hepatorenal syndrome). There are concers regarding a negative impact of TIPS on cardiocirculatory function. However, effects of TIPS on hemodynamics as well as renal and hepatic function are not well investigated.

OBJECTIVES. To investigate the effects of TIPS on hemodynamic parameters and hepatic and renal function as well as vasoactive hormones.

METHODS. Prospective study in 16 ICU patients with cirrhosis of the liver treated with TIPS. Before and after TIPS insertion: Advanced hemodynamic monitoring using transpulmonary thermodilution (PiCCO, Pulsion Medical Systems Germany). Doppler ultrasound for determination of renal resistance index (RI). Assessment of laboratory markers of hepatic and renal function as well as norepinephrine, aldosterone, plasma renin activitiy (PRA), antidiuretic hormone (ADH) and Pro Brain Natriuretic Peptid (proBNP).

RESULTS. TIPS was performed successfully in all patients. No major complications occurred. TIPS insertion lead to a significant increase of central venous pressure (12.0 ± 5.4 vs. 17.6 ± 6.2 mmHg; $p = 0.000$) and heart rate (77 ± 16 vs. 84 ± 20; $p = 0.026$) and a significant decrease of porto-systemic pressure gradient (29.9 ± 8.2 vs. 12.0 ± 3.5 mmHg; $p = 0.000$) and mean arterial pressure (87 ± 11 vs. 75 ± 13; $p = 0.031$). After TIPS insertion cardiac index (3.8 ± 1.2 vs. 4.4 ± 1.4; $p = 0.003$) and global end-diastolic volume (731 ± 120 vs. 783 ± 107; $p = 0.015$) increased significantly, whereas systemic vascular resistance index decreased significantly (1,680 ± 560 vs. 1,463 ± 609; $p = 0.015$).

RI was not different before and after TIPS placement (0.77 ± 0.07 vs. 0.78 ± 0.10; $p = 0.859$).

Following TIPS, prothrombin time decreased slightly but significantly (58 ± 17 vs. 54 ± 16; $p = 0.005$) and serum bilirubin increased significantly (2.4 ± 1.5 vs. 3.0 ± 2.2; $p = 0.040$). Serum creatinine (1.6 ± 1.4 vs. 1.5 ± 1.3; $p = 0.001$) and blood urea nitrogen (30.6 ± 21.4 vs. 27.3 ± 22.2; $p = 0.012$) were significantly lower already 24 h after TIPS.

Endogenous norepinephrin (805 ± 676 vs. 1208 ± 1278; $p = 0.075$), aldosterone (578 ± 942 vs. 285 ± 445; $p = 0.241$), PRA (7.2 ± 13.5 vs. 4.9 ± 7.3; $p = 0.241$) and ADH (5.2 ± 2.2 vs. 5.8 ± 3.5; $p = 0.695$) did not change significantly 24 h after TIPS insertion. proBNP was significantly higher 24 h after the TIPS procedure (1773 ± 2007 vs. 2371 ± 2299; $p = 0.013$).

CONCLUSIONS. TIPS is an effective and save treatment option to reduce porto-systemic pressure in cirrhotic patients. Regarding hemodynamic parameters GEDVI and CI increase significantly after the TIPS procedure. No circulatory failure was observed after TIPS placement. Renal function improved after TIPS insertion.

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ARTERIAL AMMONIA IN PATIENTS WITH HYPOXIC HEPATITIS

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INTRODUCTION. Hypoxic hepatitis (HH)is a condition occurring in up to 10% of all ICU admissions [1]. While in patients with acute liver failure, elevation of arterial ammonia levels has been linked to cerebral complications and increased mortality, the role of arterial ammonia in HH patients is unknown.

OBJECTIVES. Our study aims at evaluating arterial ammonia levels in patients with HH. Furthermore, we wanted to elucidate the potential consequences of high ammonia levels in these patients.

METHODS. Arterial ammonia levels were measured and documented in 72 HH patients without liver cirrhosis who were admitted to the medical ICU. ICU mortality and overall 28-day-survival were documented. COX regression was performed to describe the impact of ammonia levels on mortality. Mann–Whitney Test was used for comparison of metric variables.

RESULTS. Overall median arterial peak ammonia level in our patients was 65 µmol/L (41.9–100.6 µmol/L), whereas median arterial peak ammonia value was significantly higher in ICU non-survivors compared to survivors (77 (53–119.2) vs. 52.9 (36.4–71.1); $P < 0.01$). SAPS II and SOFA score were significantly higher in ICU non-survivors ($P < 0.01$ and $P < 0.05$, respectively). COX regression revealed that arterial peak ammonia levels were significantly associated with higher 28-day-mortality ($P < 0.01$), even after adjustment for SAPS II.

Median arterial peak ammonia levels in patients with verified brain edema were significantly higher than in patients without (130.7 µmol/L (92–349.7 µmol/L) vs. 70.6 µmol/L (43.2–81.7 µmol/L); $P < 0.05$) after exclusion of patients following cardiopulmonary resuscitation with consecutive hypoxic brain damage.

CONCLUSIONS. Our results suggest that increased levels of ammonia are associated with high mortality and can lead to brain edema in patients with HH.

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1173

THE INTRODUCTION OF CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT) TO A REGIONAL INTENSIVE CARE UNIT: DEMOGRAPHICS, DOSE DELIVERY AND CIRCUIT LIFE

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INTRODUCTION. Acute kidney injury (AKI) is known to occur in up to 25% of ICU admissions, a fifth of whom will require CRRT[1]. These patients place considerable morbidity, mortality and financial burdens on critical care services[2]. In recent years CRRT has become an established treatment in our institution providing an opportune juncture to examine our outcomes and clinical practice.

OBJECTIVES.

1. To determine demographics and outcomes for patients receiving CRRT in our unit
2. To measure mean circuit life and dose delivery
3. To ascertain level of compliance with anticoagulant policy

METHODS. We performed a retrospective audit of all patients treated with CRRT in the Regional Intensive Care Unit for Northern Ireland over a 16 month period from May 2008 to August 2009. Data was obtained from electronic patient records and the local Intensive Care National Audit and Research Centre (ICNARC) case mix programme.

RESULTS. 103 patients (72 males, 31 females) were treated with CRRT in the 16 month audit period, all of whom received continuous venovenous haemofiltration (CVVH). Mean duration on CRRT was 5.8 days (IQR = 2–7).

SUMMARY STATISTICS FOR CRRT PATIENTS

	CRRT Patients	Rest of ICU Population	P values
Age (years)	61.3	55.0	<0.001
Admission APACHE	24.3	17.3	<0.001
ICU Length of Stay (Days)	12.3	8.2	<0.01
ICU mortality	47%	19%	<0.001
Hospital mortality	60%	28%	<0.001

53% of patients had a diagnosis of sepsis and 21% of patients were admitted under the neurosurgical team, the latter of which may have contributed to the relatively low anticoagulant use of 54%. Systemic heparinisation was the sole anticoagulant used, but compliance with local protocols was poor with 48% of APPTs below the therapeutic range and 46% of infusions commenced at the wrong rate. 68% of filter changes were due to clotting and mean filter life was 32 h. Despite this, dose delivery was acceptable, with 84% of prescribed dose delivered.

CONCLUSIONS. As previously reported[1], our demographic data confirm the relatively poor outcome of patients needing CRRT. We have identified areas where care for these patients could be optimised and endeavour to do this locally via improved protocol design and an ongoing educational programme. Many of the components of CRRT could be incorporated into care bundles, but certain aspects of treatment remain controversial[3] which may be a barrier to their adoption. Given the high numbers of neurosurgical patients in our unit, consideration should be given to the use of regional anticoagulation such as citrate.

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1174

ADMISSION SERUM LACTATE IS A STRONG PREDICTOR OF OUTCOME IN CIRRHOTICS ADMITTED TO ICU, AND WHEN ADDED TO THE LIVER-SPECIFIC SCORES OF MELD OR UKELD, IMPROVES THEIR RESPECTIVE PREDICTIVE VALUE

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INTRODUCTION AND OBJECTIVES. Accurate prognostic indicators of patient survival in an intensive care unit (ICU) help guide clinical decision making. Factors known to portend poor prognosis in acutely ill cirrhotics in ICU include the need for mechanical ventilation, development of shock, renal failure and sequential increase in the number of failing organs. While serum lactate is now an established marker of survival and/or the need for transplantation in fulminant liver failure, its impact on critically ill cirrhotics is less well known.

METHODS. We retrospectively studied 133 consecutive acutely ill cirrhotics admitted to the ICU between 2005 and 08 at the Royal Free Hospital, a tertiary referral centre in liver diseases and transplantation. Data were collected on demographic variables, aetiology of liver disease, liver-specific prognostic scores [Child-Turcotte-Pugh (CTP), Model for end-stage liver disease (MELD), United Kingdom model for end-stage liver disease (UKELD)], and acute illness scores [acute physiological score and chronic health evaluation (APACHE II), sequential organ failure assessment score (SOFA)]. In addition, serum lactate levels at 0, 24 and 48 h were also recorded. Multivariable logistic regression analysis was performed, and the discrimination ability of each of the above-mentioned scoring models in predicting ICU and hospital survival of these patients was evaluated using the area under the receiver operating characteristic (ROC) curve.

RESULTS. The ICU and hospital non-survivors—43/133 (32.3%) and 57/133 (43.4%) respectively—had similar demographic features as the survivors, but had significantly higher mean admission MELD, UKELD, SOFA and APACHE II scores, as well serum lactate levels on admission. Serum lactate at admission and particularly at 24 h had a better discriminative accuracy for mortality ($AUC = 0.737$ and 0.764) compared with liver-specific prognostic scores, MELD ($AUC = 0.732$ and 0.720), MELD-Na ($AUC = 0.338$ and 0.554) and UKELD ($AUC = 0.698$ and 0.695). Acute illness scores exhibited a rather poorer predictive power, both APACHE II ($AUC = 0.632$ and 0.571) and SOFA ($AUC = 0.688$ and 0.716). Adding lactate to MELD and UKELD scores further improved their outcome prediction potential (AUC MELD-lactate = 0.737 and UKELD-lactate = 0.717).

CONCLUSIONS. Serum lactate is a powerful independent tool in predicting survival of acutely ill cirrhotics on ICU. Persistent hyperlactataemia after aggressive resuscitation for 24 h may reflect native liver's inability to metabolise it. In that case, should lactate not be incorporated in the liver function scoring models such as CTP, MELD or UKELD?

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1175

SEVERE BACTERIAL INFECTIONS AFTER LIVER TRANSPLANTATION (LT): AN EPIDEMIOLOGICAL STUDY

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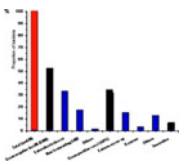
INTRODUCTION. Better immunosuppression has reduced the incidence of rejection but has increased patient's susceptibility to opportunistic infections and cancer.

OBJECTIVES. To describe the incidence, the main clinical and microbiological features of documented bacterial infections within 1 year after LT, to determine the factors associated with infection.

METHODS. retrospective observational monocentric study including all LT patients from 2003 to 2008. We studied demographic data (sex, age, SAPS II at admission, Child Pugh score, underlying liver disease), perioperative characteristics (duration of ischemia and of surgery, amount of red blood cell packs transfused, vassopressor use during surgery, external biliary tract drainage), infection characteristics (all documented biliary, pulmonary, surgical site, urinary, central venous access infections and their microbiological features) and outcome parameters (ICU length of stay, duration of mechanical ventilation, ICU mortality)

RESULTS. 274 transplant recipients were analyzed. The main underlying liver disease was alcohol and hepatitis C virus related cirrhosis. No perioperative parameters were associated with infection within 1 year after LT. Ninety three patients presented 237 infections, 2 [1–4] per patient. The main sites of infection were biliary tract, urinary tract infections and pneumonia. The first episode occurred 12 [6–39] days after surgery. Among the infections, 428 pathogens were isolated, mainly gram negative bacilli (53%). Among the Enterobacteriaceae, 14% were ESBL producers and 70% resistant to ciprofloxacine. Non fermentative gram negative bacilli represented 18% of all the pathogens diagnosed and the first episode occurred 61 [24–86] days after surgery. *S. aureus* was uncommon, but in more than 50% of the episodes *S. aureus* was resistant to methicillin. Infected patients had significantly longer mechanical ventilation (1 [1–1] vs. 2 [1–9] days, $p < 0.05$) and longer ICU stay (9 [7–13] vs. 11 [8–17] days, $p < 0.05$). Mortality was significantly higher in infected patients (14/93 (15%) versus 10/181 (6%), $p = 0.013$).



Bacteria involved in infections in the first year

CONCLUSIONS. One third of LT recipients present a documented bacterial infection within 1 year after surgery. We found a high prevalence of ciprofloxacin resistance and a low incidence of S.aureus witch was often resistant to methicillin. Non fermentative gram negative bacilli represent 18% of the pathogens and should be taken in account for treatment of the most severe patients.

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EFFECTS OF LARGE-VOLUME PARACENTESIS ON HEMODYNAMICS IN PATIENTS WITH CIRRHOSIS OF THE LIVER AND ASCITES

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INTRODUCTION. Patients with advanced cirrhosis and ascites often display circulatory dysfunction which might be deteriorated after paracentesis. Influence of paracentesis and particularly the volume removed on circulatory function is not well investigated.

OBJECTIVES. The aim of our study was to evaluate the influence of paracentesis on hemodynamic variables assessed using transpulmonary thermodilution (TPTD) in patients with cirrhosis and ascites.

METHODS. Prospective study in 29 patients with cirrhosis and ascites. Assessment of hemodynamic variables using TPTD (PiCCO-2-System, Pulsion Medical AG) immediately before and after paracentesis. Medical ICU, university hospital.

RESULTS.

Patients: 53 paracenteses (mean 6,162 ± 3,100 ml: 765–14,675 ml) in 29 patients (14 female, 15 male; mean age 58.6 ± 8.0 years) with cirrhosis (etiology: 25 alcoholic, 3 hepatitis, 1 cryptogenic). APACHE II score on ICU admission 23.4 ± 8.8, SAPS II score on day of paracentesis 38.1 ± 12.6.

Analysis of all paracenteses: After paracentesis, systemic vascular resistance index (SVRI) and central venous pressure (CVP) significantly decreased from 1,299 ± 525 dyn s cm^{-5} m^2 to 1,248 ± 518 ($p = 0.025$) and from 15.7 ± 6.7 mmHg to 13.9 ± 5.6 ($p = 0.013$), respectively. Mean arterial pressure (MAP) did not change (83 ± 13 mmHg vs. 78 ± 18; $p = 0.075$), neither did heart rate (HR) (88/min vs. 89; $p = 0.986$). No decrease in cardiac index (CI) (4.66 ± 1.45 l/min/m^2 vs. 4.73 ± 1.49; $p = 0.19$), no change in global end-diastolic volume index (GEDI) (857 ± 171 ml/m^2 vs. 869 ± 218; $p = 0.894$). Extravascular lung water index (ELWI) raised from 10.1 ± 3.6 ml/kg to 10.8 ± 3.8 ($p = 0.039$). Changes of CI correlated with GEDI ($r = 0.635$; $p < 0.01$) and CVP ($r = 0.304$; $p < 0.05$). All paracenteses were performed without complications. To investigate whether there are differences in hemodynamic changes in a subgroup of large-volume paracenteses (LVP), we separately analysed 36 patients undergoing paracentesis ≥5,000 ml: SVRI significantly decreased from 1323 ± 561 to 1256 ± 560 ($p = 0.016$). ELWI raised from 9.6 ± 3.0 to 10.4 ± 2.7 ($p = 0.041$). A trend to a decrease in CVP slightly failed significance (15 ± 7 vs. 14 ± 6; $p = 0.070$). In this subgroup, CI increased from 4.61 ± 1.45 to 4.76 ± 1.58 ($p = 0.04$), which was not observed in totality of patients. Neither MAP (82 ± 12 vs. 80 ± 17; $p = 0.333$) nor HR (87 ± 17 vs. 90 ± 19; $p = 0.578$) changed significantly. No change in GEDI (851 ± 179 vs. 880 ± 233; $p = 0.565$).

CONCLUSIONS. Paracentesis of 6162 ± 3100 ml resulted in significant reduction of SVRI and CVP, probably due to reduced intraabdominal pressure. Increase in ELWI might be due to higher absorptivity of the lung following decrease of intrathoracic pressure by paracentesis. Preload variable GEDI did not change significantly. In the subgroup of LVP CI significantly increased. Regarding this positive effect of paracentesis particularly after removal of large amounts of ascites as well as multiplied risks of repeated paracenteses, a restriction of the amount of ascites removed cannot be justified.

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EXTRACORPOREAL LIVER SUPPORT THERAPY

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INTRODUCTION. Extracorporeal liver support therapy is in its infancy but is valued as a detoxification treatment option for patients with cirrhosis who have rapid worsening of their liver function. We report the use of Prometheus®, a new extracorporeal liver support system allowing the removal of protein bound and water soluble toxins by fractionated plasma separation and absorption (FPSA) in a patient with Wilson's disease (WD) who developed rapid worsening of their liver function.

METHODS. A 26-year-old female patient, diagnosed with WD since the age of 17, was initially treated in an irregular pattern with penicillamine. Therapy was discontinued. Now, 2 years later, she developed acute decompensated liver failure with hepatic encephalopathy with a MELD 29. Liver transplantation (LT) was the treatment option for this patient. But, in this case, the rapid and adverse evolution of the liver failure with renal failure and the unknown waiting time for a emergency liver donor in our country led us to use the Extracorporeal liver support therapy.

RESULTS. After 5 h 30 min of therapy we reduced the amount of bilirrubin for less than a half, we increase the urinary output and next day the patient went to liver transplant, stable, with a renal function improved.

CONCLUSIONS. Acute liver failure due to WD is most of the time fatal without emergency LT. This case report highlights discontinuation of chelants treatment in a patient with WD. As the patient progressed to decompensated liver cirrhosis with encephalopathy, LT was the only treatment option but while we don't get a donnor, we can use, for a short period of time, an Extracorporeal liver support therapy as a very useful bridge. Results from two studies presented at the recent EASL 2010 Congress have shown that treatment with extracorporeal devices may not confer a survival advantage for severe liver failure patients, despite positive dialysis effects. However, results among a small sub-group of patients show promise like severely ill patients with hepatorenal syndrome type 1 or a MELD score over 30.

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Perioperative care: Abdominal problems: 1178–1191

1178

EFFECT OF PRUCALOPRIDE, NEOSTIGMINE AND METOCLOPRAMIDE ON COLONIC MOTILITY *IN VITRO*

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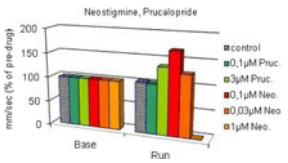
INTRODUCTION. Postoperative motility disturbances frequently occur in critically ill patients and affect all parts of the gastrointestinal (GI) tract. Effective treatment of colonic motility disorders is still limited—only neostigmine, an inhibitor of acetylcholine and prucalopride, a 5-HT-4 receptor agonist are clinical available (1). Metoclopramide is used to stimulate the upper GI tract and seems to have no effect on colonic motility.

OBJECTIVES. The aim of this in vitro study was to compare the prokinetic potency of those substances.

METHODS. A tissue bath with guinea pig colonic segments fixed on a polyacrylic tray allows the evaluation of the transit time (TT), the time necessary for a wooden pellet to perambulate. A decrease of the TT reflects stimulation, and an increase inhibition of peristalsis.

After stable peristalsis activity the effect of increasing concentrations of prucalopride, neostigmine or metoclopramide on TT were evaluated. Dose response curves were constructed, two way ANOVA (Sigma Stat) was used for statistics, p values ≤ 0.05 were considered to be significant.



Effect of prucalopride and neostigmine on motility

RESULTS. Prucalopride stimulates normal peristalsis in vitro only in the highest tested concentration of 3 µM ($p < 0.05$). Neostigmine's prokinetic effect was limited to a small concentrations range (0.1 µM, $p < 0.05$), the concentration of 0.03 µM had a moderate, but not statistically significant prokinetic effect and the highest tested concentration (1 µM) lead to a complete block of peristalsis (Fig. 1). Metoclopramide, as expected, was devoid of any effect on colonic motility.

CONCLUSIONS. This experimental setting is a reliable method to evaluate the effect of different substances on colonic motility *in vitro*. Prucalopride's prokinetic activity is concentrations dependent and limited. Neostigmine is well known to improve colonic motility, but it seems imperative that the drug's effective dose range be use—higher concentrations have inhibitory effect on peristalsis.

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1179

COMPARISON OF AN INDWELLING BOWEL CATHETER SYSTEM INPUT AND OUTPUT VIA GRAVITY IRRIGATION IN BURNS AND OTHER SKIN DISEASES

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INTRODUCTION. A bowel catheter is useful in preventing wound infections in bed-ridden patients with burns or skin diseases and the bowel can be a source of body fluid removal.

OBJECTIVES. Determine if bowel irrigation is applied uniformly across diagnostic categories in the Burn Unit. The hypothesis is that with capillary leakage and third space accumulation, output in patients with bowel catheters, who have Burns/Toxic Epidermal Necrolysis (TENS) will be greater than in patients with other dermatologic conditions.

METHODS. This was a 24 month retrospective study of 35 intensive care patients: 22 (Burn/TENS and 13 Other (necrotizing fasciitis, dermatologic diseases, ulcers). ActiFlo™ (Hollister, Inc, Libertyville, IL) bowel catheter was utilized. Tap water irrigations were performed from 0 to 1,000 cc/24 h. Statistical analysis was performed with the following program SAS v9.2 mean ± S.D., median, interquartile range, and Wilcoxon rank sum test.

RESULTS. The mean ± S.D. % total body surface area involvement and length of stay in Burns/TENS was 56 ± 27% and 46 ± 37 days vs. 11 ± 10% and 53 ± 31 days in the Other group. The bowel catheter was utilized for 69 ± 20% of the hospital stay in the Burn/TENS group vs. 55 ± 44% in the Other group. The start day for the two groups did not differ significantly: 10 ± 9 post admission in Burns/TENS vs. 5 ± 4 day post admission in the Other group. The volumes were approximate. In Burns/TENS, the bowel received (median) [500 (IQR), 0–600] cc/24 h irrigation fluid compared to 500 (IQR, 0–1,000) in the Other group, $p < 0.0001$. The bowel catheter output in Burns/TENS was (median) 400 (IQR, 0–1,000) cc/24 h compared to 600 (IQR, 120–1,000) in the Other group, $p < 0.0001$.

CONCLUSIONS. There was statistically more Irrigation fluid input and Bowel fluid output in the Other skin condition group compared to the Burns/TENS group. Severity of illness, start time for irrigation, the number of irrigations/time period, and sepsis may have affected this result. Reasons for the disparate treatment in this study are being investigated.

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ABDOMINAL SURGERY IN BURN PATIENTS: THE RISE OF ABDOMINAL COMPARTMENT SYNDROME HAS NOT ECLIPSED DEAD GUT

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INTRODUCTION. Historically, abdominal surgery has been a high-risk, high-mortality event in the critical care of burn patients.

OBJECTIVES. We hypothesized that changes in care–to include ulcer prevention, recognition of abdominal compartment syndrome (ACS), and aggressive fluid resuscitation–have resulted in changing indications for, and mortality from, abdominal surgery in these patients.

METHODS. We analyzed data for 1979–1995 (Period A; 2,797 patients) and 1996–2006 (Period B; 3,153 patients) at a single burn center. The transition between periods was marked by a new facility under new leadership. Statistics by Chi square, Exact, or Mann–Whitney U tests.

RESULTS. See Tables.

TABLE 1 INDICATION FOR SURGERY BY PERIOD

Period[1]	Biliary	NOMI	Ulcer	ACS	Other	Total[2]
A	9 (23%)	8 (21%)	5 (13%)	1 (3%)	16 (41%)	39
B	6 (7%)	23 (26%)	0	44 (49%)	16 (18%)	89

Data are # of patients (row percentages in parentheses). Biliary: biliary disease; NOMI: nonocclusive mesenteric ischemia with infarcted small and/or large bowel; Ulcer: Curling's ulcer of stomach and/or duodenum. [1]$p < .001$ for indication. [2]$p < .001$ for total number of surgeries as fraction of admissions.

TABLE 2: ACS VERSUS NOMI (PERIODS A AND B COMBINED)

INDICATION	Mort (%)[3]	Age (years)	TBSA (%)[4]	Full (%)[5]	Inhal	Day[6]
ACS	86	39 ± 18	62 ± 23	50 ± 28	51	6 ± 16
NOMI	61	37 ± 21	47 ± 21	30 ± 23	55	14 ± 13

Data are means ± SD. Mort: Mortality; TBSA: total body surface area burned; Full: full-thickness burn size; Inhal: (+) inhalation injury; Day: day postburn of surgery. [3]$p = .011$. [4]$p = .007$. [5]$p = .002$. [6]$p = .024$.

CONCLUSIONS. Despite advances in critical care, the number of patients undergoing abdominal surgery has doubled. ACS now accounts for half of all laparotomies, but no progress has been made in reducing laparotomies for NOMI. The mortality for these conditions remains very high. Improved methods of ensuring gut perfusion, while avoiding over-resuscitation and preventing ACS, are needed for patients with severe thermal injury.

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ANESTHESIA FOR PROLONGED LAPAROSCOPIC SURGERY IN A STEEP TRENDELENBURG POSITION: A REVIEW OF 80 CASES OF ROBOTIC RADICAL PROSTATECTOMY

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INTRODUCTION. As laparoscopic procedures have expanded the types of surgery, the procedures have become more demanding and required longer lasting operation time and also performed in the elderly patients. Long lasting laparoscopic procedures have potential hazard of postoperative pulmonary complications including atelectasis, gas embolism, subcutaneous emphysema, and pneumothorax, etc.

OBJECTIVES. Robotic radical prostatectomy involves extreme changes in patient position and often associated with a longer operative time than other commonly performed laparoscopic procedures. This review discusses the anesthetic considerations in robotic radical prostatectomy while analyzing potential risk factors related to pulmonary complications.

METHODS. We retrospectively reviewed the medical records of all the patients who had undergone robotic radical prostatectomy at our institution. Among the total patients of 80, aged 49 to 82 years, 58 patients were capable of spontaneous respiration at the end of surgery (Group I) whereas 22 patients needed assist ventilation (Group II). The demographic characteristics, coexisting diseases, anesthesia and operation time, anesthetic agents, the amounts of blood loss, infused fluid and transfused blood products were compared between the groups.

RESULTS. The mean age of the patients was 67.2 ± 7.3 years. The mean operation times were 445.3 ± 210.3 min (range, 235–1250 min). Age, body mass index (BMI) and ASA status did not differ significantly between the two groups, whereas operation time, the amount of blood loss and the incidence of transfusion were significantly higher in the group II. Although 3 patients with subcutaneous emphysema and atelectasis needed prolonged ventilator care for 48 h, the incidence of atelectasis and subcutaneous emphysema was similar between the groups.

CONCLUSIONS. Prolonged laparoscopic surgery in a steep Trendelenburg position has a high possibility of postoperative respiratory insufficiency and the possible contributing factor is a long operation time.

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1182

THE COUGH REFLEX AFTER ESOPHAGECTOMY DETERMINE THE LENGTH OF POSTOPERATIVE VENTILATOR DAYS AND ICU STAY

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INTRODUCTION. After the esophagectomy for esophageal cancer the cough reflex may disappear due to the injury of a lung branch of vagus nerve during mediastinal lymphadenectomy and the absence of the cough reflex might affect postoperative respiratory management.

OBJECTIVES. We examined the frequency of postoperative cough reflex and its effect on postoperative clinical outcome retrospectively.

METHODS. We examined the patients who admitted into the ICU after the esophagectomy with lymphadenectomy during the period from September, 1999, to February, 2010. In addition to usual criteria for extubation we removed their tracheal tube if the cough reflex was identified when one milliliter of half saline was distilled into their trachea. If the cough reflex was absent until 7 days after the operation the patient underwent tracheostomy and after that they weaned from the ventilator.

RESULTS. There were 125 patients (F/M 24/101), and their mean age was 58.5 ± 7.8. Cough reflex were confirmed by seventh postoperative day in 95 patients (76%) but residual 30 patients underwent tracheostomy because of absence of cough reflex (Table 1). The length of cough absent days was correlated with the length of ventilator days ($p = 0.037$) and the length of ICU stay ($p < 0.0001$), but not with the length of postoperative hospital stay ($p = 0.502$).

POD OF COUGH REFLEX RESTORED AND ICU STAY

POD of cough reflex restored	n	ICU stay (days)
0	8	3.1 ± 0.6
1	27	4.7 ± 4.1
2	10	4.8 ± 1.2
3	14	6.2 ± 1.5
4	13	8.1 ± 4.9
5	12	8.0 ± 1.3
6	6	9.5 ± 2.7
7	5	8.6 ± 0.5
>8	30	9.0 ± 4.3

CONCLUSIONS. Postoperative ICU stay and ventilator days after the esophagectomy were dependent on restoration of cough reflex.

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EFFECTS OF PEEP APPLICATION ON ARTERIAL OXYGENATION AND MINUTE VENTILATION DURING LAPAROSCOPIC CHOLECYSTECTOMY OPERATIONS

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INTRODUCTION. The technique of laparoscopic cholecystectomy carried with carbon dioxide pneumoperitoneum may lead to adverse events in mechanical, hemodynamic and respiratory systems as a consequence of physiopathological changes such as increased intraabdominal pressure. It may cause hypoxemia, hypercapnia, hemodynamic instability and impairment of oxygenation. Decreased functional residual capacity, ventilation/perfusion imbalance and sympathetic stimulation effects of CO2 that is absorbed from peritoneum are basic problems. In perioperative period, application of mechanical ventilation and anesthesia should be reviewed because of these physiopathological mechanisms.

METHODS. In this study, we aimed to investigate the effects of 5 cmH_2O PEEP application on ETCO2, minute ventilation and arterial oxygenation during laparoscopic cholecystectomy operations. For this reason, the study included total 40 patients and they were randomly divided into two groups. Same anesthetic protocol was applied in both groups. For general anesthesia induction; 1 mg/kg dose of fentanyl, 2 mg/kg dose of propofol were administered. Following this procedure endotracheal intubation was applied with 0.15 mg/kg dose of cisatracurium. Patients received %50 O2–%50 N2O (mixture with equal amounts) with 0.8–1.2 MAC end-tidal sevoflurane for anesthesia maintenance. Before CO_2 insufflation, respiratory parameters were recorded on the respiratory apparatus adjusting ETCO2 32–36 mmHg, respiration rate 12/min., inspiration/expiration rate 1:2, Vt: 8–10 ml/kg. Patients were ventilated by volume controlled mechanical ventilation. Heart beats, mean arterial blood pressure and peripheric O2 saturation (spO2), ETCO2, minute ventilation(V) and peak airway pressure(PIP) values of all patients were recorded just before insufflation (T0). After recording, 5 cmH_2O PEEP was applied to the first group (Group 1). PEEP wasn't applied to the 2nd group (Group 2). These parameters were repeated in 5 periods such as 5 (T1) and 30 (T2) minutes after insufflation, preexsufflation (T3) and postexsufflation (T4) in both groups. Before insufflation, respiration rate (12/min) and ETCO2 (32–36 mmHg) values were adjusted as planned in both groups and minute ventilation was also adjusted. At the same time, total insufflated amount of CO2 for distending abdomen was recorded. Arterial blood gas analyses were made just before induction (while patients were breathing normal room air, T0), 30 min after induction (T2) and just before the end of the operation (T4).

RESULTS. In our study, we found that minute ventilation to stabilize ETCO2 32–36 mmHg was significantly increased in group 2 in which PEEP was not applied ($p < 0.01$). None enhancement was needed in minute ventilation in Group 1 and arterial oxygenation was significantly increased in Group 1 ($p < 0.01$).

CONCLUSIONS. Application of PEEP in laparoscopic operations provides decreasing of minute ventilation and recovery of arterial oxygenation.

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ATORVASTATIN ATTENUATES COGNITIVE IMPAIRMENT FOLLOWING NEPHRECTOMY IN MICE

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INTRODUCTION. The existence of postoperative cognitive dysfunction (POCD) as a complication of non-cardiac surgery in the elderly has been demonstrated with a rate of 25.8% at 1 week and 9.9% at 3 months postoperatively[1]. It is indicated that the pathophysiology consists of a hippocampal neuroinflammatory response to the trauma associated with surgery[2].

Aside from the cholesterol lowering effects of statins, as a class of drugs they have been shown to exert anti-inflammatory effects and have the potential to be therapeutic in neuroinflammatory disorders[3].

OBJECTIVES. We tested the hypothesis that atorvastatin improves memory retrieval post unilateral nephrectomy in a murine model.

METHODS. C57/BL6 mice were randomly allocated into 4 groups ($n = 8–10$/group): control plus placebo, control plus atorvastatin, nephrectomy plus placebo and nephrectomy plus atorvastatin. Animals were given either a placebo (0.4 ml normal saline) or 250 μg in 0.4 ml normal saline of atorvastatin by gavage once a day for 5 days. On day 4 all animals underwent fear conditioning training using a conditional stimulus of a 70 dB tone and an unconditional stimulus of a 0.70 mA electric shock. On day 5 the surgical animals underwent unilateral nephrectomy, whilst the control animals received no surgery. At post-surgical day 3 all animals were tested for hippocampal dependent memory retrieval using the fear conditioning paradigm, with freezing response to the 70 dB tone as a marker of memory retrieval. All animals were then terminated.

RESULTS. Surgery evoked a reduction in hippocampal dependent memory retrieval in the nephrectomy plus placebo group as measured by % freezing time (mean ± SD: 40 ± 16) when compared to the control plus placebo group (70 ± 19; $p < 0.01$); a situation mimicking POCD. This change was obviated in the nephrectomy plus atorvastatin group (59 ± 16; $p > 0.05$ vs. control plus placebo).

CONCLUSIONS. Our data suggested that atorvastatin has the potential to improve postoperative cognitive performance in a murine model of POCD. The proven safety of the drug along with its already widespread use and cost effectiveness would permit rapid instigation of a human randomized controlled trial to explore efficacy in the clinical setting.

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PREVALENCE OF INTRA-ABDOMINAL PRESSURE MEASUREMENTS DURING NUTRITION DAY

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INTRODUCTION. Intra-abdominal pressure (IAP) is a prognostic factor for ICU morbidity and mortality (1). Gastro-intestinal failure (GIF) is difficult to quantify and recent studies suggest a combination of IAP together with the success or failure of enteral feeding to define GIF as a SOFA subscore (2).

OBJECTIVES. This study looks at the prevalence of IAP measurements during nutrition days held in 2009 and 2010.

METHODS. Patients admitted to the ICU and included in the nutrition day database in whom IAP measurements were performed either via gastric or bladder route were studied.

RESULTS. In 2009, IAP was measured in 61 out of 1442 patients (4.2%) from 28 ICUs. In 27 of the 61 patients (44.3%) the IAP values were missing. The mean IAP was 11.7 ± 8. In patients in whom IAP was measured SAPS II score was 50.3 ± 13.9 with a mortality of 44.1% (compared to a SAPS II around 40 ± 16 and a mortality of 26% in the other patients). In 2010, IAP was measured in 68 of 935 patients (7.3%) from 29 ICUs. In 23 of the 68 patients (33.8%) the IAP values were missing. The mean IAP was 15.4 ± 14.8. In patients in whom IAP was measured mortality was 41.7% compared to 32% in the other patients.

CONCLUSIONS. The preliminary results of the analysis of the data obtained during nutrition day in 2009 and 2010 show a positive trend with regard to the prevalence of IAP measurements in these patients: there was an increase in patients with IAP measurements from 4.2 to 7.3% and a decrease in missing IAP values from 44.3 to 33.8%. Mortality in patients with IAP measurements was higher. There is still a lot of work to do before IAP can be incorporated into a SOFA subscore to define GIF. The prevalence of IAP measurements during next nutrition day data collection needs to be increased by sensibilisation of the participating centres.

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AN AUDIT OF HYPOTENSION AND ITS MANAGEMENT POST-OPERATIVELY IN MAJOR ELECTIVE GASTROINTESTINAL SURGERY

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INTRODUCTION. Hypotension in the post-operative period is common but guidelines recommend its prevention/treatment [1]. Epidurals are common practice following major surgery in many institutions and can prevent pulmonary complications [2] but have also been associated with falls in blood pressure when compared to other analgesic techniques [3]. Fluids therapy is a common intervention for hypotension but fluid overload has been associated with worse outcomes in surgical patients [4]. We decided to audit the incidence and management of hypotension in the surgical high dependency unit of a large tertiary referral hospital.

OBJECTIVES. To determine the incidence and management of hypotension in the surgical high dependency unit in pancreatic, upper GI and lower GI patients.

METHODS. We prospectively looked at 48 patients who underwent major upper GI, lower GI or pancreatic surgery involving epidural analgesia. The first 24 h of care from onset of anaesthesia was closely looked at with regards to fluid management, epidural management and actions taken on episodes of hypotension or severe hypotension (defined as systolic blood pressure of <90 and <80 respectively). Each episode of hypotension was looked at to determine the actions taken at that point.

RESULTS. Of the 48 patients looked at, 17 were major pancreatic, 17 lower GI and 14 upper GI patients. 40 (83%) had at least one episode of hypotension, with 11 (23%) having at least one episode of severe hypotension. Mean Fluid in during the first 24 h was 6523 ml, with a mean fluid balance of 4133 ml. There was no difference between the doses of epidural local anaesthetic in 24 h between the hypotensive and non hypotensive groups ($p = 0.275$). Management of hypotensive episodes was variable, but the most common intervention at episode one was fluid bolus (80%) and discontinuation of epidural was most common at episode two (39%). Use of vasopressors for hypotension was very low with only two infusions being started altogether.

CONCLUSIONS. Hypotension is very common in our high dependency unit. Fluid balance in our patients was far more positive that we had expected. Management of hypotension was variable. We plan to institute a protocol for hypotension and fluid administration to determine if improvements can be made.

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FACTORS PREDICTING RELAPAROTOMY IN SEVERE SECONDARY PERITONITIS

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INTRODUCTION. A significant number of patients with severe secondary peritonitis (SSP) may require more than one laparotomy to achieve definitive control of the intra-abdominal-infection (IAI). However, the factors predicting need for relaparotomy have not been widely characterized.

OBJECTIVES. To identify predictive factors associated with the need for relaparotomy in patients with SSP.

METHODS. Adult SSP patients undergoing laparotomy between 2004 and 2009 included within a single-center peritonitis registry (PERIT) were collected. Patients subjected to relaparotomy were studied. We excluded patients with severe peritonitis secondary to appendicitis. APACHE II and SOFA score at ICU admission after the initial laparotomy were recorded. Variables with a p value <0.1 in a bivariate analysis were included in a multivariate logistic regression for further analysis of predictors for need for re-laparotomy.

RESULTS. Two-hundred forty-seven patients were obtained from PERIT registry. A total of 212 patients with SPP were included in the analysis. Eighty seven patients (41%) required relaparotomy. Median number of re-laparotomies was 3. Most SPP were associated to colon (n = 94, 44.3%), small intestine (n = 83, 39.2%) and biliary tract (n = 33, 15.6%) perforations. Cultures were positive in 74.5% of first laparotomy: gram negative bacteria were isolated in 53.3%, gram positive bacteria in 16.5% and fungi in 4.7%. Hospital mortality was 17% (n = 36). Multivariate analysis is described in the Table 1.

TABLE 1 MULTIVARIATE ANALYSIS FOR PREDICTORS OF RE-LAPAROTOMY

≥1 relaparotomies	Odds ratio	P > z	[95% conf. interval]	
APACHE II > 15	3.28	0.000	1.69	6.35
Post-operative peritonitis	3.40	0.001	1.64	7.05
Generalized peritonitis	2.97	0.015	1.24	7.14
SOFA > 4	2.83	0.002	1.46	5.48

Predict model: 76.8% (goodness of fit test, p = 0.699)

[Predicts]

CONCLUSIONS. Post-operative peritonitis, generalized peritonitis, APACHE II > 15 and SOFA > 4 were highly predictive of the need for re-laparotomy in SSP patients.

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MANAGEMENT IN THE ICU OF PATIENTS BEFORE AND AFTER BARIATRIC SURGERY

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INTRODUCTION. Many patients who are operated for morbid obesity situations are under home CPAP support for the whole day or during night sleeping hours.

OBJECTIVE. To assess the evolution of bariatric surgery operated patients and identification of factors influencing the outcome.

PATIENTS AND METHODS. Prospective interventional study, 114 patients undergoing bariatric surgery between 2005 and 2009. Patients were admitted to the ICU the day before the intervention, obtaining a blood gas analysis. To those under home ventilatory support (case group, 73 patients) CPAP (PEEP 5 cm of water, FiO2 0.21) was applied by nose mask during 8 h immediate before surgery and 8 h after (if they have been extubated after surgical procedure). Patients not on home CPAP were the control group (41 patients). We collected patient data, lung function tests, serial blood samples, complications during their stay in ICU and in the ward, and status (alive/dead) at discharge from ICU and hospital.

RESULTS. Eighty six (75.5%) patients were women, and overall mean age was 43.46 ± 9.62 years. The body mass index was 49.04 ± 6.73. Most common comorbidities were hypertension (55.3%) and the obstructive sleep apnea syndrome (59.6%). Most common complication during ICU stay was low urine output (29%.) The average ICU length stay in ICU was 2.4 ± 0.76 days. Survival during their stay in ICU was 100%. At follow-up found that the most common complication in the room were infections (22.3, 11.6% surgical wound infection, 10.7% systemic infection). The mean hospital stay was 11.31 ± 10.71 days. The mortality rate was 1.8%. The previous need of home CPAP and its use during the ICU stay previous to surgery, when comparing the case to the control group did not show significant differences neither in blood gases controls after surgery nor in any other evolution studied parameters.

CONCLUSIONS. In obese patients scheduled for surgery, the previous use of CPAP has not shown an improvement in blood gas parameters. The use of CPAP in the hours before and immediately after surgery has not been associated with better postoperative oxygenation. Combined ICU-Surgery Dpt. action in these cases seem to contribute to better patient outcomes.

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THE INFLUENCE OF BUMETANIDE (A LOOP DIURETIC) ON INTRA-ABDOMINAL PRESSURE IN CRITICALLY ILL PATIENTS: A RETROSPECTIVE STUDY

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INTRODUCTION. Excessive fluid resuscitation can cause intra-abdominal hypertension (IAH) due to increased intra-abdominal volume or decreased abdominal wall compliance. This can lead to secondary abdominal compartment syndrome (ACS), a condition associated with high morbidity and mortality. The World Society for the Abdominal Compartment Syndrome (WSACS) has recommended restriction of fluid administration and removal of excess fluids as non-invasive techniques to decrease intra-abdominal pressure (IAP). Ultrafiltration has been successfully used in this setting. There are no literature data on the use of diuretics for this indication.

OBJECTIVES. The aim of this study is to evaluate whether the use of bumetanide (a loop diuretic) in critically ill patients treated at the Ghent University Hospital was associated with a decrease in IAP.

METHODS. We reviewed electronic patient records on patients admitted to the Ghent University Hospital ICU between November 2003 and January 2010 for patients who received bumetanide in continuous infusion and IAP monitoring on the same days, regardless of the reason for diuretic administration. On these patients, demographic data, IAP values, 24 h fluid balance and outcome data were recorded. Several subgroups were defined: patients with and without IAH (as well as different grades of IAH), patients with a negative fluid balance of over −500 and −1,000 mL/24 h and combinations of these groups.

RESULTS. Two hundred sixty-six patients receiving bumetanide in continuous infusion while under IAP monitoring could be identified, for a total of 877 patient days. Mean age and mean APACHE II score were 60.0 ± 15.6 years (range 5–92) and 22.2 ± 7.3. Mean IAP at the start of the infusion day was 13.3 ± 4.3 mmHg. IAH, defined as a mean IAP of 12 mmHg or higher, was present in 62.6% of the patient days. Mean fluid balance was +1,518.8 ± 1,946.1 mL/24 h (not taking insensible fluid loss into account). IAP was decreased after one day of bumetanide infusion in 57.7% of patients with a negative fluid balance vs. 50.5% of patients with a positive fluid balance, showing a trend towards statistical significance (Chi-square test, p = 0.066). This trend could not be confirmed in the subgroup of patients with IAH (p = 0.48). Using Pearson's correlation testing, there was no significant correlation between fluid balance and the change in IAP achieved after 1 day of bumetanide infusion (R = −0.007, p = 0.82) in the general group. No significant correlations between fluid balance and change in IAP could be found in any of the predefined subgroups.

CONCLUSIONS. The use of bumetanide in continuous infusion was not associated with a decrease in IAP on the following day in our institution. As diuretic use is recommended by the WSACS as a non-invasive technique to lower IAP in selected patients, prospective studies are needed to evaluate the effect of diuretics on IAP.

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AWARENESS OF AND ATTITUDES REGARDING INTRA-ABDOMINAL HYPERTENSION AND ABDOMINAL COMPARTMENT SYNDROME: RESULTS FROM AN INTERNATIONAL SURVEY (WSACS STUDY 003)

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INTRODUCTION. The results from several surveys on physicians' knowledge of intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) between 2000 and 2005 have demonstrated a general lack of clinical awareness. Many ICUs never measure intra-abdominal pressure (IAP).

OBJECTIVES.
1. to assess the clinical awareness of IAH and ACS;
2. to determine how IAP is measured and IAH/ACS are managed since the publication of the Consensus Definitions and Recommendations for treatment on IAH/ACS in 2006 and 2007.

METHODS. The WSACS Executive Committee created an interactive online survey (http://www.wsacs.org/survey.htm), accessible from January 2007 until December 2008.

RESULTS. The survey was completed by 2244 responders. They were doctors (70.5%), nurses (15.9%) and doctors in training (8.7%). Primary training was intensive care medicine (30.0%) (trauma)surgery (19.4%) and anaesthesiology (16.8%). Most came from North America (53.0%) followed by Europe (31.6%), Asia (7.2%), South America (4.8%), Australia (2.0%) and Africa (1.4%). 2.9% were members of the WSACS. Eighty five percent were familiar with IAP/IAH/ACS. 69.4% knew about the concept of Abdominal Perfusion Pressure. 28.4% were aware of the consensus definitions on IAH/ACS on WSACS.org. Ninety two percent treated at least 1 patient with ACS in the last year. The majority considered the cut-off for IAH to be at least 15 mmHg (74.9%), and believed the cut-off for ACS was higher than the current consensus definition for most respondents (60.2%). Organ dysfunction was only considered to be a problem for 67.8% of the respondents at levels of 20 mmHg or higher. Bladder measurement was used most frequently (91.9%), but the majority used instillation volumes well above the current standards; frequency of measurement was highly variable. Three percent did not measure IAP. The indications for IAP monitoring most frequently mentioned are: Abdominal surgery, massive fluid resuscitation and acute pancreatitis. Whereas surgical decompression was frequently mentioned and used as a treatment for IAH/ACS, medical management options such as paracentesis, were only used by about half of the respondents. Criteria for deciding to decompress the abdomen were predominantly the combination of IAP and organ dysfunction (74.4%), followed by the degree of organ dysfunction alone (8.9%), the cause of ACS (6.3%), the evolution of organ dysfunction (4.3%) and the evolution of IAP (2.1%) After initial decompressive laparotomy the open abdomen was treated with a VAC in 39.2% of cases, in 24.4% with a Bogota bag (silo), in 21.2% with temporary abdominal mesh and 2.9% immediate primary fascial closure or other techniques (6.7%).

CONCLUSIONS. The results of this survey show that most of the respondents claim to be familiar with IAH and ACS, yet the knowledge of published consensus definitions, measurement options and clinical management is inadequate.

1191

EVOLUTION OF THE INTENSIVE CARE WORKLOAD ASSOCIATED WITH THE DEVELOPMENT OF A BARIATRIC SURGICAL SERVICE

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INTRODUCTION. Bariatric surgery is a growing speciality with resource allocation issues, including the provision of intensive care beds. Morbidly Obese patients have a spectrum of co-morbidities, which lead particularly to cardio-respiratory complications in the peri-operative period.

OBJECTIVES. We set out to quantify the intensive care workload and changes to that workload over the first 4 years following the transfer of a Specialist Bariatric service to our hospital.

METHODS. A prospectively collected bariatric surgical database was cross-referenced to the ITU database (Ward-Watcher) to identify admissions to the 10-bedded Critical Care Unit of all patients who had undergone any bariatric procedure. For each patient identified; demographics, reason for admission, level of support, length of stay and outcome were recorded. Data were grouped into 12-month periods for trend analysis.

RESULTS. Between May 2006 and April 2010, 1561 bariatric procedures were performed in our hospital. The majority (1508) were elective procedures (906 gastric bypasses, 470 gastric bands, 127 revisions, 10 other). Fifty-three (3.5%) were urgent or emergency procedures (32 endoscopies, 21 re-operations). Median age of all patients was 43 years (range 17–73), median BMI was 50 kg/m^2 (range 23–103), median weight was 144 kg (range 65–353). Only 22% of patients were male. There were 139 admissions to the Critical Care Unit post operatively, utilising a total of 331 critical care bed days. 92 (66%) were discharged within 24 h. Patients admitted had a median age of 47 years (22–65) and a median weight of 161 kg. 36% were male. Fourteen patients were invasively ventilated, 16 received non-invasive ventilation; 11 required inotropic support and 3 required haemofiltration. As a proportion of the total ITU workload during this 4 year period, the 331 bed days was 2.98% of the total of 11121 Critical Care Bed days.

TABLE 1

	Year 1 and 2	Year 3 and 4	P value
Total Procedures	538	1043	
Level 2 bed days	187	86	
Level 3 bed days	36	22	
% of Total ICU bed days	4.4	1.8	<0.0001
Bed days/100 procedures	41.4	10.4	<0.0001

CONCLUSIONS. Introduction of a new Bariatric Surgical service has considerable resource implications for the Critical Care Unit. As experience is gained the demand for both level 3 and level 2 beds reduces. A mature Bariatric Surgical Service requires around 10 ICU bed day for every 100 procedures performed.

End of life care: 1192–1204

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INTERNATIONAL HETEROGENEITY OF REGULATIONS IN EMERGENCY RESEARCH: A NEW MEDICOLEGAL RISK?

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INTRODUCTION. Research in emergency situations and especially in resuscitation field raises important ethical and regulatory issues. The globalization of the resuscitation science through multicentric trials for example highlights the need for a more consistent approach to regulatory aspects to enable the science to grow while protecting human rights.

OBJECTIVES. The purpose of this analysis is to compare the different regulations approaches in emergency research in North America (Canada, USA) and in Europe (European Directive, France).

METHODS. A systematic analysis of regulatory issues related to emergency research in 3 different countries (2 in North-America and 1 in Europe) and of the Directive 2001/20/EC of the European Parliament and of the Council).

RESULTS. USA: Y = 1996, W = Yes/Explicit, E = Yes, PD = Y, CC = Yes, S = Yes, DC = Yes

Canada: Y = 1998, W = Yes/Explicit, E = Yes, PD = No, CC = No, S = Yes, DC = Y

Europe: Y = 2001, W = No, E = Yes, PD = No, CC = No, S = Yes, DC = No

France: Y = 2004, W = Yes/implicit, E = Yes, PD = No, CC = No, S = Yes, DC = Yes

Y = Year of implementation, W = Waiver of consent procedure, E = Ethics Committee (National/Local, PD = Public disclosure, CC = Community Consultation, S = Surrogate, DC = Deferred consent (patient/proxy)

CONCLUSIONS. This analysis emphasizes the lack of international standardization of regulatory measures and ethical decisions. However some countries like the US seem to advance in the democratic process by mandating additional regulatory measures (community consultation, public disclosure to the communities) prior to initiation of clinical investigation; nonetheless, there is little evidence of their effectiveness. Many challenges are raised. Firstly, the variability in regulations, and consequently in local board's assessments, is problematic, pleading for international regulations. Secondly, the current heterogeneous ethical review process and demanding unsubstantiated regulatory measures poses a risk to all when it is not evidence based and it is applied inconsistently between countries, within a country and worse at the level of each individual hospital review board. It puts the investigator at risk for unnecessary criticism and the community at risk as it is unknown if we truly consult or inform our target communities about waiver of consent research through our current ethical and regulatory processes. Globalization and evaluation of the ethical and regulatory processes are urgently needed; regulatory community has to work towards a standardized evidence-based process upon which to base regulatory decisions.

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PERCEIVED HOPELESSNESS AFTER ICU CARE IS A PREDICTOR OF LONG-TERM SURVIVAL

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INTRODUCTION. In research outside the intensive care field it is known that a high score for the psychological factor "perceived hopelessness" experienced by healthy individuals increases risk of death several fold.

OBJECTIVES. The aim of this study was to examine if the score of the psychological factor "perceived hopelessness" may predict long term mortality (mean or high perceived hopelessness score) when assessed post ICU care in former ICU patients.

METHODS. Prospective, multicenter study in three mixed ICU's in Sweden. Questionnaires, including the 2-item hopelessness scale, demographic data and previous illnesses, were sent 6 months after discharge to all former adult ICU patients who thereafter were followed for another 3 years. A reference group of 6093 individuals from the uptake area of the hospitals served as controls.

RESULTS. 980 (59%) patients returned the questionnaires. The ICU patients reported significantly higher mean scores in perceived hopelessness score compared with the general population, 2.5 (SD 2.2) compared with 2.1 (SD 2.1) ($p < 0.001$), and 40% (n = 392) of the ICU patients perceived a mean or high hopelessness score compared with 36% of the general population ($p < 0.001$).

The ICU patients who died during the follow-up period reported a significantly higher perceived hopelessness score (n = 123) 3.7 (SD 2.5) ($p < 0.001$) as compared with those who survived up to 3 years after discharge (n = 857) 2.4 (SD 2.1). In a logistic regression model the long term mortality for the ICU group was found to be affected by: pre-existing disease [odds ratio (OR):2.2], age (OR: 1.04) and perceived hopelessness score (OR: 1.18).

CONCLUSIONS. The new and interesting finding of this study is that ICU patients score higher on "perceived hopelessness" than a control population and this increase is predictive for the post ICU mortality. Furthermore, the size of this effect is significant and only exceeded by pre-existing disease and age.

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THE ROLE OF A MEDICAL EMERGENCY TEAM IN LIMITATION OF MEDICAL TREATMENT AND END OF LIFE CARE: A 5 YEARS SINGLE CENTER RETROSPECTIVE STUDY

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INTRODUCTION. Hospital Medical Emergency Teams (MET) were introduced to identify and treat acutely unwell ward patients in order to reduce serious adverse events. An additional role of the MET appears to involve decisions about limitation of medical treatment (LOMT). We performed a retrospective observational study to evaluate what proportion of MET calls was associated with LOMT issues.

OBJECTIVES. To estimate the proportion of MET reviews involving patients with a not-for-resuscitation (NFR) order and the timing of MET calls in relation to admission and death or discharge from hospital. To compare the patient characteristics and outcome for MET calls associated or not associated with LOMT issues.

METHODS. We obtained Hospital Research Ethics Committee approval. We performed a retrospective observational study involving five-year (August 2005–April 2010) in a single tertiary Australian hospital. We obtained information on demographics, on the MET review and hospital outcome. LOMT included NFR orders, not for MET orders and palliative care plans.

RESULTS. We analysed 4829 MET reviews in 3629 patients. Table 1 and Fig. 1 summarize major findings for overall population and the two subgroups of patients with or without LOMT.

Fig. 1 Flow diagram MET population

TABLE 1 CHARACTERISTICS OF MET POPULATION

	Overall MET population	No LOMT subgroup	LOMT subgroup	P value
Age[b]	69 (± 17.2)	65.1 (± 17.4)	78.7 (± 12.1)	<0.001
Sex (male)	1994/3629 (54.9%)	1453/2585 (56.2%)	520/1032 (50.4%)	0.016
Surgical	1892/3629 (52.1%)	970/2585 (37.5%)	688/1044 (65.9%)	<0.001
Days after admission[a]	3 (8)	3 (7)	4 (9)	0.003
Days before discharge[a]	8 (16)	10 (16)	5 (12)	<0.001
Unplanned ICU admissions	516/4829 (10.7%)	463/3390 (13.7%)	53/1039 (5.1%)	<0.001
LOS[a]	14 (19)	14 (21)	13 (16)	<0.001
Hospital mortality	915/3629 (25.2%)	390/2585 (15.1%)	525/1044 (50.3%)	<0.001

LOS hospital length of stay
[a]Mean (± standard deviation);
[b]Median (interquartile range).

Patients with LOMT care plan were older, more likely to have medical diagnoses, were reviewed later during their hospital stay and closer to their hospital discharge or death. Fewer LOMT patients were admitted to ICU. Hospital length of stay was shorter, mortality in LOMT care patients was double that of non-LOMT patients. However, more 50% of patients with LOMT were discharged alive from the hospital.

CONCLUSIONS. More than one third of MET activations deal with LOMT issues. Although the mortality of these patients is high, a large proportion survives to hospital discharge.

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SURROGATE DESIGNATION: CAN WE TRUST OUR RELATIVES?

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INTRODUCTION. Evaluation of the patient experience in Intensive care (ICU) frequently depends on reports from surrogates such as relatives. There is a concern regarding the validity of the surrogate opinion which might not represent the values of the incapacitated patient and treatment decisions therefore maybe biased [1]. Others have found that there is a strong preference within a population for utilizing relatives as surrogate decision-makers in the event of admission to ICU and this attitude is not influenced by ethnicity, religion or education level [2].

OBJECTIVES. The objective was to measure the ability of the relative to answer on behalf of the patient. A further wish was to determine the validity of their surrogate responses.

METHODS. A retrospective study, which surveyed relatives of patients who had died within a critical care service during a 2-year period (2005, 2006). The 31 item questionnaire allowed for the collection of quantitative and qualitative data with respect for each item to overcome the limitations of the quantitative format which may not be sensitive to all the issues which can surround the provision of end-of-life care [3]. For 3 items, relatives were asked specifically to grade their capacity to represent the patient.

RESULTS. Quantitative data from the 3 items designed to test the relatives' perception of their ability to act as surrogates indicates that relatives considered they could respond to these items for 46% (average) of instances. When the relative did answer on the patient's behalf, the level of concordance between the surrogate (relative) and the patient's perceived opinion was 60% suggesting that when the relative is willing to act as surrogate the response is likely to have validity. (Table 1).

TABLE 1 CAPACITY OF RELATIVES TO ACT AS SURROGATES

Question	Surrogacy responses on behalf of the patient*	Similar response (concordance) from relative and on behalf of patient*
1. Adequate information	53 (70)	62 (42)
2. Felt involved in decision making	47 (62)	62 (36)
3. Received adequate spiritual support	37 (61)	57 (32)
Average (total respondents)	46 (133)	60

* Percentages shown with numbers in brackets

Results from the qualitative data indicates that the low (46%) level of willingness to answer these questionnaire items reflected a reluctance to answer on behalf of a sedated or ventilated patient, rather than an inherent inability to represent the patient.

CONCLUSIONS. The response rate to the 3 items vindicates concerns regarding the ability of relatives to represent the patient in ICU settings and supports a need for further study. Where the relative is willing to act as surrogate, concordance does exist. Qualitative data clarified quantitative results and was instrumental in promoting a better understanding of the concerns of relatives who have a family member admitted to ICU.

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DECISION MAKING PROCESS OF THERAPY RESTRICTION IN HUNGARIAN INTENSIVE CARE UNITS

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INTRODUCTION. Throughout the world decreasing number of patients receives all available medical therapies in intensive care units (ICU). The majority of patients that died in ICU were provided some kind of therapy restriction. An important conflict strains between clinical practise, bioethical principle and jurisdiction laws; the solution of this conflict is more and more urgent. Therapy restriction has also important economical aspects since the number and cost of available treatments constantly increase. Our survey studied therapy restriction procedures in Hungary for the first time.

METHODS. In 2007 we performed a survey with questionnaire among intensive care physicians. Questionnaires were sent out electronically to 743 registered members of the Hungarian Society of Anaesthesiology and Intensive Care. Respecting anonymity we have statistically evaluated 103 replies (14%) with t test and ANOVA. We grouped intensive care physicians based on gender, years spent in work, religion and type of department they were working, and we compared data from these groups.

RESULTS. Intensive care physicians generally make their decisions alone, based on the patient's long-term life prospects and physical status (3.75/5 points). They are slightly influenced by the opinion of the patient (2.57), the relatives (2.14) and other medical personnel (2.37). If the physician sees any chance of recovery but the patient or relative requests treatment restriction then 67.3% of physicians that completed the forms would continue therapy against the will of the patient or relative. Only 27.7% would accept the patient's/relative's opinion and autonomy in such a case and would stop therapy. In fact 28.3% of physicians would make their decisions without considering or even against the opinion of patient if they think therapy is useless. If there is no chance of recovery despite medical treatment 3% of physicians stop the treatment, 8.1% would continue it without informing the patient or the relatives, 17.2% informs the relatives but continues useless treatment irrespective of the will of the patient or relative. Having analyzed the groups we found two significant differences. In case of useless treatment physicians working in university hospitals more often choose treatment restriction without informing relatives ($p < 0.001$) then those working in non-university hospitals. Physicians who declare themselves as atheist rather choose the continuation of treatment without informing relatives ($p = 0.007$).

CONCLUSIONS. The Hungarian practise of end of life decisions among intensive care specialists is paternalistic, physicians make their decisions alone, do not consider the requests of the patient or relatives. Our goal is to strengthen patient autonomy and to support their opinion by training ICU physicians. On the other hand it is inevitable to define what useless medical treatment exactly is and to introduce this category in medical ethics and also in jurisdiction practise.

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AN AUDIT OF END OF LIFE PRACTICES IN AN INDIAN CANCER HOSPITAL ICU

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INTRODUCTION. Little information on end-of-life (EOL) decisions and practices is available from Indian ICUs. We audited EOL practice in our ICU, a 34 bed ICU-HDU of a tertiary cancer referral centre in Mumbai, India.

OBJECTIVES. To determine the frequency and processes of EOL care at our centre.

METHODS. Between October 2007 and December 2009, 150/388 (39%) patients staying in the ICU for more than 1 day, underwent some form of EOL care in the ICU. ICU staff notified investigators whenever an EOL decision was made. We recorded demographic details, documentation of the EOL care process in the case notes, and interviewed ICU staff to determine the EOL care processes involved.

RESULTS. 97 patients (65%) were male, 53 (35%) were females. Mean age was 42.4 ± 2 years. ICU stay was 6.7 ± 6.3 days, admission APACHE II score was 18.1 ± 7.8 which increased to 24.9 ± 9.4 on the day of EOL care decision. 33% patients had metastatic cancer. Reasons for initiating EOL care were refractory acute illness in 53%, advanced cancer in 51%, brain death in 11%, and lack of finances in 11%. EOL discussions were initiated by the family in 11%, and by the ICU medical team in 89% patients. 16 families wanted to take the patient home to die. The ICU consultant was involved in all discussions with the family, the primary consultants in 91% and primary team residents in 79%. Nurses were involved in only 3 patients. Agreement on EOLC was reached after 1 discussion in 70%, 2 discussions in 22%, and 3 discussions in 8% of cases. Documentation of the EOL care process was not done in 51% cases. Withholding of life support (WH) was practised in 110/150 patients (73%) and Withdrawal of life support (WD) in 27%. Intubation was withheld in 14.5% patients, cardiopulmonary resuscitation in 50%, inotropes in 76% and dialysis in 8%. Regarding WD, only 3/40 patients were extubated and the ventilator withdrawn in another 7/40 patients. Inotropes were withdrawn in 20 patients (50%). Reduction of FiO2 0.21 without discontinuing mechanical ventilation was the commonest mode of WD, in 35 patients (88%). All patients received morphine infusions during LOLS/WOLS. Family members were present by the bedside in 61% cases.

CONCLUSIONS. WH is preferred over WD. Documentation of the EOL process does not occur in a significant proportion of cases. Nurses are rarely involved in the EOL care decision making process. Legal issues may be barriers to good EOLC in our ICU, and perhaps in India.

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CARING AT END-OF-LIFE: VISION AND ATTITUDE OF A BRAZILIAN ICU STAFF

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INTRODUCTION. Complex issues related to the end-of-life (EOL) care are present in every day activity in intensive care units (ICU), as so as in media. Until this year, in our country there is no specific legislation regulating interruption of treatment in terminal patients.

OBJECTIVES. To know the point of view of the staff is essential to understand their beliefs, attitudes and decisions.

METHODS. Between November 2008 and February 2009, a research form was done in a Brazilian private general ICU with 23 beds. The following items were analyzed: profile of the interviewed; their opinion about end of life questions: fear of death, fear of experience pain before death, the best place to die, advanced directives, decision-making process, therapeutic withhold of mechanical ventilation, nutrition, fluid management, antibiotics, vasoactives drugs, sedation and analgesia in patients which death is imminent and irreversible.

RESULTS. About 84.41% of our ICU team answered the research ($n = 65$). The mean age is 32.61 years (SD 6.74), 58.50% of female, 58.50% married, 50.85% Protestants and 38.50% Catholics and ICU professional experience of 6.75 years (SD 4.65). Using a visual analog scale (0, no fear to 10, the worst fear possible) the team pointed 5.96 as their fear of death; the fear of suffering pain before death was 8.17. For 44.60% of the responders, the best way to die would be with their lovely ones, no matter if at home or at hospital. Only 9.20% would prefer to die an ICU. The majority of the team (88.25%) would share the EOL decision-making process with the family instead only by the medical staff (52.30%). About 73.10% would leave an advanced directive with their therapeutic preferences like do not resuscitation orders. The ICU team agreed on the withdrawal of vasoactives drugs (41.50%), antibiotics (57.00%), nutrition (18.50%) and mechanical ventilation (1.53%) in patients out of treatment.

CONCLUSIONS. Our results showed the staff vision about their own death and their opinion about the end-of-life care issues. In developing country as Brazil there is a still gap between everyday practice and the current legislation. Fortunately, the debate about EOL issues has increased in last years. The end-of-life discussions and decisions should begin by respect to points of view of all involved: patients, family, medical staffs with a legal support of the society's beliefs and expectations.

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END-OF-LIFE DECISIONS IN GREEK INTENSIVE CARE UNITS: A MULTICENTRE STUDY

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INTRODUCTION. Intensive care may prolong the dying process in patients who have been unresponsive to the treatment already provided. Withholding and withdrawal of life-sustaining therapy are ethically acceptable and common worldwide practices.

OBJECTIVES. To examine the frequency, types and rationale of life-support limitation in Greek intensive care units (ICUs), the clinical and demographic parameters associated with it, and the participation of relatives in the decision-making process.

METHODS. Prospective observational study conducted in 8 Greek multidisciplinary ICUs. We studied all consecutive ICU patients who died, excluding those who stayed in the ICU <48 h or were diagnosed with brain death. 306 patients comprised the study population [mean age 64 ± 17 (SD) years, mean APACHE II score on admission 21 ± 7].

RESULTS. Of patients studied, 41% received full support including unsuccessful cardiopulmonary resuscitation (CPR). 48% died after withholding of CPR, 8% after withholding of other treatment modalities besides CPR, and 3% after withdrawal of treatment. Patients in whom therapy was limited had a longer hospital ($p = 0.01$) and ICU ($p < 0.01$) stay, a lower admission GCS score ($p < 0.01$), a higher APACHE II score 24 h prior to death ($p < 0.01$), and were more likely to be admitted with a neurological diagnosis ($p < 0.01$). Patients who received full support were more likely to be admitted with either a cardiovascular ($p = 0.02$) or trauma diagnosis ($p = 0.05$), and to be surgical rather than medical ($p = 0.05$). The most important factors affecting the physician's decision to provide full support were reversibility of illness and prognostic uncertainty; the physician's religious beliefs and legal concerns had minimal impact. The main factors guiding the decision to limit therapy were unresponsiveness to treatment already provided, prognosis of underlying chronic disease, and prognosis of acute disorder; old age was not a determinant, while economic cost and lack of ICU beds seem to play no role. Relatives' participation in decision-making occurred in 20% of cases and was more frequent when a decision to provide full support was made ($p < 0.01$). The principal reason for not discussing end-of-life dilemmas with relatives was the fact that the family was thought not to understand (60%) Advance directives were rare (1%).

CONCLUSIONS. Limitation of life-sustaining treatment is a common phenomenon in Greek ICUs. However, in a large majority of cases, it involves the withholding of CPR only. Withholding of other therapies besides CPR and withdrawal of support are infrequent. Physician has a dominant role in decision-making.

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PRELIMINARY RESULTS FROM THE APPROPRICUS STUDY (APPROPRIATENESS OF CARE IN THE ICUS)

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INTRODUCTION. Advances in medical technology enable more lives to be saved but sometimes may merely prolong the dying process and the suffering of patients and their families at the end of life. ICU healthcare workers who provide aggressive care to patients not benefiting from it, have moral distress and are at risk for burnout.

OBJECTIVES. The primary objective of this study is to determine the prevalence of inappropriate or non-beneficial care in ICU patients as perceived by their ICU healthcare providers, as well as the reasons for this perception. Second, we want to determine which factors are associated with the perception of inappropriate care.

METHODS. A descriptive survey design is used. A single-day cross-sectional evaluation of perceptions of inappropriate care among 2,327 ICU healthcare providers in 85 ICU centres in 10 European countries will take place on May 11th 2010. Questionnaires will be administered to ICU healthcare providers (nurses, head nurses, junior and senior ICU physicians) providing bedside care to adult ICU patients on that particular day. In this study, inappropriate care is defined as a patient care situation that is similar to one or more of seven scenarios. These scenarios were created based on the literature and a multidisciplinary conference attended by experts in intensive care, geriatrics, and palliative care.

RESULTS. The cross-sectional study will take place on May 11th 2010. Preliminary results will be given at the ESICM conference.

CONCLUSIONS. We have designed a one-day cross-sectional study to record inappropriate or non-beneficial care in European ICU's. Results will be available for the ESICM conference.

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1201

OBTAINING RETROSPECTIVE CONSENT IN INCAPACITATED INTENSIVE CARE PATIENTS

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INTRODUCTION. Since the introduction of the Mental Capacity Act in the UK in 2007, the impact within research in the intensive care environment has not been elucidated. Since many of the patients are incapacitated and therefore unable to consent, it is now stipulated by the ethics committee that the researcher must make reasonable attempts to identify a consultee, failing this, nominate a person unrelated to the research project to be consulted. In order to comply with the Mental Capacity Act, retrospective consent must be obtained, once the patient regains capacity.

OBJECTIVES. The aim of the study was to highlight the difficulties in obtaining retrospective consent, evaluate the methods used and demonstrate the adaptations made to increase retrospective consents.

METHODS. This explorative analysis investigated the process of obtaining consent in 246 patients enrolled in an observational study on critically ill patients. Consent was obtained on admission if the patient had capacity. Assent from the patient's next of kin or a legal professional representative was obtained before enrolment in patients who lacked capacity. After discharge from ICU, a member of the research team re-visited these patients to explain their involvement in the research, its purpose, procedures, implications and any further participation required by the subject. At this point, the patient could consent or withdraw from the study. If the patient decided to withdraw from the study, all data collected and samples stored were destroyed. The researcher visited the patient for a minimum of two visits; firstly to explain the study; secondly to establish if the patient has retained the information and to gain retrospective consent.

RESULTS. 246 patients were recruited within the time period of which 44 (17.7%) died. In 65 (26.2%), consent was obtained on admission as the patients had capacity, 36 (14.6%) were discharged prior to obtaining retrospective consent, 10 (4%) lacked capacity on the researcher's visits, and 1 patient (0.4%) withdrew from the study. 90 patients (36.3%) were successfully consented retrospectively. Overall, the researchers performed 221 visits to obtain from the 137 patients for whom retrospective consent was required.

CONCLUSIONS. The process of recruiting patients who lack capacity within the intensive care unit is challenging and time consuming. Stipulations set by the ethics committee to seek retrospective consent once the patient has regained capacity, has a major impact on research staff time and finances. Detailed recommendations as well as guidelines how to assess capacity in the post-ICU patient and how the assessment of capacity has to be applied to Intensive Care research are needed to fully comply with ethical and legal requirements.

REFERENCE(S). None.

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PATIENTS' EXPRESS ADVANCE RESUSCITATION DIRECTIVES AFTER ICU DISCHARGE

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INTRODUCTION. Most patients with acute critical illness are not able to make decisions about limitation of life-supporting treatment. A such decision should be based on treatment preferences which should be previously expressed by the patient as an advance directive.

OBJECTIVES. We wanted to know if patients expressed to surrogate decision makers, after ICU discharge, specific resuscitation directives, and we have investigated any factors related to the patients and their illness or care process that might be associated with this.

METHODS. We reviewed patients admitted in the ICU between December 2008 and May 2009. A random sample of 60 survivor patients has been defined. Seven patients were excluded (3 for language barrier, 2 died, 2 were no more reachable). Fifty three patients took part in semistructured interview at 6–12 month post ICU discharge. The questionnaire discussed in detail the aspects of advance directives. Patients had also completed a quality of life questionnaire (Euroqol 5D), and we calculated the EQ-5D visual analog scale. We reviewed medical records in ICU data base: age, gender, length of stay, SAPS II, BMI, length of ventilator support and central venous catheterization as well as prescription of transfusion, hemodialysis or adrenergic agonist. Multivariate logistic regression was practiced to investigate any factor associated to expression of specific resuscitation directives after ICU discharge.

RESULTS. After ICU discharge, 60% of interviewed survivors expressed specific resuscitation directives to an appropriate identified surrogate (written "living will" or oral statement). EQ-5D visual analog scale was 58 ± 19. On multivariate regression analysis, only one studied variable was significantly associated to the post-ICU expression of specific resuscitation directives: age (odds ratio = 0.94, $z = -2.1$, $p = 0.035$).

CONCLUSIONS. After ICU discharge, a majority of our patients expressed to surrogate decision makers specific resuscitation directives, especially the younger patients. Our findings suggest that surviving to ICU is an opportunity to specify oral or written directive, and both may help to illuminate future decision making from the patient's perspective.

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APPLICABILITY OF PALLIATIVE QUALITY MEASURES TO END OF LIFE CARE IN ICUS IN THE UK AND ISRAEL

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INTRODUCTION. Previous studies have demonstrated that there are differences in intensive care units between and within countries in: patient and family members' preference for involvement in decisions about end of life care; end of life care practices and the role of health professionals in shared decision making [1, 2]. An extensive body of work in the United States has identified a series of Palliative Quality Measures (PQM) for end of life care in intensive care units [3]; the applicability of these measures in other countries has not been tested.

OBJECTIVES. The aim was to identify the extent to which the palliative quality measures identified in previous studies apply to intensive care units in the UK and Israel. Objectives were to: (1) Establish validity, reliability and feasibility for the PQM tool in ICUs in Israel and the UK, (2) Explore the views of ICU nurses in Israel and the UK regarding what makes a 'good' death in ICU and compare findings with items in the PQM tool.

METHODS. Patient record review (n = 65 patients), individual and focus group interviews with nurses (n = 32) in four ICUs in Israel and three ICUs in the UK.

RESULTS. Pain assessment and pain management were the PQM most commonly documented across all units in the two countries; pain management was also the priority goal of a 'good death' across most interviews. Most of the PQM from the original tool were considered important but documentation practices varied by individual ICU. Documentation of social work support and spiritual support was different in the two countries.

CONCLUSIONS. In common with the original work, pain was considered the most important symptom to keep under control during end of life care. Quality of care provided cannot always be gleaned from documentation alone.

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CANCER PATIENTS' CARE AT THE END-OF-LIFE IN A CRITICAL CARE ENVIRONMENT: PERSPECTIVES OF FAMILIES, PATIENTS AND PRACTITIONERS

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INTRODUCTION. Innovations in cancer care requiring intensive support, and improved cancer patient survival in and out of critical care, have led to greater numbers of cancer patients than ever accessing critical care. Current research points to 1 in 6 of all patients dying in general critical care units (ICNARC, 2009), and even higher numbers for cancer patients (Studnicki et al 1994; Iwashyna, 2004). While palliative care is an established domain in cancer, for critical care patients end-of-life care (EOLC) is often problematic. This research explores the provision of EOLC for cancer patients in a critical care unit.

OBJECTIVES. To explore the issues around EOLC provision for cancer patients in a critical care unit through family, professional and patient experiences. To explore how a diagnosis of cancer impacts upon EOLC provision for critically ill patients.

METHOD. A Heideggerian phenomenological interview approach was undertaken, in order to gain personal experiences. Families of those patients who died after decisions to forgo life-sustaining treatment (DFLSTs) were interviewed. Patients who were seriously critically ill (APACHE II > 25 or had received CPR) who experienced critical care were also interviewed, since patients' views about EOLC provision are very rarely explored. Doctors and nurses also contribute their vision for, and experiences of, EOLC in a cancer critical care unit. Thirty seven participants were interviewed.

RESULTS. Tensions between treating families versus treating patients impacted on timeliness of EOLC. Achieving a good death was possible through caring activities that made best use of technology to prevent prolonged dying. Decision-making and EOLC could be difficult to separate out which, in turn, affects prospects for EOLC. Three main themes included: *Dual Prognostication; The Meaning of Decision-Making;* and *Care Practices at EOL: Choreographing a Good Death*. These themes outlined the essence of moving along a continuum toward patients' deaths and the impact that had on opportunities for care and a good death.

CONCLUSIONS. Cancer affected the trajectory in unexpected ways. The trajectory could be very quick, especially in unexpected death and some newly diagnosed cancers. Even in the face of a life-limiting and serious disease like cancer, death could be unexpected. The rapidity of trajectory related to cancer diagnosis, prognosis, withdrawal and patient demise significantly impacted on the potential for, and timing of, EOLC. A sentiment of moving on from historical practices around critical care for cancer patients, and related poor prognoses, was overwhelmingly agreed on but important caveats in cancer prognostication remains.

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Physiotherapy in the ICU:1205–1214

1205

PEAK EXPIRATORY AND INSPIRATORY FLOWS CHANGES DURING HIGH FREQUENCY CHEST WALL OSCILLATION (HFCWO) VIA THE VEST® AIRWAY CLEARANCE SYSTEM IN MECHANICALLY VENTILATED PATIENTS

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INTRODUCTION. In mechanically ventilated patients, adequate airway clearance may facilitate improved gas exchange. Optimal airway secretion clearance been associated with a PEF/PIF ratio >1.1 (kim et al. 1990; Bredge Mccarren 2006). Oscillation frequency (Hz) determinates relations among peak expiratory and inspiratory flows. To our knowledge, there is not a previous description of the effect of variable oscillation frequencies on PEF/PIF ratio in mechanically ventilated patients.

OBJECTIVES AND METHODS. This study was performed in 71 mechanical ventilated patients in assist control ventilation mode. Subjects were treated with high-frequency chest wall oscillation (HFCWO) via The Vest® Airway Clearance System. The effects of various frequency settings on airway clearance and ventilatory parameters were evaluated during 45 min of therapy (5 Hz/15 min, 10 Hz/15 min and 15 Hz/15 min). We recorded inspiratory and expiratory resistances (RIns;RExp), peak flows and gas exchange pre- and post-HFCWO therapy.

HFCWC CHANGES

	Resistances (cmH_2O/L/seg) R-Ins	Resistances (cmH20/L/seg) R-Exp	Flow Peak insp-flow (L/min)	Flow Peak exp flow (L/min	Ratio PEF/ PIF
Pre-HFCWO	16	18.78	42.15	42	0.9
5 HZ	16.3	20.2	33	41	1.24
10 HZ	15.5	19.6	34.6	39	1.12
15 HZ	14.4	17.3	35.5	37.32	1.05
Post-HFCWO	19.95	17.86	34.4	32.5	0.94

RESULTS. Oscillation at 5 and 10 Hz showed optimal PEF/PIF ratio. Gas exchange: Pre- versus post-HFCWO: PaO_2 [PaO_2: 57.41 ± 16 vs. 73.75 ± 28] ($p = 0.04$) and pH [PH: 7.36 ± .05 vs. 7.37 ± .05 p .029] ($p = 0.029$) exhibited statistically significant clinically positive changes as a result of HFCWO therapy.

CONCLUSIONS. These data suggest that oscillation settings of 5 and 10 Hz provided more optimal PEF/PIF ratio (>1.1). Our data also suggests that airway clearance using HFCWO may facilitate improved gas exchange in mechanically ventilated patients. Further study is required to confirm these results

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1206

EFFECTS OF INTRAPULMONARY PERCUSSIVE VENTILATION AS COMPLEMENTARY TECHNIQUE IN NONINVASIVE MECHANICAL VENTILATION DURING EXACERBATIONS OF COPD

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OBJECTIVES: We hypothesized that the use of intrapulmonary percussive ventilation (IPV) could effect hypercapnia/acidosis and airway secretions control during treatment with Noninvasive Mechanical Ventilation (NIPPV) in exacerbations of COPD associated with bronchial secretions.

METHODS. Prospective multicenter study. The study was performed in the medical ICU of 3 Spanish university hospitals members of the Spanish IPV Working Group. We enrolled COPD exacerbation patients with secretions and the need for NIPPV in ICU. Criteria of exacerbations of COPD are: a respiratory frequency ≥25/min, a $PaO_2 > 45$ mmHg and pH ≤ 7.35. We define two IPV strategies as complementary treatment during NIPPV to evaluate the effects of IPV. *Strategy Group I*: NIPPV at first line and combination of IPV in early periods without NIPPV in spontaneous breathing and pH ≥7.35. *Strategy Group II:* First line of IPV with mouthpiece/face mask and oxygenation previous to the application of NIMV with pH < 7.35. In both groups daily sessions IPV were applied by for 30 min/3 day by mouthpiece or face mask during stay in ICU. NIPPV was applied with BiPAP Ventilator (Respironics) and face mask with BiPAP mode. Cardiopulmonary monitoring, clinical and arterial blood gases were evaluated. Therapy was considered as successful when patients did not need NIPPV support and clinical and arterial blood gases returned to baseline.

RESULTS. 65 patients with COPD exacerbation were admitted in ICU for NIMV, age 70 ± 12 years, male (90%) 15 were excluded for severe hypoxemia (PaO_2:$FiO_2 \leq 200$) associated with pneumonia (5/15) and cardiac insufficiency (10/15). Fifty patients were enrolled in the study.

Strategy Group I: (n = 25): Thirty minutes of IPV showed a significant decrease in respiratory rate, increase in pH respect pre IPV/pCO_2 mmHg from [pH 7.26/76.6 mmHg to pH 7.34/76.6 mmHg] after IPV treatment ($p < 028$; $p < 043$) and improved airway clearance.

Strategy Group II (n = 25): after NIPPV with control of arterial blood gases [pH 7.38/ 52 mmHg] and IPV treatment showed improved clearance of airway secretions without significant change in Ph/PCO_2 [pH 7.39/50 mmHg] ($p < 0.162$). Hospital stay was significantly shorter in the IPV group than in the control group (6.8 ± 1.0 vs. 7.9 ± 1.3 days, $p < 0.05$). UCI stay (G I: 3 ± 1; GII: 4 ± 2); failure (GI: 1/25; GII:0 %).

CONCLUSIONS. Trial of IPV session have ventilatory effects in COPD patients admitted at ICU for exacerbations associated with important bronchial secretions and is useful as complementary technique during NIPPV.

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1207

IS HEAD-UP TILT-TABLE REHABILITATION BETTER THAN SITTING IN A CHAIR FOR VENTILATED ADULTS IN INTENSIVE CARE IN TERMS OF IMPROVING LUNG FUNCTION?

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INTRODUCTION. Physiotherapy intervention is a fundamental part of the patient stay in an intensive care unit (ICU) and treatment is often aimed at maintaining/improving respiratory function. Physiotherapists use the upright posture to elicit these improvements and sitting in a chair and standing with a tilt-table are commonly used interventions. To date there are no published reports comparing the efficacy of these interventions in ventilated subjects.

OBJECTIVES.

- To compare the effects of these two positioning techniques employed with ICU patients.
- To measure changes in respiratory rate, tidal volume and minute volume during these positioning interventions.
- To measure functional residual capacity during positioning interventions.
- To measure the change in metabolic demand during positioning interventions.

METHODS. Convenience sampling of ventilated subjects meeting the inclusion criteria was employed. Subjects acted as their own controls undergoing sitting in a trauma chair and standing on a tilt table at 70 degrees in random order on the same day. Respiratory rate (RR), tidal volume (V_T), ventilation (V_E) and oxygen consumption (VO_2) were measured at minute intervals during baseline and intervention for 10 min. Functional residual capacity (FRC) was measured once at rest and following each intervention. Measurements were recorded using the "E-COVX" module for the "GE Carestation ventilator".

RESULTS. 10 subjects were recruited. No adverse events occurred during interventions. Significant increases from baseline RR ($p < 0.0001$), V_E ($p < 0.0001$) and VO_2 ($p = 0.009$) occurred during the tilt table intervention. There was an increase in FRC during tilting of 0.6 L which failed to reach significance. Significant increases from baseline RR ($p < 0.0001$), VO_2 ($p = 0.024$) and a decrease in V_T ($p = 0.015$) occurred with the chair intervention.

CONCLUSIONS. These interventions are safe in a critical care population. Increased muscular activity associated with upright interventions elicited expected elevations in VO_2. The tilt-table produced an increase in V_E driven by an increased RR at the expense of V_T. V_E was not elevated during chair sitting despite an increased VO_2 and was accompanied by an unexpected decrease in V_T.

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1208

INTER-RATER RELIABILITY OF THE AUSTOMS THERAPY OUTCOME MEASURE IN AN ADULT CARDIOTHORACIC INTENSIVE CARE POPULATION

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INTRODUCTION. UK guidelines about rehabilitation after critical illness highlight the need for outcome measures to determine patient progress and efficacy of treatment [1]. There is no consensus about the most appropriate measures of patient function. The AusTOMs [2] tool was designed by therapists in Australia to measure activity and function across nine scales assessing structural and functional difficulties and ability to perform activities. Scales are split into four domains (impairment, activity limitation, participation restriction and distress/wellbeing) and scored from 0 to 5 with 0.5 intervals allowed. Acceptable inter-rater variation is defined as an absolute difference of 0.5. AusTOMs has not been appraised in patients recovering from critical illness.

OBJECTIVES. To prospectively determine the inter-rater reliability of the AusTOMs physiotherapy scales in adult patients who had undergone cardiothoracic surgery and required critical care admission for over 5 days.

METHODS. The therapy (physiotherapy and occupational therapy) team underwent a 1 h teaching session using the AusTOMs handbook prior to commencing the trial. AusTOMs was then used over eight consecutive weeks during the weekly therapy goal setting meeting. Each week a patient was selected to be scored using the most appropriate functional scales. The clinical history was presented to the team by the therapist leading the patient's care. Therapists were then asked to independently score patients across the four domains for each scale. Reasons underlying differences in scores were explored by group discussion. The difference between the 10th and 90th centiles of the initial scores was calculated for each domain as a measure of inter-rater variability.

RESULTS. 6–8 therapists were present at each meeting. Respiratory function and musculoskeletal movement related function were the most common scales used. The mean difference between 10th and 90th centiles was greater than 0.35 (± 0.21) for all domains.

INTER-RATER RELIABILITY OF AUSTOMS SCALES

	Respiratory system functions (impairment)	Respiratory system functions (activity)	Musculoskeletal Movement related functions (impairment)	Musculoskeletal Movement related functions (activity)	Participation restriction	Distress/ wellbeing
Mean 10–90th percentile range of scores awarded	0.75	0.35	1.03	0.35	0.88	0.66
SD of 10–90th percentile of scores awarded	±0.43 (0.32–1.18)	±0.21 (0.14–0.56)	±0.65 (0.38–1.68)	±0.33 (0.02–0.68)	±0.51 (0.37–1.39)	±0.52 (0.14–1.18)

None of the scales/domains showed consistent inter-rater reliability over the 8 week period. Overall the activity limitation domains of each scale showed the least inter-rater variance of scores. Clinical experience of therapist did not appear to influence scores.

CONCLUSIONS. The AusTOMs outcome measure showed poor inter-rater reliability when evaluated over an 8 week period on our intensive care unit. Further work is ongoing to evaluate the ability of AusTOMs to reveal changes over time when scored by therapists.

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1209

SETTING REHABILITATION GOALS IN THE ADULT INTENSIVE CARE POPULATION

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INTRODUCTION. UK guidelines on the rehabilitation of patients after critical illness highlight the importance of establishing and reviewing individualised rehabilitation goals for all patients that are at risk of developing physical and non-physical morbidity [1]. Our institution's practice is to create objective goals that are SMART—Specific, Measurable, Achievable, Realistic and Timed [2].

OBJECTIVES. The aim of this audit was to prospectively collect data regarding the setting of rehabilitation goals in a group of patients admitted to a cardiothoracic intensive care unit.

METHODS. All consecutive patients admitted under the Intensive Care team in November 2009 were included. Data regarding the timings of initial physiotherapy assessment, goal setting, and concomitant sedation were collected using a structured questionnaire completed by the treating physiotherapist.

RESULTS. 30 patients were admitted under the critical care team. 29 patients were assessed by a physiotherapist within 24 h of admission. Of these 29, 21 had SMART goals set within a median of 7 days of initial assessment (range 1–29 days). There was a correlation between level of consciousness and the number of days taken to set goals. Patients who were fully conscious or drowsy on initial contact ($n = 11$) had a SMART goal set in a median of 3 days. By contrast patients who were sedated/paralysed on initial assessment ($n = 18$) had goals set in a median of 12 days. Initial goal setting did not include other therapists or the family. Goals fell in to 5 categories, range of movement, hoisting out to chair for periods of time, sitting on the edge of the bed, transferring out to the chair by standing and mobility goals—i.e. walking set distances. The maximal interval between reviews of the patients' goals was 7 days.

CONCLUSIONS. Most patients had SMART goals defined and regularly reviewed. However, despite physiotherapy assessment within 24 h of admission, there was often a delay in setting these objective goals. The need for continuous sedation acted as a barrier to explicit setting of goals. The results emphasised the need to improve patient and family/carer involvement with initial goal setting in order to be compliant with UK standards.

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1210

ELECTRICAL MUSCLE STIMULATION: A FORM OF EXERCISE TO IMPROVE MUSCLE STRENGTH IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Critical illness polyneuromyopathy (CIPNM) is a frequent complication in ICU patients characterized by severe muscle weakness, for which no effective preventive means has been proposed so far. Electrical muscle stimulation (EMS) training has induced beneficial effects on CHF, COPD, and in-hospital patients.

OBJECTIVES. Investigation of EMS effects on muscle strength and exploration of issues in relation to handgrip dynamometry in ICU patients.

METHODS. One hundred seventy two consecutive patients with APACHE II score ≥13, were randomly assigned to the EMS ($n = 86$, age: 62 ± 18 years, APACHE II: 18 ± 5) or the control ($n = 86$, age: 59 ± 18 years, APACHE II: 18 ± 5) group. EMS sessions applied daily in muscles of both lower extremities. The strength evaluation of various muscle groups of the upper and lower extremities was made clinically upon awakening with the MRC scale, ranging from 0 to 5 (normal strength) for each group. The same scale was also employed in the diagnosis of CIPNM (MRC < 48/60). A subgroup of these patients also performed handgrip dynamometry.

RESULTS. Fifty seven patients (EMS: 28, control: 29) were finally evaluated. EMS patients scored higher than controls ($p \leq 0.05$) in wrist flexion, knee extension, ankle dorsiflexion and right side hip extension, while they tended to perform higher in all other muscle groups (p: 0.20–0.10) (Table 1).

TABLE 1 MRC SCORES [MEDIAN (INTERQUARTILE RANGE)]

	Left side		Right side	
	EMS group	Control group	EMS group	Control group
Shoulder abduction	4.0 (1.0)	4.0 (2.0)	4.0 (1.0)	4.0 (2.0)
Forearm flexion	5.0 (0.5)	4.5 (1.5)	5.0 (0.5)	4.5 (2.0)
Wrist flexion	5.0 (0.0)*	5.0 (1.5)	5.0 (0.0)*	5.0 (1.0)
Hip flexion	4.5 (1.0)	4.5 (2.0)	4.5 (1.0)*	4.0 (2.0)
Knee extension	5.0 (0.5)*	4.5 (2.0)	5.0 (0.5)*	4.5 (2.0)
Ankle dorsiflexion	5.0 (0.0)*	5.0 (1.0)	5.0 (0.0)*	5.0 (1.0)

Collectively, EMS group performed higher MRC scores [median (interquartile range)] than controls in the legs [29 (3) vs. 27 (10.5), $p = 0.04$] while it tended to perform higher in the arms [28 (4) vs. 26 (10.5), $p = 0.11$]. Overall MRC score was higher in the EMS group [56 (7) vs. 52 (18.5), $p = 0.05$]. Handgrip strength was evaluated in 21 patients (EMS group: 12, control group: 9), with EMS patients tending to perform higher than controls [(mean ± SD) 21.4 ± 10.8 vs. 14.8 ± 10.7 kg, $p = 0.18$). CIPNM was diagnosed in 3 patients in the EMS group (10.3%) in comparison to 12 patients in the control group (41.4%) ($p = 0.01$)

CONCLUSIONS. EMS in ICU patients has a systemic beneficial outcome in strength, affecting not only muscle groups stimulated but also groups not applied. This form of exercise, being safe, well-tolerated and applicable in subjects unable to co-operate, constitutes an effective means of strength preservation, CIPNM prevention and early mobilization in critical illness. Handgrip, in addition, may be a useful surrogate tool in clinical diagnosis of CIPNM, and further research is needed to define proper reference values.

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MANUAL HYPERINFLATION WITH OR WITHOUT RIB-CAGE COMPRESSION IN MECHANICALLY VENTILATED PATIENTS

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BACKGROUND. Secretion removal is major aim of respiratory physiotherapy in intensive care. Manual hyperinflation provides a tidal volume to the lungs that is greater than baseline. It is effective in secretion clearance and is frequently used [1, 2]. There is a limited evidence that addressed the effects of combining rib-cage compression and suctioning on oxygenation, ventilation, and airway-secretion removal in mechanically ventilated patients [3].

OBJECTIVES. The aim of this study was to investigate the effects of manual hyperinflation administered in combination with expiratory rib-cage compression on lung compliance, gas exchange, and secretion clearance in mechanically ventilated patients.

METHODS. Twenty-two intubated, mechanically ventilated, and hemodynamically stable patients were studied. The patients received manual hyperinflation, with or without expiratory rib-cage compression, with a minimum 3-h interval between the two interventions. Manual hyperinflation with or without expiratory rib-cage compression was performed for 5 min before endotracheal suctioning. Respiratory mechanics and hemodynamic variables were measured 5 min before (baseline) and then 5 and 20 min after the interventions. Arterial blood gases were determined 5 min before (baseline) and 20 min after the interventions. Secretion clearance was measured as sputum weight. The two measurements were obtained on the same day.

RESULTS. No significant differences were observed in gas exchange and secretion clearance between the two interventions ($p > 0.05$). In each case, static lung compliance and tidal volume improved significantly at 5 min post-intervention ($p < 0.01$), whereas at 20 min post-intervention, only static lung compliance had improved significantly above baseline ($p < 0.01$).

CONCLUSIONS. Our results suggest that the addition of expiratory rib-cage compression to manual hyperinflation does not improve lung compliance, gas exchange, or secretion clearance in mechanically ventilated critically ill patients.

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1212

CARDIAC RESERVE IS A DETERMINANT OF THE RESPONSES TO EARLY MOBILIZATION IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Recently, there has been an interest in mobilization of acutely ill patients who are in an intensive care unit (ICU). In the literature, the major safety issues while mobilizing critically ill patients has been outlined. Cardiac reserve [(CR) (% of age predicted maximal heart rate)] and respiratory reserve [(RR), ratio of partial pressure of oxygen in arterial blood to the inspired fraction of oxygen (PaO_2/FiO_2)] are the important factors that can affect the ability to tolerate the mobilization. Patient who has RR more than 300 and CR lower than 50% is considered to have sufficient reserve to tolerate mobilization [1,2].

OBJECTIVES. The aim of this study was to compare the effects of mobilization on respiratory and hemodynamic parameters in patients with sufficient and insufficient respiratory and/or cardiac reserve.

METHODS. Mobilization events are divided into two groups (sufficient, insufficient) according to the pre-mobilization CR (sufficient, <50%; unsufficient, >50%) and RR (sufficient, >300; insufficient, <300). Heart rate (HR), systolic/diastolic/mean arterial blood pressure (SBP, DBP, MABP), respiratory rate (RsR) and percutaneous oxygen saturation (SpO_2) were recorded from the monitor. Respiratory and hemodynamic parameters were collected just prior to the mobilization, just after the completion of the mobilization when the patient had been returned the supine position and 5 min of the recovery period and compared between the groups.

RESULTS. A total of 87 abdominal surgery patients (47 male, 40 female) received 113 mobilization treatments in ICU. The mean age was 60.1 years, mean body mass index (BMI) was 24.9 kg/m^2, mean APACHE II score was 20.5 and mean ICU stay was 7.3 days. Mobilization events included 88 (78%) sitting on the edge of the bed, 12 (11%) standing, 13 (11%) walking to chair and sitting in the chair. 85% (96) of mobilization events had insufficient RR and 15% (17) of mobilization events had sufficient RR. 74.3% (84) of mobilization events had insufficient CR and 25.7% (29) of mobilization events had sufficient CR. All respiratory and hemodynamic parameters were found similar in sufficient RR and insufficient RR group at all stages of the mobilizations ($p > 0.05$). SpO_2 was higher, while HR and RsR was lower at all stages in sufficient CR group compared to insufficient CR group ($p < 0.05$).

CONCLUSIONS. Resting HR and CR may affect the safety of mobilization, for this reason it is important to consider respiratory and hemodynamic parameters prior to and while mobilizing the ICU patients.

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1213

RESPIRATORY AND HEMODYNAMIC RESPONSES TO MOBILIZATION OF THE CRITICALLY ILL OBESE PATIENTS

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INTRODUCTION. Obesity is a chronic disease and a major health problem. Obesity in critically ill patients is associated with a prolonged duration of mechanical ventilation and intensive care unit (ICU) length of stay [1].

OBJECTIVES. The aim of this study was to investigate the effects of mobilization on respiratory and hemodynamic parameters in the critically ill obese patients.

METHODS. Extubated critically ill obese patients [body mass index (BMI) > 30.00 kg/m^2)] were included as soon as their cardiorespiratory stability allowed mobilization protocol. Mobilization was defined as sitting in the bed, sitting on the edge of the bed, standing, walking to chair and sitting in the chair. Heart rate (HR), systolic/diastolic/mean arterial blood pressure (SBP/DBP/MABP), respiratory rate (RR) and percutaneous oxygen saturation (SpO_2) were recorded from the monitor. Respiratory and hemodynamic parameters were collected just prior to the mobilization (supine position), just after the completion of the mobilization when the patient had been returned the supine position and 5 min of the recovery period. All parameters were compared with initial values. The ratio of partial pressure of oxygen in arterial blood to the inspired fraction of oxygen (PaO_2/FiO_2) was calculated from the arterial blood gas samples before and after the mobilization.

RESULTS. A total of 31 obese patients (15 male, 16 female) received 37 mobilization treatments in ICU. The mean age was 63.3 years, mean BMI was 32.2 kg/m^2. Mobilization events included 26 (70%) sitting on the edge of the bed, 3 (8%) standing, 8 (22%) walking to chair and sitting in the chair. Any deterioration in clinical status was occured during the mobilization. RR increased significantly after the completion of the mobilization compared to initial values ($p < 0.05$). SpO_2 increased significantly and the all other parameters were similar ($p > 0.05$) after the 5 min of the recovery period compared to initial values. Mobilization resulted in a significant increase in PaO_2/FiO_2 ratio ($p < 0.05$).

CONCLUSIONS. Early mobilization in ICU promotes respiratory reserve in obese patients. Mobilization can be performed safely patients by providing cardiorespiratory parameters continuously monitored in order to prevent adverse effects in critically ill obese patients.

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1214

BENEFICIAL EFFECTS OF RESPIRATORY PHYSIOTHERAPY IN CRITICALLY ILL PATIENTS VENTILATED FOR MORE THAN 48 H: A RANDOMIZED, CONTROLLED TRIAL

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INTRODUCTION. The use of respiratory therapy for patients with a variety of lung disease is a standard in medical care [1], including in the intensive care unit (ICU) setting [2]. In this context, it is widely accepted the routine use of physical therapy in several situations in the intensive care, such as the care of critically ill patients not requiring ventilatory support, assistance during the postoperative recovery and the assistance to critically ill patients requiring ventilatory support [3]. At present definitive recommendations cannot be made regarding the use of respiratory physiotherapy for decreasing relevant clinical outcomes in critical ill patients requiring mechanical ventilation.

OBJECTIVES. This study aimed to determine the impact of providing chest physiotherapy on the duration of mechanical ventilation, intensive care length of stay, intensive care and hospital mortality in mechanically ventilated patients.

METHODS. Single-centre, randomized, controlled trial in a university hospital general intensive care unit (ICU). Were included in the study 139 patients aged more than 18 years, admitted to the ICU needing mechanical ventilation for longer than 48 h. Physiotherapists provide group intervention (P) with the intensity and frequency of therapy they felt appropriate based on their assessment of the likely treatment benefit. Control patients (group C) only received suctioning, decubitus care and general mobilization.

RESULTS. Primary outcomes were ICU and hospital mortality regardless of the cause of death. Secondary outcomes were length of ICU and hospital stay, length of mechanical ventilation, weaning and extubation failure. Patients in the P group more frequently achieved parameters to start weaning, but there were no significant differences between P and C groups on weaning and extubation failure, length of mechanical ventilation and length of ICU stay. There was fewer hospital, but not ICU, mortality in the P group.

CONCLUSIONS. We demonstrated that respiratory physiotherapy decrease hospital mortality and suggest that this effect was, in part, secondary to the effect of the intervention on weaning from mechanical ventilation.

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Short and long-term outcomes after ICU discharge: 1215–1228

1215

INCIDENCE AND CONSEQUENCES OF COGNITIVE IMPAIRMENTS AFTER CRITICAL ILLNESS

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INTRODUCTION. Critical illness can cause diverse cerebral dysfunctions ranging from unconsciousness to minor cognitive impairments (MCI). Severe cerebral dysfunction, as delirium, is known to affect outcome after critical illness but it is uncertain whether minor impairments affect mortality or morbidity [1].

OBJECTIVES. The primary aim of this study was to estimate the incidence of MCI in a group of general ICU survivors immediately after ICU stay and three and 12 months after discharge. Secondary we wanted to explore if type of cerebral dysfunction after ICU discharge affected mortality and morbidity.

METHODS. Patients admitted to our general ICU were included prospectively. Inclusion criteria: age >18 years, ICU stay >24 h. Exclusion criteria: Previous or present cerebral damage or disease and drug/alcohol abuse. Patients without delirious symptoms were screened with Mini Mental State Examination (MMSE). Patients with MMSE > 24 were examined neuropsychologically with Cambridge Neuropsychological Test Automated Battery (CANTAB) to investigate for MCI. The group was neuropsychologically assessed at 1–2 weeks, 3 and 12 months after ICU discharge.

RESULTS. We included 80 patients. 11/80 (14%) were delerious and 14/80 (18%) were not delerious but had MMSE < 24 after ICU stay. Of the 55 patients with MMSE ≥24, 28 were possible to classify as having MCI or not. 18/28 (63%, 95% CI: 45–83%) were found to have a MCI after ICU discharge. On 3 and 12 months these numbers were respectively: 11% (95% CI: 0–20%) and 10% (95% CI: −1 to 21%) There was an increased risk of both death and being institutionalised at both 3 and 12 months regarding delirious patients and patients with MMSE < 24 compared to patients with MMSE > 24. No such differences were found regarding patients with or without MCI. (Tables 1 and 2).

TABLE 1 ODDS RATIO OF DEATH

Cerebral function at ICU discharge	Death 3 months		Death 12 months	
	OR	95% CI	OR	95% CI
MMSE > 24 (55/80)	1	–	1	–
Delirious (11/80)	**61.9**	**4.5–860.1**	**24.3**	**3.8–158.4**
MMSE < 24 (14/80)	**19.3**	**1.1–335.6**	**7.8**	**1.3–47.8**
No MCI (10/28)	1	–	1	–
MCI (18/28)	NA	NA	0.06	0.001–3.6

TABLE 2 ODDS RATIO OF BEING INSTITUTIONALIZED

Cerebral function at ICU discharge	Institution 3 months		Institution 12 months	
	OR	95% CI	OR	95% CI
MMSE > 24 (55/80)	1	–	1	–
Delirious (11/80)	**13.4**	**2.3–77.5**	**443.0**	**10.4–18798**
MMSE < 24 (14/80)	**8.5**	**1.6–44.9**	**138.2**	**1.1–18075**
No MCI (10/28)	1	–	1	–
MCI (18/28)	5.4	0.5–62.5	NA	NA

CONCLUSIONS. The incidence of MCI after critical illness is high on discharge but drops on 3 and 12 months after. Severe cognitive impairments affect mortality and morbidity, but minor cognitive impairments do not.

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MID-TERM SURVIVAL OF PATIENTS UNDERGOING CARDIAC SURGERY

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INTRODUCTION. Evaluation of outcomes of patients undergoing cardiac surgery is a useful tool to measure the quality of care.

OBJECTIVES. This study analyzes mid-term survival and risk factors associated with survival of patients undergoing cardiac surgery in Son Dureta hospital.

METHODS. 1938 patients were consecutively operated from November 2002 to December 2007. Patients who were discharged alive from hospital were followed until December 2008. We did Kaplan–Meier survival analysis and logistic regression study of variables associated with mid term mortality.

RESULTS. In-hospital mortality was 1.96% (95% CI: 1.36–2.60%). Information was available on 1,844 (97%) of 1,900 patients who survived until hospital discharge. At the end of the follow-up period, observed mortality was 6.5% (CI 95%: 5.4–7.7%). Survival probability at 1, 3 and 5 years of follow-up was 98, 94 and 90%, respectively. The mean time of follow-up was 3.2 years (range 0.01–6.06). Patients ≥70 years showed a lower survival rate than patients <70 years of age (log rank < 0.0001). Age ≥70 years, history of severe ventricular dysfunction (EF <30%), diabetes mellitus, preoperative anemia and hospital stay were independently associated with mid-term mortality.

CONCLUSIONS. Mid-term survival of patients alive after hospital discharge was very satisfactory. Mid-term mortality varied according to age and several preoperative chronic diseases.

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1217

FAMILY RECEPTION, INFORMATION AND PARTICIPATION TO CARE IN INTENSIVE CARE UNITS: A FRENCH SURVEY ON PRACTICES AND OPINIONS OF CAREGIVERS

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OBJECTIVES. To investigate the modalities of family reception, information and participation to care in intensive care units (ICU) in France; and to test the agreement of caregivers with policies and their opinion on purposed modifications.

METHODS. A closed-ended questionnaire was developed by the Nurse congress commission of the Société de Réanimation de Langue Française (SRLF). An invitation to complete it online was sent by email to caregivers registered on the SRLF push-list. Results were analyzed by ICU or by respondent.

RESULTS. 731 caregivers working in 263 ICUs completed the questionnaire (65% were nurses, 24% were doctors, 9% were nurse's aides, 86% worked in adult ICUs and 14% in pediatric ICUs). 7% of adult ICUs (n = 222) had unrestricted policy but 58% had a visiting time of less than 4 h per day. At the opposite, 59% of pediatric ICUs (n = 41) had unrestricted policies. 63% of the respondents working in ICUs with a visiting time <4 h per day considered very useful or essential to enlarge visiting periods but 29% of them considered this enlargement as unhelpful. At the opposite, 9% of the respondents working in ICUs with unrestricted policy found very useful or essential to reduce visiting periods. 81% of caregivers working in ICUs with unrestricted policy but only 35% of caregivers working in other ICUs thought that an unrestricted policy was able to improve often or systematically the relations with families. Moreover, only 8% of caregivers working in ICUs with unrestricted policy but 46% of caregivers working in other ICUs thought that an unrestricted policy disturbs the organization of care. 96% of respondents found very useful or essential to give information in a dedicated room whereas it was often or systematically done in only 52% of ICUs. Identically, 97% of respondents found very useful or essential to give information to proxies with the patient's nurse whereas it was often or systematically done in only 54% of ICUs. Some cares were often or systematically programmed for family participation in 56% of pediatric ICUs but in only 0.5% of adult ICUs. Indeed, proxies often or systematically participated in nursing in 66% of pediatric ICUs but never in adult ICUs. At the opposite, proxies often or systematically participated in tracheal aspirations in only 5% of pediatric ICUs and in 0.1% of adult ICUs.

CONCLUSIONS. More than half of respondent's adult ICUs are closed but caregivers working in ICUs with unrestricted policy perceive it favorably. Some improvements are also expected by caregivers on the use of dedicated rooms for information and on the participation of nurses in meetings with families. Finally, participation of families to care is not a practice of French adult ICU caregivers.

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"RESIDUAL" SYMPTOMATOLOGY FOLLOWING INTENSIVE CARE: STUDY FROM 1 YEAR AFTER DISCHARGE

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OBJECTIVES. To evaluate which symptoms patients may exhibit following discharge from ICU and their relation to the length of time spent in the unit as in-patient.

METHODS. Included: Patients with dysfunction of two or more organs in the first 24 h, admitted and discharged from ICU during 2008. Excluded: neurocritical and politrauma patients. Contact 1 year following discharge; questions were asked concerning symptoms related to a period in intensive care that presented following discharge and which were not present prior to admission. In the case that the patient was not contacted, the next of kin was asked.

RESULTS. 154 patients included. General characteristics during admission to ICU: 63% male; age 60.2 ± 17.5 years; SOFA* 7 ± 2.8; APACHE** II 16.8 ± 6.4; APACHE** IV 57 ± 18.8; length of stay in ICU: 5.1 ± 28.4 days; 42.9% were on invasive mechanical ventilation and 17.5% on non-invasive mechanical ventilation. Data collection was carried out over 18 ± 4.4 months, on average 19 months (range: 12–26 months). 18.2% (28 patients) had died at the time of contact. The person contacted was the patient in 33.3% of the cases, the spouse in 13.7% and immediate family (patient's parent/child/sibling) in 43.1% of the cases. 46.6% had difficulty sleeping following discharge from ICU with an average time since discharge of 10.5 ± 8.9 months; 51.1% suffered feelings of sadness and difficulty in finding enjoyment which had persisted for 8.7 ± 8.1 months; 30.3% had experienced difficulty in concentrating over an average of 9.3 ± 8.8 months; 28.2% had suffered some form of memory loss after discharge over an average period of 8.9 ± 8.6 months; 76.5% presented with asthenia over an average of 10.8 ± 8.3 months; 64.7% had arthromyalgia over a period of 12.6 ± 8.4 months; 35.3% had experienced changes in appetite over an average of 6.6 ± 7 months; 43.3% had changes in intestinal habit over an average of 7.78 ± 9 months; of which 64.3% had diarrhoea, 30.4% constipation, and 5.4% both symptoms; 18.8% presented with headache over a period of 12.9 ± 9.2 months; 15.2% had tremors, that had not previously been present, over an average of 12 ± 7.3 months; 12.8% had experienced reduced vision, over an average period of 16.5 ± 7.1 months; 10.7% presented with speech/language problems, over an average period of 14.6 ± 8.6 months; 14.5% exhibited newly presenting changes in micturition, over 16 ± 7.7 months. Another less frequently occurring symptom was loss of hearing (1.3%).

CONCLUSIONS. Severely ill patients that are admitted to ICU frequently present with "residual" symptomatology following discharge, most notably arthromyalgia and asthenia. Many of these conditions persist for months.

* SOFA = Sepsis-related Organ Failure Assessment

** APACHE = Acute Physiology and Chronic Health Evaluation

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THE DISCHARGE REVISED ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVALUATION SCORE AS A PREDICTOR OF IN-HOSPITAL DEATH AND READMISSION AFTER DISCHARGE FROM SURGICAL INTENSIVE CARE UNIT

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INTRODUCTION. Intensive care unit (ICU) readmission rates range from 3 to 12%, in spite of initial recovery from critical illness. Previous researches report that the Revised Acute Physiology and Chronic Healthy Evaluation (APACHE II) score at either admission or discharge is an important predictor for readmission after ICU discharge. However, there are a few papers concerning the association of discharge APACHE II score with readmission after discharge from surgical intensive care unit.

OBJECTIVE. We compared the ability of the discharge APACHE II score with that of the admission APACHE II score in predicting readmission, especially early readmission within 48 h, after discharge from ICU.

MATERIALS AND METHODS. A retrospective cohort study and a review of patient records for all patients admitted to the 32-bed tertiary surgical intensive care unit (SICU) from October 2007 to March 2010 were conducted.

RESULTS. Of 4257 adult (≥18 years) admitted to the SICU, 271 (6.4%) were readmitted to the SICU during the same hospital stay. Age (OR 1.01, 95% confidence interval [CI] = 1.00–1.02, P = 0.025), male (OR 1.36 [1.04–1.78], P = 0.007), admission route from other ICUs(OR 1.78 [1.08–2.94], P = 0.024), both admission (OR 1.04 [1.02–1.06], P = 0.000)and discharge APACHE score (OR 1.04 [1.02–1.06], P = 0.001)and length of stay in SICU (OR 1.04 [1.02–1.05], P = 0.000) were significant independent factors in predicting readmission. Readmitted patients had longer LOS and higher mortality than those not readmitted (55 ± 75 vs. 15 ± 23 days, 13% vs. 0.5%, P = 0.000 respectively). With regard to early readmission within 48 h, the discharge APACHE II score, not the admission APACHE II score, was the only significant predictor (OR 1.06 [1.00–1.12], P = 0.046)

CONCLUSION. This study showed that both discharge APACHE II score and admission APACHE II score are useful predictors for readmission after ICU discharge, but discharge APACHE II score is only independent factor in predicting early readmission within 48 h after ICU discharge.

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1220

COPING STRATEGY AND PERCEIVED HOPELESSNESS ARE IMPORTANT FOR HEALTH RELATED QUALITY OF LIFE AFTER CRITICAL ILLNESS

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INTRODUCTION. Health related quality of life (HRQoL) is decreased in former ICU patients. In research outside the intensive care field it is well known that the psychosocial factors, coping strategies and perceived hopelessness affect HRQoL. However, the influence of coping and hopelessness on HRQoL after intensive care is unknown.

OBJECTIVE. The aim of this study was to examine how coping strategies and perceived hopelessness among former ICU patients compares to corresponding in a reference group. We also evaluated the effect of coping and hopelessness and ICU related factors on HRQoL.

METHODS. Prospective, multicenter study in three mixed ICU's in Sweden. Patient demographics, length of stay, APACHE II score, reason for admission and time on ventilator were collected for all adult patients. Questionnaires, including the coping instrument Pearling-Schooler Mastery Scale (PMS), the 2-item hopelessness scale, SF-36, demographic data and previous illnesses were sent 6 months after discharge from hospital to the patients. The reference group (n = 6,093) was a random selection of persons from the same catchment area as the study patients.

RESULTS. 780 (59%) ICU-patients, 18–74 years, returned the questionnaires. The patients reported significantly lower mean scores in coping 13.6 (SD 4.6, $p < 0.001$) and higher perceived hopelessness 2.3 (SD 2.1, $p = 0.006$), compared to the reference group 22.6 (SD 3.5) and 2.1 (SD 2.1), respectively. For the ICU patients the SF-36 physical summary component PCS was significantly ($p < 0.05$) affected by pre-existing disease (Beta Coefficient (β): 8.7), hopelessness (β1.3), reason for admission (β1.2), and length of stay in ICU (β 0.006). The mental component score MCS was significantly ($p < 0.05$) affected by pre-existing disease (β 2.3), hopelessness (β: 2.2), and coping (β:1.0). For the reference group coping and perceived hopelessness did not significantly affect measures of HRQoL.

CONCLUSIONS. This study indicates that coping strategies and perceived hopelessness are important for the HRQoL of previous ICU patients. However, the magnitude of these effects are smaller than that of pre-existing diseases.

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1221

IS DEPRESSION A RISK FACTOR FOR MORTALITY IN MEDICAL ICU PATIENTS?

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INTRODUCTION. Mortality on a medical intensive care unit (ICU) is estimated to occur in about 25% of patients. Its association with age, severity of illness and comorbidities is well established. For other diseases like coronary artery disease it has been shown that pre-existing depression is a risk factor for worse outcome. The role of depression regarding the outcome of ICU patients has not been investigated so far. We studied the association between pre-existing depression and mortality in medical ICU patients and present preliminary data of this ongoing study.

OBJECTIVES. Assessment of a possible association between mortality of ICU patients and prevalent depressive mood at time of ICU admission. The primary endpoint was 28-day mortality.

METHODS. Prospective cohort study. All patients admitted to a medical 8-bed ICU in a university hospital, older than 18 years, were eligible. Postoperative patients and patients who had an expected length of stay below 48 h (survey) were excluded. Patients whose cognitive function allowed appropriate comprehension and response answered the hospital anxiety and depression scale (HAD). Prevalent depressive mood at admission was defined by a score ≥8 in the depression dimension. All other patients were assessed by observer rating by next-of-kin. In this case the Hammond scale, a validated instrument for observer rating of depressive mood (cut-off ≥4), and a modified version of the HAD for observer rating (cut-off ≥10) were used. In addition APACHE II, SAPS II, SOFA, age, sex, comorbidities, reason for admission, length of ICU stay and ventilator days were recorded.

RESULTS. By now 173 patients had complete follow up data. Of these patients 53 (31%) were classified to have depressive mood at ICU admission. In total 46 patients had died by day 28 (27%). The 28-day mortality was 40% (21/53) in patients with depressive mood and 21% (25/120) in patients without ($p = 0.01$). Patients with and without depressive mood did not differ with respect to age, sex, APACHE II, SAPS II or SOFA score at admission. Multiple logistic regression analysis with 28-day mortality as the dependent variable revealed that prevalent depressive mood at the time of ICU admission was an independent risk factor for mortality (Table 1).

CONCLUSIONS. Pre-existing depressive mood is an independent risk factor for mortality in medical ICU patients.

TABLE 1 MULTIPLE LOGISTIC REGRESSION ANALYSIS WITH DAY 28-MORTALITY AS DEPENDENT VARIABLE

	OR	95% CI	p
Age	1.05	1.02–1.08	0.003
Depressive mood	2.2	1.00–4.9	0.05
APACHE II	1.003	0.97–1.08	0.38
SOFA	1.23	1.09–1.39	0.001

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LABORATORIAL DATA AT THE ICU DISCHARGE AS IN-HOSPITAL OUTCOME PREDICTORS

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INTRODUCTION. Some classical post-ICU discharge predictors of death are described, such as age, severity of disease and level of nursing care [1]. Besides these factors, some laboratorial data at ICU discharge are potential predictors of post-ICU death.

OBJECTIVES. The aim of this study was to investigate whether standard base excess (SBE), pH, lactate, hemoglobin level, creatinine, platelets, leukocytes and albumin at the ICU discharge as well as the 25% decrease on C-reactive protein concentrations (CRP > 25%) from the day pre-ICU discharge to the day of ICU discharge may be useful predictors of in-Hospital outcome.

METHODS. Patients discharged from the ICU after at least 72 h of stay were retrieved from our prospective collected data base. A multivariate analysis was performed using a backward-LR binary logistic model taking in-hospital death as a dependent variable and the cited data as independent variables.

RESULTS. 396 patients were retrieved. The average age was 49 ± 19 years old, mean APACHE II score was 17 ± 8, and the main causes of admission were septic syndromes and respiratory failure. The in-hospital mortality after ICU discharge was 18%. The ICU length of stay was 9 ± 9 days. At the time of ICU discharge pH was 7.41 ± 0.04, SBE was −0.3 ± 4.0 mmol/L, lactate was 1.9 ± 1.0 mmol/L, hemoglobin 9.6 ± 2.0, creatinine was 1.3 ± 1.46 g/dL, albumin was 2.68 ± 0.64 g/dL, platelets was 280,645 ± 166,100/mm^3, leukocytes was 10,795 ± 8,769 cells/mm^3 and the number of patients who lowered CRP at least 25% were 159 (40%). The multivariate analysis resulted in the follow independent in-hospital death predictors: APACHE II (OR 1.070, 95% CI 1.034–1.107, $p = 0 < 0.001$), SBE (OR 1.079, 95% CI 1.012–1.151, $p = 0.021$), Lactate (OR 1.033, 95% CI 1.007–1.059, $p = 0.011$), Hemoglobin (OR 0.857, 95% CI 0.737–0.996, $p = 0.044$), Albumin (OR 0.483, 95% CI 0.290–0.805, $p = 0.005$) and CRP > 25% (OR 0.480, 95% CI 0.260–0.890, $p = 0.020$).

CONCLUSIONS. This study demonstrated that SBE, Lactate, Hemoglobin and Albumin concentrations on the day of ICU discharge are independent predictors of in-hospital mortality. Moreover, the reduction on CRP levels above 25% in the last 24 h of ICU stay is a strong predictor of better in-hospital clinical outcome. We suggest that these variables together with the clinical judgment may be taken into account on the ICU discharge decision process.

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EARLY PREDICTIVE FACTORS FOR INTENSIVE CARE UNIT READMISSION

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INTRODUCTION. Readmissions to the intensive care unit (ICU) are usually associated with increased morbidity and mortality, and they may evidence the quality of patients' care. The risk for ICU readmission varies across studies, and is generally analyzed just before ICU discharge, leading to deviation of ICU team and patients' daily goals. Early prediction may improve the care for patients in risk for ICU readmission, and help developing mechanisms for its prevention.

OBJECTIVES. To analyse risk factors for readmission in intensive care unit looking at the first 24 h data after unit admission.

METHODS. The first intensive care unit admission of patients was analyzed from January to December 2009 in a medical–surgical unit. Readmission to the unit was considered those during the same hospital stay or within 3 months after intensive care unit discharge. Deaths during the first admission were excluded. Demographic data, acute illness and comorbidity prognostic scores, and use of mechanical ventilation were submitted to uni and multivariate analysis for readmission. Numeric variables were expressed as median or percentage.

RESULTS. The unit admitted 1,394 patients during 2009. Sixty-six patients died in the first ICU admission and were excluded. The readmission group was composed by 173 patients, while 1,155 patients were not readmitted. The lead time between the index admission and readmission was 7 days, and 19 (11%) died in the hospital. Patients readmitted at least once to ICU demonstrated the following different characteristics compared to control group: older age: 74 versus 68 years, $P < 0.001$; admission for respiratory insufficiency or sepsis: 31 versus 15%, $P < 0.001$; medical admission: 52 versus 29%, $P < 0.001$; higher SAPS II score: 31 versus 25 points, $P < 0.001$; Charlson index: 1 versus 0 points, $P < 0.001$; active neoplasia: 19 versus 12%, $P = 0.02$; SOFA score on ICU day 1: 2 versus 1 point, $P < 0.001$; length of ICU stay: 3 versus 2 days, $P < 0.001$. After the multivariate analysis for the risk of ICU readmission, higher age (odds 1.02 [CI 95% 1.00–1.03]), type of ICU admission (medical, odds 2.11 [CI 95% 1.40–3.17]), SOFA score (odds 1.18 [CI 95% 1.06–1.31]) and admission for respiratory insufficiency or sepsis (odds 1.71 [CI 95% 1.08–2.69]) were early associated to readmissions in intensive care unit.

CONCLUSIONS. Age, medical admission, SOFA score and respiratory- and/or sepsis-related admission are early associated with increased ICU readmission risk.

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IS HEALTH RELATED QUALITY OF LIFE AFFECTED BY AN EARLY (<3 YEARS) DEATH AFTER ICU CARE AS COMPARED WITH SURVIVING ICU PATIENTS?

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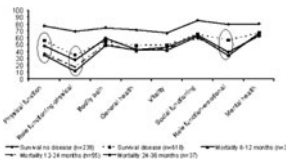
INTRODUCTION. There has been a growing interest in patient perceived health related quality of life (HRQoL) among survivors of critical illness. However, little information is available regarding patient perceived HRQoL among the patients dying within a restricted period post ICU.

OBJECTIVES. The aim of this study was to examine patient perceived HRQoL in former ICU patients that die in the period from 6 month up to 3 years after discharge from intensive care unit and the hospital.

METHODS. Prospective, multicenter study in three mixed ICU's in Sweden. Questionnaires, including HRQoL (SF-36), demographic data and previous illnesses, were sent out six, 12, 24 and 36 months after discharge to all former adult ICU patients. Data for this study were only collected among those dying before the 36 months post-ICU follow-up.

RESULTS. Of the 980 patients who returned the questionnaires 123 (12.6%) died, 31 (25.2%) between 6 and 12 months, 55 (44.7%) between 12 and 24 months, and 37 (30.1%) between 24 and 36 months. The most frequent admission diagnoses were respiratory problems n = 36 (29.3%) and gastrointestinal diseases n = 33 (26.8%). Examining HRQoL in the former ICU patients the following observations were made: (see Fig. 1). A pronounced and quantitatively large decrease in HRQoL is seen for the surviving patients with pre-existing disease as compare to the previously healthy survivors. Although already at a very low value further decreases in HRQoL for the patients dying before 3 years post ICU is significantly less as compared to the ICU patients with pre-existing disease that survives. The decrease is mainly in physical function, role physical function and role emotional function (marked in the figure).

CONCLUSIONS. Yes, health related quality of life is extensively affected, mainly in the dimensions physical function, role physical function and role emotional function. Importantly, in these two affected physical dimensions a shorter time to death increases such a decrease. The finding further stresses the importance of pre-existing diseases for the final HRQoL outcome of former ICU patients.



Mortality and HRQoL

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MORTALITY AFTER ICU DISCHARGE

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OBJECTIVE. To evaluate mortality in ICU patients after discharge.

MATERIAL. Included: Patients admitted to a polyvalent ICU during 2007 and 2008. Only in a few cases the coronary artery disease patients were admitted. Excluded: patients for elective surgery and no-complicated arrhythmias that were admitted just for implantation of a permanent pacemaker. Were evaluated 1,377 patients. Were mechanical ventilated the 84.8% of them.

METHODS. Our Unit Data Base was used. The discharge letters and the Hospital Admission Service Registry.

RESULTS. 1377 patients were included and their stay in ICU was 8.42 ± 12.59 days with a NEMS of 34.6 ± 10.8 and APACHE II score of 16.2 ± 9.1.

From the overall, 959 patients (69.6%) were discharged to the hospital ward, APACHE II 14.0 ± 7.8, hospital, stay 8.5 ± 12.5 days. 87 patients were transferred to other hospitals (6.3%). 331 patients died during their stay in ICU (24%).APACHE II 24.7 ± 8.7. NEMS 42.9 ± 8.5. Admittance time to ICU 8.0 ± 12.8. 113 patients died on the ward. (11.8% of cases discharged to the ward from ICU. Overall mortality was 32.2% (ICU mortality plus mortality on the ward). 40 critically ill patients died in the first 72 h after the transfer to the ward. ICU stay 13.3 ± 20.8 days (median 6.5) APACHE II 23.5 ± 11.0. Between the 4th and 7th day 22 patients died. ICU stay 19.1 ± 28.9 days (median 8.5) APACHE II 21 ± 9.4. On the hospital ward 51 patients died between 7 and 203 days. ICU stay 12.7 ± 15.6 days (median 6.0) APACHE II 18.3 ± 7.3. A predictive score was not used at the time of discharge despite that in the discharge letter was a note about the inviability of some patients. This note was present in 12 patients (19.3%) of the 62 patients who died in the first 7 days).

CONCLUSIONS. Our mortality after ICU discharge is 11.8%, intermediate amount some papers published in our country (23.8–3.5%). It would be useful to definite the case-mix of every ICU. It take our attention the high mortality rate amount patients who are discharge from the ICU in the first 72 h, 4.17% (6.4% a week), we do not know if the reason was the discontinuity of the clinical imput from us or on the other hand because it was prolonged the ICU support to non-viable patients.

* APACHE = Acute Physiology and Chronic Health Evaluation

** SOFA = Sepsis-related Organ Failure Assessment

** MOF = Multi Organ Failure

1226

CAUSES, RISK FACTORS AND OUTCOMES OF PATIENTS READMITTED TO A TERTIARY UNIVERSITY HOSPITAL INTENSIVE CARE UNIT IN DUBLIN

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INTRODUCTION. Despite initial recovery from critical illness requiring ICU admission, many patients remain at risk of subsequent deterioration and death [1]. Recent studies have shown readmission rates ranging between 4 and 7% [2]; this population had mortality rates six times higher and were eleven times more likely to die in hospital [1].

OBJECTIVES.

1. To calculate the readmission rate in our mixed ICU unit over a 6 months period
2. To identify risk factors associated with readmission into the ICU
3. To study the outcomes of these readmissions

METHODS. a retrospective observational study, data was collected from an ICU computer database (Metavision) and analysed manually

RESULTS. The total number of admissions in this period was 365, average patient age was 57 ± 17 with 52.4% being males. Readmissions constituted 10.5% of the total admissions with 23.8% of those readmitted within 24 h of their initial discharge. 40% of the initial discharges from the unit were made out of hours i.e. unplanned, presumably due to heavy demand on beds. Readmissions were particularly associated with patients discharged to surgical wards 23.8% and the hepatobiliary HDU 28.6%, the latter might reflect the proportion of that particular patients population received. 52.4% of the readmissions required to stay 72 h or less in ICU. The overall mortality of the patients requiring more than one admission in this 6 months period was 57.1%.

CONCLUSIONS. There is an urgent need for expanding ICU services in our hospital, i.e. extra beds, staff, outreach teams, etc in addition to investing in nursing capacity building especially in surgical wards.

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1227

THE IMPACT OF INTENSIVE CARE UNIT ATTENDANCE ON HEALTH-RELATED QUALITY OF LIFE

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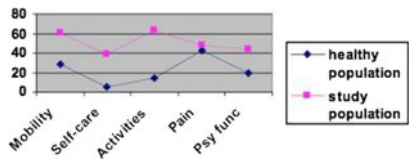
INTRODUCTION. Health-related quality of life (HRQOL) has been recognized as a relevant outcome measure for patients requiring ICU care.

OBJECTIVES. The purpose of the present study was to examine the relationship between the HRQOL of these patients and several clinical factors.

METHODS. A prospective cohort of patients over 18 years old, admitted in our surgical ICU for over 48 h, between October 2002 and June 2008 were studied. Demographics data, type of admission, neoplasia, SOFA, ASA, APACHE II scores, sepsis, renal failure, mechanical ventilation, *critical* illness *polyneuropathy*, psychiatric history, blood product transfusions, etc were recorded. EuroQol 5D questionnaire was used to measure the quality of life a year after discharge from the unit. 501 patients met the inclusive criteria, 198 died during the follow-up year after ICU outcome. 303 patients survived, 160 of them completed the questionnaire by phone. Data were analysed using the SPSS v.15. The t student statistical analysis and Chi-square test was used.

RESULTS. HRQOL in survivors was significantly worse compared to the healthy population ($p < 0.001$), except pain dimension**.**



HRQOL

Statistical analysis shows the relationship between the dimensions and the following factors; sepsis, renal failure, SOFA (first and second day score), *critical* illness *polyneuropathy*, mechanical ventilation, sedation time, previous psychiatric history and blood products transfusions ($p < 0.05$).

RELATION DIMENSIONS/FACTORS

Mobility	Psychiatric history	Renal Failure	
Self care	Sepsis	Polyneuropathy	
Activities	Blood transfusion	Mechanical ventilation	Sedation
Pain	SOFA score	Psychiatric history	Renal failure
Psych function	Polyneuropathy	Renal failure	Mechanical ventilation

CONCLUSIONS. We agree with others studies that compared with the general population, ICU survivors report lower HRQOL. Moreover, a relationship between several factors like sepsis, renal failure, SOFA (first and second day score), *critical* illness *polyneuropathy*, mechanical ventilation, sedation time, previous psychiatric history and blood products transfusions were found in our study population.

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1228

QUALITY OF LIFE IN GENERAL INTENSIVE CARE UNIT SURVIVORS

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INTRODUCTION. With increasing survival after intensive care stay research is focusing on long term outcomes, mental health, health-related quality of life and cognitive outcomes.

OBJECTIVES. To evaluate health-related quality of life and study its determinants in patients discharged from an intensive care unit (ICU).

METHODS. Retrospective analysis of data collected in questionnaires EuroQol5-D by an interview at 6 months after discharge over the last 5 years. Statistics: Pearson's Chi-square, Mann–Whitney, Kruskal–Wallis and Fisher's exact test, significance for $p < 0.05$.

RESULTS. 770 patients were interviewed, 67% were male and 49.5% trauma victims. Only 13.6% of patients had more than 4 years of education. 49.3% were healthy and 65.5% professionally active. 13.9% had a tracheotomy performed in the ICU. 60% had new complaints. Only 39.6% of the professionally active patients resumed their work. The proportion of those reporting moderate to extreme problems in the 5 dimensions studied in EQ-5D test, were: 48% mobility, 35% self care, 62% usual activities, 49% pain/discomfort and 53% anxiety/depression. EQ visual analogue scale and EQ index medians were 60 (IQR 50–80) and 68 (IQR 50–90), respectively. 15% feel worse than in the year before ICU. Men had more complaints regarding mobility, self-care and usual activities. Patients with comorbidities, even if independent in daily activities previously, had significantly more self care limitation and motor disabilities. Women had more complaints regarding pain and discomfort and also anxiety/depression. Those with psychiatric complaints had more pain and discomfort. People with anxiety/depression did not resume their usual activity. The length of stay had a significant relation with depression, complaints about mobility, personal care and usual activities. However, the ICU length of stay only had a statistic relation with the Beck scale and complaints about usual activities. The SAPSII score, had a statistical relation with PTSS, mobility, personal care, usual activities in the EQ-5D. Patients with a tracheostomy had worst quality of life.

CONCLUSIONS. Men showed more functional limitation while women showed more psychological impairment. Patients who were discharged from the ICU rarely return home in the functional level in which they left hospital. The SAPS II score correlates with the changes in the quality of life of the patients.

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Staff work conditions and well-being: 1229–1240

1229

INFECTION RISK FOR NONTUNNELED CENTRAL VENOUS CATHETERS, ACCORDING TO THE PLACEMENT SITE IN ICU PATIENTS

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INTRODUCTION. The use of central venous catheters (CVC) is indispensable in the treatment of hospitalized patients. Infection is one of the most important complications of CVC use. Bacteremia due to CVC is the third cause of nosocomial infection in ICU patients. Although its impact has not been well established, mortality is estimated at 10% and increases in ICU stays at 5–8 days

OBJECTIVES. The aim of our study was to test the hypothesis that there is a difference in infection risk for nontunneled central venous catheters (CVC), according to the insertion site, like subclavian (SCV), internal jugular (JV) or femoral (FV) vein.

METHODS. During a 11 months period, from January 2009 to December 2009, 62 patients admitted to our ICU and included retrospectively to our study. Age (mean) 57.7 years, length of stay (LOS, mean): 11.8 days, APACHE II score (at admission, mean): 16.9. In these patients, a total number of 86 CVC had been used. We looked for the insertion site according to the type of placement as first (1st), second (2nd) and third (3rd) placement We recorded the total number of CVC, the total number of CVC days, the total number and the percentage of CVC according the insertion site and the type of placement and the total number and the incidence of bacteremia due to CVC.

RESULTS. Our data are presented at the table below. We totally recorded 7 episodes of bacteremia (EB) due to CVC according to 687 CVC days, that is 10.13‰

TABLE 1

	Total	1st	2nd	3rd	EB No	EB ‰
SCV No	42 (48.3%)	24 (43.6%)	11 (55%)	7 (63.6%)	2	5.05‰
SCV days	398 (57.9%)	189 (49.8%)	132 (63.47)	77 (77%)		
Mean ± SD	9.47 ± 4.6	8.21 ± 4.6	11 ± 3.7	11 ± 5.5		
JV No	12 (13.9%)	8 (14.5%)	4 (20%)	0	1	16.39‰
JV days	61 (8.8%)	38 (10%)	23 (11%)	0		
Mean ± SD	5.08 ± 3.3	4.75 ± 3.57	5.75 ± 3.09			
FV No	32 (37.2%)	23 (41.8%)	5 (25%)	4 (36.3%)	4	17.54‰
FV days	228 (33.1%)	152 (40.1%)	53 (25.4%)	23 (23%)		
Mean ± SD	7.3 ± 5.74	6.9 ± 3.39	10.6 ± 12.4	5.7 ± 4.64		
Sum CVC No	86	55	20	11	7	10.18‰
Sum CVC days	687	379 (56.1%)	208 (30.2%)	100 (14.5%)		
Mean ± SD	8.08 ± 5.14	7.15 ± 4.1	9.9 ± 6.6	9 ± 5.64		

CONCLUSIONS. According to our data, subclavian vein was the most common insertion site used, especially as 2nd and 3rd placement and was related with the lower incidence of becteremia episodes. Although the risk of placing a CVC for inflection complications is against the risk for mechanical complications, we have to improve our CVC policy, preferring the subclavian or the jugular site of insertion, in order to minimize the infection risk for a nontunneled CVC.

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1230

BURNOUT SYNDROME IN CRITICAL CARE UNIT OF THE UNIVERSITY HOSPITAL

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INTRODUCTION. Burnout Syndrome (BOS) is typified in three dimensions: emotional exhaustion (EE), depersonalization (DP) and the lack of personal achievement (PA). It is a frequent psychopathological syndrome in medical and nursery personal with a prolonged occupational stress.

OBJECTIVES. Objectives for this study were to determinate the frequency and the risk factors associated with BOS. Secondarily, we searched several variables as civil status, age, sex, work seniority as potential risk factors.

METHODS. Inclusion criteria were to work in Critical Care Unit (CCU) the Hospital Clínico Universidad de Chile (HCUCH). This unit included 2 subunits: intensive care unit (ICU), middle care unit (MCU). The MBI® Instrument was applied between April to July of 2009. All staff of CCU were asked to response the instrument. As previously reported, BOS was defined with high EE, high DP and low PA. Risk of BOS was anything of the three dimensions positive for BOS. We gave information on specifics objectives and the schedule of a future intervention programme. For analysis, comparisons were made based on student t test, Chi-square test with Yates corrections or Fisher exact test as corresponded. For all tests we used confidence interval 95% with $p < 0.05$.

RESULTS. A total of 111 MBI® tests that included all sub-units in CCU. This is a 56% of all personal working in the CCU. BOS was found in 8.26% of cases. Women (75%), unmarried (75%), with an average of age 31.9 years old. (23–47 years old) and with a work seniority younger than 5 years (50%). EE is high (31.5%), for nurse and paramedical personals. DP was 22.5 and 31.5% to middle level, for nurse and medical doctor, and low PA in 34% for paramedical personal, with longer work seniority (more than 10 years). Risk factors were female gender, unmarried status, childless, middle aged (23–47 years old) and recent start in the job (stay younger than 5 years).

CONCLUSIONS. BOS incidence in our CCU was within previous observations in Critical Care Unit (8.26%). BOS was most frequently observed in unmarried people, without children in general. It is important to note that AE presentation was high (24.8%), as well as depersonalization (13.2%). Personal achievement was lower around a quarter of the sample. The incidence of BOS risk in our CCU was 47.9%.

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BURNOUT SYNDROME AND QUALITY OF LIFE IN INTENSIVISTS

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INTRODUCTION. Burnout is a prolonged response to chronic emotional and interpersonal stressors on the job, and is defined by three dimensions: exhaustion, cynism (depersonalization), and inefficacy. ICU physicians are exposed to several stress factors and are particularly predisposed to this syndrome.

OBJECTIVE. To describe the prevalence of burnout syndrome among intensivists and its relation to their quality of life.

METHODS. An epidemiological cross-sectional survey conducted to evaluate all adult ICU physicians in Salvador, BA (Brazil), from October to December 2006. The quality of life and burnout syndrome were evaluated respectively by the WHOQOL-Bref instrument and the Maslach Burnout Inventory (MBI). Burnout was classified into low, moderate and high levels for the three studied dimensions, according the MBI classification, and it was defined by the presence of a high level in at least one dimension. The quality of life was evaluated in four domains: physical, psychological, social relationships and environment, graduated from 0 to 100, with higher scores denoting higher quality-of-life.

RESULTS. 297 intensivists were enrolled (88.4% of the eligible population). The mean age was 34.2 ± 6.9 years and 71.7% were male. The mean time since graduation was 10.0 ± 6.7 years. Burnout syndrome was observed in 63.3% ($n = 188$) of intensivists. A high burnout level was observed in 7.4, 22.2 and 33.7%, for three, two and one dimensions, respectively. Moderate to high levels of exhaustion, depersonalization and inefficacy were found in 79.9, 51.0 and 54.8%, respectively. The mean score found in the four domains of quality of life were: physical, 68.0 ± 15.6; psychological, 64.5 ± 14.5; social relationships, 62.0 ± 19.6; environment, 60.0 ± 13.7. Intensivists with burnout syndrome had lower mean scores of quality of life in the physical (75.8 ± 13.8 vs. 63.5 ± 14.7), psychological (72.3 ± 11.3 vs. 59.9 ± 14.0), social relationships (70.6 ± 16.9 vs. 57.0 ± 19.4) and environment (66.4 ± 12.7 vs. 56.3 ± 12.8) domains ($P < 0.001$).

CONCLUSION. Intensivists presented high prevalence of burnout syndrome, which was related to lower quality of life. These data indicate that strategies must be discussed to prevent this syndrome in this population.

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USING NURSING ACTIVITY SCORES (NAS) TO ASSESS NURSING WORKLOAD ON MEDIUM CARE (MC) UNITS

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INTRODUCTION. Medium Care Units lack a validated instrument for assessing nursing workload. In order to target nursing resources effectively and efficiently, it is necessary to determine the average nursing care workload, per patient, per 8 h shift. Once an accurate workload measurement has been calculated, it is then possible to plan in the correct number of FTE's (*full time equivalent*) MC nurses, to achieve the optimum levels of nursing staff. NAS (Miranda et al. [1]) has been successfully used to measure nursing workload on an Intensive Care Unit over a 24-h period. In contrast to Intensive Care, the nursing care workload on MC is not evenly spread over a twenty four period, but tends to vary between shifts.

OBJECTIVES. The aims of this pilot study were (1) To assess the fitness of NAS as an accurate reflection of nursing workload on an MC unit. (2) To determine the nursing work load, per patient, per 8 h shift.

METHODS. Prior to the commencement of the study all thirty one nurses taking part received instruction in the content and registration of NAS. At the end of each 8 h shift, each nurse retrospectively scored their patient(s) using NAS. This consists of a check list containing twenty three items giving a possible score between 0 and 177, where 177 equates to 1.77 *Full Time Equivalent* (FTE) Intensive Care nurse. The NAS were entered in to a database and the average scores, per patient, per shift were calculated. Three hundred patients were retrospectively scored over a 2-month period in October and November 2009. Not all patients were scored on all three shifts as some patients had been transferred out of the unit before shift end. In addition any incorrectly completed forms were discarded and excluded from the study.

RESULTS.

NAS SCORES

Shift	Day	Evening	Night
Number of patients scored	269	214	247
Average NAS score per patient	43.5	43.9	36.4

The NAS did not significantly differ between day and evening shift (43.9 VS 43.5 NS). However on the night shift it was considerably lower (43.9 > 33.6, p < 0.0 5) and (43.5 > 33.6, p < 0.05). The evening shift has one less FTE Medium Care nurse, though the NAS scores did not differ between the two. This finding supports accounts from nurses working on the evening shift reporting that they are understaffed.

CONCLUSIONS. NAS can be used to determine the nursing care workload, per 8 h shift, on a Medium Care Unit. It offers an acceptable, accurate measuring tool enabling nursing staff levels to be adjusted in accordance with the needs of patients.

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1233

DOCTORS' ALERTNESS DURING NIGHT: NOCTURNAL ATTENTIONAL PERFORMANCE (NAP) PILOT STUDY

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INTRODUCTION. Medical errors occur more frequently during the night [1]. At the same time sustained attention deteriorates [2].

OBJECTIVE. To explore attentional performance of doctors on a short-time test during day and night shift as contributing cause of medical errors.

METHODS. This multicenter pilot study included 14 doctors working at (pediatric) intensive care units (ICU). Subjects were randomly assigned to two groups: one was first tested during day, then during night, while the other was tested in reverse order. The *d2 Test of Attention* [3] was used to assess attentional performance. Total performance (Tn-F) score, standardized for age and level of education, was used to express attentional performance. Subjective, 1-to-10 scores were gathered in two questionnaires.

RESULTS. Figure 1 displays standardized total performance scores of 14 doctors. Measured attentional performance showed high intra- and interpersonal variability and did not differ between both shifts ($p > 0.9$). In contrast, doctors expected alertness to be decreased (7.5 ± 1.7 and 6.1 ± 1.7 (mean ± SD) on subjective 1-to-10 scale during day and night shifts, respectively; $p < 0.02$) and the chance of making errors to increase (from 3.3 ± 1.7 to 6.2 ± 1.3 (mean ± SD); $p < 0.01$) during night shifts.

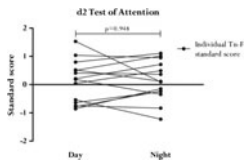

Figure 1

CONCLUSIONS. Physicians working at ICU are aware of the risk of making errors during night shifts. However, we showed that doctors perform equally during night and daytime when confronted with a short-time challenging task. Consequently, a discrepancy between measured attentional performance and expected alertness was observed. These results suggest nocturnal alertness might be comparable to daytime during short-lasting tasks that elicit a high level of stress and motivation (e.g. testing, medical emergency). Further research is needed to elucidate if long-lasting (routine) tasks reflect decreased sustained attention and contribute to medical errors.

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WORK AND HEALTH CONDITIONS OF THE INTENSIVE CARE UNIT PHYSICIANS IN SALVADOR, BRAZIL

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INTRODUCTION. Burnout syndrome is a response to prolonged occupational stress that involves three main dimensions: emotional exhaustion, depersonalization, and reduced personal accomplishment.

OBJECTIVES. The aim of this study was to describe the prevalence of burnout syndrome, socio-demographic characteristics, and working conditions among intensive care physicians in the city of Salvador, Bahia State, Brazil.

METHODS. A cross sectional study investigated of 333 Intensive Care Unit Physicians. Information about doctors' physical health, mental health (evaluation of Burnout syndrome through Maslach Burnout Inventory/MBI), living habits and work conditions was collected in an individual, self-reported, mailed questionnaire.

RESULTS. We studied 297 physicians, the majority of whom were male (70%). Mean age and time since graduation were 34.2 and 9 years, respectively. High levels of emotional exhaustion, depersonalization, and reduced personal accomplishment were found in 47.5, 24.6, and 28.3%, respectively. Prevalence of burnout syndrome, defined as a high score in at least one dimension, was 63.3%, while prevalence was 7.4% for all three dimensions. In conclusion, burnout syndrome was common in this sample of ICU physicians.

CONCLUSION. The prevalence of burnout syndrome high level. The observed work and health conditions point out the need of deep changes in the Intensive Care Unit Physicians work organization.

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COMPLIANCE TO VAP BUNDLES IN A MULTI SPECIALTY ICU-CAN WE ACHIEVE ZERO VAP?

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INTRODUCTION. VAP is the leading cause of death amongst HAI. Hospital mortality of ventilated patients who develop VAP is 46% compared to 32% for ventilated patients who do not develop VAP. VAP prolongs number of ventilator days, ICU stay, and length of hospital stay. The Ventilator Bundle is a series of interventions that, when implemented together, will achieve significantly better outcomes than when implemented individually. Key components are:·Elevation of the Head of the Bed, Daily, Sedation Vacations, Readiness to extubate assessment, Peptic Ulcer Disease ProphylaxiS, DVTProphylaxis

OBJECTIVES. (1) To apply VAP bundles and understand its compliance among nursing staff. To try to achieve a 95% compliance in individual component. (2) Whether increasing compliance leads to decrease in VAP. (3) Is it possible to achieve zero VAP?

METHODS. The study had three phases: (1) Observation phase (January–June 2009) We just observed the incidence of VAP without any application of bundles. (2) Intervention phase (July–September 2009). A lot of effort was done to educate nurse about VAP bundles and its components. The intervention included: (a) Creation of worksheet containing VAP bundle elements and nurse were educate how to fill it. (b) Certificate course were run to educate nurse about the VAP bundle and its benefits. (c) Weekly discussion with nursing in charge and clinical instructors to understand compliance to bundle and problems. (d) Random inspection checks o understand compliance. (e) Orientation class for new joinees by physician intensivist. (f) In service education of vap bundle by clinical instructors. (3) Study phase (October 2009–March 20110). (a) We calculated the overall compliance to bundle and its individual components. (b) We calculated the vap incidence after bundle application. (c) Could we achieve zero vap?

RESULTS. A) (1) Observation phase: The incidence of vap was extremely high in our ICU. It was 11.0 per 1000 ventilator days. (2) Intervention phase: we could decrease the incidence of vap to 8.8 per 1,000 ventilator days. (3) Study phase: We could achieve zero vap. (4) We could achieve 100% compliance to 3 components of bundle viz: head of bed elevation, stress ulcer and DVT prophylaxias. (5) In the study phase we improved upon 2 other components of bundle i.e. sedation vacation and readiness to extubate to 56.5 and 63.8% respectively. (6) Overall improvement in the bundle compliance may have lead to zero vap

CONCLUSIONS. (1) 95% compliance in individual components is achievable although we could obtain only in 3 components. (2) Increase in compliance leads to decrease in vap incidence. (3) Zero vap is achievable

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1236

PHYSICIANS' OPINION ABOUT COMPETENCIES OF THE TRIAGE NURSE IN HUNGARIAN EMERGENCY DEPARTMENTS

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BACKGROUND. The structure of the Hungarian Emergency Care has changed in the last decade, new positions and staffs appeared in Emergency Departments (ED). The exact competency of these new positions was not determined; therefore there were no standard competencies in every hospital especially for triage nurses. There is no special training for triage nurses in Hungary.

AIMS. Our goal was to assess the physician's opinion about potential competencies of a triage nurse.

METHODS. A representative cross sectional study design was applied with self-fill-in questionnaire about physician's attitude related to skills of triage nurses. The questionnaires were distributed between September and November 2007 in 24 (out of 31) EDs. In this survey 159 physicians' questionnaires were processed. Chi-square and Student-t test was used for comparison of variables. P values less than 0.05 were considered statistically significant.

RESULTS. 79.2% of physician would support the special training of triage nurse. 55.3% of physician suggests that the nurses use the patient's physical examination regularly in EDs. The full time (FT) emergency physician significantly would reduce the basic competencies of nursing (e.g. dressing, feeding of patient, $P = 0.008$, and $P < 0.001$, respectively) than part-time (PT) emergency physicians. Significantly greater part of the FT physician would widen the competency of triage nurses in the field of physical examination of nervous system ($P < 0.001$) and cardiovascular system ($p = 0.005$) than the PT physician.

CONCLUSION. Hungarian emergency physician would widen the competency of triage nurse, but only half of physician would like to that nurses apply physical patient examination in practice. The full time physician would give more competencies for triage nurse than part time ones, but the final field of competency will be depended on other factors.

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POSTTRAUMATIC STRESS DISORDER (PTSD) AMONG HUNGARIAN AMBULANCE WORKERS

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INTRODUCTION. Posttraumatic Stress Disease (PTSD) is a physical and psychological condition caused by chronic or acute stress. There are no previous extensive studies about PTSD among Hungarian paramedics and other ambulance service staff.

AIM. The aim of this study was to measure the level of PTSD among Hungarian ambulance workers, and explore factors which can influence it.

SAMPLE AND METHODS. 411 Hungarian ambulance workers were involved to this cross-sectional study (147 ambulance drivers, 173 ambulance nurses, and 91 ambulance team leaders: medical doctors and ambulance officers). Self filling questionnaire were used for data collection, including Briere's Trauma Symptom Checklist, and socio-demographic questions. Chi square test, independent T test and variance analysis were used for comparison of variables.

RESULTS. The average PTSD-points of ambulance workers was 20. There was significant association between level of PTSD and gender: women's average 23, men's average 18 PTSD-points ($p = 0.049$). There were no correlations between level of PTSD and type of settlement, location of ambulance station and level of education. Those who would need psychological support ($p = 0.01$), and those who had psychologically traumatic experiences in the last 2 years have significantly higher PTSD-points ($p = 0.01$).

CONCLUSIONS. Hungarian ambulance workers are exposed with many effects which can lead PTSD. Professional psychological support is needed in order to cope with PTSD successfully.

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HAND HYGIENE PRACTICES IN AN INDIAN ICU

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INTRODUCTION. Healthcare-associated infections (HCAI) are estimated to affect 1.4 million people worldwide, causing longer hospital stay, increasing hospital costs and excess mortality [1]. Hand hygiene represents the single most effective way to prevent healthcare-associated infections. Compliance with hand hygiene amongst healthcare workers (HCW) has been demonstrated to be quite low at 40% [2].

OBJECTIVES. To quantify the degree of compliance to hand hygiene norms in the ICU and to assess the short term success of strategies to improve hand hygiene compliance.

SETTING. 34 bedded Medical-Surgical ICU in a Tertiary care centre.

DESIGN. Prospective observational.

METHOD. Unobtrusive observer (single person). Observed over sessions of 1 h. The compliance was calculated as :Number of times the staff performed hand hygiene/Number of hand hygiene opportunities. The number of hand hygiene opportunities was based on the WHO tools [3]: before touching a patient, before clean/aseptic procedures, after body fluid exposure risk, after touching a patient and after touching patient surroundings.

RESULTS. See TABLES:

HAND HYGIENE COMPLIANCE RATES

Health care staff	Observations (compliance %) Jan	Observations (compliance %) Feb	Observations (compliance %) March
Doctors	30 (25)	15 (45)	10 (30)
Nurses	34 (68)	30 (56)	40 (79)

PATIENT DATA

	January	February	March
Total admissions	240	206	218
Patient-days	832	724	621
APACHE IV (Mean)	75.7	76.39	77.22
Mortality %	13.75	13.59	13.76

CONCLUSIONS. The overall compliance was unsatisfactory but nurses fared better than doctors. The compliance improved in the third month after introducing supervision programs in the second month

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EVALUATION OF TRAINING IN CAM-ICU AND RASS SCORING BY CRITICAL CARE NURSING STAFF FOR THE ASSESSMENT OF BRAIN DYSFUNCTION IN ICU

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INTRODUCTION. ICU delirium represents a form of brain dysfunction that in many cohorts has been diagnosed in 60–85% of patients receiving mechanical ventilation. Delirium is a common but complex clinical syndrome characterized by disturbed consciousness, cognitive function or perception, which has an acute onset and fluctuating course and is associated with poor outcomes. And yet, it can be diagnosed and treated. In the UK, reporting of delirium is generally considered to be poor. In light of updated NICE guidelines on delirium due out this year, specialist clinical assessment will soon become gold standard as a means of diagnosing and reducing the prevalence of this condition in the ICU setting. NICE recommends that CAM-ICU (Confusion Assessment Method) be used by healthcare professionals who are trained and competent in the diagnosis of delirium. On our 16-bed unit, we are currently implementing CAM-ICU assessments to be performed twice daily (at the commencement of each nursing shift) as well as RASS (Richmond Agitation and Sedation Scale) scoring on an hourly basis for all patients.

OBJECTIVES. To implement training of all our ICU nursing staff in the use of CAM-ICU and RASS scoring. To periodically validate and reinforce earlier training, so as to improve assessment and reporting of delirium.

METHODS. Our 'Delirium Group' comprising both nursing and medical staff, taught CAM-ICU and RASS to 48 staff members using multimedia presentations in small groups and/or individual teaching sessions over 6 weeks. Scoring of CAM-ICU and RASS was subsequently audited on 3 occasions post training. Discrepancies were discussed and post-audit retraining provided where necessary.

RESULTS. The following audit and validation data were generated on our unit as documented in Table 1. No statistical analysis was undertaken. We anticipate focusing on the challenges encountered and strategies used in managing this change in our ICU practice.

TABLE 1 AUDIT AND VALIDATION DATA

Outcome measured	Audit 1 (March 11)	Audit 2 (March 22)	Audit 3 (April 22)
Hourly RASS score achieved	82%	82%	91%
Twice daily CAM-ICU scoring achieved	66%	65%	66%
Inaccurate CAM-ICU scoring	11%	12%	0%
CAM-ICU not undertaken	34%	23%	0%

CONCLUSIONS. This early appraisal suggests an improvement in the uptake and quality of delirium assessment and reporting undertaken by staff in ICU. It also highlights the need for continual education and training to maintain standards of assessment of delirium.

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RESISTANCE TO ORGANIZATIONAL CHANGE: CONTRIBUTOR FACTORS QUALITATIVE ANALYSIS

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INTRODUCTION. The resistance to change is produced not only by a simple cause-effect relationship, but by different factors relationship. We have studied some of these main factors explaining the barriers to provide the optimal health care.

OBJECTIVES. Detection of "resistances to change" before starting a "Patient Safety Program" in a Intensive Unit Care.

METHODS. The factors causing resistance to change based on multisource data. Qualitative technical methods were used: brainstorming and focal groups. The data collection elaboration was created by the collaboration of ICU Nurse, Quality Department Nurse and external reviewers. Finally, the main factors were classified in different categories. Each category was scored by 1 to 5 according to gravity and prevention possibility. Finally, priority was given to more serious and easier prevention problems.

RESULTS. The most serious problems for ICU professional was the historical factors. The easier solution problems were "the lack of information" and all evaluators were agree with it. We arranged the factors in order to the next classification (Tables 1 and 2).

TABLE 1

	ICU medical doctor		ICU nurse		Nurse of Quality Unit		External Safety Expert	
	Gravity	Prevention possibility	Gravity	Prevention possibility	Gravity	Prevention possibility	Gravity	Prevention possibility
Fear to the unknown things	4	5	2	2	2	3	2	2
Lack of information	4.3	2.3	5	1	4	2.7	3	3.7
Historical factors	5	5	5	5	3.3	2.6	3	2.3
Threats to the status quo	4.3	5	5	5	3.3	2.6	3	5
Threats to the payment	1	1	1	1	1	1	2	2
Low organisational confidence	5	5	4.3	4.6	3.3	3.7	3	4
Fear to the failure required	1.2	1.4	3.6	3.5	3.5	2	3	3

TABLE 2

	ICU medical doctor	ICU medical doctor	ICU nurse	ICU nurse	Nurse of Quality Unit	Nurse of Quality Unit	External Safety Expert	External Safety Expert
	Gravity	Prevention Possibility	Gravity	Prevention Possibility	Gravity	Prevention Possibility	Gravity	Prevention Possibility
Resistance to new experimental things	1.3	2.5	2.1	2.5	4	2	3.4	4.6
Low organisational flexibility Rise of the task work Decrease in the work responsibilities Dread to not being able to learn new skills required	4.3	4.6	4.6	5	3.6	3.3	3.5	3.5
Rise of the task work	2.3	3.6	4.6	3.6	3	2	3.5	5
Decrease in the work responsibilities	1	1	2.3	2.3	4	4	3	4
Dread to not being able to learn new skills required	1.2	1	2	2.3	3	2	3	4

DISCUSSION. All investigators were agreed with the low importance of problems with payments and low prevention probability of low organisational flexibility, so they were agreed on not to work about them.

The ICU professionals were more pessimistic and have lower confidence in prevention possibilities but they showed more confidence about the capacity to learn new skills. They weren't worried about resistance to do experimental things. Probably, historic factors play an important role in this pessimistic attitude. On the other side, Quality and Safety Experts have more experience in prevention programs and they put all their trust in its. After doing the analysis, we chose the "lack of information problem" to plan prevention activities. We consider it is a serious and real problem but at the same time, easy of prevent.

CONCLUSIONS. The implementation of the Patient Safety Program in the ICU means a real cultural change. The priority analysis could help to plan strategies in order to avoid the program failure.

Safety and safety attitudes: 1241–1254

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IMPACT OF ADMISSION TIME ON MORTALITY IN AN INDIAN INTENSIVE CARE UNIT WITH ROUND-THE-CLOCK INTENSIVIST COVERAGE

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INTRODUCTION. High mortality in patients admitted during off hours has been attributed to inadequate staff levels, but only a few studies have assessed the impact of 24-h intensivist coverage on intensive care unit (ICU) mortality.

OBJECTIVES. To assess the influence of time of admission on mortality for non-elective patients admitted to ICU with 24 h in-house intensivist coverage.

METHODS. Retrospective study analyzing data from for all admissions in a medical ICU during a 15 months period. Patients were divided into two groups according to time of admission: regular hours (Monday–Saturday 9 a.m.–5 p.m.) and off hours (Monday–Saturday 5 p.m.–9 a.m., Sunday). Patients were compared with regard to demographics, severity of disease, ICU course and outcome. Primary outcome measure was ICU mortality.

RESULTS. Out of 653 admissions, 262 (40.12%) patients were admitted in regular hours and 391 (59.88%) during off hours. There was no significant difference in age ($p = 0.07$), sex ($p = 0.434$), baseline severity of illness ($p = 0.272$), need for organ support, days on mechanical ventilation ($p = 0.181$) and length of ICU stay ($p = 0.065$). ICU mortality was 14.9% and 16.4% in patients admitted in regular and off-hours, respectively ($p = 0.689$). Relative risk of death for admission in after-hours was 1.018 (95% CI; 0.952–1.088), with odds ratio of dying being 1.119 (95% CI; 0.726–1.726).

COMPARISON BETWEEN REGULAR AND OFF-HOUR ADMISSIONS

Parameter of interest	Regular hours (n = 262)	Off-hours (n = 391)	p value
Mean age, years ± SD	60.08 ± 19.5	57.4 ± 17.9	0.070
Sex, males (%)	157 (59.9)	221 (56.5)	0.434
Mean APACHE II score ± SD	14.07 ± 8.3	14.84 ± 9	0.274
Need for mechanical ventilation (%)	69 (26.3)	104 (26.6)	1.000
Days on mechanical ventilation ± SD	5.13 ± 6.1	4.03 ± 4.4	0.181
Need for renal support (%)	31 (11.8)	61 (15.6)	0.214
Need for inotropic support (%)	59 (22.5)	106 (27.1)	0.218
Mean ICU stay, days ± SD	5.44 ± 5.8	4.65 ± 5.1	0.065
ICU mortality (%)	39 (14.9)	64 (16.4)	0.689

CONCLUSIONS. Full time intensivist coverage ensures continuity of care. Hence, off hours admissions are not associated with any increased mortality. These observations could have important clinical and organizational consequences. Based on the findings of this study, we suggest that, wherever possible, full-time intensivist cover should be available in ICU.

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MEDICAL PERSONNEL RECOGNITION OF THE MANAGEMENT OF CUFF OF ARTIFICIAL AIRWAY

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INTRODUCTION. After placing artificial airway, various complications associated tube placement had been developed. The patient suffered from tracheal ulceration, tracheal stenosis and pneumonia, because higher pressure of cuff balloon could compress tracheal wall and lower of it could develop aspiration from oropharyngeal and stomach to lung.

OBJECTIVES. We concerned about whether medical personnel could recognize management of the cuff of artificial airway or not.

METHODS. We asked to doctors and nurses working in intensive care unit of Konyang University Hospital, Daejeon, Republic of Korea. We asked 12 questions with 18 contents of questionnaire that was composed of methods of set initially, maintenance and appropriate pressure of cuff.

RESULTS. 96 of medical personnel replied to us. Most of them had worked in intensive care unit, so they had placed of artificial airway. 86.4% of them used manometer to adjust the cuff. We could find that nurses had more cognition compared to doctors for it (94 vs. 76%). Only 28.5% of doctors described pressure of the cuff in medical record. 89 of medical personnel replied that they knew the appropriate range of cuff pressure. 37% (32/89) of them replied that the range of cuff pressure was kept with 25–30 mmHg and 34% (30/89) was 20–25 mmHg. 70% of nurses in the ICU knew that range of cuff pressure was 15–25 mmHg. Most of them knew complications of high and low pressure of the cuff. 69.8% of medical personnel monitored the cuff balloon during receiving mechanical ventilation and they used manometer to adjust it. 78% of nurses knew that the cuff should be adjusted continuously, but 58% of doctors did. Interval measuring the cuff pressure was 38% of once a day, 38% of three times a day, 17% of more than four times a day

CONCLUSIONS. Most of the medical personnel knew to keep appropriate cuff balloon to prevent various complications of artificial airway. They had insufficient cognition about maintaining the cuff balloon and appropriate level of cuff pressure. That was more prominent in doctors than nurses

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QUALITY OF INTERHOSPITAL TRANSPORT OF THE CRITICALLY ILL: IMPACT OF A MOBILE INTENSIVE CARE UNIT WITH A SPECIALIZED RETRIEVAL TEAM

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INTRODUCTION. Interhospital transfer is occasionally required as a consequence of limited therapeutic options or because of a need for a higher intensity of medical care that cannot be given in rural Intensive Care Units. Along with the potential benefit for the to be transferred patient, transport may also lead to hemodynamic and pulmonary deterioration. In order to minimize additional risk of interhospital transport of critically ill patients, a Mobile Intensive Care Unit with a specialized retrieval team was established in our university hospital-based intensive care unit. From March 2009, transport of the critically ill patients in our adherence region are performed by MICU.

OBJECTIVES. In this prospective audit adverse events and patient stability during MICU transfers were assessed and compared to our previous data on transfers performed by standard ambulance [1].

METHODS. All transfers performed by MICU from March 2009 until December 2009 were included. Data on fourteen vital variables were collected at the moment of departure, on arrival and 24 h after admission. Variables before and after transfer were compared using the Paired-Sample test. Major deterioration was expressed as a variable beyond a predefined critical threshold and was analyzed using the McNemar test and the Wilcoxon Signed Ranks test. Results were compared to the data of our previous prospective study concerning interhospital transfer by ambulance.

RESULTS. 74 interhospital transfers over a 10-month period were evaluated. Systolic blood pressure, glucose and haemoglobin were significantly different at arrival compared to departure, although never significant values for major deterioration were reached. An increase of total number of variables beyond threshold at arrival was found in 38% of patients, 32 percent exhibited a decrease of one or more variables beyond threshold and thirty percent showed an equal number of trespassed thresholds. There was no correlation between the patients status at arrival and the duration of transfer or severity of disease. ICU mortality was 28%.

Compared to standard ambulance transfers of ICU patients performed in 2005, there were far less adverse events: 12.5 vs. 34%, which in the current study were merely caused by technical (and not medical) problems. Although mean APACHE II score was significantly higher, patients transferred by MICU showed less deterioration in pulmonary parameters during transfer than patients transferred by standard ambulance.

CONCLUSION. Transfer by MICU imposes less risk to critically ill patients compared to transfer performed by standard ambulance and has therefore resulted in an improvement of quality of interhospital transport of ICU patients.

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CLINICAL DIAGNOSES AND AUTOPSY FINDINGS: DISCREPANCIES IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Previous studies in adult intensive care units (ICUs) reported rates of pre-mortem to post-mortem discrepancies ranging between 7 and 32% depending on the population studied. And, most of them were retrospective studies, which included small number of patients.

OBJECTIVES. To compare clinical and pathological diagnoses and to determine the types of errors in a large and multidisciplinary ICU-patient population.

METHODS. We conducted a prospective study of all consecutive autopsies performed on patients who died in the ICU of the Hospital Universitario de Getafe, Madrid, Spain, between January 1982 and December 2007. The diagnostic errors were classified in two categories: class I errors that were major misdiagnoses with direct impact on therapy, and class II diagnostic errors which comprised major unexpected findings that probably would not have changed therapy.

RESULTS. Of 2,857 (18.1%) deaths during the study period, autopsies were performed in 866 patients (30.3%). Autopsy reports were finally available in 834 patients. Major missed diagnoses were noted in 154 patients (18.5%). 63 patients (7.5%) had class I discrepancies, 43 relating to the underlying primary disease, 16 relating to the cause of death, and 4 relating to both underlying primary disease and cause of death. 95 patients (11.4%) had class II discrepancies, 48 relating to the underlying primary disease, 45 relating to the cause of death, and 2 relating to both underlying primary disease and cause of death. The most frequently missed diagnoses were pulmonary embolism, pneumonia, invasive aspergillosis and endocarditis. The autopsy did not determine the cause of death in 22 patients (2.6%). Our rate of diagnostic discrepancy remained relatively constant over time. The median error rate was 8.5% [interquartile range (IR), 4.6–9.1%] for class I errors and 13% [IR, 7.2–14.5%] for class II errors.

CONCLUSIONS. This study found significant discrepancies between clinical diagnoses before death and post-mortem findings. This reinforces the importance of the post-mortem examination in detecting otherwise unexpected diagnoses and improving the quality of care of critically ill patients.

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UNPLANNED EXTUBATION AND REINTUBATION RATE IN ICU PATIENTS

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INTRODUCTION. Unplanned extubation is associated to a high risk of reintubation end correlates with increased risk of nosocomial pneumonia. On the other hand, reintubation significantly increases morbidity and mortality in critical ill patients, increasing the incidence of ventilator associated pneumonia (VAP) rate and makes the airway management risky.

OBJECTIVES. The aim of our study was to test the rate of unplanned extubation as well as the reintubation rate in our ICU, in order to evaluate the efficiency of our airway and weaning time protocols.

METHODS. During a nearly 4 year's period, 216 patients admitted to the ICU, mean age: 61.8 years, mean APACHE II score: 18.5, mean LOS: 13.5 days, with predicted and actual mortality: 31.1 and 22.47% respectively. From these, 191 were intubated and included retrospectively in our study. 109 patients were extubated, while the others either underwent bedside percutaneous tracheostomy or died. We concerned that the number of days of mechanical ventilation were about equal to the number of days of intubation. Reintubation was defined as the need to reintubate during the first 48 h after extubation.

RESULTS. We recorded four episodes of unplanned extubation. Three of them caused by malfunction of the tube due to secretions and airway obstruction and one of them was undesired extubation caused by the patient himself. The total number of days of intubation was 2,111, mean ± SD: 11.06 ± 11.87, min: 1, max: 51 days. Therefore the rate of unplanned extubation was 1.897‰, while the standard limit is below 15 ‰. The total number of reintubations was 19, while the total number of scheduled extubations was 109. Therefore, the reintubation rate was 17.43%, while the standard limit is below 12%.

CONCLUSIONS. The recorded rate of unplanned extubation was low in our ICU patients, below the acceptable limit, assuming that our sedation and airway management policy is effective. On the other hand, the recorded rate of reintubation was high in our study, above the acceptable limit. Although a low rate of reintubation might indicate excessively long mechanical ventilation times, this did not recorded to our study. Nevertheless, our data suggest that we have to improve further our weaning time protocols, making the extubation procedure safer, and avoiding risk factors for VAP.

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ARE ACADEMIC RANDOMISED CONTROLLED TRIALS (RCTS) SAFER? PROTOCOL VIOLATION REPORTING IN RCTS PUBLISHED IN HIGH-IMPACT JOURNALS

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INTRODUCTION. Poor study conduct, leading to excessive protocol violations (PVs), may result in false negative randomised controlled trials (RCT). PVs such as *inappropriate enrollment* of patients with a contraindication to the study treatment may lead to excess harm in the active intervention group [1] and *failure to deliver the study intervention* according to the study protocol may underestimate true treatment efficacy [2]. Full reporting of PVs may aid in the interpretation of RCT results however there are no published reviews on this topic [3].

OBJECTIVES. To determine reporting rates for key types of PVs and to investigate study characteristics that may be related to reporting.

METHODS. Eighty consecutive RCTs published in four major journals (NEJM, JAMA, BMJ and The Lancet) were reviewed. Medline (http://www.PubMed.org) was searched to identify eligible RCTs. Consecutive full text publications were retrieved until 80 RCTs were identified (20 from each Journal). The search was conducted in April 2009.

RESULTS. The 80 included RCTs were identified from 101 consecutive publications. Publications were excluded because they were subgroup or economic analyses of a previously published RCT [6], not a RCT [5], not published in the target journal [4], systematic reviews [2], or other reason [5]. Median trial size was 700 participants (range: 20 to 162,387). 13/80 (16%) of RCTs were single centre, 58/80 (72%) were Industry funded and 21/80 (26%) reported negative findings. Overall 71/80 (89%) of RCTs reported some form of PV, these included: 51/80 (63%) patient compliance; 40/80 (50%) discontinuation of study intervention due to safety; 32/80 (40%) study intervention-related researcher error; 16/80 (20%) inappropriate enrollment and; 8/80 (10%) technical errors in randomisation. Multi-centre RCTs may be more likely to report study intervention-related researcher errors (44% of multi-centre trials vs. 15% of single centre trials, $P = 0.06$). Academic trials were less likely to report discontinuation of study intervention due to patient safety (38% of Academic trials vs. 80% of Industry trials, $P = 0.002$) and were less likely to report technical errors in randomization (5% of Academic trials vs. 23% of Industry trials, $P = 0.03$).

CONCLUSIONS. Multi-centre trials are accepted to be organizationally complex. On-site education may be required to reduce errors in study intervention delivery attributable to the research team. It is possible the apparent excess harm attributable to Industry trials is a reporting artifact however, if it is real, it must be addressed. Additional research is required to investigate patient safety-related PVs and technical randomization errors, which may be lower in Academic trials.

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PATIENT SAFETY IN INTENSIVE CARE UNITS: THE ROLE OF NURSING RELATED UNTOWARD OCCURRENCES

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INTRODUCTION. Patient Safety is an increasing research field, but few studies have focused their attention on Intensive Care Units (ICUs). ICUs are high-risk environments extremely vulnerable to adverse event (AE) occurrence.

OBJECTIVES. To determine the occurrence of adverse events and harmless incidents related to nursing activities in ICUs, characterizing their nature and identifying AE potential risk factors.

METHODS. A prospective cohort was conducted in four ICUs of a 1100-bed academic, tertiary-care urban hospital in Sao Paulo, Brazil, enrolling critical ill patients older than 15 years from July to August 2009. Nursing Harmless incidents (N-INC) and nursing AE (N-AE) were identified by daily monitoring of medical and nursing rounds and also by chart reviews. Demographic characteristics, clinical severity on admission (APACHE II-score), length of stay, and the nursing team workload (Nursing Activities Score-NAS) were also recorded. The association with the occurrence of AE was analyzed by multivariate logistic regression.

RESULTS. Among the 54 enrolled admissions, a total of 1298 nursing-care related untoward occurrences were identified (mean ± standard-error: 24.04 ± 3.5 occurrences): 101 N-AE affecting 29 admissions (53.4%) and 1197 N-INC involving 53 admissions (98%). The most common N-INC were: failures in following the daily nursing prescription (559 incidents in 59% admissions), errors in collecting and sending samples for testing (164 incidents in 68% admissions) and failures in recording information in patient charts (145 incidents in 74% admissions). Regarding N-AE, skin lesions including dermatitis and pressure ulcers predominated with 64 events in 27 admissions (50%). Nursing-staff worked overloaded in the studied ICUs; with NAS mean scores of 63.76% ± 3.22. A prolonged length of stay (>3 days) and nursing working overloaded (NAS > 50%) remained as strong independent risk factors associated to the occurrence of N-AE, with adjusted OR of 21.84 and 18.63, respectively ($p < 0.05$).

CONCLUSIONS. This study was essential to determine the incidence of N-INC and N-AE in the sudied ICUs. The nursing staff worked highly overloaded. In this prospective cohort, we identified that the N-INC were extremely frequent, corresponding to more than 90% of all nursing-related failures, and affected 98% of the studied admissions. N-AE, also frequent, affected more than 50% of admissions. The occurrence of at least one N-AE presents a strong and significant association with nursing-workload and length of stay. This study shows the importance of studying Patient Safety in specific settings like ICUs, disclosing its particularities, in order to improve the quality in healthcare.

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PATIENT SAFETY IN INTENSIVE CARE UNITS: WHAT SORT OF ADVERSE EVENTS ARE RELATED TO PHYSICIAN'S ACTIVITIES?

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INTRODUCTION. Intensive care units (ICUs) are complex settings with critically ill patients, submitted to invasive care, involving a multidisciplinary team, requiring urgent high-risk decision-making, taking place in an expensive structure with new technologies of increasing complexity. All these conditions facilitate the occurrence of Adverse Events (AE).

OBJECTIVES. To determine the occurrence of harmless incidents and AE related to physician's competences in ICUs, disclosing their potential risk factors.

METHODS. This study was conducted in 4 medical ICUs of a 1,100-bed academic tertiary hospital in Sao Paulo (Brazil), enrolling critically ill adult-patients from July to August 2009. Harmless incidents (MD-INC) and AE(MD-AE) related to physician activities were identified by daily monitoring of medical and nursing rounds and by chart reviews. Demographic characteristics, APACHE II-scores, Charlson-Comorbidity Index, and length of stay were also recorded. The association with the occurrence of MD-AE was analyzed by multivariate logistic regression.

RESULTS. Fifty out of 54 enrolled admissions suffered at least one physician related untoward event, with a total of 415 occurrences. Physician related problems were only surpassed by the nursing related category. More than a quarter of the identified occurrences were actually MD-AE (108 events) affecting 24 admissions (44%). Hypoglycemia not related to insulin administration was the most important detected MD-AE, with 49 episodes in 18 admissions. The next most frequent MD-AE were the injuries related to medical procedures like central line catheters, mechanical ventilation and intubation: 31 events in 19 admissions. Metabolic changes and cardio-respiratory instability were the most important MD-AE related damages. As much as 307 MD-INC were identified Problems related to recording necessary information in medical charts and those regarding daily monitoring (like not asking indicated tests or performing incomplete clinical evaluation) were the most frequent MD-INC, with 183 and 100 incidents respectively. A strong and significant association with the occurrence of at least one MD-AE was identified regarding length of stay >3 days and Apache scores >13 points, with adjusted OR estimates of 5.77 and 3.20, respectively ($p < 0.05$).

CONCLUSIONS. This prospective study was essential to identify the proportion of our ICU admissions affected by MD-INC and MD-AE, disclosing their nature. Our MD-AE rates, affecting more than 40% of admissions, were higher than those described in prior general studies, including not only ICUs. Among the detected MD-AE, hypoglycemic episodes not related to insulin administration predominated, indicating important deficiencies regarding nutritional support. Severity on admission and length of stay were important risk factors for the occurrence of at least one MD-AE.

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INCIDENT REPORTING SYSTEM: COMPARISON BETWEEN STAFF AND EXTERNAL OBSERVER

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INTRODUCTION. A systematic measurement and analysis of unintended events (UE) have been recommended for patient safety and improvement of quality of care in critically ill patients. However, a spontaneous reporting system may be inefficacious in intensive care unit (ICU) because of a poor data collection, particularly by physicians staff.

OBJECTIVES. The aim of this study was to evaluate the reliability of a staff spontaneous event report by comparison with events collected by an external observer in a surgical intensive care unit (ICU).

METHODS. To facilitate the reporting and the analysis, we identified a series of events with a serial number and a colour code related to their for each of the following 5 macro-phases: ICU bed booking, admission procedures, patient stay, discharge and emergency procedures. A specific structured form including UE's code and colour, date and hour of the event and type of patient has been prepared and proposed to staff 1-week for each month after a proper phase of education. The report was voluntary and anonymous and the data collected during the morning shift from September to December 2009 have been compared to those collected from an external observer.

RESULTS. In the studied period, healthcare staff reported 53 UEs: 51% collected by nurses, 47% occurred during the morning shifts and 67% were classified as moderate or severe. The rate of UE in the morning shift was 12 UEs per 100 patient days. The external observer identified 55 events in 8 morning shifts with an incidence of 76 UEs per 100 patient days. The violation of isolation rules for patient with multi-drug resistant bacteria infection both by ICU staff and surgical consultant was the UE observed more frequently by the staff (26%) and by the external observer (35%).

CONCLUSIONS. The above data indicated that:

1. in our ICU the incidence of UE is very high, particularly for compliance to isolation of infected patients and
2. the spontaneous reporting system under-estimated largely the real incidence of UEs.

A series of specific activities have been put in action in 2010 for improving the adherence to protocols of patient isolation (i.e. staff audit on transmitted infections in 2009) and for increasing the spontaneous UEs reporting (i.e. coloured panel, questionnaire administration).

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THE DIFFERENCE BETWEEN SELF-REPORTED AND INDEPENDENTLY AUDITED MEDICATION ERRORS IN AN INDIAN ICU

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INTRODUCTION. Quantification and evaluation of medication error is an integral component of quality and safety assurance. Towards this purpose an honest appraisal must be made of what we do.

OBJECTIVES. To quantify the number of self-reported and independently audited medication errors.

SETTING. A 34-bed medical-surgical ICU in a tertiary care hospital in India

DESIGN. Prospective observational evaluation. Interventions: none

STUDY POPULATION. 2,179 patients, during the 9 months July 2009–March 2010.

METHODS. Medication errors were identified by voluntary reporting by nurses and doctors and were recorded on critical incidence reporting forms. Medication administration and documentation errors were identified by daily review of charts by an independent observer (clinical pharmacologist).

Measurements: Opportunities for error = No. of random samples audited × 10 R's (10 R's = Right Patient, Right Medication, Right Dose, Right time and frequency, Right Route, Right Documentation, Right Compatibility, Right Evaluation, Right Education, Right to refuse medication). Percentage of errors = (observed/opportunities for error) × 100.

RESULTS. Among 7056 patient days, only 8 errors were reported as critical incidents by healthcare staff (1.13/1,000 patient days).The total number of patient records audited was 1,650 and possible opportunities for error was 11,635. The number of documented errors was 209. The mean percentage of errors/month was 2.

CONCLUSIONS. A large difference was found between audited medication errors and voluntary critical incident reporting in an Indian setting. The above data highlights the inherent underestimation in voluntary self reporting in a milieu where this practice is new. Systematic auditing is therefore mandatory to ensure patient safety. Self reporting methods need to be strengthened through education and non-punitive remedial measures.

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USE OF THE BOW-TIE METHOD FOR A PROSPECTIVE RISK ANALYSIS OF IN HOSPITAL TRANSPORTATION OF INTENSIVE CARE PATIENTS

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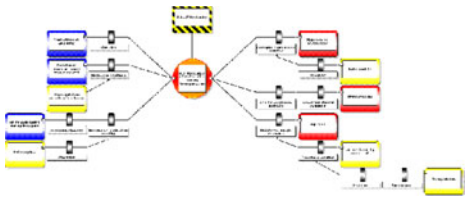
INTRODUCTION. In hospital transportation of Intensive Care (IC) patients for diagnostic procedures or therapeutic interventions is daily routine. The majority of IC patients are mechanically ventilated and vasoactive medication dependent. Transportation of these patients outside the safe environment of the ICU is potentially harmful, because several risks are present.

OBJECTIVES. Incidents, related to the transportation of ICU patients, with adverse outcome are rare. Nevertheless we believed that the actual number of incidents is significantly higher than the ones reported in our Incident Registration System. Therefore a prospective risk analysis was performed, using the Bow-tie method. We used this method to improve patient safety and quality of in hospital transportation of ICU patients.

METHODS. The Bow-tie method was performed at the ICU of the Academic Medical Centre of the University of Amsterdam, The The Netherlands. The ICU contains 32 operational beds and approximately 120 nurses and 30 medical doctors are employed. The study was performed by the Committee on Patient Safety and Quality (CPSQ). Using the Bow-tie method, supported with purchased software (BowtieXP by Governor's) multiple Bow-tie diagrams were made: (1) Incidents with the inevitably use of lifts, (2) Incidents with bed-side equipment, (3) Ventilation-related incidents, (4) Monitoring-related incidents, (5) Incidents concerning lines and devices, (6) Medication-related incidents and (7) Patient-related problems. An example of a Bow-tie diagram:



MEDICATIONRELATED INCIDENTS

RESULTS. The great majority of defence barriers, as reported in the Bow-tie diagrams, were already effective. After analysis a list of recommendations to improve patient safety and quality during transportation was composed: 1. Revision of the Transportation protocol
2. Implementation of a checklist together with at least 30 min preparation time
3. Improving education, certification and supervision by staff members
4. Changes in design of bed-side equipment
5. Use of a lift (priority)-badge
6. Improvement of the incident registration system.

The results were presented and discussed in our weekly meeting on patient safety and healthcare for all ICU personnel. By the end of this year all the recommendations will be implemented in our ICU.

CONCLUSIONS. We improved the safety and quality of in hospital transportation of ICU patients by performing a prospective risk analysis. Bow-tie is a good instrument to identify health care risks.

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INCIDENCE OF PHRENIC NEUROPATHY RELATED TO INTERNAL JUGULAR AND SUBCLAVIAN VEIN CATHETERIZATION: A PROSPECTIVE STUDY IN PATIENTS ADMITTED IN AN INTENSIVE CARE UNIT

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INTRODUCTION. The phrenic nerve could easily be injured during the catheterization of subclavian and internal jugular veins. After an exhaustive bibliographic review, we only have found case reports of phrenic neuropathy.

OBJECTIVES. To determine the incidence of phrenic neuropathy associated with the catheterization of internal jugular and subclavian veins, without ultrasound support, in patients admitted to an ICU.

METHODS. A prospective study was performed by following patients admitted in the ICU between October 2008 and May 2009. A normal neurography of both right and left phrenic nerves at the moment of their admission was the main inclusion criteria. After this baseline study, a new neurography was repeated weekly (Chen and Resman method, Sinergy Medelec), during their stay and at the moment of being discharge from ICU. Simultaneously, all vascular subclavian and internal jugular vein catheterization were registered. A final neurography and a fluoroscopy study were performed after being discharged from hospital.

RESULTS. 40 patients were included and two hundred and ten neurographies of both right and left phrenic nerves were performed. 14 patients did not receive any vascular punctures in the cervical region during the follow up period, acting as control group. 26 patients underwent a total of 48 vascular catheterization, 43 in subclavian vein (89.6%) and 5 in internal jugular vein (10.4%). A phrenic neuropathy was diagnosed in 4 patients. This represented an incidence of 15% (4/26) of phrenic neuropathy per patient and 8% (4/48) related to subclavian and internal jugular vein catheterization. In relation to patients without phrenic nerve injury who underwent subclavian and internal jugular vein catheterization, patients affected of phrenic neuropathy had longer mechanical ventilation time (33 $\pm$ 36 days vs. 19 $\pm$ 13, $p = 0.3$) and longer average stay time in ICU (49.7 $\pm$ 35 days vs. 25 $\pm$ 14, $p = 0.08$), although these differences have not statistical significance. We did not find significantly differences related to age (53 $\pm$ 9 vs. 55 $\pm$ 18, $p = 0.2$) and APACHE II index (16 $\pm$ 3.5 vs. 15.8 $\pm$ 5.8, $p = 0.4$) between both groups (Wilcoxon Two-Sample Test). We performed a control neurography of 2 case patients after being discharged from hospital. We checked the CMAP phrenic nerve reappearance after 3 weeks and 6 months of being diagnosed its neuropathy, respectively.

CONCLUSIONS. We found an incidence of phrenic neuropathy of 15% per patient and 8% related to subclavian and internal jugular vein catheterization, during the follow-up period. The time of reappearance of phrenic CMAPs after being detected its neuropathy points to a neuroapraxia or partial axonotmesis as pathogenic type of injury.

DISCUSSION. Phrenic neuropathy has to be considered in cases of difficult weaning of unclear etiology. The catheterization of subclavian and internal jugular veins should be recommended employing ultrasound support.

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ADEVERSE EVENTS AND NEAR MISS IN SPANISH ICUS. SYREC STUDY

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INTRODUCTION. SYREC project aims to improve ICU patient safety. The project includes an epidemiological study. We present the main results.

OBJECTIVES. To estimate the near miss (NM) and adverse events (AE) rate in Spanish Intensive Care Units (ICUs). We study the incidence and nature. Finally, we classify and analyze its severity.

METHODS. Multicenter prospective observational cohort study. Inclusion criteria: patients admitted to the 79 participant ICUs during the 24-h observation period. During this period, NM and AE detected and reported inside and outside ICU were included. Only outside ICUs were considered when its were the reason for admission. We evaluate the kind of incident, severity and preventability. Data collection studied under the distribution of frequencies.

RESULTS. 1,017 patients were included. 1,424 incidents were reported in 591 patients, 943 were NM and 481 AE. Risk: The median risk of NM was 73% versus AE 40%. 22.1 incidents per patient admitted. Incidence rate: the incident rate median was 5.89 per 100 patients per hour ICU stay, the NM of 3.47 per 100 patients per hour ICU stay and that of AE, 2.04 per 100 patients time of stay in ICU. The 66% of the incidents reported have been NM and 34% AE. This incidents causing temporary damage in the 29.50% of occasions and in the 4.28% permanent damage, compromised the patient's life or contributed to death. Classification of incidents (Table 1).

TABLE 1 CLASSIFICATION OF INCIDENTS

	Number of NM	% row	% column	Number of AE	% row	% de column	Number of incidents	% row	% column
Drugs	294	84%	31.2%	56	16%	11.6%	350	100%	24.6%
Mecanical ventilation and artificial airway	107	74.3%	11.3%	37	25.7%	7.7%	144	100%	10.1%
Lines, catheters, and drains	133	89.9%	14.1%	15	10.1%	3.1%	148	100%	10.4%
Equipment	207	94.5%	22%	12	5.5%	2.5%	219	100%	15.4%
Diagnosis	87	73.7	17.3	31	36.3%	6.5	118	100%	8.3%
ICU management	81	39.1%	8.6%	126	60.9%	26.2%	207	100%	14.5%
Procedures	29	41.4%	3.1%	41	58.6%	8.5%	70	100%	4.9%
Nosocomiial infections	0	0%	0%	116	100%	24.1%	116	100%	8.1%
Others	5	9.6%	0.5%	47	90.4%	9.8%	52	100%	3.7%

CONCLUSIONS. Our study shows a high individual risk. Our ICUs services present a high-risk environment. Therefore we have to go into the developement of epidemiological studies depth, in order to create further strategies supporting patient safety.

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COMMUNICATION: A KEY FACTOR IN THE PATIENT SAFETY?

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INTRODUCTION. Communication problems are often a contributing factor in patient safety problems

OBJECTIVES. To assess the impact of communication problems among the ICU's professionals on patient safety, as the problems of communication on ICU's professionals have been identified as one of the most important factors on patient safety problems.

METHODS. Multicenter prospective observational cohort study. Inclusion criteria: patients admitted to the 79 participant ICU's during the 24-h observation period. During this period, ISD and EA detected and reported inside and outside ICU were included. Only outside ICU's were considered when its were the reason for admission. We evaluated the importance of communication as a contributing factor to the mentioned incidents, depending on the kind of incident, severity and preventability. We analyzed the qualification of professional worker who detected the communication problem. The data collection presented as the frequency distribution, and its association contrasts with the chi square test. Null hypothesis was rejected at the $p < 0.05$.

RESULTS. 1,017 patients included. 1,424 incidents were reported. During the study period, 145 communication problems were reported as a contributing factor to 120 incidents. 60% of the communication problems were reported in relation to drug related incidents. The incidents were classified as incidents without damage (ISD) (98) and adverse events (AE) (22). The 80.69% of the problems contributed to ISD appearance and the 19.31% to EA appearance. The communication problems was responsible of the some avoidable problems (96.67%). The nurses reported the 74.48% of the communication problems. All these differences were statistically significant.

CONCLUSIONS. Communication problems were only detected in a 8.45% of the incidents. These were mainly associated to administration medication problems, incidents without damage and avoidable incidents. The nursing staff showed a greater sensitivity to the communication problems that doctors.

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Prevention and diagnosis of kidney injury: 1255–1267

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COMPARISON BETWEEN SERUM CYSTATIN-C AND SERUM CREATININE-BASED EQUATIONS TO ESTIMATE GLOMERULAR FILTRATION RATE IN CRITICAL PATIENTS

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INTRODUCTION. Importance of renal assessing in intensive care unit (ICU) patients is unquestionable for a correct drug dosing, fluid requirements or decisions for renal replacement therapies. Serum creatinine (SC) is a very common biochemical parameter in clinical practice for assessment of renal function. Many equations have been designed to estimate creatinine clearance based on SC, but their capacities for providing a correct estimate of glomerular filtration rate (GFR) are suboptimal. This is even worse in critically ill patients due to malnutrition and/or immobilization. In clinical practice, despite its limitations, 24 h-urine creatinine clearance ($CrCl_{24h}$) is used as a reference method to determine GFR. Data show that Cystatin-C could be promising as an endogenous filtration marker in ICU settings.

OBJECTIVES. To assess in a medical ICU population whether the Arnal-Dade formula of cystatin-C clearance (CC) developed from serum cystatin-C (SCC) shows better predictive performance of GFR than SC-based formulae, as regards to patients' renal function: $CrCl_{24h} \geq 60$ mL/min 1.73 m^2 or $CrCl_{24h} < 60$ mL/min 1.73 m^2.

METHODS. Prospective observational study including 241 samples of 131 ICU patients. Demographic [age, sex, race, height and weight] and biochemical [(SC, SCC, serum albumin, blood urea nitrogen and $CrCl_{24h}$)] data were collected. Comparisons were done between CC and (1) the reference ($CrCl_{24}$), and (2) three SC-based equations: Cockroft-Gault (CG), Modification of Renal Disease (MDRD) and four-variable Modification of Renal Disease (fv-MDRD). Correlation coefficients, bias and precision were evaluated.

RESULTS. All formulae showed notable bias from the reference method. Interestingly, all equations based on SC-values clearly overestimated $CrCl_{24h}$ (CG: 19.6%; MDRD: 1.1%; fv-MDRD: 27.5%), whereas CC showed underestimation of these $CrCl_{24h}$ (CC: −17.5%). In the $CrCl_{24h} \geq 60$ mL/min 1.73 m^2 group ($n_{\geq 60} = 146$; 89 patients), CC showed the best correlation indexes (CC-$CrCl_{24h}$; $r^2 = 0.296$, $r = 0.544$), the second most biased (−16.7%) and the worst precision (24.9%). In this group, MDRD was the least biased (−2.4%) and the most precise (21.3%). In the $CrCl_{24h} < 60$ mL/min 1.73 m^2 group ($n_{< 60} = 95$; 54 patients), CC was the worst correlated with $CrCl_{24h}$ ($r^2 = 0.214$, $r = 0.462$), in contrast to MDRD ($r^2 = 0.299$, $r = 0.547$). In terms of precision, MDRD showed again better results than CC: 33.5% vs. 38.9%, respectively.

CONCLUSIONS. In our ICU population, CC did not demonstrate a clear improvement on the remainder SC-based formulae in either of the two groups according to $CrCl_{24h}$. However, in a patient with high MDRD values and suspicion of low GFR, CC could be useful as guidance before obtaining the definitive confirmation by $CrCl_{24h}$.

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STANDARD EQUATIONS THAT ESTIMATE GFR DO NOT ACCURATELY PREDICT CREATININE CLEARANCE IN CRITICALLY ILL PATIENTS WITH ACUTE KIDNEY INJURY

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INTRODUCTION. There are well established and robust techniques for measuring and categorizing renal function in people with chronic kidney disease (CKD). A number of rapid bedside estimates of renal function have been devised incorporating routine daily measurements, such as serum creatinine, in combination with demographic data (e.g. Cockroft-Gault, the MDRD series). The addition of serum cystatin C measurements to some equations may also improve accuracy of estimation. The current and accepted categorical classification of Acute Kidney Injury (AKI: AKIN/RIFLE) has been useful epidemiologically but does not provide a continuously variable measure of severity of AKI which would be valuable for both clinical management and research.

OBJECTIVES. Previously published abstracts have suggested a role for eGFR in describing renal function in the critically ill but a more comprehensive analysis was needed.

METHODS. 37 (21 male) (mean age 72 range 38–90) critically ill patients with AKI were recruited. A 4 h creatinine clearance (^{4}CrCl) (previously validated as a measure of renal function in critically ill patients) was measured and simultaneous blood sampling was done for creatinine, urea, albumin and cystatin C. Various equations used to estimate GFR were compared to ^{4}CrCl with regression and Bland-Altman analysis. All patients had a ^{4}CrCl of <60 mL min per 1.73 m^2

RESULTS.

RESULTS

	*CrCl	1 Cr	Cock croft and Gault	aMDRD	MDRD 6
Mean eGFR	27.1	53.43	35.5	33.3	35.53
Range	8–51	13–119	11–63	9–87	9–79
Bias		−26.3	−8.4	−6.2	−5.14
1.96 SD		28	13.72	18.6	16.66
% error		52	39	56	47
r^2 $p < 0.01$		0.64	0.82	0.72	0.75

	MDRD 7	Cystatin C 1	Cystatin C 3	Cystatin C 4
Mean eGFR	28.8	43.24	41.03	39.68
Range	8–71	17–85	16–79	15–79
Bias	−1.6	−16.11	−13.89	−12.54
1.96 SD	16.6	20.14	19.36	16.6
% error	58	46	47	42
r^2 $p < 0.01$	0.71	0.71	0.71	0.70

CONCLUSIONS. While equations which estimate GFR correlated reasonably with 4 h creatinine clearance in critically ill patients with AKI they did not predict creatinine clearance sufficiently accurately to add value to current approaches. With modifications, eGFR estimates may become more useful in the future for this patient group but there is no justification for applying these equations at present

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URINARY KIDNEY INJURY MOLECULE (KIM-1) IS AN EARLY MARKER OF SEPSIS-INDUCED ACUTE KIDNEY INJURY

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INTRODUCTION. Although sepsis induced acute kidney injury (AKI) is well-recognized, its diagnosis still relies on measurement of serum creatinine concentration and urine flow, which change slowly and have low specificity and sensitivity. Kidney injury molecule (KIM-1) has been identified as a promising biomarker for early detection of AKI [1].

OBJECTIVES. To validate urinary KIM-1 as an early marker for acute kidney injury in patients with sepsis.

METHODS. Prospective observational study included 43 consecutive adult patients with sepsis admitted to surgical ICU and 11 healthy controls. Urine samples were collected on admission to the ICU and 48 h later. Urinary KIM-1 levels were measured with commercially available enzyme-linked immunosorbent assay (ELISA) kits. AKI was diagnosed using AKI Network criteria [2]. Patients were managed independently by the ICU team. Hemodynamic and laboratory parameters were measured daily, until ICU discharge or death.

RESULTS. Urine KIM-1 levels were significantly higher in patients with sepsis both on admission to ICU (1,057.2 pg/ml) and 48 h later (933.5 pg/ml) then in healthy controls (267.6 pg/ml). KIM-1 levels on admission were lower in non-survivor group then in survivor group ($p < 0.05$). The area under the receiver operating characteristics curve for urinary KIM-1 level indicated that it was good predictor of sepsis outcome but not a good predictor of AKI as defined by AKIN.

CONCLUSIONS. Urinary KIM-1 is elevated early in patients with sepsis suggesting that sepsis-related renal injury affects proximal tubules. Higher levels of KIM-1 could predict better outcome of sepsis.

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ORGAN HEALING AND FIBROSIS: INTERCELLULAR CONTACTS AND *B*-CATENIN PLAY A MAJOR ROLE IN EPITHELIAL SMOOTH MUSCLE EXPRESSION

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INTRODUCTION. Epithelial-mesenchymal transition (EMT), a key process in tissue development and repair, has also been identified as a major mechanism in fibrogenesis. The cytokine TGFβ has been shown to induce transformation of epithelial cells into matrix-forming and smooth muscle actin (SMA)-expressing myofibroblast (MF) via EMT. The other prerequisite is an injury-induced loss of intercellular contact, including adherens junctions (AJs). The classical experimental method to induce AJ disruption is the uncoupling of E-cadherin-mediated contacts by Low Calcium Medium (LCM). This concept has been termed as the two-hit model of EMT (1). β-catenin, a scaffold protein of the AJ, released by cell contact injury, can act as a transcription factor and has been shown to facilitate EMT. However, the mechanism whereby cell contact injury promotes EMT is not understood. Our recent studies have shown that Smad3, one of the main signal transducers of the TGFβ pathway is a strong inhibitor of epithelial SMA expression, by interfering with myocardin-related transcription factor (MRTF) [2]. The latter is the main driver of the SMA promoter, through it association with serum response factor (SRF). Intriguingly, β-catenin can bind to Smad3.

OBJECTIVES. To clarify the mechanisms whereby AJ injury promotes SMA expression.

METHODS. AJs were manipulated in kidney tubular cells, either by siRNA-mediated down-regulation of E-cadherin, β-catenin or through chemical uncoupling of AJs by LCM. Protein expression was detected by Western blotting and immunofluorescence microscopy, protein-protein interactions were monitored by co-immunoprecipitation, and the activity of the SMA promoter was determined by luciferase reporter assays.

RESULTS. Knockdown of E-cadherin promoted β-catenin translocation to the nucleus and induced a threefold rise in the TGFβ-triggered SMA expression. Conversely, silencing of β-catenin strongly suppressed the two-hit (TGFβ + LCM)-induced activation of the SMA promoter, and inhibited SMA protein and mRNA expression by 50%. The same stimuli induced strong association of β-catenin with Smad3. Transfection of cells with a β-catenin expression vector dose-dependently prevented the inhibitory action of Smad3 on the MRTF-induced activation of SMA promoter. Moreover the active (myogenic) MRTF-SRF complex was restored, as β-catenin preempted Smad3's inhibitory effect on the complex.

CONCLUSIONS. These studies define a novel mechanism whereby epithelial injury activates the myogenic program, a central process in organ fibrosis. Our results imply that β-catenin, liberated from the injured AJs, facilitates the activation of the myogenic program by preventing or mitigating the inhibitory action of Smad3 on MRTF. These hitherto unknown interactions among Smad3, β-catenin and MRTF represent novel targets to lessen fibrogenesis.

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DISCREPANCIES BETWEEN ACTUAL AND ESTIMATED RIFLE CLASS AND THE EFFECT OF URINE OUTPUT

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INTRODUCTION. The RIFLE classification for acute kidney injury (AKI) is based on relative changes in serum creatinine (SCr) and on urine output (respectively $RIFLE_{SCr}$ and $RIFLE_{uo}$). The criteria that lead to the worst possible classification determines the final RIFLE class ($RIFLE_{final}$). The $RIFLE_{SCr}$ require an actual pre-morbid baseline value. When this value is unknown, current recommendations are to estimate the baseline SCr by the Modification of Diet Renal Disease (MDRD) equation [1]. This method was shown to result in bi-directional misclassification of the $RIFLE_{SCr}$ class, however, the impact of this method on the $RIFLE_{final}$ class were not reported [2].

OBJECTIVES. We compared the maximum $RIFLE_{SCr}$ based on the premorbid SCr ($aRIFLE_{SCr}$) with that based on the estimated SCr ($eRIFLE_{SCr}$) and determined the effect on the $RIFLE_{final}$

METHODS. Prospective observational study during a 6-month period in patients of ≥18 years admitted to the ICU for at least 48 h and with a known pre-morbid SCr. The lesser of ICU-admission SCr and premorbid SCr was defined as the actual baseline. Likewise, the lesser of ICU-admission and MDRD based SCr was defined as the estimated baseline. In each patient we calculated the worst AKI score during the first seven ICU days, based on respectively the $aRIFLE_{SCr}$, $aRIFLE_{final}$, $eRIFLE_{SCr}$ and $eRIFLE_{final}$.

RESULTS. A pre-morbid SCr was available in 101 (39%) out of the 259 analyzed patients. Mean age and APACHE II score were respectively 64 ± 13 years and 22 ± 7. The frequency of misclassification of $RIFLE_{SCr}$ and $RIFLE_{final}$ are shown in Tables 1 and 2 respectively.

RIFLESCR ACCORDING TO ACTUAL AND ESTIMATED SCR

Maximal eRIFLESCr	Maximal aRIFLESCr				
	No-AKI	Risk	Injury	Failure	Total
No-AKI	**51 (50.5%)**	3 (3%)	1 (1%)	0	55 (54.5%)
Risk	10 (9.9%)	**9 (8.9%)**	2 (2%)	0	21 (20.8%)
Injury	5 (5%)	4 (4%)	**4 (4%)**	1 (1%)	14 (13.9%)
Failure	0	1 (1%)	2 (2%)	**8 (7.9%)**	11 (10.9%)
Total	66 (65.3%)	17 (16.8%)	9 (8.9%)	9 (8.9%)	**101 (100%)**

RIFLEFINAL ACCORDING TO ACTUAL AND ESTIMATED SCR

Maximal eRIFLEfinal	Maximal aRIFLEfinal				
	No-AKI	Risk	Injury	Failure	Total
No-AKI	**16 (15.8%)**	1 (1%)	0	0	17 (16.8%)
Risk	1 (1%)	**29 (28.7%)**	0	0	30 (29.7%)
Injury	0	1 (1%)	**23 (22.8%)**	1 (1%)	25 (24.8%)
Failure	0	0	2 (2%)	**27 (26.7%)**	29 (28.7%)
Total	17 (16.8%)	31 (30.7%)	25 (24.8%)	28 (27.7%)	**101 (100%)**

The $eRIFLE_{SCr}$ overestimated AKI in 22 (21.8%) patients and underestimated AKI in 7 (7%) patients, while the $eRIFLE_{final}$ overestimated AKI in 4 patients (4%) and underestimated AKI in 2 patients (2%).

CONCLUSIONS. Estimating the SCr baseline results in bi-directional misclassification of the $RIFLE_{SCr}$ class. The original RIFLE classification, however, is based on SCr and urine output criteria. When the urine output is taken into consideration the impact of a surrogate baseline on the misclassification of AKI is less pronounced.

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1260

ASSESSMENT OF INCREASED GLOMERULAR FILTRATION RATE IN ICU PATIENTS

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INTRODUCTION. Increased glomerular filtration (GFR) or hyperfiltration has been reported in ICU patients, and may be associated with inadequate antibiotic drug concentrations, and as a consequence, worse outcomes. Routine creatinine measurements lack sensitivity and specificity. Hence, assessment of hyperfiltration may be problematic.

OBJECTIVES. Evaluation of methods for assessment of GFR in a cohort of ICU patients with hyperfiltration.

METHODS. Single center prospective cohort study in the ICU of the Ghent University Hospital. Inclusion criteria were age ≥18 years, informed consent, urinary creatinine clearance (Ccr) >120 mL/min on the day preceding the study, and presence of urinary catheter, central venous catheter and arterial catheter. GFR was assessed with an urinary inulin clearance (Cin) as gold standard, and compared to serum creatinine and Cystatin, 2 and 24-h Ccr, the Cockcroft-Gault (CG), MDRD and MDRDs equations for GFR, and cystatin-C based equations for GFR (Hoek, Filler, Larsson, Le Bricon). Comparison was with the Wilcoxon test and the Pearson correlation coefficient. Bias was assessed by the mean difference between Cin and different methods, precision by standard deviation (SD) of the bias.

RESULTS. 23 patients were included in the study, 74% were male, and median age was 50 y (interquartile range, 36–62). APACHE II score on admission was 14.6 (SD 7), and SOFA score at time of study was 2 (SD 2.1). Cin was 129.6 (SD 72.5) mL/min, creatinine 0.49 mg/dL (SD, 0.19), and Cystatin C 0.79 mg/dL (SD 0.60). There was a relative good correlation between Cin and 1/Cystatin C ($r = 0.542$, $p = 0.008$), and no correlation with 1/creatinine ($r = 0.149$, $p = 0.424$). Comparisons with Cin are illustrated in the Table.

ASSESSMENT OF GFR VS. CIN

	Mean (SD)	P (vs. Cin)	Correlation coefficient (p)	Bias	Precision
Ccr 2-h	169.9 (61.3)	0.052	0.287 (0.195)	−42.3	−198 to 114
Ccr 24-h	156.2 (79.9)	0.134	0.308 (0.163)	−30.1	−207 to 147
Hoek	114.8 (31.2)	1.000	0.536 (0.008)	18.0	−105 to 141
Larsson	128.8 (40.5)	0.678	0.558 (0.006)	2.4	−116 to 121
Filler	143.6 (41.2)	0.210	0.550 (0.007)	−12.8	−132 to 107
Le Bricon	119.9 (30.3)	1.000	0.542 (0.008)	13.1	−110 to 136
CG	173.9 (58.4)	0.017	0.159 (0.479	−39.2	−206 to 128
MDRD	295.1 (116.9)	<0.001	0.086 (0.704)	161.2	−413.2 to 90.7
MDRDs	183.5 (73.2)	0.031	0.142 (0.530)	−45.2	−222.6 to 132.3

CONCLUSIONS. In a cohort of ICU patients with hyperfiltration, none of the tested methods for assessment of GFR were adequate compared to the gold standard Cin. The Cystatin C derived equations, especially Larsson, performed best for assessment of GFR, because bias was minimal, however, precision was weak.

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WHOLE-BLOOD NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) AS A PREDICTOR OF ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Acute kidney injury (AKI) in the intensive care units (ICU) is associated with a high in-hospital mortality, between 45 and 60% of cases. Early detection of AKI could be crucial to develop therapeutic strategies that could modify the AKI course as far as possible. Blood and urinary concentrations of NGAL are early biomarkers of AKI [1]; NGAL is also an acute phase protein which can be elevated in other processes like systemic immune response system (SIRS), sepsis and septic shock. Most studies about the NGAL value to predict AKI were done in patients after cardiac surgery and little information exists regarding NGAL usefulness in critically ill patients.

OBJECTIVES. To analyze: 1. the capacity of whole-blood NGAL (wbNGAL) to predict AKI—evaluated by RIFLE score—in critically ill patients and,

2. the wbNGAL values in patients with SIRS, sepsis or septic shock.

METHODS. NGAL was measured in whole-blood by a point-of-care device (Triage® NGAL Test, Inverness Medical Innovations) at admission and 48 h later in patients admitted to a general ICU. Patients were classified both by RIFLE score at admission and 24 and 48 h later and by wbNGAL concentrations at admission. To the later classification, the cut-point for AKI prediction was obtained by ROC curve analysis. wbNGAL values at admission were compared in patients with SIRS, severe sepsis or septic shock. Clinicians were blinded to NGAL results.

RESULTS. The study included 100 consecutively-admitted patients (40 female) with mean age 59.1 ± 17.8 years, and length of ICU stay of 10.3 ± 9.6 days. Seventy-one developed SIRS, 9 severe sepsis and 20 septic shock. Eigtheen patients developed RIFLE F score, 14 of them at ICU admission; extracorporeal renal therapies were required in 9 cases. When patients were classified according to their RIFLE score at 24 h of admission, wbNGAL values at admission were 71 (60–167) ng/mL in 61 patients with RIFLE 0, 186 (87–330) ng/mL in 7 with RIFLE R, 381 (299–445) ng/mL in 10 with RIFLE I and 558 (246–1,060) ng/mL in 15 with RIFLE F ($p = 0.0001$). Four patients were discharged before 24 h [wbNGAL 384 (60–783) ng/mL]; whereas the 3 patients who died before 24 h had wbNGAL at admission of 685 (187–862) ng/mL. The area under ROC curve of wbNGAL at admission for AKI prediction was 0.84 (95% confidence interval 0.76–0.91, $p = 0.0001$), with an optimal cutoff value of 178 ng/mL with 77% sensitivity and 79% specificity. Fifty-five patients have NGAL ≤ 178 ng/mL. wbNGAL concentrations at admission were 81 (60–187) ng/mL in 71 patients with SIRS, 261 (193–481) ng/mL in 9 patients with severe sepsis and 623.5 (361–798) ng/mL in 20 patients with septic shock ($p < 0.0001$).

CONCLUSIONS. Whole blood NGAL concentrations measured at ICU admission appeared as an useful predictor of AKI in critically ill patients; in addition, wbNGAL concentrations showed an increasing pattern from SIRS to severe sepsis and septic shock.

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COMPARISON OF MEASURED AND ESTIMATED CREATININE CLEARANCE METHODS TO ASSESS RENAL FUNTION IN CRITICALLY ILL PATIENTS

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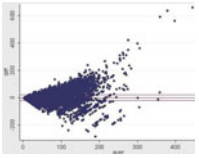
INTRODUCTION. In intensive care unit (ICU) patients, kidney function is monitored by the creatinine clearance (crcl). It can be measured by two methods. Urinary crcl (Ucrcl) is directly measured, using the urinary and serum creatinine. But commonly crcl is estimated from serum creatinine (Scr) alone, as estimated glomerular filtration rate (eGFR); using equations validated in chronic kidney diseases. There is paucity of literature on validation and comparison of these methods in ICU (Hoste).

OBJECTIVES. We compared 4-h timed Ucrcl and eGFR in the newly admitted critically ill. We also sought to ascertain the incidence of high crcl and the agreement between 2 methods in this subgroup.

METHODS. Retrospective, single-centre cohort of 2788 consecutive admissions to ICU. Simultaneous measurements on first day in ICU, were compared using Bland Altman method. Patients with high crcl (>150 ml/min) were separately examined.

RESULTS. The limits of agreement was −70 to 91, indicating poor agreement between the methods for clinical use. The mean bias was 7.34 mls/min. (c.i. 5.78–8.89) for the entire cohort and 21 ml/min. (c.i. 18–25 ml/min.) for those with normal crcl (90–150 ml/min.), with Ucrcl higher than eGFR. There were 249 patients with high crcl, where the bias was higher (103 ml/min., c.i. 88–117 ml/min.).



UCRCL AND EGFR AGREEMENT

CONCLUSIONS. In critically ill patients there is poor agreement between Ucrcl and eGFR, more pronounced at high creatinine clearances. In clinical practice it may be important to measure Ucrcl as well, particularly in high crcl group.

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IS CYSTATIN C AN EARLY PREDICTOR OF ACUTE KIDNEY INJURY, DIALYSIS INITIATION AND OUTCOME IN CRITICALLY ILL PATIENTS?

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AIMS. Potentially effective therapeutic interventions for acute Kidney Injury (AKI) are currently delayed due to paucity of early predictive biomarkers. The RIFLE criteria allow assessing the degree of renal dysfunction. We evaluated whether Cystatin C (Cys C) is an early predictive biomarker for AKI in a heterogenous population in the Intensive Care Unit (ICU). We also assessed the correlation of Cys C with the need for Renal Replacement Therapy (RRT) and the outcome (death) of critically ill patients (pts).

METHODS. Upon admission in the ICU, initial severity illness scores were calculated and the values of serum CysC and serum creatinine(Cre) were determined for up to 30 days. Pts were scored daily for the presence of AKI using Cre and urine output criteria of the RIFFLE system. AKI was diagnosed by having any of the R, I or F RIFLE criteria.

RESULTS. We studied 58 critically ill pts with APACHE score >13 (males 67%, mean age 62.6 ± 18.7 years), admitted in the multidisciplinary ICU of Hospital "Evangelismos". Of those patients, 40% developed AKI, 33% needed RRT and 53% died. A multivariate logistic regression analysis revealed an independent association between CysC_max (maximum value of CysC during pts ICU stay) and the need for continuous venovenous hemodiafiltration (CVVHDF) (OR = 3.77, $p < 0.006$), after controlling for possible confounding factors [gender, age, Apache II and maximum value of Cre during pts ICU stay (Cre_max)]. Furthermore, ROC curve analysis showed that CysC_max is superior in predicting pts who will need RRT compared with Cre_max (AUCs: 0.87, $p < 0.001$ vs. 0.82, $p < 0.001$, respectively). Cox regression proportional hazards analysis revealed an independent association between CysC_1 (CysC the day of ICU admission) and AKI (regardless of stage according to RIFFLE criteria) (HR = 2.27, $p < 0.028$), after adjusting for possible confounding factors [gender, age, Apache II and Cre the day of ICU admission (Cre_1)]. A ROC curve analysis on the day the patients developed the early stage of AKI (R according to RIFFLE criteria) indicated a significant overall predictive ability for CysC (AUC = 0.82, $p < 0.004$). A CysC cut-off value of 1.64 predicted the early stage of AKI with a sensitivity of 0.87 and a specificity of 0.70.

CONCLUSION. The use of RIFLE criteria gives a high incidence of AKI in the ICU setting. In this unselected population of critically ill pts, CysC seems to be superior to Cre in predicting pts who will develop AKI and will need RRT during their hospitalization in the ICU. Early identification of high risk patients may allow potentially beneficial therapies to be initiated early in the disease process, before irreversible injury occurs.

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ASSESSMENT OF RENAL PERFUSION DURING FLUID CHALLENGE USING RENAL DOPPLER

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INTRODUCTION. Doppler-based renal resistive index has been proposed as a mean to monitor renal perfusion. However, several factors influence renal resistive index including renal resistances, renal vascular compliance, or interstitial renal pressure. This may explain discrepancies regarding interest of RI in renal perfusion assessment. The purpose of this study was to evaluate changes in renal resistive index (RI) after a fluid challenge in critically ill patients.

PATIENTS AND METHODS. Prospective, multicenter, study performed on patients requiring a fluid challenge. Patients were included if under mechanical ventilation and monitored by an oesophageal Doppler. Doppler based RI was monitored before and after fluid challenge (Isotonic saline: 500 mL). Fluid responsiveness was defined as an increase in stroke volume of more than 15%. Acute kidney injury was defined accordingly to the AKIN definition. Results are reported as median [IQR].

RESULTS. 19 patients of 67 [39–78] years were included. Main reason for ICU admission was septic shock in every of the included patients. At inclusion median SOFA score was of 11 [7–14]. At study inclusion, ten patients had an acute kidney injury and 16 received vasopressors.

Of the included patients, ten (53%) were considered as having fluid responsiveness accordingly to our definition. Median resistive index before and after fluid challenge was of 0.71 [0.67–0.76] and 0.72 [0.70–0.75] respectively.

Main results are reported in the Table 1. Overall, changes in RI were not different in patients with and without fluid responsiveness.

TABLE 1 MAIN PHYSIOLOGICAL VARIABLES BEFORE (T0) AND AFTER FLUID CHALLENGE (T1)

	Total (N = 19)	No fluid responsiveness (N = 9)	Fluid responsiveness (N = 10)	P
MAP T0 (mmHg)	70 [67–78]	70 [68–79]	71 [59–74]	0.41
MAP T1 (mmHg)	79 [72–81]	79 [75–81]	78 [65–87]	0.99
Stroke volume T0 (mL)	39 [27–54]	41 [34–79]	35 [25–50]	0.12
Stroke volume T1 (mL)	45 [32–70]	45 [37–82]	43 [30–70]	0.35
Renal RI T0	0.71 [0.67–0.76]	0.77 [0.67–0.81]	0.71 [0.70–0.76]	0.30
Renal RI T1	0.72 [0.70–0.75]	0.74 [0.71–0.75]	0.72 [0.67–0.77]	0.65
Changes in stroke volume (%)	11.1% [4.3–28.4]	3.8% [0.1–7.4]	27.1% [15.4–40]	0.002
Changes in IR T0-T1(%)	+1.9% [−4.7 ± 6.2]	−4.2% [− 6.4 ± 7.2]	+2.3% [+1.7 ± 3.3]	0.28

Interestingly, RI changes were not correlated with stroke volume in patients with or without fluid responsiveness ($R = 0.48$; $P = 0.20$ and $R = 0.42$; $P = 0.27$ respectively).

CONCLUSION. Our preliminary results suggest that fluid challenge has little impact on renal resistive index. In addition, our results suggest that in critically ill patients, stroke volume has no statistical no clinically relevant impact on renal resistive index. Interestingly, this remains true for the subgroup of patients responding to fluid challenge. Additional patient are currently being included in this study in way to confirm these results and to adjust for confounding factors.

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COMPARISON OF IODIXANOL AND IOHEXOL FOR THE PREVENTION OF CONTRAST-INDUCED NEPHROPATHY

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INTRODUCTION. The contrast-induced nephropathy (CIN) is consider to be the most frecuence reason of acute renal failure in hospitalized patients. They are defined by a fixed increase (0.5 mg/dl) o a 25% rise serum creatinine level after to be exposed 24 h to the contrast. The main complications are kidney and cardiac problems and this will lead to longer hospitalization and increased mortality.

OBJECTIVES. To compare CIN occurrence after a injecting a iso-osmolar contrast (IOC, Idixanol) or a low-osmolar contrast (LOC, Iohexol) to a group of patients submitted to coronary angiography, with o without percutaneous coronary intervention (PCI). To establish unrelated CIN markers and to evaluate the efficiency of the kidney protection protocol used in our hospital.

METHODS. A prospective observational study includes 267 patients of which 129 received IOC (April to June 2009) and 138 LOC (August to October 2009). CIN risk were clasifiqued in a point-giving system and preventive treatment was based on 0.9% isotonic saline and oral Acetylcysteine for both groups.

RESULTS. The age of the group of patients who received LOC was lightly superior (65.3 ± 9.8 vs. 6.1 ± 105; $p = 0.01$) and in this group there were more female (40.6% vs. 24.8%; $p = 0.006$); in the other demographics and clinical stats there were no significant differences found. There was no different in the volume contrast average administrated (237.9 ± 109.8 cc LOC vs. 222.9 ± 99.2 cc IOC; $p = 0.7$) nor in PCI percentage (42.4% LOC vs. 39.3% IOC; $p = 0.2$). The total prevanlence of CIN was 16% in the LOC group compared to 10.4% in the IOC group. No patient included in this study needed dialysis. All cases were presented as transitory acute renal failure with spontaneous solution although longer hospitalization was required (36 vs. 96 h; $p < 0.001$). In the multivariate analysis the use of IOC was a protective factor (OR 0.48; CI 95%:0.22–0.80; $p = 0.03$). The presence of diabetes mellitus (DM) (OR 1.9;CI 95%: 1.2–4.1; $p = 0.004$), hematocrit <39% (OR 2.7; CI95%: 1.2–6.7; $p = 0.015$), acute myocardial infarction (AMI) (OR = 2.9; CI95%: 1.4–6.3; $p = 0.006$), treatment with diuretics (OR = 4.3; CI95%: 1.9–10; $p = 0.001$), were found to be independent predictors.

CONCLUSIONS. The LOC was associated to a greater number of CIN than IOC. Patients who developed CIN were significantly longer hospitalized. The use of point giving system that includes CIN's predictors like DM, hematocrit <39%, AMI, and treatment with diuretics helps us to classify CIN risk and use a correct kidney protection protocol.

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1266

URINE NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) AS A PREDICTOR OF ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS

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INTRODUCTION. The incidence of Acute Renal Failure in the intensive care unit (ICU) is around 50% of cases and is related to increase in mortality in patients who required dialysis as far as 80%. Early detection of acute kidney injury (AKI), after damage is not on set could be crucial to develop therapeutic strategies to modify the course of injury. Blood and urinary concentrations of NGAL are early biomarkers of AKI[1]; to date, little information exists regarding NGAL usefulness in critically ill patients.

OBJECTIVES. To analyze: 1. the capacity of urine NGAL (uNGAL) to predict AKI—evaluated by RIFLE score—in critically ill patients and,
2. the uNGAL values in patients with SIRS, sepsis or septic shock.

METHODS. NGAL was measured in urine sample by an automatic analyzer device (ARCHITECT ci4100®; Abbott Diagnostics) at admission and 48 h later in patients admitted to a general ICU. Patients were classified both by RIFLE score at admission and 24 and 48 h later and by uNGAL concentrations at admission. To the later classification, the cut-point for AKI prediction was obtained by ROC curve analysis. uNGAL values at admission were compared in patients with SIRS, severe sepsis or septic shock. Clinicians were blinded to NGAL results.

RESULTS. The study included 76 consecutively-admitted patients (29 female) with mean age 59.6 ± 17.6 years, and length of ICU stay of 10.4 ± 10 days. Fifty-four SIRS, 6 severe sepsis and 16 septic shock. Thirteen patients developed RIFLE F score, 9 of them at ICU admission; extracorporeal renal therapies were required in 6 cases. When patients were classified according to their RIFLE score at 24 h of admission, uNGAL values at admission were: 26 (10–81) ng/mL in 48 patients with RIFLE 0, 163 (49–998) ng/mL in 5 with RIFLE R, 357 (151–596) ng/mL in 8 with RIFLE I and 384 (31–539) ng/mL in 10 with RIFLE F ($p = 0.02$). Five patients were excluded, three died before 24 h with uNGAL 816 (17–1,029) ng/mL and two were discharged before 24 h with uNGAL 182 (13–352) ng/mL. The area under ROC curve of uNGAL at admission for AKI prediction was 0.84 (95% confidence interval 0.74–0.92, $p < 0.0001$), with an optimal cutoff value of 114 ng/mL with 69% sensitivity and 84% specificity. Forty-seven patients have Ungal ≤ 114 ng/mL. uNGAL concentrations at admission were 30 (10–132) ng/mL in 54 patients with SIRS, 36 (10–235) ng/mL in 6 patients with severe sepsis and 400 (126–592) ng/mL in 16 patients with septic shock ($p = 0.001$).

CONCLUSIONS. Urine NGAL concentrations measured at ICU admission appeared as a useful predictor of AKI in critically ill patients; in addition, uNGAL concentrations showed an increasing pattern from SIRS to severe sepsis and septic shock.

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1267

THE RIFLE CLASSIFICATION FOR ACUTE KIDNEY INJURY: USING CALCULATED BASAL VALUE OF CREATININE OVERESTIMATES THE INCIDENCE OF ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Two previous studies using the RIFLE criteria in intensive care patients have found the incidence of acute kidney injury (AKI) to be 36 and 67%. However, these studies used calculated basal value of creatinine in a considerable proportion of their patients, which is a possible source of error.

OBJECTIVES. The aim of this study was to investigate the incidence and severity of acute kidney injury in intensive care patients using true baseline creatinine values.

METHODS. This was a retrospective study of all patients admitted to the intensive care units of Landspitali University Hospital (LSH) during the year 2007. Serum creatinine was found from hospital records but search for baseline values of serum creatinine was also conducted in other laboratories and health care facilities in the country. The severity of acute kidney injury was estimated by the RIFLE classification.

RESULTS. 1026 adult patients were admitted to the intensive care units at LSH during the year 2007 (mean age 60.6 ± 17.8 year, 61.1% males). A reliable baseline serum creatinine value was found at LSH for 71% of patients but by extending the search we identified a baseline value in over 99% of the patients. According to RIFLE classification 231 (22.5%) had acute kidney injury, 83 risk, 70 injury and 78 failure. However, if baseline creatinine was calculated in the 29% of patients that did not have a baseline value at LSH, as practiced in previous studies, additional 58 patients were diagnosed with AKI leading to a falsely higher incidence of 28.1%. Mean age of patients with AKI was 67 compared to 58 by those who did not develop AKI ($p < 0.001$). Hospital mortality of patients with AKI was four times higher (40.7%) than of those who did not develop AKI (9.1%).

CONCLUSIONS. The incidence of AKI in intensive care units of LSH is about 22.5%, which is lower than reported in recent studies. The incidence presented in this study is, however, in 99% of cases based on true baseline data on kidney function, while in previous studies using the RIFLE classification kidney function was estimated from a calculated creatinine value in a sizeable proportion of patients, possibly resulting in overestimation of the incidence of AKI.

1269

THIAMINE DEFICIENCY IN CRITICAL CARE PATIENT: ASSOCIATION WITH VITAMINS INVOLVED IN HOMOCYSTEINE METABOLIC ROUTE

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INTRODUCTION. Critical care is a patient susceptible to nutritional deficiency, especially in vitamin. B_1, B_2, B_6, B_{12} and Folic vitamins are involved in Homocysteine (Hcy) metabolic route. It has been demonstrated that low Hcy levels are associated with normal folic and B_{12} vitamin, and with lower cardiovascular risk.

OBJECTIVES. The aim of this study was to define the status of Hcy and B vitamins at admission and 7 days of ICU stay in critically ill patients, and to evaluate its relationship between them.

METHODS. A prospective study was done on critically ill consecutive patients with inclusion criteria: ≥18 years old, SIRS and APACHE II >15. Hcy, B12 and folic plasma levels were measured by enzymoimmunoassay and enzymatic method. for B1, B2 and B6 in erythrocyte. Permission was obtained from an institutional ethical committee and written informed consent was asked.

RESULTS. At 0 and 7 days of ICU stay 50 and 53% of patients were B_1 deficient, respectively. 12 and 20% were B_{12} deficient on both times, respectively. Folic levels show significant differences between 0 and 7 days of ICU stay. We found association between B_2 vitamin and Hcy at admission and 7 days. No differences were found between 0 and 7 days Hcy values.

CONCLUSIONS. Adequate status of vitamins is needed to be monitored at admission and during ICU stay of patients that may have prognostic and perhaps therapeutic implications. Development of B vitamin deficiencies may be associated with different metabolic and clinical alterations that are attributed to other causes or are unknown, but complicate evolution of critically ill patient. Measurement and monitoring of Hcy and B vitamin complex is important to prevent the development of serious and potentially fatal complications in critically ill patients.

Miscellaneous: 1268–1280

1268

ENERGY EXPENDITURE IN CRITICALLY ILL PATIENTS: COMPARATIVE ANALYSIS OF PREDICTIVE EQUATIONS AND INDIRECT CALORIMETRY

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INTRODUCTION. Careful determination of the energy requirements should be part of the first care applied to critically ill patients since the metabolic changes provoked by acute disease make nutritional evaluation a difficult clinical exercise.

OBJECTIVES. The aim of this investigation was to compare the resting energy expenditure (EE) calculated by Harris-Benedict equation (EE_{HB}) with the resting EE measured by indirect calorimetry (EE_{IC}) in critically ill patients under mechanical ventilation. Three sources of body weight were used to calculate the EE_{HB}, including: BW1 = portable scale measured, BW2 = Ideal body weight calculation = Male: 22.5 × Height^2, Female: 21.5 × Height^2 and BW3 = Predicted Body Weight Calculation = Male: 50 + 0.91 (height [cm] 152.4), Female: 45.5 + 0.91(height [cm] 152.4).

METHODS. One-hundred fourteen patients were included in this investigation. Energy expenditure was calculated by the Harris-Benedict equation (EE_{HB}) and measured by indirect calorimetry (EE_{IC}). Indirect calorimetry was performed during 30 min. Energy expenditure also was performed through Harris Benedict equation using real body weight and ideal body weight.

RESULTS. Resting energy expenditure calculated with the Harris-Benedict equation using the BW1 showed a significant (<0.0001) but low relative correlation ($r = 0.58$) with EE_{IC}, with a mean bias of 26.1 kcal day^{-1} and the limits of agreement ranging from −605.6 to 553.3 kcal day^{-1} as detected by the Bland-Altman analysis. The use of BW2 and BW3 yielded worse correlation indexes with EE_{IC} ($r = 0.34$, $p < 0.0001$; $r = 0.35$, $p < 0.0001$, respectively) with Bland-Altman analysis showing worse level of agreement and higher variability as compared to EE_{IC} (mean bias of 136.7 kcal day^{-1}, limits of agreement = −816 to 542.5 kcal day^{-1}; mean bias of 135.5 kcal day^{-1}, limits of agreement = −825 to 554 kcal day^{-1}, respectively).

CONCLUSIONS. These findings suggest that REE_{IC} seems to be more appropriate than EE_{HB} to accurate measure of EE in critically ill patients under mechanical ventilation. Moreover, the alternative methods to calculate the ideal body weight (BW2 and BW3) yielded decreased accuracy of the EE in critically ill patients.

GRANT ACKNOWLEDGMENT. We are thankful to Fundação de Amparo ao Ensino, Pesquisa e Assistência (FAEPA) do Hospital das Clínicas and Faculdade de Medicina de Ribeirão Preto-USP for financial support.

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THE PRESENCE OF AN ALLELE WHICH CODES FOR FUNCTIONAL CYP3A5 REDUCES THE EFFECT OF AKI ON HEPATIC MIDAZOLAM METABOLISM IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Cytochrome P450 3A (CYP3A), the most abundantly expressed cytochrome P450 enzymes in liver, are responsible for the metabolism of over 50% of drugs used across several therapeutic classes. In adults, CYP3A is represented primarily by the major isoform, CYP3A4, and a polymorphically expressed isoform, CYP3A5. Individuals with at least one wild-type *CYP3A5*1 allele* synthesise functionally active enzyme while homozygotes for the **3 allele* are functional non-expressers of the enzyme. The presence of functional CYP3A5 increases the hepatic metabolism of CYP3A substrates such as tacrolimus. CKD is known to reduce the hepatic metabolism of drugs via the CYP3A enzyme system and we have shown, recently, that AKI has a similar effect and that the length of time with AKI is the most important variable. We hypothesise that expression of functional CYP3A5 may reduce the impact of AKI on hepatic drug metabolism as has been shown to be the case for drug interactions with the imidazole antifungals.

METHODS. 72 (45 male) (mean age 72 range 23–90) critically ill patients with no AKI and varying degrees of severity of AKI were recruited. Midazolam concentration was measured 4 h after intravenous administration as a probe-drug for hepatic CYP3A 4/5 enzyme activity (T_4 [midazolam]). This is a validated method for testing CYP3A activity in critically ill patients. Patients were excluded if they were on any known CYP3A4/5 inhibitors.

RESULTS. Two patients with severe AKI had unexpectedly high T_4 [midazolam]. Figure 1 demonstrates the following: Without a CYP3A5*1 allele, the rate of midazolam metabolism increased with duration of AKI ($r^2 = 0.24$; $p < 0.0001$) (solid line). Patients who had at least one *1 allele (dashed line) were protected from the inhibitory effect that AKI has on hepatic drug metabolism (significant difference between the correlation lines $p = 0.011$). If the two major outliers are removed (dotted grey line) from the *3/*3 group ($r^2 = 0.23$; $p < 0.001$), the correlation lines remain statistically different ($p = 0.048$).

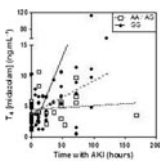

Figure 1

CONCLUSIONS. The presence of an allele which codes for functional CYP3A5 protects critically ill patients from the inhibitory effect of AKI on the hepatic metabolism of midazolam.

1271

BICARBONATE WITH $PACO_2$ AND CALCEMIA NORMALIZATION DOES RESTORE CARDIOVASCULAR PERFORMANCE IN SEVERE LACTIC ACIDOTIC RATS

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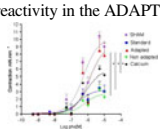
INTRODUCTION. Lactic acidosis during shock is responsible for myocardial failure, vascular hyporesponsiveness and a decrease in sensitivity to vasopressor agents. Sodium bicarbonate is a proposed treatment to correct acidosis, although with deleterious cardiovascular effects. Indeed, hypocalcemia and hypercapnia, both powerful myocardial depressants, are the main side effects of the administration of this therapy [1].

OBJECTIVES. Already studied in experimental models of isolated lactic acidosis, the cardiovascular effects of sodium bicarbonate administration have never been explored after correction for hypocalcemia and hypercapnia.

METHODS. We therefore compared, in a rat model of severe lactic acidosis (pH < 7.2, hyperlactatemia >3 mmol/l) induced by a state of controlled hemorrhagic shock, the cardiovascular effects of: (1) standard resuscitation plus administration of sodium bicarbonate with correction for calcemia and $PaCO_2$ ("ADAPT" group, n = 5); (2) standard resuscitation plus administration of sodium bicarbonate without correction for $PaCO_2$ and calcium ("NONADPAT" group, n = 5); (3) standard resuscitation; ("STAND" group, n = 5); (4) standard resuscitation plus calcium administration ("CALC" group, n = 5). Evaluation at steady and shock state, 60 min and 120 min was focused *in vivo* on arterial gas and myocardial contractility (Emax) by conductance catheter. *Ex vivo* vasoreactivity was tested on mesenteric arteries (300 µm) by myography. Sodium intakes were equivalent between groups.

RESULTS. Our model displayed a profound acidosis from 7.31 to 7.18 ± 0.01 ($p = 0.02$) and hyperlactatemia from 2.8 ± 0.4 to 9.2 ± 0.6 mmol/l ($p < 0.01$). Emax decreased from 2.5 ± 0.33 to 0.54 ± 0.06 mmHg/µl $p = 0.01$. In the ADAPT group, at 60 min, pH was normalized at 7.36 ± 0.01 ($p = 0.04$). Furthermore, Emax was enhanced at 332 ± 43% ($p < 0.001$) (STAND: 145 ± 26%, NONADAPT: 94 ± 18%, CALC: 234 ± 52%). The cumulative dose of infused norepinephrine was significantly lower in the ADAPT group 145 ± 26 µg/kg compared to other groups (STAND: 344 ± 10 µg/kg, NONADAPT: 438 ± 10 µg/kg, CALC: 423 ± 103 µg/kg, $p = 0.02$). *Ex vivo* mesenteric vasoreactivity in the ADAPT group was normalized (graph 1).



Mesenteric vasoreactivity to phenylephrine

CONCLUSIONS. In severe lactic acidosis, infusion of sodium bicarbonate after correction of its side effects improves myocardial function and vasoreactivity.

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1272

THE PREVALENCE AND CONSEQUENCES OF 25-HYDROXYVITAMIN D DEFICIENCY IN THE CRITICALLY ILL

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INTRODUCTION. 25-hydroxyvitamin D deficiency may have clinical consequences for intensive care patients [1]. The prevalence and significance of 25-hydroxyvitamin D deficiency in the intensive care unit have not been fully determined. A recent study of an unselected group of ITU patients [2] has suggested low ITU admission 25-hydroxyvitamin D levels are common.

OBJECTIVES/HYPOTHESES TO BE TESTED. Royal Free Hospital Intensive Care Unit patients exhibit low circulating levels of 25-hydroxyvitamin D. Circulating levels of 25-hydroxyvitamin D decrease further during the course of hospital admission. Admission circulating levels of 25-hydroxyvitamin D affect ITU morbidity and mortality

METHODS. All ITU admissions were assessed within 72 h of presentation and patients who were deemed to have the potential to require admission for at least 1 week were included. Demographic and clinical data were obtained in a prospective manner. Results were recorded from samples obtained at admission, 7 days and 28 days. Standard ITU nutrition protocols were used. No interventions were performed.

RESULTS. Clinical and outcome data were obtained for 40 patients. No significant differences between APACHE 2, SAPS 2 or APACHE 3 scores for survivor and non-survivor groups at either ITU or Hospital discharge were noted. 60 further patients await complete data analysis. 0% (0 of 39 for whom results were available) achieved an adequate (>75 nmol/l) circulating 25-hydroxyvitamin D level. 3 patients (7.7%) demonstrated levels within the insufficient range (50–75 nmol/l). 2 patients (5.1%) did not have any detectable 25-hydroxyvitamin D. The remaining 34 patients (87.2%) were either in the deficient (41.0%, 25–50 nmol/l) or severely deficient (46.2%, 10–25 nmol/l) ranges. Admission 25-hydroxyvitamin D levels in survivors and non-survivors were compared at ITU and Hospital discharge. No significant differences between the four groups (P > 0.05, ANOVA) were observed, indicating that in this data set, admission 25-hydroxyvitamin D levels do not appear to alter or determine clinical course. Mean 25-hydroxyvitamin D levels were compared at admission, Day 7 and at Day 28. No significant differences between the three groups (P > 0.05, ANOVA) were identified. No significant differences between the mean 25-hydroxyvitamin D levels of the survivors and non-survivors at Day 7 or Day 28 were apparent (small numbers).

ADMISSION 25-HYDROXYVITAMIN D LEVELS

	ITU	Hospital
Survivors	28.1 ± 3.4	29.9 ± 3.7
Non-Survivors	29.9 ± 5.6	28.2 ± 4.8

MEAN 25-HYDROXYVITAMIN D LEVELS

	Admission	Day 7	Day 28
Mean 25-hydroxyvitamin D levels (nmol/L)	29.5 ± 2.6	28.14 ± 2.5	25.5 ± 2.8

CONCLUSIONS. The majority of patients were profoundly 25-hydroxyvitamin D deficient. We were unable to detect a significant difference in the admission 25-hydroxyvitamin D levels of survivors and non-survivors at ITU or hospital discharge. A trend to reducing levels of 25-hydroxyvitamin D with duration of admission was noted and remained common in both survivors and non-survivors.

Analysis of the full data set of 100 patients is warranted.

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1273

EFFECT OF SALINE INFUSIONS ON QUANTITATIVE ("STEWART'S") ACID-BASE ANALYSIS IN PATIENTS UNDERGOING INTERVENTIONAL NEURORADIOLOGY PROCEDURES

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INTRODUCTION. Large volumes of 0.9% sodium chloride (NS) can contribute to metabolic acidosis in patients with septic shock [1,2] and patients undergoing surgical procedures [3]. Patients with neurological illness can receive significant quantities of NS, chosen primarily for its iso-osmolar properties.

OBJECTIVES. NS is commonly used as maintenance and resuscitation fluid by the anaesthetist, and as intravascular flushes by the radiologist during prolonged interventional neuroradiological (INR) procedures. This pilot feasibility study aimed to ascertain the effect of NS infusion on acid-base measurements in patients undergoing INR procedures under propofol-remifentanil anaesthesia.

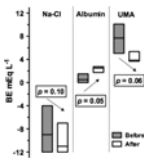
METHODS. We collated routine electrolyte, albumin and acid-base data of 5 patients who underwent coil/glue embolisations of intracranial aneurysms and vascular malformations, both before and after the procedure. Base excess (BE) was partitioned into the effects of sodium chloride difference (Na-Cl), albumin, lactate and unmeasured anions (UMA), using the Stewart-Fencl-Story approach [4]. All values are reported as medians (ranges). The Wilcoxon signed-rank test was used for analytical statistics.

RESULTS. Serum albumin decreased significantly:

SERUM MEASUREMENTS

Median (ranges)	Before	After	p value
Sodium (mEq/L)	137 (135–138)	141 (137–143)	0.06
Chloride (mEq/L)	107 (104–109)	112 (110–117)	0.06
Albumin (g/dL)	40 (36–42)	32 (31–35)	0.05

BE became more negative in all 5 patients (0.2 mEq L^{-1} before vs. −2.8 mEq L^{-1} after; $p = 0.06$). Sodium chloride difference and UMA both contributed to this base *deficit* (changes of 2.0 mEq L^{-1} and 3.9 mEq L^{-1} respectively). The fall in serum albumin had the opposite effect (contributing 2.0 mEq L^{-1} to base *excess*). Lactate made a negligible contribution.



BASE EXCESS CONSTITUENTS

CONCLUSIONS. A trend to widening Na-Cl and rising UMA contributed to an increasingly negative BE in patients undergoing prolonged INR procedures. Dilution of serum albumin partially ameliorated these BE changes. These changes may become clinically relevant to acid-base interpretation when severe dysnatraemias and fluid shifts occur in a diverse group of patients with neurological illness. The osmolar consequences of using 'balanced salt solutions' also have to be considered. There is a need for further studies of acid-base analyses in neurocritically ill patients.

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1274

HYPOCHOLESTEROLEMIA IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Total cholesterol (TC) is reduced as part of an acute-phase response to many disorders, including infection, malignancy, surgery and burn injury. This decrease occurs early in the course of critical illness and it has also been associated with nosocomial infections and increase magnitude of organ dysfunction. Although the mechanism is still unknown, cytokine release may be one important factor; there is a significant inverse relationship between cholesterol and C-reactive protein, IL-6 and IL-10. Some authors have concluded that cholesterol is an independent predictor of mortality.

OBJECTIVES. Evaluate the prevalence of low levels of cholesterol on admission and its variations during the first 24 h in critically ill patients.

METHODS. Prospective descriptive study with 41 patients randomly selected who were admitted to a Medical Surgical ICU from January to April 2010. Serial blood samples were collected on admission and on the morning of day 2; the Acute Physiology and Chronic Health Evaluation (APACHE) II score were computed and demographic data as well as ICU mortality were considered.

RESULTS. One patient died within the first 24 h, with the lowest TC on admission (TC-0) registered (54 mg/dL). There were included 40 patients: 27 male (67.5%), mean age 64.7 years, APACHE II score 11. There were 23 (57.5%) patients with low cholesterol (≤ 160 mg/dL) on admission and 33 (82.5%) on the day 2; mean TC-0 was 147.3 mg/dL and TC on the day 2 (TC-1) 114.8 mg/dL. There were reported a decrease in TC in 34 (85%) subjects. Patients with infection/septic shock (n = 7) had the lowest TC-0 (136 mg/dL), the greatest decrease (34.8%) and the highest APACHE II score (18); the post-surgery and trauma (n = 16) and non-septic shock (n = 3) groups had similar TC-0 (144.2 vs. 143.6 mg/dL) and decrease (27.1 vs. 27.8%), although the APACHE II score were different (9 vs. 14); patients with cardiovascular disease (n = 7) registered 24.7% decrease in TC, and TC-0 176.3 mg/dL. The overall mortality rate was 12.5% (n = 5), all deaths were in the lower-cholesterol group. Survivors versus non-survivors had TC-0 149.2 versus 134.0 mg/dL; TC-1 112.6 versus 97.2 mg/dL; TC decrease 21.4 versus 27.5% and APACHE II score 11 versus 22.

CONCLUSIONS. Critically ill patients had low cholesterol on admission in the ICU and become more hypocholesterolemic at an early point in their illness. These findings show a trend toward increasing mortality rate in patients with infections, shock and cardiovascular disease.

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EFFICACY OF RECOMBINANT HUMAN ERYTHROPOIETIN IN CRITICALLY ILL ANAEMIC SEPTIC PATIENTS

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INTRODUCTION. Anaemia commonly complicates the course of critically ill patients. By ICU day 3, approximately 95% of patients have Hb concentrations below normal. About 85% of patients with an ICU stay greater than 1 week receives blood transfusion with a significant increase in mortality rates compared with non transfused patients. rHuEPO was approved for human use in June 1989.

OBJECTIVES. To investigate the erythropoietic response to hight dose of a weekly schedule of recombinant human erythropoietin (rHuEPO) in critically ill anaemic septic patients.

METHODS. A total of 60 patients admitted to the intensive care unite (ICU) were enrolled in this study, patients were randomized to receive either rHuEPO or not, 30 patient did to form the rHuEPO group, 30 did not to form the control group.

RESULTS. The EPO treated group of patients showed significant increase in reticulocyte count compared with baseline $p < 0.001$, as well as with the control group $p < 0.006$. The EPO treated group exhibited also a significant increases in Hb concentration compared with baseline $p < 0.001$ as well as the control group <0.0 3. All patients in the control group received RBC blood transfusion 100%, while only 83.33% of the EPO group did. The EPO treated group showed significant decreases in their APACHE II score during the study period compared with baseline $p < 0.001$ as well as with the control group $p < 0.05$. The EPO treated group showed no significant difference in their SOFA score compared with baseline $p < 0.923$, however the control group exhibited continuous and significant increase in their SOFA score throughout the study period compared with their baseline $p < 0.003$, there was no significant difference in the final outcome recovery, mortality or morbidity $p < 0.337$, $p < 0.286$ respectively.

CONCLUSIONS. The administration of rHuEPO to critically ill anaemic septic patients is effective in raising their reticulocytic counts, Hb concentrations and in reducing the total number of units of RBCs they require. In addition there was a trend toward better in hospital clinical course, increased recovery and decreased mortality in the rHuEPO group.

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1276

PHARMACOKINETICS OF ORAL VERSUS INTRAVENOUS THYROXINE (T4) IN ORGAN DONORS

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INTRODUCTION. Thyroxine replacement therapy has become commonplace in the management of organ donors to reverse hemodynamic instability and homeostasis, yet the pharmacokinetics of thyroxine are unknown in this patient population [1,2]. Since T3 is only available in oral form, we studied the pharmacokinetics of oral versus intravenous T4 to determine if oral administration is suitable.

OBJECTIVES. (1) to study the pharmacokinetics of oral versus iv T4 therapy; (2) to determine if oral thryoxine therapy is suitable.

METHODS. With ethics approval and signed consent from the substitute decision maker, 34 patients who were determined to be neurologically dead and consented for organ donation, were randomized to receive either an oral or intravenous dose of T4 (2 mcg/kg). All patients received an oral and iv preparation; one of which was a placebo. This study was also double blinded and randomization occurred in blocks of 4–6. Free serum levels of T4 and T3 were measured hourly until the time of organ procurement. The area under the curves (AUC) were determined and compared using.

RESULTS. There were 15 patients (13 males) in the oral versus 17 patients (8 males) in the iv group, with an average age of 61 ± 14 vs. 53 ± 17, respectively. There was no significant difference at baseline or 6 h between groups for hemodynamic variables, free T4, free T3 or TSH levels. The only exception was MAP where it was higher at baseline in the oral group and there was a significant increase at 6 h in the iv but not the oral group (77–96 vs. 91–89 in the oral). The AUC for T4 was greater for the iv group (301 pmol/l/12 h) compared to the oral group (274 pmol/l/12 h). There was no statistically significant difference in any of the levels from 0 to 12 h between the oral and iv groups. Oral bioavailability of T4 was 91%.

CONCLUSIONS. Administration of iv T4 resulted in a slightly greater AUC compared to oral administration. However, oral bioavailability of T4 in our population was very high, at 91%. T3 is currently the recommended thyroid replacement in neurologically dead organ donors. However, intravenous T3 is unavailable in many jurisdictions. IV T4 has been used as a substitute. Our study shows that in this select population, oral bioavailability is high suggesting that oral T4 may be a reasonable alternative. Further work is needed to determine whether there was a difference in the number and rate of organ retrieval in the oral versus intravenous groups.

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1277

ORNITHINE-ASPARTATE COMPLEX ADMINISTRATION IN THERAPY OF ACUTE NECROTIZING PANCREATITIS IN CHRONIC ABUSE PATIENTS

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INTRODUCTION. Specific characteristics of metabolic derangements occurring in critical illness is domination of developing catabolic state particularly in acute necrotizing pancreatitis. As a result, we faced such a problem as developing a clinically apparent protein-calorie deficiency which is resistant to standard nutritional support. The treatment of acute necrotizing pancreatitis in chronic abuse patients is difficult to handle for the clinician and should include sufficient energoplastic supply.

OBJECTIVES. In our research we aimed to assess the efficacy of adding of ornithine-aspartate complex in carbohydrate metabolism in chronic abuse patients with acute necrotizing pancreatitis.

METHODS. 56 comparable chronic abuse patients with acute necrotizing pancreatitis (control group $N = 28$, mean age 45.1 ± 8.5; Ornithine group $N = 28$, mean age 44.0 ± 8.1) received early parenteral nutrition from the moment of admission to hospital with universal system "three-in-one". Ornithine group also received ornithine-aspartate complex by parenteral administration (40 g/day). On the second day the patients were admitted parenteral nutrition and tube feeding 24 h/day. The volume of parenteral nutrition was gradually decreasing. Biochemical and metabolic endpoints were measured at baseline and on 6th day (nitrogen balance, amino acids spectrum, plasma whole protein, transferring concentrations, glucose and insulin levels) at the Clinical Laboratory

RESULTS. In all patients metabolic disturbances with protein status and carbohydrate metabolism shifts were revealed. Dynamic of the whole protein, albumin/protein ratio and nitrous balance in both group showed similar tendency of metabolic improvement. Dynamic of essential and nonessential amino acids concentration remained normal showing adequate energoplastic supply in both groups. Glutamine concentration in Ornithine group remained stable and even increased by the 6th day of nutritional support, while in Control group glutamine concentration was decreasing, and by the 6th day of nutritional support it was below normal values. In Ornithine group higher levels of endogenous insulin at normal values of glucose and faster Fisher index improvement were detected.

CONCLUSIONS. Administration ornithine-aspartate complex in therapy of acute necrotizing pancreatitis in chronic abuse patients, probably, may influence on disease outcome.

In Ornithine group duration of delirium tremens causes was 4 ± 1 days versus Control group (6 ± 1 days). Restoration of metabolic activities confirms adequate nutritional support in both groups but ornithine-aspartate complex adding provides faster improvement of protein and carbohydrate metabolism.

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COMPARISONS OF NUTRITIONAL INDEXES INCLUDING PREALBUMIN AND SEVERITY SCORING SYSTEMS AS PROGNOSTIC INDICATORS IN SURGICAL INTENSIVE CARE UNIT PATIENTS

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INTRODUCTION. Prealbumin level was known as sensitive indicator for assessing the severity of critically ill patients. However, there is a little data showing the correlation between the serum prealbumin levels and the patient's outcome.

OBJECTIVES. This study was designed to evaluate the nutrition indexes including serum prealbumin level as prognostic indicators of patient recovery in critically ill patients with comparing severity scoring systems.

METHODS. We selected 59 patients over 16 years old, supplied with total parenteral nutrition (TPN) for more than 7 days in surgical intensive care unit, Ajou University Hospital, Suwon, Korea. The serum prealbumin, albumin levels and total lymphocyte count were measured at the first, 3rd, 5, 7, 10, 14th days of nutrition support care by TPN. We checked APACHE (acute physiology and chronic health evaluation) II score, SAPS (simplified acute physiology score), MODS (multiple organ dysfunction score) and SOFA (sequential organ failure assessment) score of patients.

RESULTS. There were 43 male patients and 16 female patients with mean age 54.3 years. The mean day of SICU staying was 13.2 days. We compared two groups; survivor group ($N = 49$) and non-survivor group ($N = 10$). There were significant statistical differences in ICU staying days ($p = 0.021$), APACHE II score ($p < 0.001$), SAPS ($p < 0.001$), MODS ($p = 0.007$) and SOFA score ($p = 0.005$) between two groups. However, serum prealbumin level ($p = 0.370$), albumin level ($p = 0.444$) and total lymphocyte level ($p = 0.584$) did not showed significant difference between two groups. Receiver Operating Characteristic curve showed low accuracy of serum prealbumin level as a prognostic factor (area = 0.559). Prealbumin level showed correlation with albumin ($r = 0.561$), however did not show correlation with APACHE II ($r = -0.151$), SAPS ($r = -0.056$), SOFA ($r = -0.056$) and MODS ($r = -0.076$).

CONCLUSIONS. Nutrition indexes including prealbumin did not correlated with clinical outcome of critically ill patients.

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ROLE OF ZINC ON ANTIOXIDANT STATUS IN CRITICALLY ILL PATIENT

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INTRODUCTION. Zn^{2+}-deficiency is linked to inflammatory processes mediated by reactive oxygen species that are increased in those lacking circumstances. Measurement and monitoring of Zn^{2+} is important to prevent the development of serious and potentially fatal complications in critically ill patients

OBJECTIVES. The aim of this study was to define the status of Zn^{2+} in plasma and erythrocytes at admission and 7 days of ICU stay in critically ill patients, and to evaluate its relationship with another antioxidant biomarkers as Mg^{2+} and superoxide dismutase (SOD).

METHODS. A prospective study was done on 54 critically ill consecutive patients with inclusion criteria: ≥18 years old, SIRS and APACHE II > 15. Zn^{2+} and Mg^{2+} were measured by flame Atomic Absorption Spectrophotometry (AAS) in wet-mineralized samples of erythrocyte. Mg^{2+}-and Zn^{2+}-content in administered nutrition was recorded daily during the 7 days of studied stay, and %RDIs were obtained. SOD activity was measured by spectrophotometry with an enzymatic method in erythrocytes. Permission was obtained from an institutional ethical committee and written informed consent was asked.

RESULTS. At admission 36.5 and 30.6% of patients were deficient in erythrocyte Zn^{2+}- and Mg^{2+}-, respectively, increasing to 49 and 41.2% at seventh day of ICU stay. There were significant differences between initial and final levels ($p < 0.05$, in both elements). A significant correlation was found between Zn^{2+}-administered by nutritional (PE and/or E) treatment (94% below RDIs) and erythrocyte Zn^{2+}-content ($p < 0.05$) at seventh day, and erythrocyte Zn^{2+}-level is positively associated with erythrocyte Mg^{2+}-level content ($p < 0.02$) and SOD activity ($p < 0.05$) of critically ill patients.

CONCLUSIONS. Adequate intake of Mg^{2+}- and Zn^{2+}-, and Mg^{2+}- and Zn^{2+}-levels in erythrocyte are needed to be monitored at admission and during ICU stay of patients and may have prognostic, and perhaps therapeutic, implications. Development of Mg^{2+}- and Zn^{2+}-deficiencies during an ICU stay may be associated with different metabolic and clinical alterations that are attributed to other causes or are unknown, but complicate evolution of critically ill patient.

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ANAEMIA DOES NOT AFFECT PHYSICAL QUALITY OF LIFE, ACTIVITIES OF DAILY LIVING OR ACTUAL PHYSICAL FUNCTION DURING MEDIUM TERM RECOVERY FROM CRITICAL ILLNESS

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INTRODUCTION. Physical function is impaired following critical illness [1]. Anaemia is a common complication of critical illness and has the potential to influence physical function [2]. It is not known whether anaemia affects the physical components of quality of life, the ability to carry out the activities of daily living (AODL) or the actual physical function of patients during recovery from critical illness.

OBJECTIVES. To determine the physical quality of life, ability to perform activities of daily living and actual physical function in a cohort of ICU survivors dichotomised on the presence of anaemia at 3 months following ICU discharge.

METHODS. Patients requiring >48 h of invasive ventilation or non-invasive ventilation plus one other organ failure were recruited from a general ICU population. Patients with a pre-existing haematological condition were excluded. Baseline and characteristics of ICU stay were recorded. The patients were assessed with the SF-36 quality of life questionnaire (PCS), The Frenchay Activities Index (FAI) of AODL recalled for pre-morbid status and at 3 and 6 months, and the 6 min walk test (6 MWT) for actual physical function at 3 and 6 months following discharge from ICU. Organotopic measures of haemaglobin, creatinine, serum C-reactive protein and albumin concentration were also recorded. The results were dichotomised on the presence of anaemia at 3 months for statistical analysis. Baseline characteristics were compared with Student's t test. A 2 way ANOVA was performed on the PCS and FAI score as well as comparisons with t test between each time-point. The distance walked as part of the 6 MWT was compared with Mann–Whitney U test.

RESULTS. Patients who remained anaemic at 3 months were older, had a longer ICU stay and had a greater requirement for inotropes during their ICU stay. The PCS score of quality of life and the FAI score was significantly impaired in both groups during follow up, but there was no effect of anaemia. The results of the t tests showed that there was a significant difference between the groups at 6 months for PCS but not for FAI scores. The distances walked were severely impaired compared to the normal population (170 and 228 m at 3 and 6 months for anaemic group and 240 and 358 m for non-anaemic) in both groups was not significantly different between the two groups. The non-anaemic group did increase the distance walked significantly from 3 to 6 months. There was no difference between albumin, CRP and creatinine concentrations between the groups.

CONCLUSIONS. Anaemia is common following critical illness but does not appear to affect the physical aspects of recovery during medium term rehabilitation. This may be due to an overwhelming degree of symptom burden from other complications of critical illness impairing physical function to such a degree that the effects of anaemia are negligible in the medium term.

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Basic research in sepsis: Pathophysiology 2: 1281–1294

1281

INFLUENCE OF PLASMA OF SEPTIC PATIENTS ON MITOCHONDRIAL FUNCTION

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INTRODUCTION. It is well established that mitochondria are affected by septic shock. Although decreases in number and function has mainly been described in skeletal muscle, also other organs seem to be affected and it has been hypothesized that mitochondrial dysfunction might be involved in the development of organ failure.

OBJECTIVES. To study the effect of plasma of patients with septic shock on mitochondrial function in vitro to potentially later on identify a central factor affecting mitochondria in all tissues during sepsis and leading to multiple organ failure.

METHODS. After sacrificing 6–8 week old Sprague-Dawley rats, mitochondria from soleus muscle were isolated through homogenization and a series of centrifugations. Mitochondrial function was assessed by measuring of oxygen consumption, using an oxygraph containing a Clarke-electrode, after addition of ADP. Before these measurements, mitochondria were incubated with plasma from septic patients or healthy volunteers, respectively, for 30 min. In our second series, the mitochondria were incubated with different concentrations of IL-6, TNF-α or buffer. Respiration rates were measured in the presence of ADP (state 3; a measure for the oxidative capacity to produce ATP) and without the presence of ADP (state 4; a measure for the amount of uncoupling). Respiratory control ratio (RCR; a measure for the respiratory efficiency of the mitochondria) was calculated by dividing state 3 by state 4 activity. All measurements were related to citrate synthase activity to compensate for the amount of mitochondria. Statistical differences between the groups were analyzed using a Student's t test.

RESULTS. ADP dependent (state 3) respiration was 98% higher and RCR 165% higher in the mitochondria incubated with plasma from the septic patients compared to those incubated with plasma from healthy volunteers (Table). There were no significant differences between the groups incubated with preservation buffer or the different cytokines (Table).

TABLE 1

	State 3 (nmol O_2 ml^{-1} units CS^{-1})	RCR
Patients		
Control plasma	32 ± 5	4.6 ± 3.1
Septic patients	64 ± 17*	12.2 ± 4.0*
Cytokines		
Control buffer	75 ± 20	14.9 ± 2.2
1 mM IL-6	87 ± 18	12.3 ± 2.2
100 mM IL-6	92 ± 19	12.7 ± 1.7
TNF-α	57 ± 13	14.1 ± 4.0

Mean ± SD
CS citrate synthase
* $p < 0.05$ versus control

CONCLUSIONS. Plasma from patients with septic shock increases mitochondrial respiration and efficiency compared with control plasma. This increase does not seem to be initiated by the cytokines in our experiment. Future research will try to identify the factor responsible for this effect.

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ISOLATION AND IDENTIFICATION OF INFLAMMATORY SPECIFIC PROTEINS IN INTERSTITIAL FLUID IN SKIN DURING ACUTE OVERHYDRATION

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INTRODUCTION. Microvascular fluid loss from the intravascular to the interstitial space generates tissue edema and is one of the major challenges in emergency and intensive care medicine. Isolation of interstitial fluid (IF) from skin makes it possible to study the microcirculation and proteins in this environment both during normal as well as pathophysiological conditions such as acute inflammation.

OBJECTIVES. By studying bio-markers from proteomic analysis by mass spectrometry in an inflammation model, we wanted to find proteomes that could be important in explaining inflammation.

METHODS. We have applied a recently described centrifugation method in a porcine model and compared it with implanted wicks. In nine anesthesized piglets we compared the methods and evaluated the IF, by overhydrating the pigs with 3000 ml of acetated Ringer's solution for 1 h, and thereafter continuously supplemented for 1 h according to fluid losses. IF was isolated from implanted dry wicks, wet wicks and by centrifugation of excised skin. The methods were evaluated by the ability to reflect overhydration and to show the expected composition of plasma proteins in IF by use of HPLC. The IF was also processed further with mass spectrometry to find possible tissue degradation or inflammation due to overhydration. *Statistics*: by SPSS v 13.0 and GraphPad Instat (version 3.05). Significance level: $p = 0.05$.

RESULTS. Colloid osmotic pressure in IF was significantly lowered after overhydration for all the tree methods. Wet wicks $p = 0.05$, dry wicks $p = 0.001$, skin samples $p = 0.05$. HPLC of IF collected with centrifugation after overhydration, identified peaks representing molecules smaller than albumin. Mass spectrometry of the same IF identified several proteins associated with inflammation: alpha-1-antichymotrypsin and Lumican, the latter a protein identified as a modulator of inflammation.

CONCLUSIONS. We have introduced a new centrifugation method for isolation of IF from the skin of pigs. By further analysis of IF isolated by centrifugation we were able to distinguish proteins found only in the IF of the pigs overhydrated with Ringer's acetate. These proteins could be associated with an inflammatory condition in the skin caused by massive overhydration, again causing tissue degradation. Identification and validation of proteomic biomarkers can be a useful tool in future treatment of inflammation in general, and in sepsis in special.

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1283

PRELIMINARY SCREENING OF THE EXPRESSION OF MICRORNA IN LYMPHOCYTE STIMULATED BY LPS

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INTRODUCTION. MicroRNA must be the first expression and control the immune response of lymphocyte, what kinds of Expression of MicroRNA in Lymphocyte Stimulated by LPS have not been known yet.

OBJECTIVES. To detect the expression of microRNA in lymphocyte that was stimulated by lipopolysaccharide with the technique of gene microarray, and screen the specific expression of microRNA.

METHODS. This experiment was divided into two procedures. The first procedure is to choose two kinds of cell strains, including Jurkat cell strain (comes from leukemia) and CCRF-CEM cell strain (comes from acute lymphocyte leukemia).we cultivate this two kinds of cell strains to mature stage, then inoculate every kind of cell strain into four culture dishes, two culture dishes was stimulated by 1 μg/ml lipopolysaccharide(study group), and the other two culture dishes serve as blank control(not stimulated by 1 μg/ml lipopolysaccharide). Eight hours later, we extracted the microRNA in each culture dish. The second procedure is to use the technique of gene microarray to analysis the difference expressions of microRNA.

RESULTS. According to the results of gene microarray, the expression of microRNA-7-1 decreased significantly in study group compared with control group in CCRF-CEM cell strain (Log2 (G2/G1) = −0.41, $p < 0.05$); the expressions of microRNA-1208 and microRNA-769-3p have a decrease trend in study group compared with control group in CCRF-CEM cell strain ($0.05 < P < 0.10$); the expressions of microRNA-16, microRNA-339 and microRNA-3p have a increase trend in study group compared with control group in CCRF-CEM cell strain ($0.05 < P < 0.10$). the expressions of microRNA-181a-2 and microRNA-720was no difference between study group compared with control group in Jurkat cell strains stimulated by LPS($P > 0.05$).

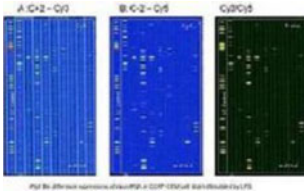

Fig. 1 expressions of microRNA in CCR-CEM

CONCLUSIONS. The expression of microRNA-7-1 decreased significantly in CCRF-CEM cell strain stimulated by LPS, microRNA-7-1 maybe join in the control the immune response of lymphocyte. More studies were needed.

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1284

HYPOPERFUSION AND HYPERPERMEABILITY EFFECTS OF THE PLATELET ACTIVATING FACTOR PAF IN THE ISOLATED PERFUSED RAT SMALL BOWEL

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INTRODUCTION/OBJECTIVES. PAF induces intestinal endothelial and epithelial barrier dysfunction and contributes to the development of sepsis. The mechanisms of PAF actions are not well-understood.

METHODS. A recently developed isolated model of the rat small bowel [1] was used. The following groups were studied: (1) PAF (n = 5), 2) PAF + PAF antagonist (ABT491, n = 6), 3) PAF + thromboxane (SQ29548) and leukotriene (MK571) antagonist (SQ/MK, n = 6), 4) PAF + rho kinase inhibitor (Y27632, n = 3), 5) thromboxane agonist (U46619, n = 3), 6) thromboxane agonist + rho kinase inhibitor (U46/Y27, n = 3), 7) PAF + inhibitor of acid sphingomyelinase (ASMase) (imipramine, n = 4) and 8) PAF + inhibitors of ASMase and cyclooxygenase (acetylsalicylic acid) (Imi/ASA, n = 5). All receptor antagonists and enzyme inhibitors were administered continuously 15 min before the end of a 60 min equilibration period. PAF or the thromboxane agonist were applied as boli. The dynamic pressure responses and the fluid shifts in the organ were recorded continuously.

RESULTS. The area under the pressure response curve and the volume shift [vascular fluid loss (ml) within 15 min after stimulation normalized to intestine dry weight (g)] are shown in Figs. 1 and 2.

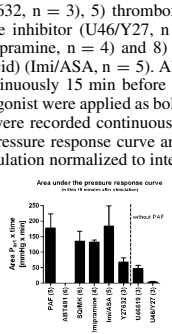

Figure 1

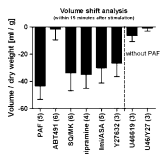

Figure 2

CONCLUSIONS. Our data indicate that the vasoconstriction mediated by the PAF and thromboxane receptors is linked to the intracellular rho kinase pathway. Imipramine and ASA seem to stabilize the intestinal barrier and reduce the vascular fluid loss.

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1285

SRC-DEPENDENT ICAM-1 PHOSPHORYLATION AND NO PRODUCTION IN PULMONARY MICROVASCULAR ENDOTHELIAL CELLS MEDIATES NEUTROPHIL EXTRAVASATION DURING ACUTE INFLAMMATION

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INTRODUCTION. Polymorphonuclear neutrophil (PMN) extravasation is a critical component of the host defense mechanism that can also result in oxidative tissue injury. This process first requires PMN adhesion to endothelial cells (ECs) and then subsequent transendothelial migration (TEM) from the vasculature. Intercellular adhesion molecule-1 (ICAM-1) on the EC surface is required for firm adhesion of PMNs. The interaction of beta2 integrins on PMNs with ICAM-1 on the EC surface induces ICAM-1 clustering and activation, and then subsequent outside-in signaling is thought to facilitate neutrophil transmigration. ICAM-1 activation is known to increase Src kinase activity as well as NO production in ECs. However, the mechanism by which PMN binding triggers ICAM-1-dependent Src and eNOS activation as well as their role in neutrophil TEM is not well understood.

OBJECTIVE: We tested the hypothesis that ICAM-1 activation of Src signaling and subsequent stimulation of eNOS-derived NO production is required for PMN extravasation during acute inflammation.

METHODS. The in vivo model of carrageenan-induced acute lung inflammation in wild-type (WT), ICAM-$1^{-/-}$, and eNOS$^{-/-}$ mice was used in parallel with in vitro endothelial cell culture studies to assess ICAM-1-dependent signaling mechanisms that mediate PMN infiltration during acute lung inflammation.

RESULTS. Carrageenan-induced PMN infiltration into the lung and activation of Src and eNOS were significantly reduced in ICAM-$1^{-/-}$ mice. In HUVECs expressing native mouse ICAM-1 or phospho-defective Tyr^{518}Phe ICAM-1 mutant, we observed that ICAM-1 activation via Ab cross-linking increased Src activity and NO production in a manner dependent on Tyr^{518} ICAM-1 phosphorylation. Phosphatase-dead SHP2 mutant (Cys^{463}Ser) blocked ICAM-1 cross-linking induced Src activation, and thus SHP2 recruitment to activated ICAM-1 may play an important role in sustaining Src activity by dephosphorylating Src negative regulatory Tyr^{529}. In addition, ICAM-1 cross-linking promoted the phosphorylation of Akt at Ser^{473} and eNOS at Ser^{1177} leading to sustained NO production. Both Akt and eNOS phosphorylation and resultant NO production were sensitive to Src inhibitor PP2 and PI3-kinase inhibitor wortmannin, suggesting ICAM-1 activation stimulates the Src-PI3 K-Akt-eNOS pathway in endothelial cells. In vitro, PMN transmigration was dependent on ICAM-1 phosphorylation and NO production. Consistent with this, in the in vivo model of carrageenan-induced acute inflammation we observed that PMN infiltration into the lung was significantly reduced in eNOS$^{-/-}$ mice.

CONCLUSIONS: Acute inflammation or ICAM-1 cross-linking *in vitro* results in Src-dependent ICAM-1 phosphorylation, sustained endothelial cell Src signaling, and eNOS-derived NO production which play critical roles in mediating neutrophil extravasation and infiltration in the lung.

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1286

MITOCHONDRIAL FUNCTION OF MONOCYTES IN HYPOBARIC HYPOXIA

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INTRODUCTION. Prolonged hypobaric hypoxia leads to systemic oxidative stress similar to severe inflammation and might serve as a model for human sepsis. In the context of a high altitude expedition human subjects can safely be submitted to prolonged hypoxia and the resulting changes in mitochondrial function can be explored in a controlled fashion. The effect of hypoxia on immune cells—key players in the pathophysiology of sepsis—is of particular interest.

OBJECTIVES. To measure mitochondrial function of monocytes during prolonged hypobaric hypoxia.

METHODS. Serial blood samples were collected and oxygen saturation was measured in twelve climbers before and throughout a high altitude climbing expedition to Pik Lenin (7,134 m). Measurements were performed at 440 m (baseline) and at the altitudes of 3,600 m (day 1), 4500 m (day 4) and 5,400 m (day 9) above sea level. Pure monocytes were isolated by the use of an antibody-antigen mediated immunomagnetic cell isolation procedure and lysed for determination of activities of mitochondrial enzymes cytochrome c oxidase and citrate synthase. Repeated measurements ANOVA followed by least significant difference (LSD) post hoc test were used to compare results on different altitudes.

RESULTS. Mean oxygen saturation was 91 ± 3% on 3,600 m, and decreased to 86 ± 3% on 4,500 m and 81 ± 5% on 5,400 m ($p = 0.001$). We observed an increase in citrate synthase activity on all altitudes compared to baseline levels ($p = 0.003$). Compared to the baseline, prolonged hypobaric hypoxia induced an increase in the mitochondrial respiratory chain enzyme cytochrome c oxidase enzymatic activity only at 4,500 m ($p = 0.003$). Normalization of cytochrome c oxidase enzymatic activity by citrate synthase activity (relative enzymatic activity) yielded a decrease in relative cytochrome c oxidase enzymatic activity during hypoxia on 3,600 and 5,400 m (Fig. 1). Expressing cytochrome c oxidase enzymatic activities as a ratio to citrate synthase is intended to act as a safeguard for potential differences in mitochondrial enrichment.

CONCLUSIONS. The data demonstrates that prolonged hypobaric hypoxia leads to a decrease in relative cytochrome c oxidase activity. This is due to an increase in citrate synthase activity as a marker enzyme for the mitochondrial matrix representing mass and/or number of mitochondria which is not counterbalanced by a corresponding increase of cytochrome c oxidase activity.

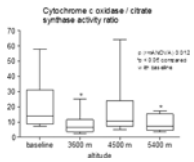

Figure 1

1287

METABOLOMIC ANALYSIS OF PULMONARY TISSUE IN EXPERIMENTAL SEPSIS

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INTRODUCTION. The usefulness of metabolomic analysis (mass spectroscopy [MS] and magnetic resonance spectroscopy [MRS]) for the study of the pathophysiology and diagnosis of sepsis is unknown.

OBJECTIVES. To define the pattern of change in metabolites by MRS in experimental sepsis.

METHODS. Male SD rats (weight 325–375 g) underwent cecal ligation and puncture or sham procedure (n = 8 per group), and 24 h after surgery were euthanized. Pulmonary tissue was extracted for magic angle MRS (HR-MAS) and processing by the R Metabonomic package. A supervised statistical analysis of main components (MC) was performed on the processed spectra.

RESULTS. The MC analysis discriminated both group (septic and nonseptic) indicating a different metabolite profile. In addition, the analysis of MC loading revealed 4 displacement positions in the discrimination between groups with a variation in the signal intensity of 50%.

CONCLUSIONS. Metabolomic analysis of pulmonary tissue by MRS is a potentially useful technique for the detection of biomarkers in sepsis.

GRANT ACKNOWLEDGMENT. Instituto de Salud Carlos III, FIS 08/1726, Fundación Mutua Madrileña.

1288

NEURO-IMMUNOMODULATION OF HUMAN CD14 + CD16 + NEUTROPHILS IN SEPSIS

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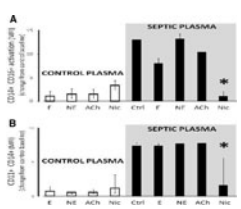
INTRODUCTION. CD14 + CD16 + neutrophils are a key subset of phagocytes associated with severe bacterial sepsis [1]. Their characteristics, and potential neuro-immunomodulation, have not been explored in humans neutrophils exposed to septic plasma from ICU patients.

OBJECTIVES. To assess the effect of adrenergic/cholinergic neurotransmitter molecules on human neutrophil adhesion and activation markers following exposure to human septic plasma.

METHODS. With IRB approval, neutrophils were isolated from 5 healthy volunteers (Ficoll density gradient separation) and incubated for 24 h with either plasma from healthy volunteers or septic patients plus pathophysiological concentrations of epinephrine (E), norepinephrine (NE) or acetylcholine (ACh) and nicotine (Nic) to assess potential parasympathetic-related neuro-immunomodulation. Flow cytometry (DAKO Cyan) measured expression on neutrophils of CD11, CD14, CD16 antibody markers and viability. Median values are shown; analyzed by ANOVA.

RESULTS. Neutrophils were unaffected by NE, E, ACh or Nic after incubation with plasma from healthy volunteers. After incubation with septic plasma, marked neutrophil activation occurred (p = 0.02). However, Nic reduced CD14 + CD16 + activation (*Fig. A) by 95% (median (35–97%; 25th–75th centiles); p = 0.01). Nic also attenuated CD11 expression, suggesting reduced neutrophil adhesion (*Fig. B). Neutrophil viability was similar across drug and plasma treatments.



Figs. A, B

CONCLUSIONS. These preliminary data suggest that nicotine attenuates both the activation and adhesion of human neutrophils exposed to human septic plasma, but does not affect viability.

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1289

TIME TO RESUSCITATION: EFFECTS ON MITOCHONDRIAL FUNCTION AND OUTCOME IN EXPERIMENTAL SEPSIS MODEL

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INTRODUCTION. Sepsis may impair mitochondrial functions.

OBJECTIVES. The aim of this study was to evaluate the potential impact of lag between sepsis initiation and start of treatment on mitochondrial respiration.

METHODS. 24 animals [40.1 ± 4.1 kg] were randomized (n = 6/group) to a control group (Group I) and three groups resuscitated at 6 (Group II), 12 (Group III), and 24 (Group IV) hours, respectively, after fecal peritonitis induction. Fecal peritonitis was induced with instillation of 2.0 g/kg of autologous feces via intra-peritoneal drain. Resuscitation was performed according to the SSC and ESICM sepsis guidelines for 48 h. Respiration of permeabilized skeletal muscle fibers and their isolated mitochondria was assessed at baseline and after 6, 12, 24, 48 and 72 h, when applicable, or before death occurred, if earlier. At the end of the experiment, also isolated brain, hepatic and myocardial mitochondrial respiration was measured using high resolution respirometry (Oxygraph-2 k, Oroboros Instruments, Innsbruck, Austria).

RESULTS. Mortality (33%, each) and organ dysfunction was highest in groups III and IV. In these two groups, different pattern of changes of skeletal muscle mitochondrial complex I-dependent respiratory control ratio (RCR) were observed (Table 1). No significant differences between groups were observed for complex I- and II-dependent RCR values of hepatic, myocardial and brain mitochondrial respiration (Fig. 1). There were no significant differences between the groups for any of the complexes in permeabilized skeletal muscle fibers mitochondrial respiration (data not shown).

CONCLUSIONS. Despite the high mortality observed in groups resuscitated at later time points after induction of sepsis, end organ mitochondrial function assessed using physiological substrates was preserved. Despite significant changes in skeletal muscle mitochondrial respiration efficiency in the two groups with the highest mortality, our findings do not support the view that mitochondrial dysfunction plays a major role in the pathogenesis of multiorgan dysfunction in experimental sepsis.

GRANT ACKNOWLEDGMENT. Swiss National Fund, nr: 3200-061988; Stiftung für die Forschung in Anästhesiologie und Intensivmedizin.

TABLE 1

Glutamate/malate-RCR (mean ± SD)	Group	N	Baseline	0 h	24 h	48 h (end)	*p* (ANOVA-time effect)	*p* (t–g interaction)
	Group I	6	11.5 ± 5.7	8.1 ± 2.7	5.7 ± 2.7	6.7 ± 3.1	0.07	0.008
	Group II	6	10.8 ± 2.3	8.5 ± 3.7	8.9 ± 4.8	5.3 ± 3.6	0.14	
	Group III	6	7.7 ± 3.4	12.6 ± 2.3	9.6 ± 1.8	6.1 ± 5.2	0.03	
	Group IV	6	12.8 ± 5.7	7.0 ± 2.4	6.8 ± 1.9	12.0 ± 5.1	0.05	

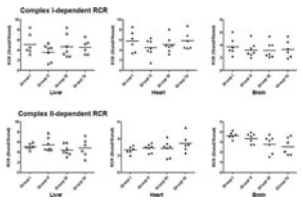

Figure 1

1290

DOWN REGULATION OF ADIPONECTIN AND ADIPONECTIN RECEPTOR EXPRESSION IN ADIPOCYTES TREATED WITH LPS

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INTRODUCTION. Adipose tissue is an endocrine organ which produces signalling proteins involved in inflammation and glucose homeostasis [1]. One of these proteins, adiponectin, promotes glucose utilisation and fatty acid oxidation and thus improves insulin sensitivity via its two receptors, AdipoR1 and AdipoR2 [2]. Adiponectin expression has been shown to be reduced in type II diabetes, obesity and endotoxaemia [2, 3]. Adiponectin also exhibits anti-inflammatory properties [4]. In this study, we have examined whether adiponectin and its receptor gene expression changes in murine adipocytes stimulated by LPS.

METHODS. 3T3–L1 adipocytes were grown in culture media (DMEM with 10% fetal calf serum) until confluent. Pre adipocytes were differentiated with the addition of 10 mg/ml insulin, 1 mM dexamethasone and 100 mM IBMX. Media was changed every 48 h. Cells were treated on day 12 with 100 ng/ml, 1 or 10 mcg/ml LPS (Escherichia coli, Sigma-Aldrich). Cells were harvested at 4 and 24 h. mRNA levels were determined by RT PCR in a 12.5 µl reaction volume consisting of 12.5 ng of reverse transcribed cDNA mixed with optimal concentrations of primers and probe and qPCR^{TM}Core kit (Eurogentec, UK) in 96-well plates on a Mx3005P detector.

RESULTS. Cell response to LPS was confirmed using IL6 as a reference gene. Expression of adiponectin mRNA was significantly reduced in cells treated with 10 µg/ml LPS harvested at 4 h (7.1 fold p = 0.002). There were no changes in cells treated with lower concentrations of LPS. There were no changes at 24 h. R1 gene expression was significantly reduced following treatment with 100 ng/ml LPS at 4 h (1.5 fold p = 0.04), but treatment with higher concentrations did not change expression. There were no changes at 24 h. R2 expression levels were significantly reduced at 4 h in the 1 and the 10 mcg/ml groups (2.6 fold p = 0.02 and 4 fold p = 0.01) respectively. There were no changes at 24 h.

DISCUSSION. Our results add to the evidence that changes occur in the adiponectin system during inflammation. In this model, we observed rapid reduction (at 4 h) in adiponectin at high dose LPS, R1 at low dose LPS and R2 at medium and high doses. There were no changes in expression levels at 24 h. This suggests that a rapid change in the adiponectin system may occur in response to LPS but this change is not maintained at 24 h. In a previous study, our group has shown reduced adiponectin gene expression in adipose tissue depots in LPS induced endotoxaemia [3]. It is interesting that different concentrations of LPS induce different changes within the adiponectin system. Further studies are needed to elucidate whether reductions in both adiponectin and its receptor may contribute to the inflammatory changes and hyperglycaemia commonly observed during sepsis.

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1291

A PROLONGED MURINE ENDOTOXEMIA INFUSION MODEL: A NEW MODEL TO INVESTIGATE THE INFLUENCES OF THE ARGININE: NO METABOLISM ON ENDOTHELIAL DYSFUNCTION IN SEPSIS

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INTRODUCTION. A key factor in organ perfusion and endothelial (dys)function is nitric oxide (NO) production by Nitric Oxide Synthases (NOS). NOS produces NO and citrulline (CIT) from arginine (ARG). Metabolic pathways of ARG-NO metabolism in human sepsis are characterized by a decreased ARG *de novo* synthesis and increased ARG breakdown by arginase. Previous experimental studies with acute bolus injection of endotoxin did not result in decreased ARG de novo synthesis, indicating this to be an inappropriate model to study human metabolic ARG-NO disorders in sepsis. Therefore, there is a need to develop a prolonged endotoxin infusion model to study these disturbances which underly endothelial dysfunction.

OBJECTIVES. To develop a model of prolonged LPS administration in mice to assess the LPS induced changes in NO release, microcirculation, glycocalyx degradation and endothelial dysfunction.

METHODS. Mice received a continuous intravenous endotoxin (LPS, 200 μg total) or sterile saline infusion for 18 h. Intracellular NO levels were determined by in vivo NO spin trapping (30 min) with Fe-DETC complexes. After NO trapping, the animals were sacrificed, arterial blood sampled and tissues snap frozen in liquid nitrogen. The trapping yield of the nitrosyl-Fe^{2+}-DETC complex (MNIC) in tissues was quantified at 77 K. Amino-acid concentrations in plasma were measured by HPLC. Side-stream dark-field imaging was used to evaluate the glycocalyx density.

RESULTS. Glycocalyx degradation was increased in the LPS-treated animals (0.3 μm, $p < 0.05$) compared to controls. Intracellular tissue NO concentrations were two- to threefold higher in the LPS-treated mice compared to controls (liver, kidney, heart, gut). The number of infiltrating MPO-positive cells increased significantly during endotoxemia. Levels of both plasma ARG and CIT were significantly lower in LPS-challenged mice than in controls, whereas plasma ornithine levels were significantly higher.

CONCLUSIONS. In this new developed murine sepsis model, the prolonged infusion of LPS resulted in increased glycocalyx degradation and associate endothelial leakage. The enhanced NO levels correlated with decreased plasma levels of ARG and CIT. Our murine model with prolonged infusion appears applicable as a model for the human clinical situation, enabling adequate investigation of the influences of the ARG-NO metabolism on endothelial dysfunction in sepsis.

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TNFA REDUCES MUSCULAR EXCITABILITY BY A PKC MEDIATED PHOSPHORYLATION OF VOLTAGE GATED SODIUM CHANNELS

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INTRODUCTION. Critical illness polyneuromyopathy is a muscular weakness occurring in intensive care unit. One of the major risk factor is sepsis. An early decrease in membrane excitability was described [1] but corresponding mechanisms are imperfectly known. TNFa is released in the first time of sepsis and could be involved in the physiopathology.

OBJECTIVES. The aim of our study was to investigate TNFa effects on muscular voltage gated sodium channels (Nav) in an in vitro model.

METHODS. Early effects of TNFa on Nav were analysed by macro-patch clamp on muscular fibers isolated from rat peroneus longus. Measurements were performed on control fibers and after addition of TNFa at concentrations ranging from 2.5 to 100 $ng.mL^{-1}$. The effects of chelerythrine, a specific inhibitor of protein-kinase C (PKC), were also tested. Experimentations were realised in a laboratory with permission of experimental research on animals and under the supervision of an authorized person (no 29-028).

RESULTS. TNFa produced a concentration-dependant inhibition of Nav currents (Fig. 1). Maximal inhibition (75% of control current) was observed with concentrations from 50 ng mL^{-1} and above. This decrease was fast: 40% of maximum inhibition was observed in less than 5 min. Moreover, chelerythrine inhibited TNFa action on Nav.

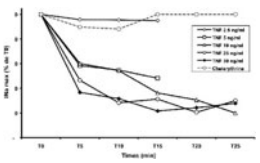

Figure 1

CONCLUSIONS. In our experimental model, TNFa induce a rapid and concentration dependant decrease of muscular Nav currents like observed in chronic sepsis [2]. As this effect is too quick to be a transcriptional one, and as it is blocked by chelerythrine, it can be assumed that TNFa action is mediated by a Nav phosphorylation secondary to PKC activation. In conclusion we evidenced that TNFa reduce muscle excitability in the early stages of sepsis. Further studies are needed to obtain a precise description of TNFa mechanisms.

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1293

NAD(P)H OXIDASE IS IMPORTANT FOR REGULATING LUNG INJURY IN RESPONSE TO LIPOPOLYSACCHARIDE (LPS)

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RATIONAL: Superoxide (O_2^-) is increased in sepsis, and thought to cause tissue injury, but O_2^- may also contribute to cell signaling and regulation of the immune response. NAD(P)H oxidase in leukocytes and the vascular wall is a major regulated source of O_2. We hypothesized that mice deficient in the p47phox (KO) component of NAD(P)H oxidase would have less pulmonary inflammation than wild type (Wt).

METHODS. We treated Wt or KO mice with IV saline or LPS and assessed lung injury by:
1. wet-dry-weight ratio;
2. leak of Evans Blue (EB) labeled albumin; and
3. histological score for edema.

We used myeloperoxidase activity to indicate neutrophil (PMN) accumulation in lungs, and measured accumulation of macrophages and neutrophils in bronchial alveolar lavage (BAL). Apoptosis was assessed by tunnel staining. We also expression of ICAM-1, an adhesion molecule, and nitric oxide synthase (NOS) enzymes, eNOS and iNOS (western and northern analysis) as well as nitrotyrosine formation.

RESULTS. Lung injury was increased in both groups. Surprisingly there was greater EB leak in KO than Wt at 2 h and a greater edema score at 4 and 8 h. PMN and macrophage accumulation in BAL were the same in both groups at 2 h but greater in KO mice at 8 h. Myeloperoxidase activity was similar at 2 h post LPS in KO and Wt indicating that similar accumulation of PMN in the lungs. Apoptosis was increased in both groups at 4 h, but resolved in Wt at 24 h and persisted in KO. Nitrotyrosine was increased in both groups but appeared higher in KO. Expression of eNOS and iNOS increased in both groups but was greater in KO than Wt.

CONCLUSIONS. In contrast to our prediction, lung injury was greater in p47phox KO mice which indicates that this complex is not essential for lung injury. However, the injury was more severe and prolonged in KO mice indicating that O_2^- may regulate the inflammatory response.

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ROLE OF IMMUNE CELLS STIMULATION ON THE INTRACELLULAR AND EXTRACELLULAR EXPRESSION OF CALGRANULINS S100A8 AND S100A9

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INTRODUCTION. Septic shock remains the main cause of mortality in the ICU, thus a persistent challenge. Recently, DNA and mRNA analysis by microchip and gene expression by real time PCR highlighted 2 proteins S100A8, S100A9 and their complex, known as the calgranulins, as potential key prognostic markers for this disease: those two proteins, whose expression seems to be restrained to phagocytes cells are newly recognized components in sepsis-induced inflammation. Moreover, they were shown to be at significantly higher concentrations in the plasma of septic shock patients that were going to die. In the contrary, those who were to survive saw their plasmatic concentration decrease, all severity scores in between the 2 population being the same.

OBJECTIVES. The aim of this study was to determine the repartition of these proteins in immune cells, their intracellular variation, at baseline and after cell activation and finally to understand the relation between their intracellular and extracellular expression.

METHODS. We used an in vitro model close to the immuno-inflammatory aggression that is septic shock. We stimulated in vitro for 1, 3 and 6 h whole blood from healthy volunteers using agonists found in the inflammatory storm that is septic shock (LPS, fMLP, GMCSF, IFNg). We also induced death cell, either using an apoptotic agonist, or by necrosis technics. We then analysed the intracellular variation of the calgranulins using flow cytometry technics. The extracellular quantification was made using ELISA methods. All the statistic analysis were made using a Mann-Whitney test.

RESULTS. We showed in this work for the first time that the intracellular repartition of the calgranulins is different depending on the type of cell: the complexe is the main form in the monocyte cytoplasma, whereas S100A9 is the main intracellular form of the PMN. This repartition remains after cell activation. We also checked the absence of calgranulins in lymphocytes. After cell activation we showed that intracellular S100A8, S100A9 and S100A8A9 increased, but at different levels depending on the cell and the agonist used. Extracellular S100A8 also raised after cell stimulation, but the concentration found were very low compare to those found in the plasma of septic shock patients.

CONCLUSIONS. Together, these results suggest a different regulation depending on the form of the protein and of the cell and thus of proper distinct function of each monomer and of the complex. In the limits of our model the increased concentrations found in the plasma of patients with a septic shock can't be explained by immune cell activation.

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GRANT ACKNOWLEDGMENT. Fonds d'Etude et de Recherche du Corps Medical

Drug intoxications and poisoning: 1295–1306

1295

SMOKE INHALATION IMPACT IN CO INTOXICATION: LARGER INDICATION OF HYDROCOBALAMINE COULD BE BENEFIT?

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INTRODUCTION. The carbon monoxide (CO) poisoning is a leading cause of death by poisoning. It may be pure or mixed during inhaling exhaust fumes. The specific character of this study is to look at smoke poisoned patients unhurt of any burn.

OBJECTIVE. Compare the patients poisoned to the CO with or without smoke inhalation

METHODS. Prospective cohort study realized between 01/01/2006 and 30/12/2009 including all CO poisoned patients treated with hyperbaric oxygen. Following parameters were seized: age, sex, date of admission, SOFA, the source of the intoxication, the gravity CO score, the initial clinical examination (realized by first aid), biology, the rate of HbCO, the Murray score and the rate of complication.

RESULTS. 405 patients were included in the study. The sex ratio was 61%, the mean age was 42 ± 18 years and the global mortality was 5, 9%. Among the 405 patients 29% were poisoned by smoke (S group), 60% by pure CO (C group) and 11% by exhaust fumes. More than 30% of the exhaust fumes victims were suicide origin. This characteristic is associated with neurological impairment induce by ingested drugs. Then, their neurological status is impossible to link to the CO poisoning. We have therefore decided to exclude this group. The SOFA score was higher in the S group compared with the C group (0.38–2.17; $p < 0.0001$). A CO score equal to 4 was present in 33 versus 1% respectively in S versus C group ($p < 0.001$). In the under group of patients having a CO score at 3, 0% (0/101) of CO poisoned patients versus 18.4% (7/38) of smoke poisoned patients were ventilated ($p < 0.001$). These patients were intubated either during transport or in the intensive care and none of them received hydroxycobalamine during the first aid (before intubation). The laboratory data showed in the S group a higher lactates level (2.2 vs. 3.9 mmol/l; $p = 0.005$) and lower initial PaO_2/F_IO_2 ratio (365 vs. 306; $p = 0.002$). Nine percent of the S group present a Murray score at 4 versus 0% for C group ($p < 0.0001$). Pneumonia, shock and death were significantly more frequent in the S group (respectively 8.6 vs. 0.8%, $p < 0.0005$; 11.2 vs. 0.8%, $p < 0.0001$; and 17.9 vs. 1.2%, $p < 0.0001$)

CONCLUSIONS. As expected the smoke poisoned group has a higher mortality than pure CO group (mortality 17% vs. overall mortality 5.9%). At equivalent CO gravity score, mortality and complications are always more frequent in the smoke poisoned group. The smoke poisoned group has a high risk of degradation. Those patients require specific monitoring and support and probably early administration of hydroxycobalamine.

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ANTITHROMBIN ADMINISTRATION REDUCES THE NEED FOR INOTROPES IN BURN SHOCK PATIENTS

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INTRODUCTION. Burn shock is characterised by immediate hypovolemia reversed by sufficient fluid resuscitation and delayed myocardial dysfunction induced by systemic activation and myocardial accumulation of neutrophils, which needs inotropes. Plasma levels of antithrombin (AT), which interacts with neutrophils and mediates anti-inflammatory properties, are reduced by up to 50% in burn patients.

HYPOTHESIS. AT administration and maintaining higher plasma levels of AT can reduce the need for inotropes in burn shock patients.

METHODS. We performed a retrospective cohort study of burn shock patients admitted to a single tertiary care center over 7 years period. Patients were eligible for inclusion if they were received fluid resuscitation with Ringer's solution and colloid according to clinical guidelines. Data were abstracted including demographic, burn injury characteristics, resuscitation fluid volume, the type of colloid and the average of plasma AT levels within 72 h after burn injury. Administration of fresh frozen plasma and/or recombinant human AT was defined as AT administration. The decisions of AT administration and inotropic support (dopamine or dobutamine) were made by the attending intensivists. Primary outcome measure was the need for inotropes within 72 h after burn injury. Cox regression model was used to estimate the risk reduction by AT administration and average of AT levels.

RESULTS. Of 44 eligible patients, 23 (52.3%) needed inotropes (Inotrope group) and 21 (47.7%) did not need inotropes (non-Inotrope group). Compared to Inotrope group, non-Inotrope group was significantly more often received AT administration (20/21 [95.2%] vs. 14/23 [60.9%], $p = 0.01$) and had higher average of AT levels (81% [78–93] vs. 67% [59–79], $p = 0.0046$), however, there were no significant differences in other clinical variables. Multivariable Cox regression analysis showed that the need for inotropes was significantly associated with AT administration (adjusted relative risk [RR] 0.21, 95% CI 0.07–0.68, $p = 0.0087$) and higher average of AT levels (adjusted RR 0.71 each 10% increase, 95% CI 0.51–0.98, $p = 0.038$).

CONCLUSION. Our findings suggested that AT administration can reduce the need for inotropes in burn shock patients. Further study in the prospective setting is warranted to establish the efficacy of AT administration.

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ARGON PROVIDES NEUROPROTECTION AGAINST ISCHEMIA/HYPOXIA INDUCED BRAIN DAMAGE IN RAT NEONATES

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INTRODUCTION. Neuroprotection afforded by noble gases, e.g. xenon, has been well established both in vivo and in vitro [1]. Argon, another member of the noble gas family has been reported previously to have a neuroprotective property [2]. The aim of this study was to investigate whether it attenuates neuronal injury in a rat model of neonatal asphyxia.

METHODS. Seven-day-old postnatal SD rats underwent right common carotid artery ligation and then recover with their dim for 1 h. Thereafter, they were exposed to 8% O_2 balanced with nitrogen for 90 min. After 2 h, they were treated with 70% argon or 70% nitrogen (positive control group) for 90 min. The cohort pups without intervention served as naïve control. They were perfused 7 days later and their brains were sectioned and stained with 0.5% cresyl violet. Microphotographs were taken from CA area of the hippocampus near −3.6 bregma relative to adult brain at 40 × magnification. Healthy cells were counted in a blind manner and their mean value was used for data analysis.

RESULTS. The thickness of healthy layers in the right CA area of the positive control group was remarkably reduced compared with other groups (Fig. 1). Quantitative analysis revealed that argon treatment significantly increased healthy cell numbers in the right CA area of hippocampus from 36.53 ± 1.201 in the positive controls to 54.37 ± 1.162 ($P < 0.01$) (Fig. 2).

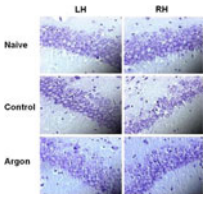

Figure 1

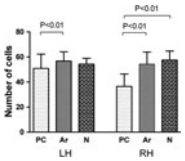

Figure 2

CONCLUSIONS. Argon is capable of protecting brain damage against ischemia/hypoxia insult in neonatal rats.

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MECHANISMS OF DEATH IN RELATION TO HIGH-DOSE CITALOPRAM IN RATS

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INTRODUCTION. Citalopram is a selective serotonin reuptake inhibitor. Citalopram toxicity is considered as weak. However, overdoses may result in serotonin syndrome, seizures, electrocardiographic abnormalities as well as respiratory failure and death. Mechanisms of severe toxicity remain unclear.

OBJECTIVES. Our objective was to study the mechanisms of death following high-dose citalopram administration in rats.

METHODS. Experimental study in Sprague Dawley rats with intraperitoneal (IP) citalopram administration; determination of the median lethal dose (MLD)using the Dixon and Bruce up-and-down method; clinical descriptive study of citalopram-induced features and measurement of alterations in respiratory pattern (arterial blood gases and plethysmography) and biological parameters including blood lactate (Scout®, EKF diagnostic), plasma and platelet serotonin concentrations (high-liquid performance chromatography–fluorometry); determination of the preventive activity on seizures and death of diazepam, cyproheptadine, and propranolol pretreatments with the determination of their minimal effective dose; comparisons using ANOVA for repeated measurements followed by Bonferroni post-test.

RESULTS. Citalopram IP-MLD was determined as 102 mg/kg in rats. Seizures were significantly increased in rats receiving 80 and 120% of citalopram MLD versus controls ($p < 0.01$ and $p < 0.05$, respectively), while death rate was only significantly increased in rats treated with 120% of citalopram MLD ($p < 0.001$). Significant decrease in body temperature was observed after 90 min in rats treated with doses >60% MLD in comparison to controls ($p < 0.05$). Occurrence of serotonin behavioural syndrome was comparable in all groups. Citalopram administration did not result in significant hypoxemia, hypercapnia, and lactate elevation, thus not supporting the hypothesis of the occurence of any significant deleterious cardiovascular effect in citalopram-induced toxicity. However, a significant moderate increase in the inspiratory time ($p < 0.05$) accompanied with an expiratory braking was observed. A significant decrease in platelet serotonin and increase in plasma serotonin concentrations were measured ($p < 0.05$). Pre-treatment with diazepam (1.77 mg/kg) and cyproheptadine (17.1 mg/kg) of rats receiving a lethal citalopram dose prevented seizures and death, while propranolol was ineffective.

CONCLUSIONS. Citalopram respiratory toxicity remains mild, while deaths result from seizures probably related to serotonin toxicity. Our observations may be helpful to better understand and manage human citalopram poisonings.

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MUSHROOM POISONING: SUCCESSFUL TREATMENT WITH SILIBININ AND *N*-ACETYLCYSTEINE (NAC)

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INTRODUCTION. Mushroom poisoning occurs universally especially during the fall season, among amateur pickers of wild mushrooms. About 90% of deaths are attributed to the ingestion of the species Amanita Phalloides. The ingestion of three mushrooms is usually fatal. The toxins released are Amatoxins, phallotoxins and vitrotoxins. Amatoxins interfere with DNA transcription.

OBJECTIVES. Although there is no specific antidote for these potent toxins, drugs like penicillin G and silibinin have been used with conflicting evidence. We successfully managed two patients with mushroom poisoning by using silibinin and NAC.

METHODS. Two members of a family, a mother 38 years old, and her son 15 years old were admitted to our ICU 36 h after the ingestion of wild mushrooms. They presented with abdominal cramps, vomiting, profuse diarrhea (>20/day), myalgias, confusion and agitation.

RESULTS. The clinical examination showed severe dehydration, tachycardia, oliguria with grade I-II hepatic encephalopathy. Laboratory exams revealed elevation of liver enzymes SGPT: 1106/880 U/L, SGOT: 1884/930 U/L. Coagulation parameters were as following: Prothrombin time 15.5″/15.1″, factor V <55%/60%, factor VII <50/55%. High ammonia levels were noted, reaching 360 and 400 ng/dl, respectively. Metabolic acidosis was also present with mild renal dysfunction. The ultrasound performed in both patients showed hepatosplenomegaly. Aggressive fluid and electrolyte replacement started upon admission. Silibinin was given at a dose of 20 mg/kg/day intravenously, in four divided doses, for three consecutive days, while NAC was given as a continuous infusion at a dose of 150 mg/kg for the first hour, 50 mg/kg for the next 4 h, and thereafter 100 mg/kg/day for the following four days. Hepatic encephalopathy, mild jaundice and renal dysfunction resolved within 48 h, and liver function tests returned to normal within 4 days. The patients recovered fully and were discharged to a medical ward.

CONCLUSIONS. Recent experimental and clinical studies have shown a strong protective and antioxidant effect against hepatic cell injury in Amanita toxicity by the administration of NAC and silibinin, either as monotherapy or as a combination therapy. Although further clinical research is required to confirm their efficacy in reducing mortality and transplantation rate, NAC has been used in our ICU in hepatic dysfunction of different etiologies with promising results.

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1300

OXYGEN CONSUMPTION IS DEPRESSED IN A SWINE MODEL OF METFORMIN INTOXICATION

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INTRODUCTION. We have recently shown that in patients with lactic acidosis due to metformin intoxication (serum drug level = 61 ± 25 μg/ml; therapeutic level is ≤4 μg/ml) systemic oxygen consumption (VO_2) can be abnormally low despite a preserved global oxygen delivery (DO_2) (1). The study, however, suffered from being retrospective.

OBJECTIVES. To prospectively clarify whether metformin primarily impairs VO_2.

METHODS. Eight sedated, paralyzed and mechanically ventilated pigs received a continuous i.v. infusion of metformin, at a rate of 1.6 g/h. The amount of metformin administered to each animal ranged from 4 and 8 g. The experiment always finished 9 h after the initiation of drug infusion. Use of sedative and neuromuscular blocking drugs, as well as ventilatory setting, were always kept constant. Serum metformin concentration was measured at the end of the experiment, using High Performance Liquid Chromatography (HPLC). Arterial pH, lactatemia, VO_2 (indirect calorimetry) and DO_2 (computed from cardiac output measured by pulmonary artery thermodilution) were recorded hourly. Data are presented as mean ± SD. Statistical testing was performed using the one-way repeated measure ANOVA and the linear regression analysis.

RESULTS. Metformin infusion produced toxic serum drug levels (77 ± 30 μg/ml; n = 5). Arterial pH drop from 7.63 ± 0.05 (prior to infusion) to 6.96 ± 0.26 (end of the experiment) (n = 8; $p < 0.001$) and lactatemia rose from 1 ± 0 to 17 ± 7 mmol/L (n = 8, $p < 0.001$). VO_2 progressively decreased (from 117 ± 37 to 66 ± 30 ml/min; n = 8, $p < 0.001$) while DO_2 did not significantly change over time (from 274 ± 74 to 239 ± 66 ml/min; n = 7, $p = 0.39$). The decrease in VO_2 was proportional to the dose of metformin administered (R^2 0.62; n = 8, $p = 0.02$) and to the serum drug level reached by the end of the experiment (R^2 0.69; n = 5, $p = 0.08$).

CONCLUSIONS. Lactic acidosis develops during metformin intoxication in the presence of a diminished VO_2 but in the absence of any clear evidence of inadequate DO_2. This finding suggests that impaired oxygen utilization, rather than availability, may have a role in the pathogenesis of metformin-induced lactic acidosis.

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PROGNOSTIC FACTORS OF POISONINGS TREATED WITH EXTRACORPOREAL LIFE SUPPORT IN THE INTENSIVE CARE UNIT

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INTRODUCTION. Massive drug ingestions may be associated with refractory cardiac failure, the reversal of which despite prolonged arrest makes extracorporeal life support (ECLS) look promising (grade C recommendation, based on case reports). Once implemented, the purpose of ECLS is to take over heart function until recovery can occur, thus minimizing myocardial work and improving organ perfusion. ECLS is feasible in the intensive care unit (ICU) (1).

OBJECTIVES. Our objective was to determine the prognostic factors of ECLS-treated patients

METHODS. Prospective study including all poisoned patients treated with ECLS in 2003–2007; surgical cannulation of femoral vessels in ICU to perform ECLS (Rotaflow®, Jostra-Maquet SA) in collaboration with a cardio-surgical team of a neighboring hospital; descriptive analysis (median [percentiles 10–90%]); univariate comparisons using Chi-square and Mann–Whitney tests.

RESULTS. Fifty-seven poisoned patients (19 M/38F, 41 years [21–59], SAPS II: 75 [49–94]) were treated with ECLS over a 4-year period in relation to cardiac failure (26/57) and arrest (31/57). Patients had ingested high doses of cardio-toxicants in 49/57 cases (chloroquine 19%, Class I-anti-arrhythmic drugs 19%, beta-blockers 14%, calcium channel blockers 11%). Sixteen patients (28%) survived, including five after prolonged cardiac arrest (maximal duration: 180 min). Death was consequent to multiorgan failure, anoxic encephalopathy or capillary leak syndrome if ECLS was performed under cardiac massage. Four patients presented with documented brain death, allowing organ donation in 2 cases. Among these patients, the heart of one flecainide-poisoned patient was successfully transplanted, after normalization of ECG and myocardial function as well as toxicant elimination under ECLS. Prognostic factors in ECLS-treated poisoned patients were as follows: QRS enlargement on admission ($p = 0.009$), SAPS II score on admission ($p = 0.005$), ECLS performance under massage ($p = 0.008$), arterial pH ($p < 0.001$), lactate concentration (10.7 [6.6–19.6] versus 15.0 mmol/l [6.2–29.5], $p = 0.003$), as well as red cell ($p = 0.008$), fresh plasma ($p = 0.003$), and platelet ($p = 0.03$) transfusions within the first 24 h.

CONCLUSIONS. To our knowledge, this is the larger series of ECLS-treated poisoned patients ever reported. ECLS appears to be an efficient salvage technique in case of refractory toxic cardiac failure or arrest, with a 28% survival rate. Our series clearly demonstrate that toxic refractory cardiac failure remains the best indication with a 46% survival rate.

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1302

SELECTIVE BOWEL DECONTAMINATION DECREASES THE RISK OF INFECTION IN PATIENTS TREATED WITH MILD THERAPEUTIC HYPOTHERMIA

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INTRODUCTION. Patients with severe brain injury are more vulnerable to infections. Prolonged hypothermic treatment may further enhance the risk of infection. Selective decontamination of the digestive tract (SDD) reduces the risk of respiratory tract infections in critically ill patients.

OBJECTIVES. Aim of the study was to investigate the incidence of infections in patients treated with hypothermia while receiving SDD.

METHODS. In this retrospective case control study 35 patients treated with prolonged hypothermia (cases) were identified and 169 patients with severe brain injury were included (controls). Propensity score matching was performed to correct for differences in baseline characteristics and clinical parameters. Primary outcome was the incidence of infection. The secondary endpoints were the micro-organisms isolated from surveillance cultures and during infection.

RESULTS. The demographic and clinical data indicated that the cases and controls were well matched. The length of stay in the ICU and duration of mechanical ventilation were comparable between the groups. The overall risk of infection during ICU stay was 20% in the hypothermia groups versus 34.4% in the normothermia group ($p = 0.388$). Pneumonia was diagnosed in 11.4% of patients in both groups ($p = 1.000$). The incidence of meningitis, wound infection, bacteremia, and urinary tract infection was low and comparable between the groups. *Staphylococcus aureus* was most frequently identified as the causative infectious microorganism in both the hypothermia (14.3%) and normothermia (36.3%) group ($p = 0.375$), followed by coagulase negative staphylococci (14.3% in the hypothermia and 27.3% in the normothermia patients, $p = 0.625$) Gram-negative bacteria were isolated from the surveillance cultures in 51.4% of patients treated with hypothermia and 31.4% of patients in the control group ($p = 0.143$). Colonization of the rectum with gram-negative bacteria was significantly more frequent in patients treated with hypothermia compared with normothermia (48.6 vs. 20.0% respectively, $p = 0.041$). In contrast, colonization of the upper gastrointestinal tract and sputum was comparable between the groups with an incidence of 14.3% in the hypothermia patients versus 11.4% in the normothermia patients ($p = 1.0$).

CONCLUSIONS. Use of SDD mitigates the increased risk of infection in patients treated with hypothermia. Based on the surveillance cultures, it seems that oropharyngeal decontamination is the most effective part of the SDD regimen in the prevention of pneumonia.

1303

ASSESSMENT OF ADEQUACY OF LOADING DOSE OF PHENYTOIN (PTN) IN ADULT INTENSIVE CARE PATIENTS USING POPULATION PHARMACOKINETICS

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INTRODUCTION. Phenytoin (PTN) is a highly protein bound anticonvulsant agent commonly employed in intensive care. Given the high morbidity associated with uncontrolled seizures in this setting, rapid attainment of therapeutic concentrations is mandated.

OBJECTIVES. To define the population pharmacokinetics (PK) of phenytoin in the critically ill, in addition to risk factors for sub-therapeutic dosing.

METHODS. Free and total PTN concentrations were measured in serum by means of high performance liquid chromatography following microfiltration, two to three times in the first 24 h after a loading dose. Population PK modelling, including intra and interindividual variability, were determined using NONMEM$^{(R)}$.

RESULTS. Fifty three patients (total of 153 plasma samples) where included in the study. Demographic and pharmacokinetic data are presented in table 1. A one compartment linear model adequately described the pharmacokinetics of loading doses of PTN. The mean clearance and volume of distribution for PTN were 0.024 L kg/h and 1.08 L/kg respectively. The loading dose was within recommended guidelines (10–20 mg/kg) for the majority of cases. Protein binding was consistently $\sim$ 90% when albumin levels were >25 mmol/L and hypoalbuminaemia was associated with higher unbound (free) PTN levels. The percentage of free and total trough levels that were therapeutic were 49% and 38% respectively

CONCLUSIONS. This study has developed a population PK model of PTN loading in critically ill patients. Hypoalbuminaemia was shown to be a critical factor in dosing requirements. In approximately 50% of patients, the trough PTN level was below the therapeutic range, suggesting that higher dosing may be required.

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DO OR DO NOT TREAT HYDROXYCHLOROQUINE OR CHLOROQUINE INTOXICATION WITH DIAZEPAM

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INTRODUCTION. (Hydroxy) chloroquine intoxications are rare but very serious. Life-threatening symptoms may occur within 30 min with progression to death within a few hours. In the Netherlands the use of diazepam is advised as first line treatment although evidence is not established and mainly provided through case-reports [1].

OBJECTIVES. To compare the effect of diazepam on mortality in (hydroxy) chloroquine intoxication to standard therapy.

METHODS. We performed an extensive MEDLINE search (1950–April 2010) with a manual reference search of identified papers. (Hydroxy) chloroquine intoxication studies and case reports in English, Dutch or French were evaluated. Patients older than 15 years with severe intoxications, based on measured concentrations or life-threatening symptoms, were included. Pooled relative risk (RR) for mortality with corresponding 95% confidence interval (CI) were calculated by means of a Fisher exact test. Our results were compared with two retrospective and one prospective study.

RESULTS. There were 32 case reports identified from which 25 case reports met our inclusion criteria. Thirteen patients received diazepam of whom two died, compared to twelve patients who did not get diazepam of whom one died. Statistical analysis demonstrated that treatment with diazepam was not associated with a lower mortality rate (RR: 1.1 CI 0.8–1.5; $p = 1.0$).Although pooling of case reports is debatable, these results were comparable to the retrospective and prospective studies that didn't show any benefit from diazepam in chloroquine intoxication [2, 3, 4]. The positive effect of diazepam may have been underestimated, due to the fact that it has been given only as rescue therapy.

CONCLUSIONS. Based on our analysis there is a lack of evidence concerning any antidotal effect of diazepam. Good supportive treatment is pivotal. If the clinical manifestations of (hydroxy) chloroquine intoxications require sedation or treatment of seizures, diazepam is a good choice based on its pharmacological profile. A prospective study which compares diazepam to sedativa with similar pharmacokinetic and dynamic profile is required to prove that diazepam has any antidotal effect.

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1305

HIGHER REQUIREMENT OF DIALISIS IN LITHIUM POISONING

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INTRODUCTION. Lithium (Li) is commonly prescribed for the treatment of bipolar disorders. However, because of its narrow therapeutic index an excessive elevation of serum lithium concentration, either during chronic maintenance therapy or after an acute overdose, can result in serious toxicity. The established treatment of severe Li toxicity is haemodialysis.

OBJECTIVES. Analyze intoxicated Li population in the Intensive Care Unit (ICU), what Renal Replacement Therapy (RRT) is being used and which risk factors are associated with higher requirements of RRT.

METHODS. Observational prospective study of 15 lithium poisoning admitted to ICU from 2004 to 2009.

RESULTS. Population: 53.3% were male ($n = 8$) with median age of 41.8 $\pm$ 16.14 years. 66.7% were suicide attempt. 53.3% were bipolar disorder and 26.7% suffered schizophrenia. Regarding medical history 20% had Arterial Hypertension, Diabetes Mellitus or COPD, 13.3% were obese, 93.3% had been treated with Li, 73.3% were smokers and 33.3% presented alcohol abuse. At admission 20% had become dehydrated, 13.3% had associated infection and in the 13.3% of the cases Li treatment had been modified in the last 2 weeks. The different types of poisoning were: acute 6.7%, acute chronic 66.7% and chronic 26.7%. Associated intoxication with other drugs was identified in the 53.3% of the cases. During the first 24 h patients presented the following signs: 73.3% neurological (mild and severe 80%), 86.7% hematologic, 60% haemodynamic, 33.3% gastrointestinal, 26.7% oliguria and 33.3% anuria. 20% needed mechanical ventilation, 33.3% vasopressors and 93.3% RRT (26.7% continuous and 66.7% intermittent dialysis).It were observed differences between the group of patients who needed >1 dialysis session (number of sessions: 2.57 $\pm$ 1.27), in comparison with those who needed only 1 session or continue RRT, in the initial Li blood concentration (5.7 $\pm$ 2.76 vs. 3.5 $\pm$ 1.28), length of stay (7.8 $\pm$ 5.9 vs. 4.1 $\pm$ 4.2 days), median APACHE II score (13.8 $\pm$ 6 vs. 16.14 $\pm$ 4.77) and Creatinine Clearance (CrCl) at admission (40.49 $\pm$ 23 vs. 73.3 $\pm$ 24.9). The presence at admission of >17,000 White Blood Cells (WBC), CrCl <40 ml/min and Na <135 mmol/l were identified as risk factors associated with >1 dialysis session requirements. There was no significant between-group difference in the initial Li and different TRR.

CONCLUSIONS. WBC >17,000/L, CrCl <40 ml/min and Na <135 mmol/l are factors that predict higher requirement of dialysis in lithium poisoning.

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CHANGES IN THE BRAIN INFLAMMATORY AND METABOLIC PARAMETERS IN A POLYMICROBIAL SEPSIS RODENT MODEL

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INTRODUCTION. Brain is one of the first organs affected in sepsis and evaluation of brain function is difficult since patients are under sedation. It has been shown that mitochondrial dysfunction may play a significant role in the pathogenesis of septic encephalopathy. Here we investigated inflammatory and metabolic parameters in a model of polymicrobial sepsis in mouse.

METHODS. Sepsis was induced by intraperitoneal injection of feces. Animal received imipenem 6 h after the procedure. Control animals received intraperitoneal saline and imipenem after 6 h. Blood Cytokines and serum lactate were measured. The animals were sacrificed by cervical dislocation. Brain slices of 400 mcm were used to measure oxygen consumption and glucose uptake.

RESULTS. Interleukin 6, MIP 1α and Interleukin 1β significantly raised in the first 6 h after sepsis induction ($p = 0.001$; $p = 0.0017$; $p = 0.0001$ respectively). In 24 h only MIP 1α was significant higher ($p = 0.0001$). Lactate was elevated 6 and 24 h after sepsis induction ($p < 0.01$ and $p < 0.001$ respectively). Oxygen consumption increased after 6 h of sepsis and drops under control values 24 h after the induction of sepsis. Glucose uptake, measured by the NBDG fluorescence, was higher after 6 h ($p = 0.0475$) and 24 h after sepsis induction.

CONCLUSION. In a murine model of abdominal sepsis, inflammatory markers, lactate production, and brain glucose uptake increased and were parallel to alterations in the mitochondrial oxygen metabolism.

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Outcome, scoring and performance in emergency medicine: 1307–1320

1307

SHORT AND LONG TERM OUTCOMES FOR ELDERLY PATIENTS MANAGED WITH INDUCED HYPOTHERMIA AFTER VF AND PULSELESS VT MAY BE AS GOOD AS FOR YOUNGER PATIENTS

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INTRODUCTION. The Royal Bournemouth Hospital has one of the highest out-of-hospital cardiac arrest admission rates in the UK. In 2005, following ILCOR/AHA guidelines [1], a cooling protocol was developed for patients with return of spontaneous circulation after advanced life support for ventricular fibrillation or pulseless ventricular tachycardia. In preparation for potential new ILCOR/AHA guidelines in 2010, the prospective database of outcomes for these patients was analysed.

OBJECTIVES. To evaluate the outcomes of therapeutic hypothermia for patients with return of spontaneous circulation following cardiac arrest.

METHODS. Outcome data from our prospective registry of cooled patients are summarised.

RESULTS. Sixty-three patients were cooled in 4 years (median age 68 years; mode 76; range 19–88 years). 84% survived to ITU discharge and 70% to hospital discharge. 98% of these were discharged home (14% to a rehabilitation hospital before home and one patient to a long term care facility). Ninety-five percent of survivors were alive at 6 months and 80% alive at 1 year with seven status results still pending. Median ITU length of stay was 3.5 days (range 1–13). Six patients required temporary percutaneous tracheostomies for airway protection and weaning from ventilation. Median duration from ITU to hospital discharge was 16 days (range 0–62).

CONCLUSIONS. This series is large by comparison to other UK centres. Survival to hospital discharge, at 6 months and 1 year were better than other published results. Although neurological outcomes were not formally assessed, we believe that the capacity to discharge home is a desirable patient outcome and represents the beneficial neurological effect of our cooling protocol. Selection bias will have undoubtedly affected our results. However the age of our patients was higher than in published trials and in other reports is considered an adverse outcome predictor. Our data would not support restricting induced hypothermia on the basis of age alone. We consider the ITU and hospital lengths of stay required to discharge these patients to be long. These data were not reported in original trials. Discharges may obviously be delayed for non-clinical reasons. This aside, neurological recovery progresses for months after cardiac arrest and discharge home may still prove possible if time is allowed. However, post-ITU resource implications should be considered when introducing a cooling protocol.

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1308

ACUTE ISCHAEMIC STROKE AND CRITICAL CARE: A 5 YEAR RETROSPECTIVE AUDIT OF ADMISSIONS TO A UK TERTIARY INTENSIVE CARE UNIT

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INTRODUCTION. Acute ischaemic stroke (AIS) is the third largest cause of mortality and the leading cause of chronic disability in the industrialized world. In some parts of Europe and the United States 26–43% of patients with AIS may be admitted to a neurological intensive care unit (ICU) for supportive therapy with 8–10% receiving mechanical ventilation [1, 2]. There are currently no agreed UK criteria for the admission of AIS patients to critical care.

OBJECTIVES. To review the incidence and outcome of AIS in our tertiary ICU over the last five years.

METHODS. A retrospective audit was performed for all AIS ICU admissions between November 2005 and November 2009. AIS was classified as thrombo-occlusive or embolic. Subarachnoid haemorrhage and primary intracerebral haemorrhage were excluded. Demographic and outcome data were recorded and compared against a mean value of all ICU admissions.

RESULTS. AIS comprised 0.8% of ICU admissions during the study period. Demographic data is presented in Table 1 as mean ± standard deviation or median (interquartile range) as appropriate. In 2008 4% (11/272) of hospital AIS admissions were admitted to ICU. 14 patients had surgical procedures including 8 decompressive craniectomies. 27% of survivors had a discharge GCS of 15/15. Mortality for unselected medical admissions over the study period was 36%.

TABLE 1

Category	Admissions (n)	Age	Male	APACHE II	Ventilator days	ICU Mortality	Hospital mortality	ICU length of stay
All ICU patients	3,856	55 ± 11	47%	19 ± 7	4.4 ± 1.2	17%	25%	5.2 (2–7)
Patients with AIS (0.8%)	29	49 ± 16	69%	17 ± 8	5.4 ± 4.9	24%	27%	6 (2–10)

CONCLUSIONS. Few patients with AIS were admitted to ICU in the study period. Their in-hospital mortality was favourable compared to unselected medical ICU admissions. Interventions such as thrombolysis may lead to increased interface with critical care. The current National Institute of Clinical Excellence acute stroke guidelines do not mention intubation or ICU admission [3]. There may be excessive pessimism in the UK regarding AIS. We believe the care of these patients should be re-evaluated in order to avoid missed opportunities to improve outcomes.

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1309

VALIDATION OF PROGNOSTIC SCORES IN BURN INJURY

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INTRODUCTION. Prognostic scores specific for critical patients were developed in order to predict mortality based on physiologic and laboratorial variables. On the other hand, specific scores for burn patients are calculated taking into consideration inhalation injury, age and total burned surface area (TBSA), among others. However, scores utilized in general ICU have not been evaluated in burn patients.

OBJECTIVES. Therefore, the aim of the present work was to validate APACHE II, SAPS 3 as well as initial SOFA in a population of patients with massive burn. These scores were compared to some specific burn patient scores, including ABSI (Abbreviated Burn Severity Index) and Estimates of the Probability of Death.

METHODS. Retrospective study employing data collected prospectively from May 2005 to February 2010 (58 months) at an ICU specialized in burn patients at a teaching hospital which is considered a reference centre in trauma care. All patients admitted during this period were included.

RESULTS. One hundred and fifty-four consecutive patients were studied (male: 73%; female: 27%), with averaged age of 37.7 ± 15.9 years and a hospital stay of 33.8 ± 28.4 days. Mortality rate of our sample was 43.5%. Incidence of inhalation injury was 45% and total burn surface area (TBSA) was the following: 35.5% of patients had 20% or less; 36.1% had 20–40% of TBSA whereas 28.4% showed 40% or more.

Area under curve of Receiver Operating Characteristic (ROC) of evaluated indexes is displayed on Table 1.

TABLE 1 AREA UNDER CURVE OF ROC OF PROGNOSTIC INDEXES

	AUC	SE	95% CI
ABSI	0.896	0.0277	0.836–0.939
APACHE II	0.864	0.0314	0.800–0.914
Estimates of the probability of death	0.828	0.0349	0.759–0.884
SOFA initial	0.802	0.0369	0.731–0.862
SAPS 3	0.872	0.0305	0.809–0.920

CONCLUSIONS. All prognostic indexes are good predictors of mortality in massive burn patients. Among them, ABSI and SAPS 3 showed the best performance.

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ANALYSIS OF HEAD CT SCANS IN CRITICALLY ILL ADULT PATIENTS

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INTRODUCTION. Computerized head tomography is routinely performed as a diagnostic tool after the occurrence of neurologic deterioration in the ICU adult patients. However, the CT findings in this setting are rarely reported. We hypothesized that the analysis of a series of cranial CTs would help to understand the neurologic conditions of the critically ill patients and improve their management.

OBJECTIVES. To analyze, over a three-month period, the head CT scans performed in the Adult ICU in the Albert Einstein Hospital in São Paulo, Brazil.

METHODS. All cranial CTs performed in the ICU patients during the studied period were analyzed by two radiologists from the Albert Einstein Hospital staff From May 1st to August 31st, 2009, according to a pre-established protocol: 1. presence of acute cerebral ischemia;
2. presence of previous cerebral ischemia;
3. presence of acute cerebral hemorrhage;
4. presence of cerebral edema;
5. cerebral aneurisms;
6. cerebral tumors and
7. normal cerebral tomography.

RESULTS. We studied 69 CT scans from 34 (49.2%) males and 35 (50.8%) females, mean age 64.43 ± 21.7 years. The head CT findings were the following: (1) presence of acute cerebral ischemia = 10 (14.4%); (2) presence of previous cerebral ischemia = 17 (24.6%); (3) presence of acute cerebral hemorrhage = 27 (39.1%); (4) presence of cerebral edema = 7 (10.1%); (5) cerebral aneurisms = 2 (2.8%); (6) cerebral tumors = 2 (2.8%) and (7) normal = 21 (30.4%).

CONCLUSIONS. The most prevalent head CT findings in ICU patients was cerebral hemorrhage followed by acute and chronic cerebral ischemic events. The high prevalence of normal scans was probably due to metabolic underlying disorders.

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1311

IS IT POSSIBLE TO PREDICT MASSIVE TRANSFUSION? UTILITY SCORES

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]**INTRODUCTION.** Massive Transfusion occurs in 3% of all civilian trauma patients. Although many trauma centers have implemented massive transfusion (MT) protocols, most of them do not have a standardized initiation policy.

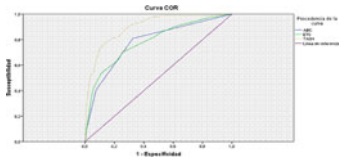
OBJECTIVES. Our purpose is to validate previously described MT scoring in our Transfusion Trauma Registry (TTR).

METHODS. Retrospective cohort of all adult trauma patients admitted to Trauma Intensive Care Unit of I level urban trauma center. Were included patients with severe trauma (Injury Severity Score ≥15) admitted from October 2006 to July 2009. We evaluated the following MT scoring and cut points (CP): TASH (trauma-associated severe haemorrhage CP: ≥16 years ≥ 18, ABC (assessment blood consumption) CP: ≥2 and ETS (emergency transfusion score) CP: ≥3, ≥4 years ≥6. These scales handle the following combinations of variables for calculation: age, sex, type of admission, mechanism, blood pressure, focussed assessment for the sonography of trauma, hemoglobin, orthopedic or pelvic trauma, heart rate. MT was defined as the transfusion of 10 units or more of packed red blood cells in the first 24 h. We study the sensitivity (S), specificity (SP), positive and negative predictive value (PPV, NPV), likelihood ratios positive and negative (LHR+ , LHR−) and area under the receiver operating characteristic curve (AUROC) of different scales for the predictive power of TM validated in the literature. 568 patients were available for analysis (77.6% men, ISS 30 ± 13, blunt trauma 93.8%). The overall MT rate was 18.8%. The following table summarizes S, SP, PPV, NPV, LR+ , LR−).

S, SP, PPV, NPV, LR+ , LR− AND SCORES

	ABC ≥ 2	TASH ≥ 16	TASH ≥ 18	ETS ≥ 6	ETS ≥ 4	ETS ≥ 3
S	43%	43%	28%	66%	81%	89%
SP	90%	96%	98%	94%	71%	36%
PPV	56%	78%	85%	66%	30%	26%
NPV	84%	86%	84%	86%	91%	92%
LR+	4.3	13.43	14	11	2.7	1.3
FR−	0.63	0.58	0.73	0.36	0.26	0.30

In the next figure and table, AUROC curves are compared for the ABC, TASH and ETS scores:



AUROC-scores

AUROC-SCORES

Score	AUROC
ABC	0.779
ETS	0.784
TASH	0.899

CONCLUSIONS. TASH showed the best predictive ability. The scores can be useful to characterize the TM population, exclusion of low-risk population and support of clinical decisions. Clinical validation requires a prospective multicenter analysis.

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OUTCOMES OF ELDERLY TRAUMA PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT

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INTRODUCTION. Though outcomes after trauma in elderly patients have been previously describe, few studies have focused on the most severely injured elderly trauma patients admitted to the intensive care unit (ICU). An understanding of the outcomes in these patients is required to help inform decision making.

OBJECTIVES. This study was undertaken to determine the mortality in elderly trauma patients admitted to the ICU at a Canadian lead trauma hospital (LHSC), and to explore factors associated with mortality. Particular attention was paid to the relationship between pre-injury anticoagulation and mortality.

METHODS. A retrospective cohort of all elderly (age ≥65) trauma patients admitted to the ICU from 1997 to 2008 was identified. Data were obtained from the LHSC trauma database. Therapeutic INR levels on admission (INR > 2.0) were used to identify pre-injury therapeutic warfarin use.

RESULTS. Of the 1209 elderly patients admitted after trauma, 355 (29%) were admitted directly to the ICU. Patients had a mean age of 75 years (± 5), and a mean injury severity score (ISS) of 27 (± 11.5). Overall mortality was 45% (161 patients), with a mean time to death of 8 days. Logistic regression identified the following factors associated with mortality: age (OR 1.07, 95% CI 1.03–1.11), ISS (OR 1.05, 95% CI 1.03–1.08), and pre-injury anticoagulation (OR 3.6, CI 1.7–7.3). Amongst patients who survived, only 30 (15.5%) were discharged home.

CONCLUSIONS. In contrast to the overall elderly population, elderly patients requiring admission to the ICU after trauma have high mortality and morbidity rates, with very few patients returning home. This study highlights the importance of therapeutic anticoagulation as a predictor of mortality. With the rising proportion of elderly patients, strategies will be required to manage the burden of injury in this population.

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VALIDATION OF A MULTIPLE-CHOICE VERSION OF THE MINI MENTAL STATE EXAMINATION IN THE ICU

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INTRODUCTION. 1/3 of intensive care unit (ICU) patients develop neurocognitive impairments. This complication affects considerably the patient's quality of life, daily activities and return to work. The Mini Mental State Examination (MMSE) is the simplest tool currently available for neurocognitive assessment and is validated in neurological populations. One of its limitations is its application restricted to patients able to speak. Up to date, there is no available version adapted to ICU patients who are deprived of speech.

OBJECTIVE. The aim of this study is to validate a visual multiple-choice version of MMSE (MC-MMSE) adapted to patients unable to speak.

METHOD. MC-MMSE was studied in 30 intubated ICU patients. For 20 of them, the inter-rater reliability was tested by 2 examiners whose passation order was randomized. For the 10 others, we studied the intra-rater reliability (test-retest). Furthermore, we compared the MC-MMSE to the original MMSE (Greco) on 3 populations: healthy volunteers (n = 26), neurological patients (n = 20) and speaking ICU-patients (n = 46).The application order of each test was randomized.

RESULTS. The **inter-rater** reliability was very good (Rho: 0.96, $p < 0.0001$). The **intra-rater** reliability was good (Rho: 0.63, $p = 0.05$). Regarding the validation: the correlations and the t test between the standard and the MC-MMSE were: healthy volunteers (Rho: 0.53, $p < 0.08$; t test: $p = 0.019$), neurological patients (Rho: 0.88, $p < 0.0001$; T test: $p = 0.02$), speaking ICU-patients (Rho: 0.82, $p < 0.0001$; T test: $p = 0.005$). The MC-MMSE showed a slightly better result for the whole test by the Bland and Altmann analysis: speaking ICU-patients (1.0 ± 2.1), healthy volunteers (0.6 ± 1.2) and neurological patients (1.5 ± 2.6). This was probably due to the recall item: speaking ICU-patients (0.9 ± 1.9), healthy volunteers (0.2 ± 0.49) and neurological patients (0.6 ± 1.2).

CONCLUSIONS. The MC-MMSE compared to the original version produces similar results independently on the population studied. However the scores with MC-MMSE were significantly better, probably because of easier recall item. Its inter- and intra-rater reliability were good. MC-MMSE could be an interesting tool to assess and monitor the neurocognitive performances of ICU patients during and after their ICU stay.

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EVALUATION OF FORECASTING FACTOR REGARDING MORTALITY IN A SERIES OF PATIENTS WITH SPONTANEOUS INTRACRANIAL HAEMORRHAGE

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OBJECTIVES. To analyze the factors associated with mortality in the intensive care admitted intracranial haemorrhages.

METHODS. Descriptive retrospective study of patients admitted from 1st January 2007 to 31st December 2009 in the intensive care unit in the Virgen de la Salud hospital (Toledo) with a spontaneous intracranial haemorrhage diagnosis.

RESULTS. There are 124 patients. Regarding associated comorbidity hypertension, dislipemy, mellitus diabetes and obstructive lung disease are analyzed, objectifying significance in relation to hypertension (24.1 vs. 50%, $p < 0.05$). In the analyse of previous treatments only anticoagulation (14.5 vs. 37.5%, $p < 0.05$) and antihypertensive (30.3 vs. 56.3%, $p < 0.05$) come out as a significative forecasting factor. The presence of hypertensive crisis defined as systolic arterial tension over 150 is not proven a forecasting factor. Analyzing the characteristics of the haemorrhage, found forecasting factors are Glasgow on groups (<8:83%, 9–12:14.9% years 13–15:2.1%, $p < 0.01$) and the ICH score with a mortality on groups of 100% for a score of 5. There are differences of significance in the mortality according to the age, classified by age groups with an age cut off of 80 years (<80 years 38.6 vs. ≥80 years 40%, $p < 0.01$). Apart from the GCS, the rest of the variables analyzed in the ICH score are not of significance; supra and infratentorial, presence of intraventricular blood neither on the divided volume over or under 30 cc although, in the latter, a $p < 0.1$ can be observed and if we only analyze the supraventricular, it comes out as significant. Other analyzed data are the time of the surgery, which is not significant, the need for mechanical ventilation, which is (42.9 vs. 15.8%, $p < 0.05$), and the days of ventilation with a mortality clearly higher on those patients with <5 days of ventilation (83%) and on those of shorter stay (lesser then 5 days 79%).

CONCLUSIONS. Let be remarked that the samples have been taken from patients admitted in the intensive care unit, losing a possible sample of less serious patients, and with a higher level of consciousness, what might explain why supra or infratentorial location and the volume don't come out as forecasting factors, since its likely that there are many small infratentorial outside the intensive care unit. We highlight also that the high mortality in the first few days can be caused by those patients who are admitted as donors, developing an encephalic death in the first days, conditioning also the data regarding the mortality on fewer days with ventilation. The finish up, we have to point out the fact that the presence of previous hypertension during the treatment might be a bad forecasting factor that should be deeper studied.

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MEDIUM AND LONG-TERM QUALITY OF LIFE IN ICU SURVIVORS WITH SEVERE THORACO-ABDOMINAL TRAUMA AND DAMAGE CONTROL LAPARATOMY

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INTRODUCTION. There is insufficient information regarding long term outcome and quality of life in trauma patients who survive damage control (DC) interventions after severe thoraco-abdominal trauma (TAT).

OBJECTIVES. We measured patient-reported outcome following surgical management with DC using a quality of life instrument.

METHODS. Survivors discharged between 3 and 18 months after severe TAT were contacted after obtaining approval by our institutional IRB. We excluded patients with neurotrauma. We applied self-response version EuroQoL questionnaire (EQ-5D) and visual analog scale (EQ-VAS: 0 (worst health)–100 (best health). EuroQoL it is based on a descriptive system that defines health in terms of 5 dimensions: mobility, self-care, usual-activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels of response: no problems (level 1), some problems (level 2) severe problems (level 3).

RESULTS. Thirty four patients were contacted. Mean ± SD age was 31.8 ± 11.6 yrs, Male were 88.2% and penetrating trauma occurred in 79.4%. Mean ± SD in severity scores were: ATI 24.4 ± 9.6, ISS 28.1 ± 8.5 and APACHE II 20 ± 6. The median time from discharge was 12 months (IQR 6–15 months). The EQ-5D dimensions in which the largest proportion of patients reported severe problems were usual-activities (work, study) and pain/discomfort 14.7% and 5.9% respectively as shown in the table. Main reason of discomfort was the presence of surgical scar in the abdomen. Median EQ-VAS score was 90 (IQR 70–100).

QOL_DC

Level of perceived problems (%)	Mobility	Self-care	Usual activities	Pain/ discomfort	Anxiety/ depression
1 (Mild or none)	73.5	85.3	61.8	50	61.8
2 (Moderate)	25.5	14.7	23.5	44.1	35.3
3 (High)	0	0	14.7	5.9	2.9
All (n = 34)	100	100	100	100	100

CONCLUSIONS. Survivors of severe trauma and DC, reported acceptable quality of life with minimal limitations with social functioning. A prospective study should assess Quality of Life in these patients from hospital discharge and systematically over time.

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PREDICTIVE FACTORS OF HOSPITAL MORTALITY FOR NEUROLOGICAL CRITICALLY ILL PATIENTS

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INTRODUCTION. The prognosis of neurological critically ill patients can be different from other types of admission and whether it is influenced by the primary neurological acute event or the medical complications during ICU stay is still a subject of debate.

OBJECTIVES. To evaluate predictive factors of hospital mortality in a cohort of patients admitted to 3 neurocritical care units.

METHODS. Neurological critically ill patients who stayed more than 2 days in the ICU were included from specialized neurocritical care units of 3 hospitals, from April 2006 to December 2009. A prospective data collection was performed, including demographic data, acute physiology scores (APACHE II and SOFA), Glasgow coma score, use of mechanical ventilation and vasoactive agents, and the occurrence of severe sepsis (according to Bone's criteria—1992). The causes of admission were divided as: ischemic stroke, hemorrhagic stroke, subarachnoid hemorrhage, status epilepticus, traumatic brain injury, elective neurosurgeries, and miscellanea. The foci of infection, microbiological data and bacteremia were analyzed from septic patients. Numeric data were expressed as median and interquartiles, while categorical data were calculated as percentage. Univariate and multivariate (logistic regression) analysis was carried out to point factors associated with hospital mortality.

RESULTS. We included 661 patients, with median age 65 years (IQ range 50–78) and 54% were male. ICU length of stay was 4 days (IQ range 2–7), and hospital mortality was 10.3%. Main causes of admission were: ischemic stroke (n = 125), elective neurosurgeries (n = 113), traumatic brain injury (n = 71), hemorrhagic stroke (n = 53), subarachnoid hemorrhage (n = 29), status epilepticus (n = 20), and miscellanea (n = 250). Severe sepsis was diagnosed on 128 (19%) patients. Lung was the most common site of infection (45%), followed by urinary tract infection (10%). Microbiological cultures were positive for 50% of patients, and 8 (6%) patients had positive blood cultures. Staphylococci was the most common bacterial isolate (n = 15), followed by Enterobacteriaceae (n = 13) and Pseudomonas sp (n = 7). Sepsis was diagnosed by the time of ICU admission on 39 (30%) patients, while it occurred during ICU stay on 110 (70%) patients. Hospital mortality was associated with age, the admission cause (higher for hemorrhagic stroke, traumatic brain injury and status epilepticus), APACHE II score, Glasgow coma score and severe sepsis on the univariate analysis. After the multivariate analysis, Glasgow coma score less than 13 points (odds ratio 6.4 [CI 95% 3.1–13.2]) and severe sepsis (odds ratio 5.9 [CI 95% 3.1–11.4]) were independently associated with hospital mortality.

CONCLUSIONS. Glasgow coma score and occurrence of severe sepsis were the main risk factors for hospital mortality of neurological critically ill patients.

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PERIOPERATIVE FACTORS ASSOCIATED TO HIGHER MORTALITY IN PATIENTS ADMITTED TO THE NEUROLOGICAL INTENSIVE CARE UNIT (NICU) IMMEDIATELY AFTER BRAIN TUMOR (BT) RESECTION

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INTRODUCTION. Brain tumors surgery is one of the main causes of admittance to the NICU. It is important to know the risk factors associated to hospital mortality of patients admitted to NICU due to this reason.

OBJECTIVES. To identify perioperative factors associated to higher hospital mortality in a series of patients admitted to NICU immediately after a BT elective resection.

METHODS. Data of 101 patients operated for BT elective resection and consecutively admitted to NICU at IMSS UMAE 1 Bajío were prospectively obtained. NICU BT database includes 269 perioperative items. We divided the series in two groups: surviving and deceased patients. Then, we analyzed the perioperative behavior differences between both groups. Either Student's t test or Chi-square test was used, as it corresponded, for the analysis of differences observed between both groups. Values of p lower than 0.05 were considered significant.

RESULTS. The hospital mortality observed in this series of 101 patients was 8.9% (9/101). Data of the nine variables showing significant differences between surviving and deceased patients groups are shown in Table 1.

TABLE 1 SURVIVING AND DECEASED PATIENTS GROUPS

Variable	Surviving patients	Deceased patients	p
Preoperative GCS	14.9 ± 0.4	11.4 ± 3.7	<0.005
Surgical time (min)	226.0 ± 104.0	294.0 ± 99.5	<0.05
Anesthetic time (min)	267.0 ± 107.1	338.0 ± 111.2	<0.05
NICU GCS, day 1	14.6 ± 1.3	5.7 ± 2.4	<0.005
NICU GCS, day 5	14.2 ± 1.5	7.4 ± 3.1	<0.005
NICU GCS, discharge	15.0 ± 0.2	7.6 ± 4.2	<0.005
Time of mechanical ventilation (h)	9.7 ± 16.7	274.3 ± 285.2	<0.005
NICU LOS (days)	2.0 ± 1.2	6.0 ± 4.2	<0.005
Hospital LOS (days)	19.2 ± 13.3	31.8 ± 12.0	<0.005

CONCLUSIONS. In our series, surviving patients operated for BT elective resection showed shorter surgical and anesthetic times, lower GSC scores along all the perioperative period, shorter time of mechanical ventilation and shorter NICU and hospital length of stay (LOS) versus deceased patients.

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PROGNOSTIC FACTORS IN NEAR-DROWNING PATIENTS RECEIVING MECHANICAL VENTILATORY SUPPORT

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INTRODUCTION. Even if hypoxic brain injury has been reported as the strongest factor affecting the poor outcome of near-drowning patients, little has been known about prognostic factors affecting the outcomes of those patients receiving mechanical ventilation.

OBJECTIVES. To define prognostic factors affecting the outcomes of patients mechanically ventilated after near-drowning.

METHODS. Medical records of 42 near-drowning patients receiving mechanical ventilation from 2001 to 2009 were reviewed, and retrospectively analyzed by univariate and multivariate logistic regression.

RESULTS. Among 42 patients, 18 (42.9%) had poor outcomes (died + transferred to other hospitals without improvement) and 24 (57.1%) had favorable outcomes (improved + transferred after improvement). According to the univariate analyses, the higher body temperature at the emergency department [the odds ratio (OR), 2.49; 95% confidence interval (CI), 1.24–5.01; P = 0.010], SOFA score (OR, 0.50; 95% CI, 0.34–0.75, P = 0.001), APACHEII score (OR, 0.80; 95% CI, 0.72–0.90; P < 0.001), Glasgow coma scale (OR, 1.72; 95% CI, 1.21–2.44; P = 0.003), mean arterial blood pressure (OR, 1.05; 95% CI, 1.01–1.08; P = 0.006), 24 h urine output (OR, 1.00; 95% CI, 1.00–1.00; P = 0.016), PaO_2/FiO_2 ratio (OR, 1.01; 95% CI, 1.00–1.02; P = 0.010), $PaCO_2$ (OR, 0.92; 95% CI, 0.86–0.99; P = 0.021), white blood cell counts (OR, 1.00; 95% CI, 1.00–1.00; P = 0.001), serum creatinine (OR, 0.19; 95% CI, 0.06–0.67; P = 0.010), and serum lactic acid (OR, 0.95; 95% CI, 0.93–0.98, P = 0.002) were associated with favorable outcomes, respectively. However, only higher body temperature as a clinical parameter and the level of serum lactic acid as a laboratory parameter were significant predictors of favorable outcomes in multivariate analyses; the OR were 2.87 (95% CI, 1.01–8.14; P = 0.048) and 0.96 (95% CI, 0.93–0.99; P = 0.011), respectively.

CONCLUSIONS. Initial body temperature and the level of serum lactic acid were two most important clinical and laboratory prognostic factor in nearly drowned patients. The outcomes were not affected by the degree of initial hypoxemia.

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PERFORMANCE OF AUTOMATED EXTERNAL DEFIBRILLATOR IN HOSPITAL RESUSCITATION

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OBJECTIVES. To determine the use of automated external defibrillators (AED) and manual defibrillators deployed in the various hospital wards (unmonitored areas) in a university hospital.

METHODS. A prospective study was performed according to Utstein style of all cardiac arrests occurred in the hospital during the first 6 months after the implantation of a new protocol of care for hospital cardiac arrest. Because of this plan automated external defibrillators were located for hospital wards and common service areas (radiology areas, outpatients, …) where one would expect a lower incidence of cardiac arrests, according to the risk map elaborated previously. In areas of greatest risk manual defibrillators previously existed. All resuscitation attempts in these areas were analyzed, excluding the emergency department because of a separate protocol against the rest of the hospital. Special attention was given to the use of AEDs by wards staff before the arrival of resuscitation team. Also a comprehensive volunteer training program was designed, but it began after the analyzed period was finished.

RESULTS. During the first 6 months we collected a total of 20 PCR in hospital wards and public areas, with a median age of 71 years and predominantly male (12 patients). The most common origin was respiratory (13 patients) followed by cardiac (4 patients). The most frequent rhythm detected was non-shockable (17 patients), only in 2 was shockable and unknown in 1. Before the resuscitation team arrival only two patients had been manually defibrillated and were never used the new AEDs.

CONCLUSIONS. The AEDs provided in the hospital were completely useless in the first months after placement, probably due to the lack of a comprehensive training plan associated to the population goal.

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APPLICATION OF NEW SCALE OF NEUROLOGICAL MONITORING FOR THE CONFIRMATION OF ENCEPHALIC DEATH IN POTENTIAL DONORS OF ORGANS

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INTRODUCTION. The scale of Basic cerebral Monitoring Modified (MBC-M) designed to be applied from the revenue of the neurocritical patient, values biochemical, and clinical variables that intervene in the cerebral dynamics (PAM, FC, Temperature, Sodium, Blood sugar, PO2, etc.). Now this score appears in proof of certainty of encephalic death

OBJECTIVES. To evaluate the scale of Basic cerebral monitoring modified in proof of certainty in Encephalic Death.

METHODS. descriptive longitudinal Study. 208 patients were studied by encephalic Death, as potential donors of organs, alerted to the Network of regional Transplant 5 (CDTOT), by units of intensive care, for 36 months, in Barranquilla's city. It was applied qualifying each of the variables in agreement to the vital opposing signs and biochemical tests brought in this moment.

RESULTS. 78.3% of the subjects were male; the average of age was 37.34 years (±sd: 16.24). The values of blood sugar, sodium, osmolaridad, tonicidad, PO2, FC, PAM, and Glasgow, determined a score of 22, qualification that there had patient with encephalic death with the scale MBCM, as a test of certainty of the scale to diagnose encephalic death in total absence of reflections of stem.

CONCLUSIONS. there is recommended the application of MBCM's scale to every neurological patient by diagnosis of encephalic death in proof of certainty, in absence of others. By the high specificity of the already demonstrated scale there is recommended that scores lower than 19 they should restate the qualification. A score of 22 is an encephalic death in absence of reflections of stem.

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Neurological conditions: 1321–1332

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TRACHEOTOMIES IN A NEUROLOGICAL ICU. INDICATIONS AND COMPLICATIONS OF THIS PROCEDURE

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INTRODUCTION. Prospective analysis of tracheostomies performed in patients admitted to a neurotrauma ICU, the reasons for its implementation, and intraoperative complications in the first week.

METHODS. All patients admitted to the ICU of neurotrauma, which underwent a tracheostomy after admission. Data were collected: affiliation, Cause of admission, average stay, cause for realization of tracheostomy, tracheostomy time delay from its indication, place of performance of the procedure (ICU or operating room), perioperative complications (event at transfer to operating room or during surgery: hypoxia, hypotension, arrhythmia, bleeding, premature extubation, false cannulation, cardiac arrest, pneumothorax or death), and postoperative complications in the first week (bleeding, difficulty in changing cannula, stomal infection, pneumothorax, death).

RESULTS. in 24 consecutives months, we included 54 patients, age 51.98 ± 19.48 years, 70.47% male, mean APACHE II at admission 16.74 +8.93 points, GCS on admission 8 ± 5 points, average stay 25.29 ± 13.10, cause of ICU admission (29.63% Brain Trauma, 22.22% Stroke, multiple trauma 16.67%, 7.41% other sources coma, 14.81% respiratory failure, 9.62% other), indication of the tracheostomies (59.26% low level of consciousness, prolonged mechanical ventilation 16.67%, 16.67% failed extubation, airway obstruction 3.7%, 3.65% others). Of the 54 tracheostomies, 35 were done in ICU at the bedside of the patient. The average time delay was 2.51 days. During the transfer of the 19 patients to the operating room, there was no serious event. There were no cases of arrhythmia, premature extubation, false cannulation, pneumothorax, or perioperative death. Intraoperative complications were: hypotension 33.33, 14.81% hypoxia/desaturation, 5.55% intraoperative bleeding. The postoperative complications were bleeding in 22.22% of cases (in 2 cases requiring surgical revision), infection of the stoma in the first week in 12.96% (in 2 cases involved serious infection requiring surgical debridement and drainage plus iv antibiotic therapy) and difficulty in changing the tube in 3.7% of cases. There were no cases of pneumothorax or tracheostomy-related death.

CONCLUSIONS. Tracheostomy is a common technique in neurotrauma ICU and the first indication was the low level of consciousness of patients. The 64.81% of the tracheostomies were performed in the ICU. There were no serious or life threatening complications. The most frequent perioperative complication was hypotension associated with anesthesia. Postoperative hemorrhage (22.22%) and stomal infection (12.96%) are two common complications, although only rarely were severe (3.7%).

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S100 B PROTEIN: HOW IS IT ACCURACY TO DETECT BRAIN DAMAGE AFTER A HEAD TRAUMA?

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INTRODUCTION. The S-100B protein is a brain-specific protein release from astroglial cells into the circulation after Traumatic Brain Injury (TBI). Researches indicate that the S-100B serum level could be a useful indicator of TBI severity, however there is not evidence enough about the role of S-100B in nonsevere Head Trauma. The hypothesis that S-100B is a useful screening tool to detect brain injury in patients with a normal level of consciousness after a Head Trauma was tested.

METHODS. A total of 115 patients with the diagnosis of Mild TBI without decrease of consciousness (according to the GCS) with at least one neurological symptom or finding like amnesia, headache, dizziness, convulsion and vomits, were prospectively included. We recorded the clinical data on admission and a blood sample before 6 h after TBI, for S-100B inmunoluminescence analysis. A routine cranial computed tomography scan (CT) was obtained within 24 h after the injury (categorized in normal or pathological). The diagnostic properties of S-100B serum levels <0.105 μg/L, for prediction of intracranial lesions revealed by CT were tested with receiver operating characteristic (ROC) analysis.

RESULTS. Seventy of the patients (60.9%) were men, with a mean (SD) age of 49.07 (20.65) years (range, 14–92 years). A total of 11 patients (9.6%) had intracranial lesions. Serum S-100β levels were significantly higher in patients with intracranial lesions than in the remaining patients. The average value of the protein in patients without intracranial lesion was 0.315 μg/L with a CI 95% (0.265–0.365 μg/L), and in those with pathological findings in CT was 0.601 μg/L with a CI 95% (0.403–0.798 μg/L). Significant differences were found between levels of S100β protein and the presence of pathological findings in the CT ($p = 0.001$) (Fig. 1). The ROC curve analysis showed that S100β protein is a useful tool to discriminate the presence of intracranial injury in CT (AUC, 0.76, 95% CI, 0.685–0.907, $p < 0.001$). S100B analyses with a cut-off level of 0.105 μg/L showed a sensitivity 100% but a specificity 19.2%. We evaluated different cut off values and in our series, the best cut off of the S100β protein is at 0.253 μg/L with a sensitivity of 100% and specificity 58%. (Fig. 2)

CONCLUSION. Determination of serum protein S-100β is a useful biochemical indicator of brain damage in head trauma. Our results show that an increase in the cut-off point of S-100β to 0.253 μg/L increases its accuracy in the prediction of the existence of macroscopical lesions.

KEY WORDS. Protein S-100B, brain injury, minor head trauma, cranial computed tomography.

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ALTERED NERVE EXCITABILITY PROPERTIES IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Critically ill patients with systemic inflammatory response syndrome frequently suffer muscle weakness due to critical illness myopathy (CIM) and polyneuropathy (CIP). Several *in vitro* studies have shown that the cause of muscle weakness is a loss of membrane excitability accompanied by membrane depolarization [1].

OBJECTIVES. We investigated membrane polarization and excitability parameters in muscle and motor nerve *in vivo* within the first week after intensive care unit (ICU) admission.

METHODS. The study was approved by our local ethics committee. Patients with SOFA scores $\geq$8 on 3 consecutive days underwent nerve conduction studies including direct muscle stimulation to categorize patients as ICU-control, CIM- (dmCMAP <3 mV) and/or CIP-patients (reduced SNAP amplitude) within the first 8 days after ICU admission. To assess excitability parameters we recorded stimulus-response behaviour, threshold electrotonus, current-threshold relationship and recovery cycle from abductor pollicis brevis muscle following stimulation of the median nerve [3]. Data are shown as median and 25%/75% percentile.

RESULTS. 16 patients were enrolled and according to nerve conduction studies we found 6 CIM-patients, 5 CIM/CIP-patients and 5 ICU-controls. Compared to healthy controls (n = 29), ICU-control patients showed membrane depolarization [reduced superexcitability: ICU-controls −15.3% (−25.2/− 5.7); healthy controls −25.3% (−29.6/− 22.4); p = 0.025]. *CIM- and CIM/CIP-patients* showed a more pronounced membrane depolarization [reduced superexcitability: CIM/CIP: −6.5% (−21.3/− 2.2); healthy controls: −25.3% (−29.6/− 22.4); $p < 0.005$ and "fanning-in" appearance in hyperpolarizing threshold electrotonus assessment: TEh [90–100 ms]: CIM/CIP: −96.1% (−106.5/− 96); healthy controls: −118.2% (−128.7/− 108.3); $p < 0.05$] and reduced membrane excitability [reduced strength-duration time constant: CIM: 0.31 ms (0.21/9.33); CIM/CIP: 0.31 ms (0.27/0.39), healthy controls 0.53 ms (0.41/0.6); $p < 0.005$].

CONCLUSIONS. We describe for the first time that critically ill patients in general show muscle- and nerve membrane depolarization, whereas patients later suffering from muscle weakness due to CIM or CIM/CIP feature additionally reduced membrane excitability. This suggests that membrane depolarization in critically ill patients is caused by energy failure leading to dysfunction of the Na–K pump, the motor of membrane repolarisation—whereas reduced membrane excitability in CIM or CIM/CIP needs an additional dysfunction of voltage gated sodium channels for example occurring in the presence of endotoxins [2].

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RATIONAL ANTIBACTERIAL THERAPY OF PATIENTS WITH CENTRAL NERVOUS SYSTEM DISORDERS

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INTRODUCTION. In intensive care patients with central nervous system (CNS) disease, the systemic inflammatory response syndrome (SIRS) criteria are often unreliable as a basis for identifying the inflammatory process. Even with the presence of some infection they could be signs of the diencephalons-catabolic syndrome. Diencephalons-catabolic syndrome like SIRS constitutes of hyperthermia over 38°C, tachypnea of over 20 per minute, tachycardia, and arterial hypertension. Thus, SIRS symptoms may occur after antibacterial treatment even if there is no infection or inflammation. We suggest a more precise method which could help to avoid the excessive antibacterial therapy and to control it in patients with CNS disease—a procalcitonin test.

OBJECTIVES. Reduce the use of wide specter antibiotics makes the control over antibacterial therapy in patients with CNS diseases more precise; reduce the number of complications related to unnecessarily long antibacterial treatment.

METHODS. After obtaining the informed concern, in our investigation we included 30 patients with different neurological disorders, who had recently transferred neurosurgical operations. All of them demonstrated SIRS symptoms on different postoperative terms. When SIRS symptoms occurred, we checked the level of procalcitonin in the patient's serum by a semi quantitative method on a disposable BRAHMS PCT-Q system. The procalcitonin level was determined against a color scale. Procalcitonin level over 0.5 ng/ml (16 patients) considered a sign of infection and in such cases we prescribed antibacterial treatment 2,000 mg of Selenase for 5–7 days. If the test result was negative (14 patients) we repeated it in 24 h and in cases with the same results, no antibacterial treatment was administered even if there were SIRS symptoms. If PCT-Q test was negative patients were sedated (fentanyl 0.8–1.5 μg/kg/h and clonidine 0.2–0.5 μg/kg/h) to achieve autonomic stability and attenuate clinical manifestation of SIRS.

RESULTS. We had not observed any cases of sepsis in both groups of patients. By mince of PCT, we had managed to reduce the quantity of wide specter antibiotics, used in neurosurgical patients for 34.7%.

CONCLUSIONS. Procalcitonin test in neurosurgical clinic let us determine the necessity of antibacterial treatment reduce the use of wide specter antibiotics, medical costs and prevent the forming of polyresistant infection.

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INTENSIVE CARE UNIT ACQUIRED WEAKNESS

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INTRODUCTION. Intensive Care Unit-Acquired Weakness (ICUAW) is increasingly recognised as a common complication of critical illness with potentially prolonged debilitating sequelae. The estimated incidence is 46% in patients with sepsis, multi-organ failure or prolonged mechanical ventilation [1] and suggested risk factors include: the systemic inflammatory response syndrome (SIRS), sepsis, higher severity of illness, hyperglycaemia, renal replacement therapy and parenteral nutrition.

OBJECTIVES. The aims of this study were to determine the incidence, risk factors and outcomes for patients diagnosed with ICUAW in Glasgow Royal Infirmary's (GRI) ICU.

METHODS. The study was undertaken in two parts, firstly as a case-control study [matched for age (within 5 years), sex and admission APACHE II score (within 5 points)] and secondly by comparing identified cases of ICUAW to a 3-month cross-sectional sample (1/10/09–31/12/09, 112 patients) of GRI's ICU patients. Data for both parts of the study was obtained from two electronic databases, WardWatcher and CareVue. CareVue was searched to identify patients with ICUAW and WardWatcher was used to identify the controls. Data collected included: patient and illness characteristics, severity of illness scoring, organ support and treatments provided, laboratory results and outcomes. Minitab software was used for statistical analysis.

RESULTS. Fourteen patients with ICUAW were identified out of 1396 patients on CareVue giving an incidence of 1%. Patients with ICUAW had significantly longer median durations of SIRS, sepsis, septic shock and multi-organ failure than case-controls (15.5 vs. 4, 13 vs. 4, 7 vs. 0.5 and 9 vs. 3 days, all $p < 0.05$) and the cross-sectional sample of ICU patients (7 vs. 2, 7 vs. 0.5, 5.5 vs. 0 and 6 vs. 1 days, all $p < 0.01$). Patients with ICUAW received higher average daily corticosteroid dosages than both control groups (152.4 vs. 0 and 152.4 vs. 0 mg, both $p \leq 0.01$). There was no consistent statistically significant relationship with the diagnosis of ICUAW and average daily blood glucose levels, renal replacement therapy or parenteral nutrition. Patients with ICUAW had longer median durations of mechanical ventilation, and length of ICU and hospital stay compared to case-controls (26.5 vs. 4.5, 26.5 vs. 6 and 49.5 vs. 23.5 days, all $p < 0.05$) and the cross-sectional sample of ICU patients (24.5 vs. 2, 26 vs. 3 and 41 vs. 15 days, all $p < 0.01$).

CONCLUSIONS. The incidence of ICUAW was very low, we hypothesise this to be explained by the absence of systematic evaluation of patients for ICUAW. The risk factors and outcomes for ICUAW were consistent with some of the published literature. Prospective study is now planned to systematically evaluate this condition.

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SURVEY OF PERIPARTUM PATIENTS ADMITTED TO A TERTIARY NEUROCRITICAL CARE UNIT

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INTRODUCTION. With increasing age, comorbidity, and socioeconomic deprivation being associated with higher risk pregnancies, there comes a potential higher risk of complications. Neurological and neurosurgical complications, which can be particularly devastating during the peripartum period, include those due to medical conditions of pregnancy (hypertensive disease, sepsis, thromboembolic disease, hypoxic-ischaemic brain injury), iatrogenic complications secondary to anaesthetic or obstetric interventions, incidental illness or injury (pharmacological alterations, trauma, tumour), and deliberate self-harm and violence.

OBJECTIVES. To ascertain the frequency of neurocritical care admissions in the West of Scotland, the nature of the admission diagnoses, the impact they have on our service (length of stay), and maternal and foetal outcome.

METHODS. Using the Scottish Intensive Care Society Audit Group WardWatcher patient database, female patients aged 14–50 years old who were admitted to the neurocritical care unit were identified (January 2008–December 2009). We manually reviewed the electronic admission note for each of these women in order to gain diagnoses; a targeted case note analysis ensued.

RESULTS. Within the 24 month study period there were a total of 915 admissions to neurocritical care, of whom 164 fulfilled the age and gender criteria; 6 admissions (0.66% of total) were for neurological complications in the peripartum period.

The age range was 18 to 45 years (*median* 31 years). Three women (50%) were intrapartum (20–36 weeks gestation) at the time of their admission, and three were postpartum (1 day–7 months). Half of admissions were due to incidental illness or injury, a third to pregnancy-related medical complications, and one case was iatrogenic in nature.

PATIENT CHARACTERISTICS

Diagnosis	Maternal outcome	Foetal outcome
Septic abortion (twin pregnancy); meningoencephalitis	Death; heart-beating organ donor	Death (twin)
Cortical vein thrombosis	Survivor	Survivor
Antiepileptic drug dose reduction (self-instigated)	Survivor	Survivor
Neuraxial anaesthesia-associated epidural abscess	Survivor	Survivor
Traumatic brain injury (RTA)	Survivor; neurodeficits	Survivor
Intracranial neoplasm	Survivor	Survivor (emergency LSCS)

Length of stay in ICU was 1 to 12 days (*median* 4.3 days). One patient sustained a residual facial nerve weakness and deafness.

CONCLUSIONS. This survey provided insight into the incidence and nature of pregnancy-related pathology requiring acute referral to a regional neurosciences centre. As highlighted in other surveys, there may be many more peripartum patients with neurological complications who are cared for in general critical care units, and do not require admission to a tertiary referral centre [1]. Further work is underway to ascertain the true numbers of neurological complications of pregnancy countrywide. Our approach represents a paradigm for the continuing audit of pregnancy-related critical care resource use in Scotland.

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IS THE PLASMA DISAPPEARANCE RATE OF INDOCYANINE GREEN (PDR_{ICG}) PREDICTIVE FOR PROLONGED INTENSIVE CARE STAY IN MULTIPLE TRAUMA PATIENTS?

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INTRODUCTION. As multiple organ failure is a leading cause of late death after severe trauma, monitoring organ function is highly relevant. Liver dysfunction is of major concern as it contributes significantly to patient outcome, ICU and hospital length of stay (LOS). Detection of liver dysfunction may be problematic because standard liver function tests (LFT) have low sensitivity and specificity. The PDR_{ICG} is considered not only a dynamic and sensitive test of liver function and splanchnic perfusion but was also suggested as a prognostic factor in the critically ill. Its value for monitoring injured patients, however, is unclear. Until now only a few studies in small trauma patient groups used PDR_{ICG}. We present data from prospective sequential PDR_{ICG} measurements in multiple trauma patients (Injury Severity Score, ISS $\geq$18).

METHODS. After approval of the local ethics committee, the PDR_{ICG} was measured within 24 h post injury (day 0) using the non-invasive LiMON system (Pulsion Medical Systems, Munich, Germany; 0.25 mg/kg ICG-PULSION). The PDR_{ICG} was measured again on days 1, 2, 3, 5, 7 and then every 3rd day until ICU discharge. Sequential organ failure assessments (SOFA) and standard LFT were done with every PDR_{ICG} measurement. ICU LOS and mortality were recorded as study endpoints.

RESULTS. We studied 68 patients [median age 32 (18–91), ISS 34 (18–66)]. Six (2–13) PDR_{ICG} measurements were available per patient. During their ICU stay, 15 patients had bilirubin elevations $\geq$34 µmol/l (2 mg/dl) but this coincided with impaired PDR_{ICG} (<18%/min) in only 3 patients. Many patients showed an early increase of PDR_{ICG} to supranormal values (>25%/min). Higher SOFA scores were indirectly associated with lower PDR_{ICG} values, particularly for SOFA scores >8. When patients were grouped by ICU length of stay (<11, $\geq$11 days, corresponding to the mean ICU LOS of the German trauma registry), logistic regression analysis identified PDR_{ICG} on day 3 as predictor of a prolonged ICU LOS >11 days. In patients with prolonged ICU LOS, significantly fewer patients showed the initial increase in PDR_{ICG}.

CONCLUSIONS. When PDR_{ICG} is measured sequentially in multiple trauma patients, the lack of the early increase to supranormal PDR_{ICG} values may be an indicator of prolonged ICU stay. Use of the traditional normal range for single PDR_{ICG} measurements may lead to underestimation of an already significantly decreased individual PDR_{ICG} in trauma patients. The usefulness of sequential PDR_{ICG} measurements for assessment of liver dysfunction and outcome prediction warrants further investigation.

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APOLIPOPROTEIN E AS A PROGNOSTIC MARKER OF BRAIN DAMAGE

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INTRODUCTION. Apolipoprotein E (APOE) is a multifunctional protein. Previous preliminary studies have suggested that polymorphism of the APOE may influence outcome after traumatic brain injury and intracranial hemorrhage, with the 4 allele being associated with poorer prognosis.

OBJECTIVES. To determine whether the presence of the 4 allele of apolipoprotein E as homozygous or heterozygous influences the prognosis of patients with acute brain damage

METHODS. We included a total of 72 patients consecutively admitted to the ICU for severe head trauma (45 cases) or intracranial hemorrhage (27 cases). APOE genotype was determined in all patients. The patient data collected on admission to the ICU were gender, age, Glasgow Coma Scale (CGS) and APACHE II score. Final outcome was assessed 6 months post admission using the Glasgow outcome scale. To determine the normal distribution of quantitative variables, we used the Kolmogorov-Smirnov test. Categorical variables were compared using Fisher exact test or Chi-square test. We used the U Mann–Whitney test or the t student test to compare quantitative variables. A p value <0.05 was considered as statistical significant.

RESULTS. The polymorphism E 4/4 was present in 9 patients (12.5%). 27 patients (37.5%) had a single allele 4 (E 2/4 or E 3/4). During the stay in the ICU, 28 patients (38.9%) were diagnosed as brain stem death. At 6 months mortality was 43.1% (31 patients) and 25 patients (36%) had good clinical recovery. Patients with single or double presence for the ApoE 4 allele showed no significant difference in mortality ($p = 0.31$) and functional status ($p = 0.45$) compared with patients who had no 4 allele. Similarly patients homozygous for the allele 4 (E 4/4) did not have higher mortality ($p = 0.35$) or worse functional outcome ($p = 0.59$) compared to other patients.

CONCLUSIONS. The 4 allele of apolipoprotein E is not associated with increased mortality or worse functional outcome in our patients.

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TIME IS BRAIN

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INTRODUCTION. Immediate reversal of warfarin with Prothrombin Complex Concentrate (PCC) and vitamin K is recommended in patients with intracranial haemorrhage [1].

OBJECTIVES. To determine whether a delay exists between the time of diagnosis of intracranial haemorrhage and the time of reversal of anticoagulation, in patients presenting within our region.

METHODS. Following approval by all audit and haematology departments a 6 month retrospective analysis was performed. We reviewed consecutive patients who received reversal of anticoagulation with PCC and Vitamin K having presenting with intracranial haemorrhage whilst on warfarin. Time of diagnosis was obtained from the time of scan and time of PCC issue was obtained from the blood bank database. Case note analysis was performed to obtain further information.

RESULTS. 47 patients were identified, 12 in the Neurosurgical centre and 35 in peripheral hospitals. The median time from scan to issue of PCC was 84 min. 14 patients were reversed within 60 min and 14 patients waited longer than 120 min to have PCC issued. No adverse thromboembolic events were encountered.

CONCLUSIONS. Avoidable delay exists between ICH diagnosis and PCC issue. PCC could be stored in the emergency department and a stat dose administered immediately after diagnosis facilitating rapid correction of INR. Repeat audit will be required to assess safety and efficacy.

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CRITICAL ILLNESS POLYNEUROMYOPATHY AFFECTS THE FUNCTIONAL ABILITY AFTER ICU DISCHARGE

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INTRODUCTION. The functional ability and muscle strength of patients in relation to the presence of critical illness polyneuromyopathy after their discharge from the ICU has not been extensively studied.

OBJECTIVES. The aim of this study was to compare the functional ability and muscle strength between these two groups of patients.

METHODS. Twenty-nine patients were evaluated (M:24, F:5) (age: 55 $\pm$ 17 years).The diagnosis of critical illness polyneuromyopathy was based on muscle strength measurement according to the Medical Research Council (MRC) of muscle strength methodology. Nine patients were diagnosed with critical illness polyneuromyopathy during their ICU stay (MRC <48/60).The patients were evaluated with MRC and Hand-Grip dynamometry (HGD) every 10 days until their discharge from the hospital. The FIM scale (Functional Independence Measure) was used to evaluate the functional ability (18–126).The first evaluation was done at the discharge from the hospital and the second one 8 $\pm$ 1 months afterwards.

RESULTS. The patients who developed critical illness polyneuromyopathy had statistically significantly lower MRC (39 $\pm$ 12 vs. 57 $\pm$ 2, $p < 0.001$) and HGD at ICU discharge (left 8 $\pm$ 5 kg vs. 23 $\pm$ 8, and right 9 $\pm$ 7 kg vs. 27 $\pm$ 9, $p < 0.001$) compared to those who did not. The muscle strength as assessed with the MRC 10 days after ICU discharge had statistically significantly lower (40 $\pm$ 11 vs. 56 $\pm$ 3, $p < 0.001$), just as the second HGD evaluation (left 11 $\pm$ 7 kg vs. 25 $\pm$ 8 and right 9 $\pm$ 7 vs. 21 $\pm$ 8 kg, $p < 0.05$).Compared to those who did not develop critical illness polyneuromyopathy, the patients who did, had statistically lower FIM values during their discharge from the hospital (49 $\pm$ 26 vs. 77 $\pm$ 30, $p < 0.05$)and 8 months afterwards (90 $\pm$ 27 vs 125 $\pm$ 1, $p < 0.05$).

CONCLUSIONS. The patients who developed critical illness polyneuromyopathy had significantly inferior muscle strength at their discharge from the ICU. These patients also had lower functional ability. This functional ability remained defected even 8 months after their discharge from the hospital. These initial findings are suggestive that the appearance of critical illness polyneuromyopathy affects the patients mobility after their discharge either from the ICU or from the hospital and persists for several months after ICU discharge. Further studies are needed to evaluate the effect of this impairment on the quality of life of these patients and also to evaluate therapeutic tools for critical illness polyneuromyopathy.

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COMPARISON OF THE EFFECTS OF MANNITOL OR HYPERTONIC SALINE SOLUTIONS ON INTRACRANIAL PRESSURE AND ELECTROENCEPHALOGRAPHY IN EXPERIMENTAL HEAD TRAUMA MODEL

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INTRODUCTION. Hypertonic saline has an osmotic effect on the brain because of its high tonicity and ability to effectively remain outside the blood-brain barrier. There may be a minimal benefit in restoring cerebral blood flow, which is thought to be mitigated through local effects of hypertonic saline on cerebral microvasculature. Most comparisons with mannitol suggest almost equal efficacy in reducing ICP but not compared their effects on EEG.

OBJECTIVES. We aimed to compare the effects of 20% mannitol, 3% or 7% hypertonic saline on hemodynamic parameters, intracranial pressure and electroencephalography in experimental head trauma.

METHODS. Bilateral craniotomy were carried out in the parietal region and head trauma was applied for all rabbits. The rabbits were randomly divided into four groups. In group I rabbits were only observed. In group II: 20% mannitol, in group III: 3% hypertonic saline and in group IV: 7% hypertonic saline was administered intravenously to achieve similar osmolar load. Electroencephalography, mean arterial pressure, heart rate, intracranial pressure were recorded before trauma and 5 and 60 min after trauma.

RESULTS. Increased intracranial pressure was significantly decreased by mannitol, 3 and 7% hypertonic saline solutions at the end of study ($p < 0.05$). But intracranial pressure values of mannitol and 7% hypertonic saline groups were lower than the other groups ($p < 0.05$). The electroencephalography scores decreased after trauma in all groups ($p < 0.05$). At end of the study, 3 and 7% hypertonic saline groups had similar electroencephalography scores with pretrauma scores ($p > 0.05$). The mean arterial pressure and heart rates increased after trauma in all groups ($p < 0.05$). Mean arterial pressure values were found lower only in mannitol group at end of the study ($p < 0.05$).

CONCLUSIONS. Our study showed that when used in intracranial hypertension treatment, 7% hypertonic saline solution is as effective as mannitol, and preserves hemodynamic parameters, and normalizes traumatic electroencephalography abnormalities better than mannitol.

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NEUROLOGICAL COMPLICATIONS OF HIV INFECTION IN CRITICALLY ILL PATIENTS: CLINICAL FEATURES, ETIOLOGY AND EARLY PREDICTORS OF OUTCOME

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INTRODUCTION. Neurological failure in HIV-infected patients has not been studied in the era of highly-active antiretroviral therapy (HAART).

OBJECTIVES. To describe neurological signs or symptoms and to identify early predictors of outcome among adult HIV-infected patients admitted to the ICU for neurological complications at the HAART era.

METHODS. We performed a retrospective study of 445 consecutive HIV-patients admitted to the medical ICU of a university hospital in Paris from January 2001 through August 2008.

RESULTS. 210 (47%) HIV-patients had evidence of neurological failure on ICU admission. Neurological findings ($n = 286$) were: delirium ($n = 94$), coma ($n = 81$), seizures ($n = 68$), intracranial hypertension ($n = 43$). Median CD4 count was 80 cells/μL [18–254]. Neurological failure revealed HIV infection in 40 (19%) patients. ICU-admission diagnoses were distributed into 3 groups: AIDS-associated CNS disease (G1): 88 (42%) patients, non-AIDS-associated CNS disease (G2): 45 (21%) patients, and general disease with neurological signs (G3): 77 (37%) patients. The leading cause of neurological failure was *Toxoplasma gondii* encephalitis ($n = 47$). Overall ICU-mortality was 30% and was not different between the 3 groups [G1: 22 (25%) patients, G2: 14 (31%) patients and G3: 26 (34%) patients, $P = .45$]. None of the HIV-related parameters (CD4 cell count, HIV viral load) were predictive of outcome. Multivariate analysis retained three factors present within 48 h of ICU admission and independently associated with in-ICU mortality: intracranial hypertension (odds ratio [OR], 5.09; 95% confidence interval [CI], 2.17–11.91; $P = .0002$), SAPS 2 score (OR, 1.59; 95% CI, 1.31–1.93; $P < .0001$) and use of vasopressors (OR, 3.92; 95% CI, 1.78–8.60; $P = .0007$).

CONCLUSIONS. Predictors of outcome in HIV-infected patients with neurological failure are identifiable at admission and depend rather on clinical presentation than on HIV-related parameters. Intracranial hypertension is a clinically relevant sign associated with an increased risk of death in the ICU.

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EVALUATION OF THE NEW ONSET SEIZURES IN THE ICU PATIENTS

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INTRODUCTION. Seizures in critically ill patients are often provoked by some underlying acute disease process metabolic, infective or vascular and are called as acute symptomatic seizures. Such seizures are often provoked situation related seizures and occur in patients who don't have epilepsy.

OBJECTIVES. To identify the causes of new onset seizures in patient admitted in medical ICU.

METHODS. All the patient admitted in ICU and who had new onset seizures were evaluated. The patients were evaluated for metabolic profile. Imaging (CT/MRI) was done whenever needed. Patients with preexisting seizure history were excluded from study.

RESULTS. 44 (29 males, 15 females) patients, who had first seizure during hospitalization in ICU were included. 43 patients had generalised and one had focal seizures. 28 patients had metabolic abnormalities. 13 (46.42%) had evidence of hepatic encephalopathy. 3 (11.36%) had only hepatic encephalopathy while rest had associated uremia, hyponatraemia, hypophosphatemia and hypomagnesemia. Out of 10 patients, who had renal failure, 4 had evidence of uremia while rest had associated hyponatraemia or hypophosphatemia. Only one patient had evidence of hypocalcemia. Imaging was done in 16 patients. 14 (30%) had abnormal CT scan results. 4 (9.09%) had intracranial hemorrhage, 4 (9.09%) had infarct, 2 (4.55%) had brain metastasis, 2 had evidence of hydrocephalus and one each had evidence of extradural hemorrhage and tuberculoma. CSF analysis was done in 7 (15.9%) patients. 3 (6.8%) had evidence of tuberculosis and 1 (2.27%) had evidence of pyogenic infection.

CONCLUSIONS. Though metabolic causes are important causes of new onset seizures in critically ill patients, imaging studies should be done in ICU patients for evaluation of first seizure.

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THE CLINICAL PROFILE OF NEW ONSET SEIZURES IN EMERGENCY SETTING

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INTRODUCTION. Seizures are common presenting problem to emergency department. The etiology of first time seizures presenting to emergency department is a vexing problem and requires full clinical assessment. The etiological profile of seizures differ between patients presenting to emergency department and patients presenting to outpatient setting.

OBJECTIVES. To evaluate the clinical and etiological profile of patients presenting to emergency department with new onset seizures.

To study the role of various investigations and CT in evaluating these patients.

METHODS. All patients admitted with new onset seizures within 72 h prior to presentation were included. All the patients were questioned and an attempt was made to assign an electroclinical syndrome to seizure. Patients were evaluated for metabolic profile, neuroimaging. CSF examination was done in those who had persistently altered mental status, infectious symptoms and fever.

RESULTS. 110 patients were admitted (1.03% of total patients who came to emergency) with history of new onset seizures. 71.8% patients were diagnosed to have acute symptomatic seizures and were placed in ILAE category 4.13 and three patients were placed in ILAE category of remote symptomatic seizures. The cause of seizures was established in 82 (74.5%) patients and remained unestablished in 28 (25.5%) patients. 14 (12.7%) patients were diagnosed to have neurocysticercosis. Other important causes were acute infarct, uremia, hyponatremia, hypernatremia, viral encephalitis, post partum eclampsia, pyogenic and tubercular meningitis. Alcohol withdrawal seizures were seen in 3.6% patients. Metabolic derangements were seen in 19 (17.3%) patients. Computed tomography was done in 88 patients and 50% had abnormal findings. MRI was done in 13 patients and 12 had abnormalities.

CONCLUSIONS. Neurocysticercosis was found to be most common cause of seizure activity in our part of country. Though Metabolic derangement can cause significant proportion of new onset seizure patients routine imaging of brain should be performed in patients with new onset seizures.

Work environment and organisational issues: 1335–1347

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SUBJECTIVE AND OBJECTIVE RESEARCH INTO THE WORKING CONDITIONS AND THEIR EFFECT ON THE HEALTH AND SAFETY OF PEOPLE WORKING IN ICU, FOCUSING MAINLY ON THE NATURAL FACTORS OF TEMPERATURE, HUMIDITY, VENTILATION, LIGHTING AND NOISE (PART 1)

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The aim of the project is the subjective and objective investigation of the conditions of work and the relation repercussions on the health and safety of people working in the ICU, focusing mainly on the natural factors that are likely to cause the Sick Building Syndrome. For this purpose a protocol of research in two phases has been planned. The first included objective measurements, with the use of suitable equipment, of the natural factors of temperature, humidity, ventilation, lighting and noise. The second phase included the subjective estimation of the working people about their own health and conditions of their work, in the particular area of the Hospital with the use of substantiated anonymous questionnaire. After the subjective and objective study and analysis of 32 questionnaires and 55 measurements of natural factors, we found that the medium temperature of the ICU was 24°C. The mean relative humidity of the ICU was 38% (highest 38.3% and lowest 37.8%). The mean ventilation rate of the ICU was 17 m^3/h (highest 28.8 and lowest <7.2 m^3/h). The mean sound pressure was 64.8 dB (highest 75 and lowest 63.5 dB). The average lighting was 331.5 Lux (160 Lux lowest and 598 Lux highest). The objective data seem to keep pace with the subjective opinions of the working people, as they were impressed in the questionnaires of subjective estimate. The objective data were compared with the subjective. The results of the research were also compared with data from the existing bibliography and current legislation, leading to a line of conclusions. (1) Insufficient and bad quality ventilation. (2) The existing temperature of the environment contributes to the appearance of Sick Building Syndrome. (3) The working environment is noisy. (4) The environment of work has problematic or insufficient lighting. (5) The ICU under study is a building area which can be characterized as "sick" if immediate action is not taken.

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SILENT MISERY: MOST SEVERE CRITICAL INCIDENTS, AS PERCEIVED BY INTENSIVE CARE NURSES

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BACKGROUND. Up to 75% of critical care nurses test positive for (symptoms of) Post Traumatic Stress Disorder (PTSD) [1, 2, 3]. It is assumed that these symptoms are caused by professional involvement in life-threatening events [3]. In a sample of intensive care nurses, we investigated which work related incidents were perceived as most distressing.

METHOD. In interviews, 12 nurses (75% female) were asked to memorize and tell about their most traumatic work related event. All interviews were recorded. After verbatim transcription, the 'most critical events' were extracted and categorized bij two independent psychologists.

RESULTS.

TABLE 1

Most severe critical events	Mentioned by N nurses
Incidents, perceived as regular in nursing, but happening under unusual circumstances (e.g. very intense family grief when a patients dies, or identification of a nurse with a family member)	6
A serious mistake made by a health care provider	2
Incidents caused by miscommunication	2
Upsetting incidents (e.g. verbal abuse)	2

None of the nurses reported major life-threatening events such as trauma-related injuries, massive bleeding or seeing patients die as their 'most critical incident'.

CONCLUSION. Not the major life-threatening events but relatively 'normal work related events' under unusual circumstances are mentioned as most critical by nurses. In contrast to major life-threatening events, these 'normal events' are usually underestimated by colleagues, and thus potentially compromise peer-support.

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A SYSTEMS THINKING ANALYSIS OF THE FACTORS WHICH AFFECT THE CARE OF ACUTELY UNWELL WARD PATIENTS IN NEW ZEALAND

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INTRODUCTION. This poster presents a qualitative system dynamics (SD) analysis of the factors which influence the care of acutely unwell ward patients in New Zealand. This systems thinking approach is commonly used in organisational research and offers a way to make sense of complex relationships between variables. This approach has previously been used in health care to demonstrate differences in mental models between policy makers and clinicians (Cavana et al., 1999). Since the factors which influence the care of acutely unwell ward patients are complex and multi faceted the qualitative SD method becomes an ideal analytic approach (e.g. see Wolstenholme and Coyle, 1983; Senge, 1990; Vennix, 1996; or Maani and Cavana, 2007).

OBJECTIVES. The aim of this study was to examine the factors which influence the care of acutely unwell ward patients from an organisational perspective. Key objectives were to determine the enablers and barriers to care from a nursing, medical and managerial (at ward and executive level) perspective.

METHODS. Using a multiple case study approach in four wards in two New Zealand hospitals, focus groups and one to one interviews were conducted with key stakeholders identified as nurses, doctors and managers. Initial coding of the data generated themes. These themes were then clustered to provide variables which were mapped to generate separate causal loop diagrams (CLDs) for each of the stakeholder groups to provide the basis for analysis. The CLDs were compared for characteristics and world views.

RESULTS. Preliminary results demonstrate a difference between clinical and managerial staff in characteristics and world view regarding the factors which affect the care of acutely unwell ward patients.

CONCLUSIONS. The qualitative SD approach has offered a novel and helpful way to make some sense of the complexity associated with caring for acutely unwell ward patients. Organizational responses that may improve care delivery to these patients should be based on frank and open discussions between staff at all levels to ensure a shared mental model as the basis for change.

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IS THERE A NEED FOR "A CARE BUNDLE" TO SUPPORT ORGANIZATIONAL DECISION-MAKING? CHARGE NURSES AND INTENSIVISTS MANAGING DAILY ACTIVITIES OF ICUS

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INTRODUCTION. A Care Bundle refers to evidence based interventions and information grouped together to improve outcomes and consistency of provided care [1, 2]. At the ICUs charge nurses and intensivists as shift leaders are responsible for daily management of unit activities. Several immediately made decisions by shift leaders are made under time pressure and high information load with inadequate information. Though we have evidence of structure and process based factors such as material and human resources, admission and discharge decisions or bed utilization, the support for information transfer and integration is poor in organizational decision-making concerning these factors.

OBJECTIVES. To identify immediate information needs of charge nurses and intensivists during the management of daily activities at the ICU and evaluate how necessary this information is for their decision-making.

METHODS. From September 2009 to November 2009, all charge nurses (n = 515) and intensivists (n = 223) of 17 university affiliated ICUs providing comprehensive care in Finland were surveyed with an on-line questionnaire using 122 statements. The questionnaire was developed based on our previous observation study and statements of our survey regarded information needs related to the ICU care activities. A rating scale from 0 to 10 (completely unnecessary-absolutely necessary) was used to assess the necessity of the information. For each statement, a response with mean 7 or over was regarded as necessary information for immediate decisions.

RESULTS. The response rate was 47.97% (charge nurses 50.1%, intensivists 43.1%). The working experience varied from 0 to 35 years (Mean 13.6, SD 7.9). Over 50% of respondents worked as a shift leader once a week or more often. 72 statements of 122 were valued as a necessary (Mean >7 or more) for immediate decision-making. Absolutely necessary information (Mean >9 or more) for immediate decision-making were assessed related to the 11 statements. These statements concerned isolations, mechanical ventilation, admissions and discharges, special treatments, patient's condition, and scheduled dates or times for surgery or other procedures.

CONCLUSIONS. Both ICU charge nurses and intensivists identified several information needs that are crucial for immediate decision-making during the whole ICU care process. Information needs of the shift leaders differed and they were strongly connected to the needs of one's professional requirements. An integrated overview and summarization of immediately needed information—a Care Bundle for organizational decision-making—at the ICUs is highly needed for ICU shift leaders. The common interests of both professionals, charge nurses and intensivists, should be emphasized when new technology-based systems are developed.

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MORAL DISTRESS AND STRUCTURAL EMPOWERMENT AMONG A NATIONAL SAMPLE OF ISRAELI ICU NURSES

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INTRODUCTION. Moral distress (MD) has been defined as knowing the "right" thing to do but not being able to do it due to institutional constraints. High levels of MD have been found among ICU caregivers. MD has been associated with increased job dissatisfaction, burnout and worker turnover. Another work-related characteristic that might be associated with MD is structural empowerment (SE) or worker perception of access to 4 sources of power in an organization (opportunity, information, support and resources). This association has been implied by others but has not been investigated.

OBJECTIVES. The objectives of this study were to determine the levels of MD and SE, and their association among a national sample of Israeli ICU nurses.

METHODS. A convenience sample of 291 ICU nurses were asked to complete 3 questionnaires: a demographic and work characteristics questionnaire, the Moral Distress Scale and the Conditions of Work Effectiveness Questionnaire-II (to measure SE).

RESULTS. The mean age of participants was 38.2 ± 9.2 years with a mean 9.6 ± years working in an ICU. Levels of MD and SE were similar to those reported in the literature, with MD frequency higher than intensity. Significant correlations were found between the frequency of moral distress and support ($r = -.18$, $p = .02$) and total SE ($r = -.17$, $p = .03$). Formal power was associated with age and seniority. Significant positive correlations were found between the elements of SE ($r = .17$–$.49$). MD frequency was not significantly correlated with MD intensity. Seniority in the ICU was associated with MD intensity ($r = .17$). MD was not found to be associated with total SE.

CONCLUSIONS. Certain aspects of SE are associated with the frequency of MD while age and seniority are more associated with MD intensity in this sample of ICU nurses. These results have implications for clinicians and administrators in terms of reducing the incidence and severity of MD associated with intensive care nursing.

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ASSOCIATION BETWEEN SEVERITY OF ILLNESS, NURSING WORKLOAD AND INFECTION IN CRITICAL PATIENTS

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INTRODUCTION. Patients admitted to the ICU have a higher risk of nosocomial infection than other hospitalized patients. Several risk factors have been identified, including severity of illness, comorbidities, invasive devices and nursing staff. Critically ill and infected patients may require high-intensity care, increasing nursing workload and decreasing time for infection control precautions.

OBJECTIVES. To verify association between severity of illness, infection and nursing workload in critical patients.

METHODS. Descriptive correlational study was carried out in three ICUs in a tertiary care, teaching public hospital, in São Paulo, Brazil, from October 2007 to April 2008. One of the ICUs was general unit (14 beds) but with a large proportion of surgical patients, clinical ICU (5 beds) and Respiratory ICU (6 beds). Demographic, clinical and patient hospitalization data were collected and applied Simplified Acute Physiology Score II (SAPS II) at admission. The nursing workload was evaluated daily using the Nursing Activities Score (NAS). All patients were followed from admission to discharge from the ICU. The data related to infection were obtained from hospital's Infection Control Committee. The associations between NAS, SAPS and variables were analyzed using chi-square tests. Linear regression was applied to verify the correlation between SAPS II and NAS.

RESULTS. 190 patients, with mean age 56.4 (± 19.3), were included in this study. Most are female (52.1%). At admission, most were surgical patients, i.e. 88 (46.3%), 42 (22.1%) had respiratory diseases and 22 (11.6%) had neurological injuries. The average length of stay in ICUs was 14.9 days and 76 (40.0%) died in ICU. The average SAPS was 41.4 points (± 16. 0) and NAS was 62.9% (± 12.3). From the total, 58 (30.5%) acquired nosocomial infection. Most frequent infection was ventilator associated pneumonia (38/65.5%). Infection was associated with high SAPS II scores ($p = 0.0349$) and showed tendency with high NAS scores ($p = 0.0587$). Severity of illness was correlated with nursing workload ($r^2 = 0.20$).

CONCLUSIONS. Severity of illness associated with infection, but high nursing workload showed only tendency with infection. Correlation between nursing workload and severity of illness was weak.

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THE SELF-PERCEIVED HEALTH BETWEEN MEDICAL-SURGICAL AND CRITICAL CARE NURSES IN HUNGARY (2003–2008)

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BACKGROUND. The health status of nursing personnel working in acute wards has an important impact on the quality of patient care. In the past years the number of acute beds has been reduced and some departments closed in Hungary. The aim of present study is to survey the self-perceived health of acute care nurses (medical-surgical and critical care) and describe the trends in their self-perceived status.

METHODS. A longitudinal study design was used to explore the self perceived health of in-hospital nurses in acute care settings (surgery, casualty, internal medicine, intensive, coronary care, emergency room) in two Hungarian hospitals in 2003 and 2008. Inclusion criteria were working in the given setting more then 2 years as a bed-side staff nurse and not being involved in managerial tasks. The data analysis was done with Chi-square, T test and ANOVA method using SPSS 14.0 ($p < 0.05$).

RESULTS. In 2003 97 nurses and in 2008 104 nurses responded the self-fill in questionnaire, making a response rate of about 80% without significant difference. The average age was 37 years. About one third of the nurses (74 persons) worked in critical care units and the rest in other acute words (127 persons). Paying attention to average scores physical load of nurses (0.7 vs. 0.5; $p = 0.004$), lack of financial appreciation (0.5 vs. 0.5; $p = 0.05$), lack of moral appreciation (0.9 vs. 0.5; $p = 0.005$) and lack of medical tools (1.2 vs. 1.1; $p = 0.012$) increased among both critical care and medical-surgical nurses between 2003 and 2008 what made a significant impact on their health status. The growing expectation against nurses work also increased in the past years (0.6; 0.4) without significant consequences in nurses' self-perceived health. The working climate decreased in both settings (0.3 vs. 0.6 $p = 0.76$) making no direct impact on nurses health status. Although the self-perceived health of nurses in different settings has increased by the scores slightly no significant change is detectable. It is more the same during the examined period at an average level.

DISCUSSION. The critical care nurses and medical-surgical nurses face more demand in the daily care and the working climate is also worsened. The self-perceived health of nurses are influenced by salient environmental factors (eg. medical tools, physical load, moral support) which can be and should be treated by managers.

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THE RELATIONSHIP BETWEEN PERCEIVED STRUCTURAL EMPOWERMENT AND PERCEPTIONS OF NURSE-PHYSICIAN COLLABORATION AMONG INTENSIVE CARE UNIT AND GENERAL WARD NURSES IN ISRAEL

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BACKGROUND. The nursing shortage is an international problem that is expected to worsen in the coming years. Studies show that one of the main reasons nurses leave the profession is their dissatisfaction with their work environment. Structural empowerment and nurse-physician collaboration are two elements of the nurses' work environment that are potentially related to one another according to Kanter's theory (1977). In addition, a nurse's clinical specialization has been found to influence perceptions related to these two concepts.

OBJECTIVE. To examine the level of perceived structural empowerment, the perceptions of nurse-physician collaboration and the relationship between these two variables, among Intensive Care Unit (ICU) nurses and general ward nurses in Israel, and to compare the groups.

METHOD. A descriptive, correlational, comparative study design was used on a sample of 84 ICU nurses and 88 nurses from Internal Medicine and General Surgery wards in a large university hospital in Israel (response rate 79%). A three section, self administered questionnaire was used to measure the study variables: the Condition of Work Effectiveness Scale-II (CWEQ-II), the Collaboration with Medical Staff Scale (CMSS) and demographic-professional background.

Results: Perceived structural empowerment was found to be moderate ($M = 19.41$, $SD = 3.66$, range = 6–30). Nurses tended to agree that there was nurse-physician collaboration ($M = 2.69$, $SD = 0.55$, range = 1–4, 1 = strongly disagree, 4 = strongly agree). A correlation was found between structural empowerment and the nurse-physician collaboration ($r = .52$, $p < 0.01$). A significant difference was found between ICU nurses and general ward nurses on their perceptions of nurse-physician collaboration ($t_{(170)} = -3.39$, $p < 0.01$; General wards: $M = 2.83$, ICU: $M = 2.55$). No significant differences were found between nurse specialization on perceived level of structural empowerment.

CONCLUSION. Nurses in this study tended to agree that there was nurse-physician collaboration on their unit/ward. Nurses who perceived themselves as having a higher level of structural empowerment, felt that there was a higher level of nurse-physician collaboration. General ward nurses had more positive perceptions about nurse-physician collaboration on their ward as compared to ICU nurses. No difference was found between the two groups on the level of structural empowerment.

RECOMMENDATION. The findings of this study can be used as the basis for the design of interventions, aimed at enhancing structural empowerment and nurse-physician collaboration, in order to improve nurses' work environment, as one of strategy to decrease the nursing shortage. Further study of additional hospitals in the country is also recommended.

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A COMPARATIVE STUDY OF CRITICAL CARE OUTREACH (CCO) REFERRALS AND INTERVENTIONS

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INTRODUCTION. CCO services are widely used within delivery of acutely ill patient care. Teams have expanded and in some hospitals 24 h cover has been instituted. Researchers are questioning the validity of Outreach services and its impact on patient outcomes. As CCO has been viewed as the panacea to all problems, data collection and analysis is fundamental in proving its financial and clinical benefits.

OBJECTIVES. This comparative study aims to evaluate retrospective data from 1 month in 2006 and 1 month in 2010. Data does not encapsulate patient outcomes; it will compare frequency of referrals and interventions. This data provides an indication to the extent CCO has participated in the care of the acutely ill over a given time period.

METHODS. Data was collected from the 4D Medicus database collating intervention data. Analysis occurred using 13 key interventions using Excel software

RESULTS. In April 2006 there were 98 referrals to CCO rising to 148 in March 2010. Fluid management increased from 30 interventions to 97. Increasing referral to the patient team and Critical Care rose at least threefold thus indicating an improvement in collaborative working practices. Patient investigations such as blood tests, arterial blood gases have quadrupled in the 4 year difference. Administration of inotropes in inappropriate environments has decreased. DNAR orders have risen dramatically resulting in a decrease of inappropriate cardiac arrest calls.

CONCLUSIONS. Whilst the validity of services has been questioned, the data itself indicates that more patients are referred and frequency of interventions has increased. Various system changes occurred during this time period such as a change of Mews trigger scores, the advent of 24 h CCO and courses such as ALERT and Survive Sepsis were introduced into the basic training of staff. It must be noted that the intention in the UK for CCO was a service that empowered staff through education to undertake this care themselves; therefore the increase in interventions could indicate that the educational approach hasn't made progress. Although the study compares 13 interventions, an increase in the type of interventions was also noted such as ward based CCO supervised CPAP and establishing a PICC line service. Therefore this highlights the changing application of interventions. Further analysis is required to look at the appropriate skills required for the delivery of safe care to the acutely ill in the ward environment. Whilst ward staff are increasingly under resourced, both in skills and manpower, CCO do provide the skills, knowledge and time to meet the shortfall in safe timely care.

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THE GROWING ROLE OF NURSES IN CRITICAL CARE: EXPERIMENTAL RESEARCH

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INTRODUCTION. Working as a critical care nurse involves situations where teamwork is essential and rapid, effective communication is of importance [1]. The education to become a specialist ICU nurse gives skills and knowledge to manage patients who are critically ill with rapidly changing conditions [2]. Experimental research is one way of contributing to the acquisition of such knowledge.

AIM. To describe how ICU nurses may contribute and perform in the experimental research process, an environment usually unfamiliar to them. We describe our experiences with regard to clinical contribution and our subjective evaluation of involvement in animal experimental research.

METHOD. Three ICU nurses in a Swedish hospital were asked to participate in a research project investigating myocardial metabolism in porcine models of shock. The tasks were anaesthesia and pain management, assisting with catheter insertion and haemodynamic monitoring the pigs during the process

RESULTS. Although the situation was new, the nursing role and function in the team were at once similar and different to the daily work situation in the ICU. One major skill learnt was the rigour of experimental measurements and sources of error, which is sometimes neglected in clinical care. Being able to observe changes due to shock in a controlled setting, we improved our ability to critically 'think ahead' in anticipation of clinical deterioration [3]. Our first-hand experiences at the animal experimental laboratory allayed many anxieties and misconceptions with this type of research.

CONCLUSIONS. The critical care environment demands skills such as the ability to accurately define and change priorities rapidly, good communication and teamwork [4]. We believe that the experimental research setting is one way of enhancing this ability.

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NURSING IN TECHNOLOGICALLY-ADVANCED ENVIRONMENT: A TURKISH PERSPECTIVE

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INTRODUCTION. It is well known that nurses who work in a technologically-advanced environments enables technology to be long-lasting. They also have power to develop new technologies that supports patient care. One of such environments are the intensive care units. Nurses carry out a care in a technology-rich environment in intensive care units. In such environments, the duties and responsibilities of the nurses are more comprehensive. Although the technology in intensive care units are discussed earlier, there is little known about what technology means for nurses in such environments.

OBJECTIVES. The aim of the study is to explain the nursing in the technologically-advanced intensive care units.

METHODS. In this phenomenologically-designed study, a face-to-face in-depth interview was performed with 20 nurses, who were experienced for 1–22 years in the intensive care unit of cardiovascular surgery clinics. During the interviews, a semi-structured form was used. Data were analysed using Colaizzi's method of data analysis. The study was approved by the Ethics Committee of the institution.

RESULTS. According to the nurses, nursing in technologically-advanced environment has three stages. These stages constituted three themes of the study: technology shock (first stage), understanding the technology-supported care (second stage), competency in technological environment (last stage). In the first stage, the nurses focus on themselves and technology; perceive the environment as frightening and complex. In the second stage, nurses gain control on technology, feel themselves safe and recognize their responsibility. In the last stage, the nurses experience anxiety related to their accountability. This anxiety may be motivating but also may be wearisome.

CONCLUSIONS. The nurses passes through three stages in a technologically-advanced environment. Helping nurses to pass through these three stages appropriately will increase the contribution of technology to the patient care, more utilization of technology by nurses and more job satisfaction.

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USE OF NURSING ACTIVITY SCORING (NAS) AND THERAPEUTIC INTERVENTION SCORING SYSTEM (TISS) DIFFERENTIATES BETWEEN INTENSIVE CARE AND MEDIUM CARE LEVEL

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INTRODUCTION. Classification of care on an Intensive Care Unit (ICU) has become an important issue for healthcare management and policy. Defining different levels of care might lead to a more effective use of nursing resources. We therefore defined criteria to differentiate the level of care between IC-level or Medium Care (MC)-level by using the interventions as listed in the NAS and the TISS. Nursing staff requirements were defined for both patient levels to analyse the effect of care-classification on the costs for nursing staff.

METHODS. We measured nursing interventions on the ICU as listed in TISS and NAS once a day in all patients admitted to the ICU between February 2009 and July 2009. TISS was used only for the listed nursing interventions, NAS was used for the translation of nursing interventions to a patient to nurse ratio. All interventions listed in the NAS and TISS scoring charts were classified according to the required level of nurse education defined subsequently as a MC-intervention or an IC-intervention. A patient was classified as MC-level if care consisted only of MC-interventions. If there was at least one IC-intervention scored, the patient was classified as IC-level. Nursing staff requirements were defined according the definitions of NAS for both care-levels; 100 NAS points is equal to 1.0 Full Time Equivalent (FTE) nursing staff.

RESULTS. A total of 530 patients were admitted to the ICU, generating 1,688 patient days. Of these, 77.5% were classified as IC-level and 22.5% were classified as MC-level. IC-level days had higher NAS scores when compared to MC-level days (45.3 ± 9.6 vs. 31.4 ± 9.2, $p < 0.001$). Nursing staff requirements according to the definitions of NAS were 2.2 ± 1.1 patients per nurse for IC-level and 3.2 ± 1.0 patients per nurse for MC-level ($p < 0.001$).

CONCLUSIONS. Both TISS and NAS can be used as instruments to differentiate the level of care on the ICU and planning of nursing staff with different nursing skill requirements. For ICU-conditions, the number of patients per nurse can be increased, resulting in lower costs. In case of the presence of a MC-unit both the nursing skill requirements and patient to nurse ratio can be changed to the level as needed by the MC-patients. Transfer of the MC-patient to this unit will lead to a more effective use of nursing staff and consequently reduce costs.

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THE USE OF THE EARLY WARNING SCORE SYSTEM IN ASSESSMENT OF PATIENTS IN POST ANESTHESIA CARE UNIT

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INTRODUCTION. Post anesthesia care units (PACU) are units where patients go under intensive nursing observation assessment until their vital functions stabilize. In these units patients condition may change rapidly and they may need close inspection as well as emergency response. Early Warning Scoring (EWS) system may make early recognition of and response to bad condition possible by observation based on systematic parameters. EWS was developed as a simple scoring system to be used at ward level utilizing routine observations taken by nursing staff. EWS is based on five physiological parameters; systolic blood pressure, pulse rate, respiratory rate, temperature and AVPU score (Alert; reacts to Voice; reacts to Pain; Unresponsive).

OBJECTIVES. The aim of this study was to evaluate EWS among patients admitted to PACU.

METHODS. EWS parameters were recorded four times from 167 patients after their admission to PACU. The First record was taken during the first admission to PACU (EWS 1), the second (EWS 2) after 15 min, the third after 30 (EWS 3) and the fourth record after 60 min. The correlation between variables like differences of four EWS, patients age, the ASA score, duration of operation were statistically examined.

RESULTS. The mean age of the patients (range; 16–89) was 43.51 ± 1.74 years. The ratio of female patients involved was 54.5 and 65.9% of patients did not have systemic illnesses and history of medicine use. The ASA score of 67.1% of patients was I, and the ratio of general anesthesia implemented patients was 55.1%. The mean duration of operation time was 82.69 ± 5.16 (range; 15–300) min, the mean duration of PACU time was 41.91 ± 1.95 (range 15–180) min. EWS means were 3.99 ± 1.51, 3.53 ± 1.41, 3.28 ± 1.38, 3.12 ± 1.35 respectively and the difference between mean scores was statistically significant ($p < 0.0001$). A probe to find correlation between EWS mean scores and patients independent variables (age, duration of operation and duration stay in PACU) showed a positive relation only between duration of operation and EWS mean scores (EWS 1; $r = 0.199$, EWS 2; $r = 0.17$, EWS 3; $r = 0.229$, EWS 4; $r = 0.230$, $p < 0.05$).

CONCLUSIONS. EWS can help to identify the patients developing bad condition. It utilizes standard clinical observations and can easily be incorporated into routine PACU practice. In addition PACU nurses should practice closer observation on patients who undergone operations of longer duration.

Protocol-guided therapy in sepsis: 1348–1359

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SURVIVING SEPSIS: IMPROVING THE EARLY TREATMENT AND RECOGNITION IN ACUTE MEDICAL PATIENTS USING AN AUDIT PROFORMA

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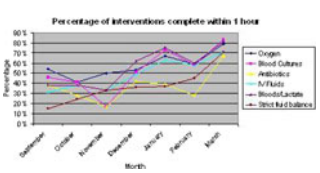
INTRODUCTION. Early treatment and recognition of sepsis is a stated aim of the surviving sepsis campaign [1] but in busy clinical environments the delivery of antibiotics and fluids can often be delayed. We describe the implementation of an audit proforma, based on the survivesepsis.org [2] resuscitation bundle, as a tool to deliver six aspects of management within 1 h of recognition sepsis.

OBJECTIVES.

1. Improve the early recognition and treatment of sepsis in acute medical patients.
2. Provide a sustainable change in the management of septic patients
3. Improve mortality and length of hospital stay

METHODS. The proforma consist of six treatment management steps, based on the survivesepsis.org "septic six": 1 Oxygen, 2 Blood Cultures, 3 Antibiotics, 4 Lactate, 5 IV fluids, 6 Strict fluid management. It is triggered by patients satisfying two or more of the systemic inflammatory response syndrome criteria. All management steps should be implemented within 1 h of the trigger time stated on the form. The forms are collected and analysed every month and the results are displayed for staff working on the medical admissions unit and accident and emergency.

RESULTS. A total of 239 forms have been collected, 30% diagnosed with severe sepsis. The progress on all six parameters is shown below.



Results

CONCLUSIONS. Over the initial seven month period we have demonstrated a sustained improvement in the rapid delivery of all six of the management parameters. Table 1 demonstrates that the proforma is reducing ventilator days and length of stay on ITU. Continued collection of data should demonstrate a sustained and statistically significant improvement.

ITU OUTCOMES

	APACHE II	Ventilator Days	Length of Stay on ITU	Hospital Mortality %	Total number of patients
Before Proforma (6 months)	18.59	3.17	3.80	45	29
After Proforma (6 months)	18.07	1.73	3.14	43	30

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CLINICAL IMPLICATION OF RESUSCITATION WITH FLUIDS GUIDED BY CENTRAL VENOUS PRESSURE IN SEPTIC SHOCK

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INTRODUCTION. The early goal-directed resuscitation has been shown to improve survival in patients presenting with septic shock. A recent systematic review demonstrated the inability of central venous pressure (CVP) to predict the hemodynamic response to fluids infusion, and it should not be used to make clinical decisions regarding fluid management in critical patients. The clinical implication of this fact in septic shock is not well-known.

OBJECTIVES. The aim of this study is to determine if the resuscitation with fluids guided by CVP has clinical implications in patients with septic shock.

METHODS. Post-hoc analysis of a patients' cohort with septic shock admitted in the Medical Intensive Care Unit since June 2007 to June 2009. All of them were treated on basis of a bundle for severe sepsis management. Chi-square analysis was used to compare categorical data. Continuous data were compared using Student's t test. We used multiple logistic regression model to assess the association between the independent variable and mortality, after adjustment for possible confusing factors (we considered variable to be confounding if the estimate of the coefficient changed by more than 10%).

RESULTS. Eighty-five patients were studied. 66% were male. Their average age was 57 ± 17 and 40% had previous chronic diseases. Severity scores: APACHE II 24 ± 8, SOFA 10 ± 4 and 76% of patients had multiorganic dysfunction. Infectious focus was respiratory in 48%. CVP mean was 12 ± 4 mmHg, ScvO2 73 ± 8% and the mean amount of fluids provided was 2840 ± 844 cc. 71% of patients needed mechanical ventilation. Hospital-stay middle was 28 days (1–160) and 10 days in ICU (1–115). ICU mortality was 34% and hospital mortality 44%. Univariable analysis showed that statistically significant factors related to mortality were: severity scores (APACHE II 26 ± 6 vs. 22 ± 8, $p = 0.05$; SOFA 12 ± 4 vs. 9 ± 8, $p < 0.00$, multiorganic dysfunction 47 vs. 26%, $p = 0.04$), infectious focus (pneumonia) (53 vs. 16%, $p < 0.00$) and volume of fluids infused (1972 ± 1025 vs. 2490 ± 1024, $p < 0.00$). When we analyzed the quantity of fluid administered in the resuscitation, those patients who achieved CVP > 14 mmHg and needed mechanical ventilation, received less volume (2591 ± 832 vs. 2982 ± 826 cc, $p = 0.04$ and 2633 ± 837 vs. 3210 ± 804 cc, $p < 0.01$, respectively). In the multivariable analysis, the amount of fluids infused adjusted by age, previous chronic disease, severity scores, CVP, ScvO2, serum lactate levels, mechanical ventilation, infectious focus and nosocomial infection were associated independently with mortality (OR 0.45, 95% CI 0.24–0.84).

CONCLUSIONS. In our patients' cohort with septic shock treated under the basis of the early goal-directed resuscitation, the volume of fluids infused was associated independently with mortality. A lower fluid administration in the resuscitation probably could be caused by the early reach of a high central venous pressure.

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BLINDING ALBUMIN AND NORMAL SALINE FOR THE PRECISE PILOT MULTI-CENTRE FLUID RESUSCITATION TRIAL: A DESCRIPTION OF THE PROCEDURE

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INTRODUCTION. Blinding of study interventions is necessary to prevent bias in randomized controlled trials (RCT). Since normal saline and 5% albumin are packaged in bags and bottles, respectively and they have different color and texture, a blinding procedure is necessary to ensure the fluids appear identical for comparative RCTs.

OBJECTIVES. To describe the blinding procedure and evaluate sterility and stability involved in the transfer and storage of study fluids in the PRECISE pilot RCT.

METHODS. A standard operating procedure for concealment, meeting pharmacy guidelines and good manufacturing practices was developed by the manufacturing pharmacist at the coordinating centre and used by all participating sites. Fluids were transferred with aseptic technique into identical 500 ml bottles under a sterile hood by the pharmacy or transfusion medicine technician then covered with an opaque wrapping. Average time to transfer of study fluids from their original packaging was recorded to understand labor involved with creating each study fluid package. Yellow intravenous tubing was manufactured to also conceal the fluid color. Six blinded bottles of normal saline and 5% albumin from the participating centers were stored at room temperature for at least 3 months. Cultures of the fluids using blood culture media and/or endotoxin levels (measured by commercial assay) were obtained to document sterility of the study fluids. Protein electrophoresis was used to assess albumin stability.

RESULTS. Transfer of the study fluids was the responsibility of the research pharmacist/technician and blood bank at 3 and 3 sites, respectively. Average time to transfer 20 containers of normal saline and 5% albumin into bottles was 65 ± 29 and 77 ± 19 min, respectively. Sterility (culture negative and/or endotoxin undetectable) of study fluids was confirmed from all bottles of normal saline and albumin that underwent testing. Protein electrophoresis of albumin samples showed a single band suggesting no degradation of albumin during transfer and storage.

CONCLUSIONS. The standardized blinding procedure developed for transfer of study fluids in this pilot RCT confirmed sterility and stability of our study fluids for 3 months. These data are important when considering the length of allowable storage time for these study fluids. Due to the resources and time involved with the transfer of these fluids for individual sites, this transfer method needs to be incorporated into budgeting and may not be feasible in the context of a large RCT.

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MANAGEMENT OF SEVERE SEPSIS IN ASIA: A PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION. The Surviving Sepsis Campaign recommends a 6-h resuscitation bundle and a 24-h management bundle to improve outcomes in severe sepsis. Compliance with and relevance of these recommendations to Asian intensive care units (ICUs) are unknown.

OBJECTIVES. The primary objective of the present study was to assess the compliance of Asian ICUs and hospitals to these bundles. The secondary objectives were to evaluate the impact of compliance on mortality, and the organisational characteristics of Asian hospitals which are associated with higher compliance.

METHODS. This was a prospective observational study of patients with severe sepsis who were admitted to the participating ICUs in July 2009. We recorded the organisational characteristics of participating centres, the patients' baseline characteristics, and the achievement of targets within the resuscitation and management bundles.

RESULTS. Sixteen countries and 150 ICUs participated, enrolling 1285 patients. Hospital mortality was 44.9%. Achievement rates for the bundle targets were: lactate measurement, 39.8%; blood cultures, 62.5%; broad-spectrum antibiotics, 64.0%; fluids ± vasopressors, 81.4%; central venous pressure, 39.7%; central or mixed venous oxygen saturation, 10.8%; low-dose steroids, 55.8%; drotrecogin alfa, 3.2%; glucose control, 27.1%; lung-protective ventilation, 11.7%. Compliance rates for the entire resuscitation and management bundles were 7.6 and 3.5% respectively. On logistic regression analysis, achievement of the targets for blood cultures, antibiotics, and central venous pressure independently predicted decreased mortality. High-income countries, university hospitals, ICUs with an accredited fellowship programme, and surgical ICUs were more likely to be compliant to the resuscitation bundle.

CONCLUSIONS. Compliance to the resuscitation and management bundles is generally poor across Asia. Given the resource limitations in Asia, the most appropriate strategy to improve outcomes in severe sepsis may be to concentrate on ensuring early administration of antibiotics after blood cultures, and appropriate fluid therapy.

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SEPSIS OVER NIGHT OR DURING DAY: GREAT DIFFERENCES IN COMPLIANCE WITH SURVIVING SEPSIS CAMPAIGN BUNDLES

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INTRODUCTION. Severe sepsis is a public health problem with increasing morbidity and mortality, and fatality rates that can be as high as 60% in septic shock. This problem prompted the development of a worldwide campaign—The Surviving Sepsis Campaign (SSC)—with the goal of reducing this mortality rate by 25% through the compliance of pre-defined bundles. The 6-h bundle comprises: serum lactate measurement, blood cultures and early antibiotic administration, as well as haemodynamic stabilization (with fluids, invasive monitoring, vasopressors and dobutamine administration as needed). The 24-h bundle is mainly addressed to intermediate and intensive care units and refers to ventilation strategy, glycaemia control, steroids in septic shock and drotrecogin alfa.

OBJECTIVES. The authors propose to evaluate if there is any difference in compliance with the SSC 6-h bundle recommendations according to the hour of hospital admission: DAY vs. NIGHT.

METHODS. Prospective cohort study off all consecutive patients admitted to a mixed intensive care unit (ICU), at a University Hospital, between 1st of December of 2004 and 31st of May of 2008. Data collected included demographic information, simplified acute physiology score (SAPS II), severity of sepsis, date and time of compliance with each of the recommendations of the 6 h bundle. Were stratified the study population in two groups according to the time of admission: DAY (08:30 a.m. to 08:30 p.m.) and NIGHT (08:30 p.m. to 08:30 a.m.).

RESULTS. During the study period, 1223 patients were admitted in our unit, of those 300 (25%) had severe community-acquired sepsis (CAS). CAS patients had a mean age of 58 ± 17 years, 178 (59%) were male. The median SAPS II was 45 and 197 (66%) had septic shock. Table 1 presents DAY versus NIGHT results.

DIFFERENCES ON 6-H SEPSIS BUNDLE COMPLIANCE

Compliance of 6-h bundle	Day	Night	p	Time of bundle achievement	Day	Night	p
Lactate measurement	48.5%	56.5%	0.171	Lactate measurement, median (IQR)	6.97 (1.27–25.18)	4.48 (0.83–14.02)	0.130
Blood cultures	37.3%	58.8%	<0.001	Blood cultures, median (IQR)	8.17 (2.74–25.54)	4.06 (1.55–10.83)	<0.001
Antibiotic administration	17.8%	32.8%	0.003	Antibiotic administration, median (IQR)	8.18 (4.25–16.17)	4.95 (2.02–9.89)	<0.001
Fluids administration	100%	100%		Venous central pressure, median (IQR)	10.94 (5.17–22.50)	7.83 (1.88–17.37)	0.214
Administration of vasopressors	99.1%	100%		Venous central oxygen saturation, median (IQR)	10.65 (8.78–22.17)	2.47 (1.02–29.64)	1.000
Venous central pressure monitoring	29.2%	44.7%	0.021				
Venous central oxygen saturation monitoring	1.8%	7.4%	0.082	Mortality rate	40%	34%	0.281

CONCLUSIONS. Unexpectedly, the compliance rate with the recommendations was significantly better over night. Although the number of nurses is constant in the 24 h, the number of doctors is lower and less differentiated in the night shift. In an attempt to find an explanation for these findings we looked at the patient flow and time span until the first medical observation in the different time periods and we found that over night admissions (between 00:00 a.m. and 08:00 a.m.) corresponded only to 10% of all admissions and were seen sooner, which might explain our findings.

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SEVERE SEPSIS AND MORTALITY ON THE ICU DURING THE SURVIVING SEPSIS CAMPAIGN

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INTRODUCTION. Sepsis, clinically defined as the systemic inflammatory response syndrome (SIRS) to infection, is a common complication. Delayed diagnosis is associated with increased morbidity, mortality and cost in the ICU. As the mortality rate of severe sepsis remains unacceptably high, a group of international expert developed guidelines in 2004, termed the Surviving sepsis campaign (SSC). The SSC group has introduced the "sepsis care bundles" into clinical practice with the goal of reducing mortality by 25% in 5 years.

OBJECTIVES. To establish degree of compliance with diagnostic and therapeutic procedures in the severe sepsis treatment. We determined the rate of compliance with resuscitation and management bundles and the impact of the compliance on the hospital mortality in patient with severe sepsis and septic shock.

METHODS. We applied the SSC bundles during the year 2004 on our department. In this study we measured the time taken to applying sepsis bundles in 240 consecutive patients with severe sepsis or septic shock from January 2004 to December 2009 (Retrospective study during 2004; Prospective study during 2005–2009). Compliance was defined as the average of the percentage compliance with each of the 13 items specified in the guideline. Mortality was recorded too. We evaluated variety of source severe sepsis and septic shock in ICU and genesis of sepsis on other departments in our hospital. Results were compared by chi squared. We disposed the abstract about SSC for physician who don't work on the ICU in our hospital.

RESULTS. Incidence of the severe sepsis and septic shock was 8.7% patients per period (240/2,752). Out of 240 patients 68 had severe sepsis a 172 septic shock. Compliance with the severe sepsis guidelines was in 2004 only 39% but in 2009 it was 68% (improved about 53.5%, $P < 0.001$). There was significant difference in 28 days mortality (in the 2004, 72%, in the 2009, 59%, $P < 0.05$).

CONCLUSIONS. Correct application of the sepsis bundles was associated with reduced mortality. But we didn't obtain 5 years mortality reduction about 25%. Sepsis bundles must be improved to guarantee clinical feasibility.

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SEVERE SEPSIS/SEPTIC SHOCK: DO WE DO WHAT WE ARE SUPPOSED TO DO?

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INTRODUCTION. *Surviving Sepsis Campaign* (SSC) reviewed in 2008 the management of patients with severe sepsis and shock septic. The objective was improving outcomes of severe sepsis. The time and accuracy of therapy administered in the initial hours after severe sepsis and shock septic change outcome. We assessed the implementation to Surviving Sepsis Campaign recommendations during the first 6 h of intervention in severe sepsis/septic shock of an academic tertiary care center.

OBJECTIVES. To monitor adherence to the recommendations of the Surviving Sepsis Campaign during the first 6 h of intervention for severe sepsis/septic shock in an academic tertiary care center.

METHODS. Observational, prospective follow-up. Patients who were admitted into the Intensive Care Unit in University Hospital Complex A Coruña (CHUAC) during the months of May–June 2009 with criteria for severe sepsis/septic shock were analyzed. We studied 5 indicators that comprise the set of intervention measures within the first 6 h of diagnosis of severe shock/septic shock.

RESULTS. Hospital mortality was 30.8% (95% CI: 9.09–61.42). The average APACHE II was 25.46 ± 9.38. The delay in initiation of antibiotic treatment was 1.23 ± 1.76 h. The average delay in initiation of resuscitation from presentation of symptoms was 3.83 ± 8.85 h. 84.62% (95% CI: 54.55–98.08) of patients achieved $ScvO2 > 70$ within the first 6 h of diagnosis.

CONCLUSIONS. Adherence to the set of measures of resuscitation from severe sepsis/septic shock is high.

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INTERVENTIONS OF THE SEPSIS RESUSCITATION BUNDLE CARRIED OUT AT THE INTENSIVE CARE UNIT LATER THAN 6 H AFTER THE BEGINNING OF SEVERE SEPSIS: IMPACT ON MORTALITY

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INTRODUCTION. Several recent studies have shown that compliance with the 6-h resuscitation bundle decreases mortality in patients with severe sepsis.

OBJECTIVES. The purpose of the study was to assess whether the completion of the sepsis resuscitation bundle within the first 6 h after ICU admission, but beyond the specific time limit of the various bundle interventions, is related to an improvement in survival in patients with severe sepsis/septic shock.

METHODS. This was a single-center prospective observational study of patients admitted to the medical-surgical ICU of an urban tertiary care teaching hospital with severe sepsis/septic shock. Patients were recruited from June 2005 to November 2009. We assessed the compliance with the different tasks included in the 6-h resuscitation bundle. Furthermore, we ascertained within the first 6 h after ICU admission the compliance with those tasks not carried out within their specific time limits; we have called this variable "bundle improvement at the ICU". Results were stratified by the number of tasks of the bundle completed before admission at the ICU, and the lag time between the beginning of severe sepsis and admission to the ICU. These late completed tasks at the ICU were related to hospital mortality by a Cox regression model.

RESULTS. We analyzed 750 consecutive episodes of septic shock (86.3%) or severe sepsis (13.7%).The mean age was 64 ± 16 years, APACHE II 22.5 ± 7, SOFA 9.0 ± 3, and global hospital mortality 34.7%. In 385 patients (51.3%) there was "bundle improvement at the ICU". Patients not undergoing additional bundle tasks out of time had higher frequency of mechanical ventilation, higher figures of $ScvO_2$ at admission, and a clear lower time from beginning of severe sepsis to ICU admission than the late bundle improvement group. Broad spectrum antibiotics administration and the achievement of the early goal-directed therapy end points were the measures implemented best at the ICU, although they were also the interventions more frequently accomplished out of the time limits. When the influence of APACHE II, residuals of SOFA, age, mechanical ventilation, and $ScvO_2$ at ICU admission was controlled by multivariate analysis, the hazard ratio (HR) showed that the "bundle improvement at the ICU" of two or more of the 6-h resuscitation bundle tasks is associated with a lower risk of mortality [HR = 0.44 (0.25–0.76); p = 0.01]. Additional tasks carried out by the ICU staff did not improve significantly mortality when at least 5 interventions had been performed within the specific time limits.

CONCLUSIONS. Implementation of resuscitation bundle within the first 6 h after ICU admission, but beyond the specific time limit of the various sepsis resuscitation bundle interventions was associated with decreased mortality in patients with severe sepsis/septic shock.

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COMPLIANCE WITH THE "SURVIVING THE SEPSIS CAMPAIGN GUIDELINES 2008" IN AN ACUTE HOSPITAL AND ITS EFFECT ON OUTCOME

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INTRODUCTION. A recent study has shown that compliance with sepsis care bundles improves the outcome in patients with severe sepsis or septic shock.

OBJECTIVES. The aims of this study were to assess the compliance rate with 6 h bundle as defined in the Surviving the Sepsis Campaign guidelines 2008 in patients diagnosed with sepsis regardless of severity and whether compliance affects the rate of mortality and/or hospital stay.

METHODS. We conducted a prospective observational study. We randomly recruited 145 adult patients from acute admissions unit and intensive care in an acute district general hospital in England who met the diagnostic criteria for sepsis. For each patient, compliance with sepsis care bundle was obtained from medical notes. The following components of the 6 h sepsis bundle were assessed: Obtaining blood cultures, initiating antibiotic therapy, measuring serum lactate and in the event of septic shock administration of fluid therapy.

RESULTS. Our study group (n = 145) consisted of 70 male patients (48.3%) and had a mean age of 71 years. Most of our patients were recruited from the acute admissions unit (n = 123, 84.8%). Focus of sepsis (presumed or confirmed) was as follows: Chest 50.3%; abdomen 17.2%; skin 11.7%; Urine 11%; others and unknown 9.8%. The rate of compliance with each aspect of 6 h bundle was as follows: 95 patients (65.5%) received antibiotics, 76 patients (52.4%) had blood cultures taken and 34 patients (23.4%) had lactate measured. Only 17 (11.7%) patients received all the three elements within 6 h of diagnosis. The incidence of septic shock in our sample was 8.97% (n = 13) of whom 84.6% (n = 11) were resuscitated with fluids. A total of 17 patients (11.7%) received all three elements of bundles within 6 h. When compared the totally compliant group (in all three elements) against those who were non-complaint in at least one element, neither the mortality rate (17.6 vs. 14.1%, p > 0.05) nor the hospital stay duration (14.7 vs. 12.5 days, p > 0.05) varied significantly. However, in those who had blood cultures taken and received antibiotics within 6 h, mortality rate (10.9%) was reduced by 50% compared to the mortality rate those who failed in one of these two elements (17.3%, RR 1.58). However, this reduction was not statistically significant.

CONCLUSIONS. In our study group, compliance with the main elements of sepsis care bundle did not cause a statistically significant reduction in hospital stay or mortality. However, prompt antibiotic therapy appears to reduce mortality in all septic patients regardless of severity.

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AUDIT OF COMPLIANCE WITH THE SEVERE SEPSIS RESUSCITATION BUNDLE IN PATIENTS ADMITTED TO ICCU

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INTRODUCTION. Sepsis is a big killer worldwide and is becoming more common. The recognition of sepsis is often delayed and management of the condition requires improvement [1]. The Surviving Sepsis Campaign represents an international collaboration between many organisations. All are committed to reducing mortality from severe sepsis. The campaign aims to do this by implementing two 'bundles' of care. The first bundle is the Severe Sepsis Resuscitation Bundle and the second the Management Bundle. This audit measures compliance with Resuscitation Bundle.

OBJECTIVES.
- Identify onset of severe sepsis
- Measure compliance with resuscitation bundle
- Calculate timing of antibiotic administration
- Record time to ICCU admission

METHODS. All admissions (n 82) to the Integrated Critical Care Unit were assessed pre and post admission documentation. Patients meeting the criteria for diagnosis of Severe Sepsis (n 35) were concurrently audited over a 4-week period. Individual and overall compliance with the bundle elements were recorded along with details of organ dysfunction at onset. Timing of antibiotic administration was also recorded. Timing of admission to ICCU was recorded and measured against percentage compliance with the bundle.

RESULTS. 82 patients were admitted to ICCU in the four week period. 35 patients had severe sepsis and 14 of those also developed septic shock. All were emergency admissions with 80% being admitted under medical specialties and 20% surgical. None of the patients were admitted to ICCU within 1 h. Time to ICCU admission varied from 80 min to 52.5 h. Percentage compliance with the bundle was between 57 and 75% for patients admitted to ICCU within 6 h of onset of severe sepsis and reduced significantly for those admitted after 16 h. All elements of the bundle were completed for 1 patient only. Compliance with the individual bundle elements were: lactate measured—45.7%; blood cultures before antibiotics—11.4%; antibiotics in <3 h—65.7%; hypotension treated with fluids—62% (based on estimated weight of 70 kg); vasopressors administered—28.6%; CVP ^{3} 8 mmHg—42.9%; $ScvO_2$ measured and ^{3} 70–0%.

CONCLUSIONS. Long and unacceptable delays in admission to ICCU were identified despite evidence of significant organ dysfunction in many of these patients. With all bundle elements being met for only 1 patient it is apparent that evidence based endpoints aimed at reducing mortality from severe sepsis are not being met despite all the bundle elements being practically deliverable. Poor compliance with taking blood cultures prior to antibiotic administration and lack of $ScvO_2$ measurement are areas requiring particular attention. Further work is recommended to identify potential contributing factors to non-compliance.

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MONITORING THE HAEMODYNAMIC RESPONSE TO A FLUID CHALLENGE: IS ARTERIAL PRESSURE SUFFICIENT?

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INTRODUCTION. International guidelines recommend that cardiac output measurement is required in addition to arterial pressure monitoring in patients with persistent shock after initial therapy [1]. Nevertheless, these recommendations are not supported by any comparison of arterial pressure and cardiac output for monitoring the effects of the most current treatments like fluid therapy.

OBJECTIVES. To evaluate in which extent monitoring the haemodynamic effects of a standardized fluid challenge with the sole arterial pressure could help for detecting the fluid-induced changes in cardiac index (CI).

METHODS. In 228 critically ill patients with acute circulatory failure deemed at receiving a 500-mL saline infusion over 20 min, we measured the systolic (SAP), diastolic (DAP), mean (MAP) and pulse (PP) arterial pressure and transpulmonary thermodilution CI before and after volume expansion.

RESULTS. Volume expansion significantly increased CI, SAP, DAP, MAP and PP by 24 ± 25%, 15 ± 19%, 9 ± 16%, 13 ± 17% and 21 ± 29%, respectively. The fluid-induced changes in PP, SAP and MAP were significantly correlated with the fluid-induced changes in CI (r = 0.56, 0.55 and 0.37, respectively). The changes (in %) in PP were significantly related to the changes (in %) in stroke volume for all quartiles but with different coefficients of correlation: r = 0.39 for the 1st quartile (36–53 years), r = 0.44 for the 2nd quartile (54–62 years), r = 0.55 for the 3rd quartile (63–74 years), r = 0.68 for the 4th quartile of age (75–88 years). CI increased ≥15% in 142 patients defined as "responders". A fluid-induced increase in PP ≥ 17% detected responders with a sensitivity of 65 [57–72]% and a specificity of 85 [76–92]%, i.e. with 6% of false-positive and 22% of false-negative cases. The fluid-induced changes in SAP exhibited similar diagnostic value. The area under the ROC curve of the fluid-induced changes in PP and SAP for detecting responders were significantly higher than for the fluid-induced changes in MAP and DAP (0.793 ± 0.03, 0.735 ± 0.02, 0.656 ± 0.04 and 0.537 ± 0.05, respectively). The area under the ROC curve of the fluid-induced changes in PP and SAP for detecting an increase in CI ≥15% was not different between patients belonging to the 1st, the 2nd, the 3rd or the 4th quartile of age (0.814 ± 0.05, 0.767 ± 0.07, 0.776 ± 0.05 and 0.0804 ± 0.06, respectively).

CONCLUSIONS. PP and SAP were the best arterial pressure values for detecting the fluid-induced changes in CI. Using the sole PP for assessing fluid responsiveness led to a non negligible proportion of false negative cases. This supports the recommendation that when a precise monitoring of fluid resuscitation is required, like in refractory shock, a direct assessment of cardiac output is required.

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AVOIDABLE CATECHOLAMINE INDUCED CIRCULATION INJURY CAUSED BY HIGH DOSES OF CATECHOLAMINES IN SEPTIC SHOCK: HYPOTHESIS OF A CATECHOLAMINE INDUCED CIRCULATION INJURY

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INTRODUCTION. Patients with septic shock need a proper fluid loading before starting high doses of catecholamines.

OBJECTIVES. Aim of our study is to show that it is possible to reduce high catecholamines in previous improper volume resuscitated patients by forced volume resuscitation combined with active dose reduction and generate the hypothesis of an avoidable catecholamine induced circulation injury.

METHODS. We studied n = 33 patients (21 m, 12f; mean age 69 ± 10 years [SE] years) with septic shock, who received high catecholamines doses (norepinephrine 18.33 [range up to 56.67] µg/min (32 pts.); Dobutamine 333.33 [up to 1,666.67] µg/min (27 pts.); epinephrine 15.00 [up to 33.3] µg/min (15 pts.), Vasopressin 100 I.E./h (1 pt.), mottled-marbled cold extremities, blood pressure in a satisfactory condition; CVP 18 (5–34) mmHg and lactate 2.6 (0.93–10.7) mmol/l after major surgery (observational study, SICU, university hospital), CO 6.45 (3.1–9.7) l/min, SVR 917 (471–2,228) dynes s/cm^{-5}, paO_2/FiO_2 247 mmHg (75–418) [median, range]. Intervention included a forced volume challenge combined with an active initiated reduction of catecholamines to achieve an adequate fluid loading status guided by passive leg rising test, course of CO, CVP, Lactate level and in 23 cases by hemodynamic monitoring [PAC n = 10; Vigileo n = 12 (Edwards), PiCCO n = 1 (Pulsion)]. It was stopped after clinical improvement with rewarmed extremities, increasing diuresis and lack of improvement of hemodynamic parameters by passive leg rising-test. Data collection included baseline characteristics, individual course of hemodynamic parameters, PAO_2/FiO_2, catecholamines, administered volume, lactate, time needed to wean from catecholamines, outcome.

RESULTS. Median catecholamine doses decreased significant in all patients: norepinephrine 0 [10]; dobutamine 166.7 [666.67]; epinephrine 3.33 [8.33] µg/min [median; range up to], $p < 0.05$ (Wilcoxon-test); volume challenge: 5.500 ml Ringer [24.000] and 1.000 ml HAES [3.500] ml (median, range up to), fluid balance during intervention: 6.750 [2.040–27.255] ml. Mean weaning time from catecholamines: 16 h [4–43 h]. All patients showed rewarmed extremities, decrease of lactate levels 2.6 mmol/l [1.10–5.4] [range]. Hemodynamic constellations were not homogenous (CO 6.25 [3.9–10.6] l/min, SVR 788 [498–1,680] dynes s/cm^{-5} but without any cardiac deterioration nor of PAO_2/FiO_2 268 [120–467] mmHg (median, range). 24 patients survived, 9 died.

CONCLUSIONS. It is possible to wean several septic shock patients from high catecholamine doses with a contemporaneous fluid challenge—the timing of this procedure depends primarily on the decision of the doctor to try it. Sustained inadequate catecholamine doses before an adequate fluid loading justify the formulation of the hypothesis of an avoidable catecholamine induced circulation injury comparable to the concept of ventilator induced lung injury and biotrauma.

Sepsis: Microcirculation and tissue oxygenation: 1360–1373

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ERYTHROCYTE PROTEINS MEMBRANE CONTENT ARE NOT ALTERED IN SEPTIC PATIENTS

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INTRODUCTION. The sialic acid content of the red blood cell (RBC) membrane decreases early in sepsis [1], and this alters the RBC shape and metabolism [2]. An increased ratio of the RBC proteins Band 3/alpha spectrin was observed in a mouse model of septic shock, suggesting a possible alteration of the RBC membrane integral/peripheral proteins ratio [3]. As there are interspecies differences in membrane composition, these observations need confirmation in humans.

METHODS. We studied RBCs from patients with (n = 15) and without (n = 9) sepsis at ICU admission and on day 3 in the septic patients. Exclusion criteria were recent RBC transfusion, hematologic diseases, cirrhosis and diabetes mellitus. Procedures included screening for RBC membrane protein alterations by cryohemolysis test and separation of the RBC membrane and skeletal proteins by polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate [4]. Comparison between groups was made by the Student's t test or the Mann–Whitney test. A p value <0.05 was considered as statistically significant.

RESULTS. The hemogram, including reticulocyte count was similar in septic and non-septic patients at ICU admission. No significant difference was observed for cryohemolysis test results and the amount of the RBC proteins (Table 1).

TABLE 1

Septic patients (n = 12)	Day 1	Day 3	P value
RBC (10.6/mm^3)	3.30 ± 0.55	3.28 ± 0.58	0.84
Ht (%)	31.5 ± 4.8	30.4 ± 4.4	0.35
Reticulocytes (10.3/mm^3)	64 ± 23	60 ± 28	0.83
Cryohemolysis test	3.8 [2.5–5.2]	3.2 [1.7–6.8]	0.32
Spectrins	614 ± 240	593 ± 244	0.61
Band 3	547 ± 185	558 ± 222	0.81
Protein 4.1	76 ± 23	81 ± 35	0.58
Glycophorins	96.7 ± 25.2	92.7 ± 33.7	0.72
Band 3/spectrins	0.92 ± 0.16	0.92 ± 0.16	1

CONCLUSIONS. RBC membrane skeletal proteins content was not altered in septic conditions. Therefore alterations in RBC rheology are mainly due to alterations in the other membrane compounds like sialic acid and/or lipids.

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EVALUATION OF A NEW MEASUREMENT METHOD OF TOTAL ANTIOXIDANT STATUS: COMPARISON WITH THE RANDOX METHOD

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INTRODUCTION. Cardiopulmonary bypass (CPB) during cardiac surgery is responsible of an inflammatory cascade eventually leading to a SIRS. Ischemia/reperfusion and blood/biocompatible material contact produce free radicals which decrease Total Antioxidant Status (TAS). Therefore, cardiopulmonary bypass (CPB) constitutes a good model to test a new TAS measurement method [1].

OBJECTIVES. Our purpose was to compare a new method (Patrol FR 08-02110) with the reference method (Randox^{TM}) during CBP.

PATIENTS AND METHODS. Patients scheduled for coronary artery bypass (CB) and aortic valve replacement (AVR) under CBP were enrolled after written informed consent in this protocol approved by local ethics committee. Anesthesia protocol was standardized with systematic use of tranexamic acid. Three blood samples were harvested: T1 = induction; T2 = 30 min. after cross aorta clamping; T3 = 24 h after induction. The Patrol method was performed after serum exposition to a photosensibilizer agent then to a laser irradiation leading to the formation of free radicals. Oxidation by those free radicals of a fluorometric sensor allowed an indirect measure of TAS. This measurement in arbitrary unit (AU) corresponded to area under curve compared to a control value from a pool serum. A value higher than 1 indicated a lower capacity for the given serum to neutralize free radicals whereas a lower value indicated a higher capacity. The same sample allowed TAS determination (µmol/L) with Randox^{TM} method. Results were expressed as absolute numbers, mean ± SD. TAS were compared with ANOVA test; $p < 0.05$ was significant.

RESULTS. The seven patients (5 male, 2 female; 71 ± 10 years old) enrolled underwent cardiac surgery (4 CB and 3 AVR) without any problem. There was no variation in TAS determination with the Randox^{TM} method: T1: 1.39 ± 0.13; T2: 1.41 ± 0.26; T3: 1.33 ± 0.15 µmol/L. Conversely a two fold significant increase was measured during CPB with the Patrol method: Ti: 1.12 ± 0.31; T2: 2.21 ± 0.60*; T3: 0.99 ± 0.34 AU. *$p < 0.001$ versus T1.

CONCLUSIONS. Oxidative stress due to overwhelming release of reactive nitrogen/oxygen species (RN/OS) is held largely responsible for sepsis-induced organ failure and mortality [2]. Up-front and/or ongoing distortion of the pro-oxidant/anti-oxidant balance is likely to play an important role in this situation and in ischemia-reperfusion. Therefore the Patrol test which appeared to be more sensible than the Randox^{TM} method could a good tool in these cases and for evaluation of new anti-oxidant treatments in critical care medicine. These results have to be confirmed in a larger population.

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SERUM LACTATE IS AN INDEPENDENT PROGNOSTIC FACTOR IN SEVERE SEPSIS

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INTRODUCTION. Sepsis is the leading cause of death in critically ill patients. Despite attempts to improve standardized strategies in resuscitation and treatment of sepsis, the morbidity and mortality remain unacceptably high. Early diagnosis and stratification of the severity of sepsis is the key to start timely the appropriate treatment. Sepsis is the systemic inflammatory response syndrome to infection; it can lead to hypoperfusion and organ dysfunction and at the cellular level to aerobic mitochondrial dysfunction. Lactate is the product of anaerobic metabolism and thus may serve as a prognostic factor in this subset of patients.

OBJECTIVES. The authors propose to test the association of the first serum lactate at hospital admission with shock and ICU mortality in patients with community-acquired severe sepsis.

METHODS. Prospective cohort study off all consecutive patients admitted to a mixed intensive care unit (ICU), at a University Hospital, between 1st of December of 2004 and 31st of May of 2008. Data collected included demographic information, first serum lactate at hospital admission, simplified acute physiology score (SAPS) II and severity of sepsis. A model of logistic regression was built with ICU mortality as dependent variable and gender, age, SAPS II, type of admission, severity of sepsis and serum lactate as independent variables. A similar one was built for shock.

RESULTS. During the study period 1,223 patients were admitted in the unit, of those 300 (25%) had severe community-acquired severe sepsis (CASS). Crude ICU mortality rate among CASS was 33%. Considering the model previously described in methods and when the variables were adjusted only gender, age, SAPS II, severity of sepsis and serum lactate were retained in the final model for ICU mortality and SAPS II nad serum lactate for shock (see Table 1).

TABLE 1 MODEL OF LOGISTIC REGRESSION (SEE METHODS)

		Adjusted OR (95% IC)for ICU mortality	Adjusted OR (95% IC)for shock
Gender, n (%)			
Male	178 (59%)		
Female	122 (41%)	0.505 (0.282–0.905)	
Age (years), mean ± SD	58 ± 17	1.017 (1.000–1.036)	
SAPS II, median (IQR)	45 (37–57)	1.035 (1.014–1.056)	1.044 (1.021–1.067)
Severity of community-acquired sepsis, n (%)			
Severe sepsis	103 (34%)		
Septic shock	197 (66%)	2.211 (1.116–4.383)	
Lactate (mmol/L), median (IQR)	2.30 (1.40–3.82)	1.209 (1.064–1.375)	1.499 (1.234–1.820)

CONCLUSIONS. A first blood lactate level was independently associated with shock and ICU mortality in patients community-acquired severe sepsis admitted in intensive care.

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DELTA CO2 (PVCO2–PACO2) AS A PROGNOSTIC FACTOR IN SEPTIC SHOCK

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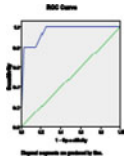
INTRODUCTION. Meeting the goals of resuscitation has shown decreased mortality in septic shock (SC), but still not set an end point to ensure adequate resuscitation. The ΔCO2 (PvCO2–PaCO2) has been proposed as an option.

OBJECTIVES. Correlates the Δ CO2 with the prognosis of SC.

METHODS. During 2009, we included patients with a diagnosis of SC in which all hemodynamic and oxygenation variables required were recorded, we excluded patients who could not collect the data and those who have orders not to attempt resuscitation. Bivariate correlation was performed by Pearson. It was determined statistically significant p values ≤ 0.05. ROC curves were constructed.

RESULTS. A total of 46 patients diagnosed with SC. Gender female 34%, age 62 ± 12 (31–83), APACHE II 23 ± 5 (14–32), days of stay in intensive care 10 ± 5 (7–32), 28-day mortality 10.8%. Lactate at admission 2.7 ± 1.7 (0.8–9.9), mean arterial pressure 76 ± 12 (50–108), central venous pressure 11 ± 3 (4–17); SvcO2 76 ± 8 (59–89), ΔCO2 6 ± 2.6 (1–11). The area under the ROC curve (AUR) for ΔCO2 at admission was 0.954, with a cutoff of 7.5, with a sensitivity (sen) of 100% and a specificity (sp) of 80% (CI 65%). The ΔCO2 at 24 h showed an AUR of 0.832, with a cutoff of 6.5 with a sen of 80% and a sp of 80% (CI 95%), with $p = 0.05$.

CONCLUSIONS. A cutoff value ΔPCO2 > 6 mmHg in the first 24 h of SC identifies patients with poor prognosis and that perhaps could benefit from more aggressive therapy resuscitation.



ROC curve initial

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THENAR MICRO-OXYGENATION IN SEPTIC SHOCK USING THE NEW DEVICE INSPECTRA 650: RELATION TO MACRO- AND MICROHEMODYNAMIC AND OUTCOME

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INTRODUCTION. Among the techniques assessing microperfusion, near infrared spectroscopy (NIRS) gained interest. More than baseline StO_2 values, the reperfusion slope after a vascular occlusion test (VOT) was the most discriminating parameter to assess microperfusion abnormalities [1, 2]. The new NIRS device (Model 650) differs from the previous Model 325 in depth of measurement (15 vs. 25 mm) and output data (1 value/2 s vs. 1 value/3.5 s), which might lead to differences in the information provided.

OBJECTIVES. To verify in septic shock (SS) using model 650 if NIRS parameters, especially the reperfusion slope, was relating with macro-hemodynamic parameters and outcome similarly to previous publications.

METHODS. Patients were prospectively included within the first 24 h of SS. SAPS II and SOFA scores, macro-hemodynamic (mean arterial pressure (MAP), cardiac output (CO), $ScvO_2$ or SvO_2); metabolic (pH, Base Excess and lactate) parameters were collected. Microperfusion data consisted in: NIRS (baseline StO_2, occlusion and reperfusion slopes (%/s), automated software); skin laser Doppler microflow (baseline flow (TPU), peak flow (TPU) and slope during reperfusion (TPU/s), measured during and after a 3 min VOT. Survivors (S) and non-survivors (NS) values were compared using non-parametric methods.

RESULTS. Median ± IQR. Fifty-five patients were included having a 29% mortality rate at day 28. SAPS II [50 (41–59) vs. 61 (58–70), $p = 0.003$] and SOFA [9 (8–11) vs. 12 (10–14), $p = 0.01$] differed between S and NS at day 1. Macro-hemodynamic and metabolic data did not differ between S and NS, except for lactate [1.92 (1.23–2.52) vs. 4.97 (1.92–11.98), $p = 0.006$]. Regarding microperfusion data, baseline StO_2 was similar between S and NS, StO_2 reperfusion slope during the first 24 h was lower in NS 0.85 (0.54–1.28) versus S (1.86 (0.90–3.53), $p = 0.02$. Laser Doppler data did not differ between S and NS. StO_2 reperfusion slope correlated with MAP (rho = 0.22, $p = 0.003$), pH (rho = 0.36, $p < 0.0001$), and negatively with SAPS II (rho = −0.35, $p = 0.009$), SOFA (rho = −0.33, $p = 0.013$), lactate (rho = −0.22, $p = 0.005$) and occlusion slope (rho = −0.3, $p < 0.0001$), but not with CO. Using univariate analysis, both SOFA at 24 h and reperfusion slope predicted similarly outcome over 28 days, with no improvement when they were combined (ROC curve).

CONCLUSIONS. This study shows different values for StO_2 measurement with the new device compared to the previous one. However, the determinants seemed to be equivalent, except for CO and MAP. Even reperfusion slope did not improve the prediction of SOFA, it was related to outcome as previously reported. We can conclude that if the number coming from the 2 machines cannot be pooled, their relations with other parameters are almost the same in SS than previously published.

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SVO_2 DOES NOT PREDICT FLUID RESPONSIVENESS IN CRITICALLY ILL SEPTIC PATIENTS

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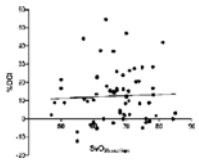
INTRODUCTION. Mixed venous oxygen saturation (SvO_2) is typically elevated in septic patients due to hyperdynamic conditions. Whether patients with elevated SvO_2 can still be fluid responsive has not been well defined.

OBJECTIVES. The objective of this study was to test whether SvO_2 can predict fluid responsiveness in these patients.

METHODS. We studied 65 patients who were monitored with a pulmonary artery catheter for severe sepsis and septic shock. Hemodynamic measurements were obtained before (baseline values) and after a fluid challenge with colloids or crystalloids. Responders were defined as those with a >10% increase in cardiac index (CI). No additional interventions were performed during the test. Student's t test and linear correlation were used for the statistical analysis.

RESULTS. Mean patient age was 70 ± 2 years and the mean SOFA score 10 ± 2. Mean arterial pressure was 71 ± 9 mmHg, cardiac index 3.0 ± 0.8 L/min/m^2, pulmonary artery balloon-occluded pressure 13 ± 3 mmHg, and heart rate 104 ± 19 bpm. Thirty-four patients (52%) responded to the fluid challenge. Responders and non-responders had similar baseline SvO_2 (67 ± 9 vs. 67 ± 8%, $p = 0.98$). Baseline SvO_2 was >70% in 13 responders (38%) and in 11 non-responders (35%). There was no correlation between changes in CI (%DCI) and the baseline SvO_2 (Fig. 1).

CONCLUSIONS. Baseline SvO_2 levels do not inform about fluid responsiveness in septic patients. A high SvO_2 does not exclude a positive response to fluid challenge.



SvO2 baseline levels in relation to %DCI

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MICROCIRCULATION IN PATIENTS WITH SEPTIC SHOCK: DOES THE NEUTROPENIA MATTER?

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INTRODUCTION. Sepsis is a disorder of microcirculation [1, 2]. Although the pathogenesis of microvascular dysfunction in sepsis is extremely complex, neutrophil activation and their interaction with endothelial cells are considered central features of sepsis-induced microcirculatory alterations. To our knowledge, however, no study evaluated the microvascular pattern of septic patients with chemotherapy-induced severe leukocytes depletion.

OBJECTIVES. To assess early microcirculatory response to sepsis in patients with and without drug-induced neutropenia.

METHODS. Demographic and hemodynamic variables together with sublingual microcirculation recording (OPS-SDF videomicroscopy) were collected in four groups of subjects: septic shock (SS, N = 9), septic shock in neutropenic patients (NSS, N = 8), neutropenia without inflammation (NEUTR, N = 7) and healthy controls (CRTL, N = 13). Except for controls, all measurements were repeated after complete resolution of septic shock and/or neutropenia (TP2). Collected video-files were processed using appropriate software tool and semi-quantitatively evaluated (functional capillary density, FCD (cm/cm^2); mean flow index, MFI [1]) [3].

RESULTS. Compared to controls, there were statistically significant microcirculatory alterations within all tested groups of patients (MFI: SS = 2.13, NSS = 1.91, NEUTR = 2.13 vs. CTRL = 3.00, $p < 0.05$; FCD: SS = 95.64, NSS = 100.77, NEUTR = 92.93 vs. CTRL = 127.43, $p < 0.001$). No differences were detected between SS, NSS and NEUTR groups. Incomplete restoration of microcirculatory perfusion was observed after septic shock and/or neutropenia resolution.

CONCLUSIONS. Microvascular derangements in sepsis did not differ between non-neutropenic and neutropenic patients. Surprisingly, neutropenia per se without measurable systemic inflammation was also associated with alterations of the sublingual microcirculation. Although we cannot exclude the role of residual neutrophils, our data could indicate that leukocytes are not the only and exclusive modulators of septic microvascular dysfunction. In addition, the role and mechanisms of microvascular changes associated with chemotherapy-induced neutropenia warrants further investigation.

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TIME SEQUENCE OF REACTIVE OXYGEN METABOLITES PRODUCTION AND SOFA SCORE IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Multiple organ failure is a leading cause of death in critically ill patients. Improvements in outcome will most rely on our capacity to measure rapidly accessible biomarkers.

OBJECTIVES. To investigate if the time sequence of Reactive Oxygen Metabolites (ROMs) production with SOFA score could be prognostic for outcome.

METHODS. The study included 33 critically ill patients (from September to December 2009) who had ROMs measured (hydroperoxides) during ICU stay, when the diagnostic criteria for sepsis (observed n = 14), severe sepsis (observed n = 11) and septic shock (observed n = 68) were present, 4–5 days and 3 weeks after the diagnosis (samples n = 93); on the same days, the SOFA score was calculated. The plasma ROMs values were assayed by a Diacron-Italia kit, applied to an automatic instrument (Olimpus AU 640). Statistical analysis was performed used Mann-Whitney test and the linear regression analysis.

RESULTS. The ROMs values and SOFA score were inversely correlated ($r^2 = 0.64$ for sepsis; $r^2 = 0.42$ for severe sepsis; $r^2 = 0.37$ for septic shock). The ΔROMs (the difference between the first and the last measurement of ROMs levels in each individual patient) was significantly different between survivors and non-survivors. Clinical characteristics of the patients are presented in Table 1. Values are presented as median and interquartile rangers. A p value <0.05 was considered as statistically significant.

CONCLUSIONS. The plasma ROMs values decreased when the critically conditions rapidly evolved towards organ failures with higher SOFA.

TABLE 1

variable	Survivors (n = 16)	Non-survivors (n = 17)	p-vlaue
Age (years)	62 (47–74)	77 (62–80)	0.007
Gendere, male sex, n (%)	17 (74)	16 (67)	0.95
SAPS II	45 (31–51)	45 (40–53)	0.52
ROMs (u Carr)	345 (228–441)	132 (76–330)	0.001
ΔROMs	−4 (−54; 43)	102 (61–330)	0.008
Length of ICU stay (days)	16 (9–32)	30 (13–49)	0.24

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KINETICS OF ADIPOSE TISSUE GLUCOSE AND LACTATE DURING CRITICAL SEPSIS

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INTRODUCTION. It remains currently unclear whether sepsis-related metabolic changes in blood are mirrored by changes in the dialysate fluid.

OBJECTIVES. The aim of the present study was to evaluate the relative kinetics of blood and adipose tissue microdialysis (MD)-derived metabolites during critical sepsis.

METHODS. Upon sepsis onset (day 1) a MD catheter was inserted into the subcutaneous adipose tissue of the upper thigh. Dialysate samples were analyzed for glucose and lactate. Sampling was performed 6 times per day for a maximum of 6 days. The daily mean values of MD measurements were calculated for each patient. Arterial blood was analyzed for glucose and lactate concomitantly with dialysate sampling.

RESULTS. Fifty-four mechanically ventilated septic patients (31 men) with a median age of 69 years (range: 21–92 years) were studied. APACHE II and SOFA score at study entry were 21 (range: 5–32) and 8 (range: 1–16) respectively. The septic syndrome was due to sepsis (n = 12), severe sepsis (n = 3) or septic shock (n = 39). Sites of infection included the lung (n = 23, 42%), the gastrointestinal tract (n = 16, 30%), or other (n = 15, 28%). Plasma glucose was consistently higher than tissue glucose; however, they both followed the same pattern of evolution, reaching a peak value on day 2(Fig. 1a). Plasma lactate was lower than MD lactate during the whole observation period, however, they both changed in parallel, with a peak value on day 1(Fig. 1b).

CONCLUSIONS. Blood and tissue metabolites have similar kinetics during the course of critical sepsis. Thus, this technique offers accurate chemical monitoring of the interstitial space in ICU septic patients.

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EFFECTS OF SODIUM BICARBONATE INFUSION ON BLOOD LACTATE LEVELS AND ACID-BASE STATUS IN A RAT MODEL OF TRANSIENT OR SUSTAINED MILD LACTIC ACIDEMIA

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INTRODUCTION. Whether it is worth to correct acidemia by infusion of alkaline solutions is a matter of discussion. There are a number of evidences against the use of alkalinization therapy with respect to the benefits of reversing pH and the side effects of sodium bicarbonate infusion [1]. Nonetheless, as recently shown by means of an on line survey, 67% of critical care physicians administer base to patients with lactic acidosis, many of which considering 7.2 as a target of pH to start treatment [2].

OBJECTIVES. To investigate the effects of bicarbonate infusion on blood lactate levels and acid-base status in a rat model of transient or sustained mild lactic acidemia.

METHODS. A total of 58 Sprague Dawley rats (352 ± 7 g) received a primed endovenous infusion of lactic acid (75 min). If inclusion criteria were met (hemodynamic stability, pH < 7.3, lactate >3 mmol/L), animals were randomized to 60 min of: A) sustained lactic acid infusion, A + B) sustained infusion + sodium bicarbonate, O) transient infusion, B) transient infusion + sodium bicarbonate. In the transient infusion (group O and B), at randomization lactic acid was replaced with normal saline. Acid-base status and lactate levels were measured over time. In a number of animals phosphofructokinase (PFK) enzyme's activity was also measured.

RESULTS. Following lactic acid infusion blood lactate rose (from 1.2 ± 0.07 mmol/L to 5.5 ± 0.23, P < 0.001), pH (from 7.426 ± 0.005 to 7.227 ± 0.009, P < 0.001) and strong ion difference (from 31.92 ± 0.54 mEq/L to 25.27 ± 0.88, P < 0.001) drop. Bicarbonate infusion normalized pH during sustained infusion of lactic acid (from 7.22 ± 0.02 to 7.36 ± 0.04 in group A + B, P < 0.001) while overshoot to alkalemic values when the infusion was transient (from 7.24 ± 0.01 to 7.53 ± 0.03 in group B, P < 0.001). Lactate rose during sustained infusion of lactic acid irrespective of bicarbonate infusion (7.4 ± 1.6 mmol/L vs. 8.0 ± 1.5, group A vs. group A + B, P = 0.670). It was higher when acid load was interrupted and bicarbonate infused (2.9 ± 1 mmol/L vs. 1 ± 0.2, group B vs. group O, P < 0.001). Bicarbonate infusion quadruplicated lactate wash-out half life (P < 0,05) and affected PFK enzyme (P = 0.067), the activity of which was correlated with blood pH ($R^2 = 0.475$, P = 0.019).

CONCLUSIONS. The effects of bicarbonate infusion differ during sustained or transient lactic acidemia. Unnecessary use of alkali perturb acid-base status and lactate metabolism potentially overcoming metabolic adaptive strategies.

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1370

STRONG IONS GAP IN SEPSIS AS OUTCOME PREDICTOR

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INTRODUCTION. Strong Ions Gap (SIG) quantifies unmeasured blood anions and it is calculated by the difference between strong cations and strong anions (all of them, dissociated in blood plasma). SIG were calculated as follows [1]:

Apparent strong ions difference (SIDa) = $(Na^+ + K^+ + Ca^{2+} + Mg^{2+}) - (Cl^- + \text{lactate})$

Effective strong ions difference (SIDe) = $2.46 \times 10^{-8} \times PCO_2/10_{pH} + A$ (A^- = protein anions: Albumin + P)

SIG = SIDa − SIDe

OBJECTIVE. To evaluate the usefulness of SIG calculation in septic shock patients correlating it with well known severity scales.

METHODS. Retrospective, observational study of all patients with septic shock as defined by the American–European consensus, admitted to the ICU from February 2009 to August 2009. Demographics, arterial blood gases, albumin, lactate and electrolytes were obtained at admittance and 24 h later; APACHE and SOFA score, central venous saturation and lactate were obtained in the same moments and were compared with SIG.

RESULTS. 30 patients with septic shock were included, 15 female (50%) and 15 male, with mean age of 73 ± 14 (35–95) years, mean blood pressure 49 ± 12 (30–70) mmHg, white blood cells 14,000 ± 1,200 (13,000–17,000), bands 9 ± 2% (6–13), creatinine 1 ± 0.2 (0.6–1.5). Results are shown in Table 1.

TABLE 1

	Admittance	24 h	p value
pH	7.3 ± 0.04 (7.28–7.43)	7.38 ± 0.02 (7.33–7.45)	<0.0001
$PaCO_2$	34.9 ± 4 (25–42)	36 ± 2 (36–40)	NS
HCO_3	18 ± 2.7 (12–24)	22 ± 1.3 (19–25)	<0.001
Bases	−3.9 ± 3.6 (−11 to −2)	5 ± 1.4 (−2 to −3)	<0.001
Anion Gap	20 ± 3.9 (13–29)	12 ± 1.6 (10–16)	<0.001
Lactate	2.8 ± 1.5 (0.7–6)	1.3 ± 0.5 (0.5–2.3)	<0.001
SIG	30 ± 2.6 (25–35)	23 ± 2 (20–27)	<0.001
SVO_2	64 ± 7.8 (50–86)	73 ± 4.2 (69–85)	<0.001
APACHE	22 ± 2 (17–27)	17 ± 1 (14–20)	<0.001
SOFA	9.4 ± 1.1 (8–13)	7.8 ± 0.6 (7–9)	<0.001

Expected values (APACHE, SOFA, SvO_2, lactate, acidosis) improved 24 h later after reanimation as well as SIG (p < 0.001). Best correlation of SIG was with APACHE at admittance (r = 0.89) and 24 h later (r = 0.75). Figure 1.

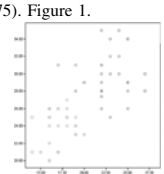

Figure 1

CONCLUSIONS. Calculation of SIG is as useful as APACHE, SOFA, SvO_2 and lactate in septic patients. Prospective studies to determine if it can predict mortality should be done.

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1371

SERUM HSP70 LEVELS, OXIDANT STATUS AND MORTALITY IN SEPSIS

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INTRODUCTION. Sepsis is an infection-initiated, inflammation-induced syndrome resulting from a complex interaction between host and infectious agents (Angus et al. 2001). The up-regulation of HSP expression and increased HSP levels inside cells was observed to exert protective effects against a variety of cellular stressors such as hypoxia, excess oxygen radicals, endotoxin, infections, and fever (Tang et al. 2007).

OBJECTIVES. To evaluate the relationship between serum HSP70 immunocontent and oxidant status in sepsis and establish a correlation with clinical outcome.

METHODS. Fifteen patients admitted to a general intensive care unit (ICU) with severe sepsis were included in the study. Up to a maximum of 12 h after sepsis diagnosis serum was collected for determination of HSP70 immunocontent by western blot and evaluation of oxidative parameters (TRAP, TBARS and carbonyl levels). For animal studies, male Wistar adult rats were subjected to animal model of sepsis (cecal ligation and puncture, CLP) or sham-operated. Immediately and 12 h after, all groups received volemic resuscitation, and the animals were divided in Sham or CLP (6 h, 12 h, 24 h and 48 h). Bronchoalveolar fluid (BALF) and serum were collected from animals. The results are expressed as means ± SE and statistical significance was assigned to $P < 0.05$.

RESULTS. HSP70 levels were increased in BALF and serum of rats subjected to CLP in a time-dependent manner; serum of sepsis patients also presented enhanced HSP70 levels. TRAP analysis of the serum indicated that sepsis patients were sub-grouped patients presenting a more pro-oxidant state (TRAP values at 140% of control), or a general antioxidant state (TRAP values at 10% of control). TBARS and carbonyl levels of the septic pro-oxidant group were significantly increased in relation to control and septic antioxidant patients. Besides, serum HSP70 levels were significantly enhanced only in pro-oxidant patients, the antioxidant septic patients had no difference in relation to control. Analysis of serum HSP70 levels in septic patients according survival outcome also indicated that HSP70 increase was correlated to mortality.

CONCLUSIONS. Serum HSP70 levels are modulated according to the oxidant status and increased serum HSP70 is associated to mortality in sepsis, while markers of oxidant damage in showed variable degrees of association to sepsis outcome.

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1372

SUPPRESSED NEUROPEPTIDE LEVELS AND ASSOCIATION WITH DISEASE SEVERITY AND PAIN LEVELS IN PATIENTS WITH MULTIPLE ORGAN DYSFUNCTION SYNDROME (MODS)

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INTRODUCTION. Critically ill patients experience high levels of stress. The pathophysiologic sequelae of stress in patients with MODS and cellular effects of stress neuropeptides have not been studied.

OBJECTIVES.

To explore:

(a) stress neuropeptides (ACTH, cortisol, prolactin, neuropeptide Y (NPY) and substance P (SP)) in critically ill subjects and controls,

(b) potential association between levels of stress neuropeptides, disease severity and pain.

METHODS. A prospective correlational study, with repeated measurements and cross-sectional comparisons. Fifty-three critically ill patients with diverse primary diagnoses and 53-age and gender-matched healthy controls were studied for 8 days. Serum neuropeptides were quantified by ELISA (NPY, SP) and chemiluminescence immunoassays (ACTH, cortisol, prolactin). Pain levels were assessed by Payen and Puntillo scales. Clinical severity was quantified by Multiorgan Failure Scoring System (MOF) and the Multiple Organ Dysfunction Score (MODS).

RESULTS. We observed:

(a) statistically significant differences between critically ill and control subjects in regard with cortisol ($p < 0.0001$), NPY ($p < 0.0001$) and SP ($p < 0.05$) levels throughout the study. Specifically, cortisol levels were higher and NPY and SP levels were lower in patients compared to controls,

(b) significant bivariate associations between stress neuropeptides ($p < 0.04$),

(c) statistically significant associations between ACTH and pain intensity levels assessed by Payen ($r = 0.391$, $p = 0.018$) and Puntillo ($r = 0.509$, $p = 0.002$) scales. There was also a constant but not statistically significant ($p = 0.1$) trend for lower SP levels in patients receiving opioids than in controls. Moreover, NPY levels were significantly lower in patients receiving analgesia ($p = 0.042$),

(d) lower ACTH and cortisol levels in survivors ($p < 0.05$)

(e) at the day of least severity, a significant association between SP levels and MOF was observed ($r = 0.29$, $p < 0.05$).

CONCLUSIONS. (a) Despite the fact that NPY and SP are stress neuropeptides, their levels appear to be decreased in MODS patients. It is worth-exploring whether critical illness may be a state of suppressed activity of some neuropeptides,

(b) the observed association between stress neuropeptide levels and survival in critical illness needs to be explore further,

(c) bedside measurement of selected neuropeptides in the future may provide an estimation of pain in uncommunicative patients.

Hence, the study of stress neuropeptides may provide new insight for the management of the critically ill.

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DECREASED PARAOXONASE ACTIVITY AND INCREASED LIPID PEROXIDATION IN CRITICALLY ILL PATIENTS WITH SEPSIS AND SYSTEMIC INFLAMMATION

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INTRODUCTION. Paraoxonase 1 is thought to play a role in preventing lipid oxidation and thus limiting production of proinflammatory mediators. Systemic inflammatory response increases oxidative stress.

OBJECTIVES. The objective of this study was to compare septic and non-septic inflammatory process in critically ill patients with respect to paraoxonase 1 activity, lipid profile and lipid peroxidation markers.

METHODS. Analyzed were serum paraoxonase 1 activity, lipid profile, oxidized low density lipoproteins and conjugated dienes in critically patients with sepsis n = 30), age/sex/APACHEII matched critically ill controls with non-septic SIRS (n = 15) and age/sex matched outpatient controls without inflammation (n = 30).

RESULTS. The activity of PON 1 was lower in septic patients (96.7 ± 47.4 U/ml) as well as in patients with non-septic SIRS (107.8 ± 39.8 U/ml) compared to healthy controls (158 ± 40.5 U/ml). The decrease in paraoxonase 1 activity, high density lipoprotein cholesterol and apolipoprotein A-1 concentrations was closely followed by the counter increase of serum amyloid A in both groups of patients. There was no difference in paraoxonase 1 activity between septic and non-septic critically ill patients. The concentration oxidized low density lipoproteins and conjugated dienes as markers of lipid peroxidation, were raised in both septic and non-septic SIRS critically ill patients as compared with healthy controls. However there was no difference between both critically ill patient groups.

CONCLUSIONS. The decreased activity of paraoxonase 1 in negative correlation with lipid peroxidation markers offers a potentially useful nonspecific marker of inflammation in critically ill patients.

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DIFFERENCES IN ENDOGENOUS VASOPRESSIN LEVELS BETWEEN SEPTIC SHOCK PATIENTS WITH OR WITHOUT HYDROCORTISONE THERAPY

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INTRODUCTION. Recent evidence indicates that combined hydrocortisone and arginine vasopressin (AVP) therapy in septic shock increases AVP plasma levels [1, 2] and may improve survival [2]. The mechanism of hydrocortisone-induced increases in AVP plasma levels remains unknown but could include enhanced release of endogenous AVP and/or decreased AVP clearance.

METHODS. This is a *post hoc* analysis of a prospective study performed in a surgical intensive care unit (ICU) from November 2005 to November 2006. Within 36 h after ICU admission, endogenous AVP plasma levels were measured in sepsis patients during the need for vasopressor support at 24 hourly intervals during 7 days. Patients <19 years, with central nervous system injury, known pathology of the AVP system, treatment with exogenous AVP before or during the study period or who refused written informed consent were excluded. Demographic and clinical data as well as the use of hydrocortisone therapy (200–300 mg/day) were documented. A Mann Whitney *U* test and multivariate linear regression model were used for statistical analysis.

RESULTS. Forty-five sepsis patients [median age, 62 (IQR, 47–37) years; admission SAPS II, 45 (33–53) pts; severest Multiple Organ Dysfunction Syndrome Score, 9 (8–10) pts; ICU-mortality, 15.6%] required vasopressor support despite adequate fluid resuscitation at ICU admission or at some time point afterwards and were included into the present analysis. Twenty-three (51.1%) patients received hydrocortisone and no patient an exogenous AVP infusion. During the observation period, endogenous AVP plasma levels did not differ between septic shock patients treated with or without hydrocortisone [4.2 (2.2–6.2) vs. 4.3 (2.7–6.1) pmol/L] both in a bivariate ($p = 0.43$) and a linear regression model adjusted for differences in disease severity (assessed by admission SAPS II) ($p = 0.38$).

CONCLUSION. No difference in endogenous AVP plasma levels was observed between septic shock patients treated with or without hydrocortisone in this analysis. Our results suggest that an increase in AVP plasma levels during concomitant hydrocortisone and AVP therapy in septic shock [1, 2] results from other mechanisms than a hydrocortisone-induced increase in endogenous AVP plasma levels.

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1375

NOCICEPTIN MRNA EXPRESSION BY NEUTROPHILS IS DOWN-REGULATED DURING CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS

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INTRODUCTION. Nociceptin/Orphanin FQ (N/OFQ) is an endogenous peptide associated with the inflammatory response; the mRNA for its precursor prepro-nociceptin (ppN/OFQ) has been identified in quantitative polymerase chain reaction (qPCR) studies in lymphocytes, monocytes and neutrophils [1, 2]. In vitro nociceptin acts as a pro-inflammatory agent, increasing chemotaxis and lymphocyte proliferation [3, 4]. In vivo it increases leucocyte activity and macromolecular leak in rat mesenteric vessels [5] and increases mortality in a rat model of sepsis [6]. Its role in human sepsis/inflammation is unknown.

OBJECTIVES. To analyse the mRNA expression of N/OFQ (by analysing its precursor ppN/OFQ) by neutrophils during cardiopulmonary bypass (CPB), as a model of the systemic inflammatory response.

METHODS. With ethics committee approval and patient consent we recruited 40 patients undergoing cardiac surgery (coronary artery bypass grafting and/or valve surgery) with CPB under standard general anaesthesia. Three blood samples were taken: at induction of anaesthesia, at 3 and 18–24 h post-CPB. Neutrophils were isolated, mRNA extracted, DNA cleaned and reverse transcribed. ppN/OFQ and GAPDH (Glyceraldehyde 3-phosphate dehydrogenase; used as a housekeeper gene) mRNA was measured by reverse transcriptase-qPCR.

RESULTS. We present the results for 34 patients (24 males, 10 females). Data from 6 patients could not be analysed as ppN/OFQ mRNA was undetermined on RT qPCR of the first sample. The median (IQR) age was 71 (61–76) years, CPB time 89 (80–117) min, aortic cross clamp time 55 (42–70) min and core temperature during CPB 32 (30–32)°C.

PPN/OFQ MRNA ΔCT

	Induction	3 h post-CPB	18–24 h post-CPB
ppN/OFQ mRNA	13.4 (12.3–14.7)	18.3 (16.6–20.3)*	16.9 (15–19.4)*

Median (IQR) ppN/OFQ mRNA concentrations expressed as ΔC_t (difference between ppN/OFQ and GAPDH Cycle threshold C_t,). *$p < 0.05$ compared to induction (by Friedman ANOVA and Dunn's multiple comparison test).

There was an increase in ΔC_t (where one cycle is a doubling of start material), indicating a 96.6% reduction in the expression of mRNA 3 h after onset of CPB.

CONCLUSIONS. During cardiopulmonary bypass there was a significant reduction in ppN/OFQ expression by neutrophils 3 h after CPB, which persisted at 18–24 h after CPB.

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SECRETONEURIN AS A PREDICTIVE MARKER FOR HYPOXIC BRAIN INJURY AFTER CARDIOPULMONARY RESUSCITATION

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INTRODUCTION. The early and precise evaluation of neurological outcome and prognosis of patients after successful cardiopulmonary resuscitation (CPR) is of great importance to determine further therapeutical strategies. Several markers such as serum levels of protein S-100B and neuron-specific enolase (NSE) have already been investigated for their reliability as early predictive markers, but results still remain controversial.

Secretoneurin (SN), a neuropeptide, is specifically expressed in endocrine, neuroendocrine and neuronal tissues but can also be induced by hypoxia in non-endocrine tissues like skeletal muscle cells. SN can also promote neurogenesis. It acts directly on neurons after hypoxia and is elevated in the serum of human stroke patients.

OBJECTIVES. In our study we aimed to evaluate secretoneurin as a new predictive marker for hypoxic brain injury after CPR.

METHODS. We performed a prospective study on all consecutive patients admitted to our intensive care unit after successful CPR. Patients with an observed event and ventricular tachycardia/fibrillation as first monitored rhythm underwent mild therapeutic hypothermia (MTH) using an intravascular cooling device targeting at a temperature of 33°C for 24 h. NSE and serum SN concentrations were measured daily up to 10 days using a radioimmunoassay (RIA). Neurological outcome was determined according to the Glasgow Outcome Scale (GOS) at ICU discharge.

RESULTS. 38 patients were enrolled in our study (29 men, 9 women) with a mean age of 62.16 ± 13.13 years. 15 of 38 (40%) patients were treated with MTH, 14 patients had good outcome (GOS 4 + 5) and 24 bad outcome (GOS 1 + 2 + 3).The mean SN levels of all patients were elevated compared to normal values (reference value: 20–22 [fmol/ml]). An about twofold increase above normal was observed on ICU admission (54.31 ± 23.87), returning to normal values within the following days (day 1: 37.41 ± 20.90 and day 2: 32.47 ± 25.14). When comparing patients with good outcome to those with bad outcome, we could detect a significant difference between SN levels at day 0 and day 1 (42.72 ± 16.99 vs. 67.55 ± 24.67; $p = 0.048$ and 26.72 ± 9.12 vs. 46.57 ± 23.95; $p = 0.012$). Furthermore, SN levels on day 0 and 1 significantly correlated with bad outcome. NSE levels were also elevated in our population over the first 5 days with a peak on day 2 (100.84 ± 162.14 µg/l). Patients with bad outcome had significantly higher NSE levels than patients with good outcome (day 0: 38.11 ± 15.21 vs. 20.74 ± 5.59; $p = 0.0001$ and day 3: 80.58 ± 43.7624 vs. 17 ± 13.15; $p = 0.010$).

CONCLUSIONS. Secretoneurin seems to be a promising new marker for the early prediction of hypoxic brain injury after CPR.

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SHORT-TERM EFFECTS OF INTRAVENOUS IMMUNOGLOBULIN ON CHANGES IN THE LEVELS OF CYTOKINES AND HMGB1 IN PATIENTS WITH SEPSIS

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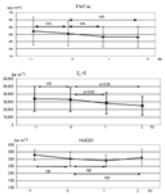
INTRODUCTION. Previous reports have indicated that intravenous immunoglobulin preparation (IVIG) reduces some types of inflammatory cytokines.

OBJECTIVES. In the present study, we studied the short-term and direct effects of IVIG with sepsis.

METHODS. 16 patients was investigated. Following the administration of 5 g of IVIG for 1 h, we took blood samples immediately following IVIG treatment and at 1 h after IVIG treatment. Blood samples taken at 1 h and just prior to IVIG administration were used as controls.

RESULTS. While there was no difference between 1 h before and just prior to IVIG treatment, statistically significant decreases were observed in the levels of IL-6 after the administration of IVIG. No significant changes were observed in the levels of tumor necrosis factor-α and high mobility group box-1.



Changes in serum TNFα, IL-6, HMGB1

CONCLUSIONS.

We confirmed the results of previous animal studies. While we reported that the administration of IVIG directly reduces the levels of IL-6 in patients with sepsis, a further prospective study of the ant-cytokine effects following IVIG treatment will be conducted in the near future.

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TIME COURSE OF PLASMA NUCLEOSOME LEVELS IN SEPSIS

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INTRODUCTION. Nucleosome, complexes of DNA and histone proteins, are released from dying and stressed cells into the blood circulation. Recent studies have shown that DNA and histone proteins may play an important role in the pathogenesis of sepsis. Little is known about the time course of circulating levels of nucleosome in septic patients.

OBJECTIVES. To investigate the levels of nucleosome in septic patients and to determine whether nucleosome could serve as a biomarker for sepsis.

METHODS. Sixty-four consecutive patients who were newly admitted in surgical intensive care unit at two university hospitals were enrolled in this study. Whole blood samples were drawn within 12 h of admission and on the third, fifth and seventh days. A last blood sample was drawn after recovery at ICU discharge in survivors or at imminent death in the cases of non-survivors. Plasma levels of nucleosome as well as cytokines IL-6 and IL-10 were detected by means of enzyme linked immunosorbent assay.

RESULTS. Fifty patients were diagnosed as sepsis and the other fourteen patients were classified as controls. Plasma levels of nucleosome were significantly higher in septic patients than in controls (two-way ANOVA, $p < 0.05$), while the levels of IL-6 and IL-10 were comparable between septic patients and controls. The septic patients presented the highest levels of nucleosome on the admission day, which was significantly different from the admission levels of nucleosome in controls (4.16 ± 3.48 vs. 1.61 ± 1.36, $p < 0.05$). The plasma levels of nucleosome between survivors and nonsurvivors showed no statistical significance.

CONCLUSIONS. Plasma levels of nucleosome may serve as a valuable biomarker for sepsis.

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TIME COURSE OF ENDOGENOUS NITRIC OXIDE INHIBITORS IN HUMAN SEVERE SEPSIS

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INTRODUCTION. Asymmetric and Symmetric dimethylarginines (ADMA, SDMA) are protein-breakdown markers; both compete with arginine for cellular transport and are excreted in urine. Moreover, ADMA is a non-selective inhibitor of nitric-oxide (NO) synthase, metabolized by a specific hydrolase whose activity in stress remains controversial. While ADMA increase is associated with adverse events, little is known about SDMA.

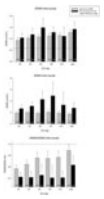
OBJECTIVES. We investigated plasma ADMA and SDMA levels during ICU stay to reveal the time-course of endogenous NO-inhibition during sepsis.

METHODS. Post-hoc analysis from a prospective RCT conducted in 3 ICUs, to study pathophysiological pathways of sepsis. ADMA, SDMA, their ratio (marker of ADMA catabolism), arginine, Interleukin-6(IL-6), Tumor-Necrosis-Factor-α (TNF-α), C-Reactive-Protein(CRP) on day 1, 3, 6, 9, 12 and at discharge in 72 consecutive severely-septic patients were measured.

RESULTS. Fasting basal glycaemia, creatinine, IL-6, TNF-α, CRP, ADMA, SDMA were higher than normal, ADMA/SDMA ratio was halved, arginine was low. ADMA was related to total SOFA and arginine, inversely related to IL-6 and CRP; SDMA was related to SAPS II, SOFA, blood urea, creatinine, arginine. ADMA/SDMA ratio was inversely related to IL-6.

In 58 ICU-survivors, creatinine, IL-6, CRP decreased over time; ADMA increased, SDMA remained stable, ADMA/SDMA ratio increased. In 14 non-survivors, creatinine, IL-6, TNF-α, CRP and ADMA were stable, SDMA increased, ADMA/SDMA ratio remained low. In both groups last ICU day confirms data trends. SDMA but not ADMA was associated to ICU-mortality.

In Figure: time course of ADMA and SDMA blood levels (mean ± standard error) during ICU stay and the last ICU day (Last); the dotted line represents the upper reference range.



Time course of ADMA and SDMA levels

CONCLUSIONS. ADMA catabolism seems to be activated during the full-blown septic phase; its increase in the advanced septic phase in surviving patients may suggest an endogenous inhibition of NO synthesis. In severe sepsis SDMA, but not ADMA, appears to be a marker of alterations in vital functions and mortality.

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HIGH-MOBILITY GROUP BOX 1 PROTEIN-HMGB-1 LEVELS AS PREDICTORS OF OUTCOME IN PATIENTS WITH SEPSIS AND SEPTIC SHOCK

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INTRODUCTION. High Mobility Group Box protein 1 (HMGB-1) is a cytokine that can mediate inflammatory response in different conditions included rheumatoid arthritis, infections, sepsis and septic shock. HMGB-1 released by activated macrophages/monocytes acts as a late mediator of sepsis. Studies have shown that serum HMGB-1 concentrations were elevated in patients with severe sepsis**.**

OBJECTIVES. In the present study, we evaluated the role of the HMGB-1 levels at the time of admission at the Intensive Care Unit (ICU) as predictor of outcome in patients with sepsis and septic shock.

METHODS. Forty-four Patients admitted to the ICU with sepsis and septic shock was recruited. Serum samples were obtained at the time of admission for the determination of HMGB-1 levels. The results were correlated with the origin of sepsis, severity, organ dysfunction, requirements of mechanical ventilation and vasoactives, days at the ICU, comorbidities and mortality at the ICU and 28 days after admission.

RESULTS. Twenty-six patients were male (68.2 vs. 31.8%). Septic shock was present in 28 patients (63.6%). The mortality rate at the ICU was 31.8% (n = 14) and 38.6% (n = 17) at day 28th. HMGB-1 levels were 34.7 ng/mL ± 39.02 (1.34–230.2 ng/mL). HMGB-1 levels were significantly higher in non-survivors at the ICU than in survivors (56.81 ng/mL ± 58.69 vs. 24.38 ± 19.18, $p < 0.05$). Higher levels of HMGB-1 in serum at the admission were correlated with a higher mortality rate in the ICU ($p < 0.05$) but not at day 28th ($p = 0.07$). These levels were not correlated with days at the ICU, requirements of vasoactives, mechanical ventilation, and APACHE score.

CONCLUSIONS. The determination of HMGB-1 levels at admission at the ICU in patients with sepsis and septic shock is a good predictor of worse outcome and lethality.

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DECREASED CIRCULATING DENDRITIC CELLS IN SHOCK: A SEVERE SEPSIS MARKER

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INTRODUCTION. Sepsis represents a complex clinical syndrome of significant morbidity and mortality. Patients with sepsis often demonstrate severely impaired immune responses. Recently, diminished numbers of dendritic cells (DCs) were reported in patients with septic shock. Early low DCs counts may be correlated to disease severity and could predict fatal outcome. However, little is known about DC number in other shock than septic.

OBJECTIVES. To evaluate and compare the circulating DCs number in patients with severe sepsis, septic or cardiogenic shock.

METHODS. In a prospective multicentric study (3 ICU), consecutive immunocompetent patients with severe sepsis (SS), septic shock, cardiogenic shock were included. Peripheral blood DC counts, measured by flow cytometry, were evaluated and compared between the three populations at admission and 24 h later. Correlation to disease severity evaluated by clinical scores and day 28 mortality was studied.

RESULTS. 100 patients were included (age 61 ± 14 years, 56 male, SOFA D0 10.5 ± 3.9, SAPS II 61 ± 18): 49 septic shock, 16 severe sepsis and 22 cardiogenic shock. Mortality at D28 was respectively 43, 14 and 59%. 13 patients presented a sepsis associated to cardiogenic shock. At baseline and at day 1, a dramatic diminution in the numbers of total DCs either myeloid (MDCs) or plasmacytoid (PDCs), was observed in sepsis (severe sepsis or septic shock) compared to cardiogenic shock patients. No difference was seen between severe sepsis and septic shock patients (Fig. 1). We did not observe any correlation between the number of total DCs at admission or at day 1 and severity of illness scores (SAPS II, SOFA and LOD score).The number of DCs is not different between non-survivors and survivors at day 28 in septic shock (Fig. 2).

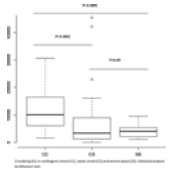

Fig. 1

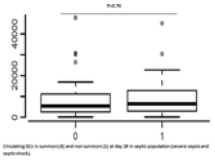

Fig. 2

CONCLUSIONS. DC reduced number is a valuable marker of severe sepsis in shock and is not affected by hemodynamic changes. It could not be used as a prognostic marker in severe septic patients.

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PRELIMINARY RESULTS FROM A PROSPECTIVE STUDY ASSESSING THE RELATIONSHIP BETWEEN STANDARD LABORATORY COAGULATION AND GLOBAL TESTS OF CLOT-FORMATION USING THROMBOELASTOGRAPHY IN PATIENTS WITH FULMINANT HEPATIC FAILURE

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BACKGROUND. The routine use of International normalized ratio (INR) to establish the coagulation status in patients with fulminant hepatic failure (FHF) may be misleading. Anecdotally, FHF patients, despite a significantly deranged INR, may display a normal or even hypercoagulable state, as recently shown, albeit in an extracorporeal setting, with frequently clotted circuits, despite raised PT, in FHF patients requiring renal replacement therapy [1].

AIM. To assess if standard laboratory coagulation tests truly reflect the coagulation state of patients with FHF.

METHODS. We prospectively studied coagulation, demographic, survival and outcome measures of FHF patients (defined by de-novo liver failure, coagulopathy-INR >1.5, and encephalopathy) admitted to the Royal Free Hospital liver and/or intensive care unit(s) (ICU), a tertiary referral centre in liver diseases and transplantation, between November 2009 to April 2010. Samples were analysed 0 and 48 h post-admission, for standard clotting tests (INR, PT, APTT, Fibrinogen and Platelets) and TEG (native, heparinase, functional fibrinogen).

RESULTS. We present the standard clotting tests and TEG results from 10 (of a required 20) patients currently enrolled, demonstrating variable degrees of encephalopathy and coagulopathy. 6/10 had paracetamol or other drug-induced FHF and the remaining 4 (2 each) being seronegative and ischaemic in aetiology. 3/10 proceeded to transplantation while 2/10 died (1 post-transplantation). The (mean ± SD) standard clotting results within our FHF patients were indicative of a marked hypocoagulable state, with a raised INR (3.88 ± 2.81), PT (46.72 ± 35.07), APTT (40.76 ± 14.94) and fibrinogen (1.99 ± 0.73). In contrast, TEG was suggestive of a hypocoagulable state in only 2/10 patients, one of which was hypercoagulable. R-time, usually reflecting clotting time, when plotted against INR exhibited wide scatter ($r^2 = 0.0566$).

CONCLUSION. In FHF, coagulation abnormalities are extremely heterogeneous and not fully reflected by standard laboratory tests. TEG, in conjunction with standard tests of coagulation may provide better understanding of individual patient's coagulation status.

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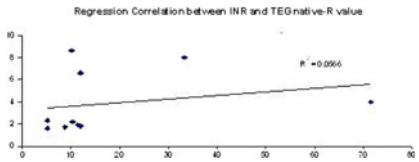

Coagulation in FHF

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MONOCYTE CD40 EXPRESSION IN SEPTIC PATIENTS

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INTRODUCTION. Recent experimental and clinical data (1, 2) support the hypothesis that costimulatory molecules, such as CD40, play an essential role in the innate immune response during sepsis. Expression of CD40 on the surface of monocytes could represent an important pathway in the modulation of the production of several key inflammatory mediators.

OBJECTIVES. To investigate whether the expression of CD40 molecule on the surface of plasma monocytes differs among the various stages of sepsis.

METHODS. A total of 32 participants (12 ICU patients with sepsis, 14 ICU patients with septic shock and 6 healthy controls) were included in the study (male patients 73.1%, mean age 46.6 ± 16.8 years). Inclusion criteria: ICU patients on mechanical ventilation with first episode of sepsis or septic shock during current hospitalization. Exclusion criteria: immunosuppression, neoplasia, autoimmune disease, cardiovascular disease. Age, gender and comorbid conditions were recorded. A blood sample for quantification of CD40 expression was obtained at the time of enrollment (day 1), and on the fifth day after the onset of sepsis; measurement was made on the same day. CD40 expression on the surface of plasma monocytes (on days 1 and 5) was assessed by flow cytometric analysis. Statistical analysis: Kruskal-Wallis test to identify difference of CD40 expression among the 3 groups was performed. Post-hoc analysis was made by Mann–Whitney U test between independent groups, using Bonferroni correction for multiple comparisons. ROC curve analysis was used to determine the accuracy of CD40 in identifying patients with sepsis or septic shock.

RESULTS. Patients with sepsis had significantly higher levels of CD40 (day 1) compared with healthy controls subjects (0.86 ± 0.41 vs. 0.34 ± 0.07, $p \leq 0.006$). On the contrary, patients with septic shock did not show any significant difference compared with controls. A ROC curve analysis for CD40 (day 1) (AUC = 0.72, $p \leq 0.05$), revealed that a cut-off value of 0.53 could predict patients with sepsis with a sensitivity of 91% and a specificity of 57%.

CONCLUSIONS. Upregulation of CD40 expression may reflect a protective phenomenon during sepsis. On the contrary, low CD40 expression could represent impaired immune function associated with more severe disease.

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GASTRIC EMPTYING IN THE SEPTIC SHOCK PATIENT WITH NOREPINEPHRINE

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INTRODUCTION. In order to increase the cardiac output in the septic shock patients, according to surviving sepsis campaign team, norepinephrine (NE) or dopamine administration was recommended. The both agents increase the sympathetic tone which antagonize against parasympathetic activity used for gastrointestinal motility (involved gastric emptying). Then, it is raised a question whether NE delayed the gastric emptying or not.

OBJECTIVES. This study was aimed to evaluate the gastric emptying in the septic shock patients with norepinephrine.

METHODS. A prospective observational study involved 54 adult septic shock patients, who received NE continuously in ICU Sardjito General Hospital (Yogyakarta, Indonesia). Patients with any head pathologies (trauma, surgical procedures for tumor or bleeding), any gastrointestinal or abdominal pathologies (diarrhea, trauma, surgical procedures for cancer, peritonitis, ileus etc.), and administrations of *metochlopramide* or *alinamin* were excluded. Nutrition fluids (100 ml) was given passively via nasogastric tube, then after 60 min the tube was aspirated. The volumes of aspirates were recorded in % as a gastric residue. Once measurement was done with time randomly for every patient. At the measurement time were recorded the dose of NE and the vital signs.

RESULTS. The gastric residues were 41.76 ± 28.11% (17 patients), 45.46 ± 25.27% (13 patients) and 13.57 ± 8.52% (7 patients) for the doses of NE of 0.1, 0.2 and 0.3 μg/kg b.w./min respectively. At the NE doses of 0.4, 0.5 and 0.6 μg/kg b.w./min, all of the gastric residues were zero (17 patients). The correlation between the NE doses and the gastric rescues was statistically significant (*p:* 0.01). The mean arterial pressures (MAP) were 84.16 ± 18.01 mmHg (ranges from 58 to 120 mmHg. There was no significantly correlation between MAP and the gastric residues.

CONCLUSIONS. The gastric emptying in the septic shock patients was not disturbed by administration of NE.

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THE EFFECT OF PHLEBOTOMY ON CYTOKINE PRODUCTION OF HUMAN WHOLE BLOOD

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INTRODUCTION. Anemia is a frequently encountered problem on the intensive care unit. Several factor lead to anemia, among which are traumatic blood loss and the drawing of blood for routine laboratory tests. It's not known how this may affect innate immunity. Hepcidin is a central regulator of iron homeostasis. It is induced in response to iron and inflammation and reduced in response to anemia and hypoxia. The suppression of hepcidin leads to the internalization and degradation of the iron exporter ferroportin on intestinal cells and macrophages, leading to the uptake of iron from the gut and the release of iron from the macrophages from the reticulo-endothelial system (RES). These cells are central to the innate immune response and the altered iron status of these cells due to suppression of hepcidin may affect the inflammatory response of these cells. We tested the hypothesis that phlebotomy in human volunteers would lead to a suppression of the innate immune response. This abstract provides data of a pilot study carried out in 3 subjects.

OBJECTIVES. To investigate the effect of phlebotomy on the innate immune response of whole blood in human volunteers.

METHODS. Three volunteers were subjected to the letting of 400 ml of blood by phlebotomy. Blood for the determination of hemoglobin and iron parameters, leucocyte count and differential, and hepcidin-25 was drawn at day 0, 4 and 7 after phlebotomy. Further whole blood stimulation was carried out at each time point by adding 0.5 ml heparin anticoagulated whole blood to a prepared tube containing endotoxin, pam3cis or RPMI as a control. Final concentrations of LPS and P3C were 10 ng/ml and 1 μg/ml respectively. These tubes were incubated at 37°C for 24 h and centrifuged for 10 min at 4,000 *g*. The supernatant was frozen at −80 until the measurement of TNF-alfa and IL-6 by ELISA. Cytokine production was corrected for the number of monocytes present. Data are expressed as mean ± SEM.

RESULTS. Hemoglobine decreased from 8.5 ± 0.3 mmol/l at baseline to 8.0 ± 06 at day 4. It returned to normal at day 7. There were no apparent changes in serum iron levels. There was however a clear decrease in serum ferritin levels from 162 ± 48 at baseline to 109 + 46 at day 7. Leucocyte count and differentiation did not show any significant changes. Hepcidin was clearly suppressed from 4 to day 7 after phlebotomy (from 6 ± 1 to 2 ± 1). TNF-alfa production dropped from 81 to 47 ng/10^7 monocytes at day 7. IL-6 production dropped from 327 to 195 ng/10^7 monocytes. Hepcidin levels correlated well with cytokine production (r^2 0.53 for TNF-alfa, r^2 0.51 for IL-6).

CONCLUSIONS. Phlebotomy leads to suppression of the innate immune response in whole blood. This could be a result of the intracellular decrease of iron in immune cells due to the systemic suppression of hepcidin. These findings are relevant to critical care patients that are subject to the repeated drawing of blood while their immune system is often compromised.

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EFFECT OF TEMPERATURE, HYPOTHERMIA AND HYPERTHERMIA, ON THE GEL POINT, FRACTAL DIMENSION AND STRUCTURE AND STRENGTH OF A BLOOD CLOT

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INTRODUCTION. Hypothermia and hyperthermia occur in many pathological states presenting to the emergency department. Both these processes are known to significantly impair coagulation pathways but as yet there is little evidence to show what affect they have on the evolving clot structure. Previous studies have attempted to determine the effect of temperature on whole blood coagulation using techniques such as thromboelastometry (TEG) but its ability to provide meaningful outcomes in terms of clot quality and structure remains elusive. Recent studies have highlighted the potential of a new technique, Gel Point (GP) and Fractal Dimension (d_f), as a functional biomarker in haemostasis.

OBJECTIVES. To explore both the changes in coagulation pathways and their associated effect on clot structure and quality based on the new biomarkers, GP and df.

METHODS. Following full ethical approval, 30 healthy whole blood samples were obtained from individuals and tested at temperatures of 27°C (n − 6), 31°C (n − 6), 35°C (n − 6), 37°C (n − 6), 41°C (n − 6). An oscillatory shear technique [1] using an AR-G2 Instrument (TA Instruments) was applied to each sample. The GP, which indicates the formation of the fibrin network, was obtained for each sample using the Chambon-Winter Gel Point criterion [2]. This method provides the basis from which d_f can be determined [3] to interpret the structural properties of the clot network. The results were compared with the standard TEG analysis.

RESULTS. Firstly**,** results showed a significant progressive change in the clot structure by this new biomarker across the whole temperature range (27–43°C). Secondly, it also highlighted a significant and meaningful correlation between coagulation pathway change (Time to GP, TGP) and the eventual clot outcome (fractal dimension). The TGP of the incipient clot was prolonged and the corresponding d_f decreased with reduced temperature values. Although, the changes in the coagulation pathway of the TEG (R time) and the rheometer (TGP) correlated, the new biomarker, d_f, provided additional structural data on the fibrin network formed and highlighted the relationship between coagulation pathway changes and the eventual fibrin clot structure.

CONCLUSIONS. In this study, we describe and quantify for the first time how temperature affects the coagulation pathways and how this impacts on the fibrin clot network, morphology and strength by using the new biomarkers, GP and d_f. The potential of these new biomarkers in determining the effects of temperature change in critical illness and injury needs to be evaluated clinically.

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