Effects of alveolar recruitment maneuvers on clinical outcomes in patients with acute respiratory distress syndrome: a systematic review and meta-analysis

**Conclusions**

Although ARMs may decrease the mortality of patients with ARDS without increasing the risk for major adverse events, current evidence is not definitive. Large-scale ongoing trials addressing this question may provide data better applicable to clinical practice.
A randomized clinical trial of an intervention to relieve thirst and dry mouth in intensive care unit patients

**Purpose:** To test an intervention bundle for thirst intensity, thirst distress, and dry mouth, which are among the most pervasive, intense, distressful, unrecognized, and undertreated symptoms in ICU patients, but for which data-based interventions are lacking.

**Methods:** This was a single-blinded randomized clinical trial in three ICUs in a tertiary medical center in urban California. A total of 252 cognitively intact patients reporting thirst intensity (TI) and/or thirst distress (TD) scores ≥3 on 0–10 numeric rating scales (NRS) were randomized to intervention or usual care groups. A research team nurse (RTN#1) obtained patients’ pre-procedure TI and TD scores and reports of dry mouth. She then administered a thirst bundle to the intervention group: oral swab wipes, sterile ice-cold water sprays, and a lip moisturizer, or observed patients in the usual care group. RTN#2, blinded to group assignment, obtained post-procedure TI and TD scores. Up to six sessions per patient were conducted across 2 days.
Results: Multilevel linear regression determined that the average decreases in TI and TD scores from pre-procedure to post-procedure were significantly greater in the intervention group (2.3 and 1.8 NRS points, respectively) versus the usual care group (0.6 and 0.4 points, respectively) \((p < 0.05)\). The usual care group was 1.9 times more likely than the intervention group to report dry mouth for each additional session on day 1.

Conclusion

This simple, inexpensive thirst bundle significantly decreased ICU patients’ thirst and dry mouth and can be considered a practice intervention for patients experiencing thirst.
Methods: This was a multicenter non-blinded randomized noninferiority trial of patients with severe sepsis who were randomly assigned to de-escalation or continuation of empirical antimicrobial treatment. Patients with severe sepsis were assigned to de-escalation ($n = 59$) or continuation of empirical antimicrobial treatment ($n = 57$). The primary outcome was to measure the duration of ICU stay. We defined a noninferiority margin of 2 days. If the lower boundary of the 95% confidence interval (CI) for the difference in patients assigned to the de-escalation group was less than 2 days, as compared with that of patients assigned to the continuation group, de-escalation was considered to be noninferior to the continuation strategy.

Results: The median duration of ICU stay was 9 [interquartile range (IQR) 5–22] days in the de-escalation group and 8 [IQR 4–15] days in the continuation group, respectively ($P = 0.71$). The mean difference was 3.4 (95% CI −1.7 to 8.5). A superinfection occurred in 16 (27%) patients in the de-escalation group and 6 (11%) patients in the continuation group ($P = 0.03$). The numbers of antibiotic days were 9 [7–15] and 7.5 [6–13] in the de-escalation group and continuation group, respectively ($P = 0.03$). Mortality was similar in both groups.

Conclusion: As compared to the continuation of the empirical antimicrobial treatment, a strategy based on de-escalation of antibiotics resulted in prolonged duration of ICU stay. However, it did not affect the mortality rate.
De-escalation strategy

After the results of the antibiogram of the suspected causative bacteria were available, the “pivotal” antibiotic used for empirical treatment was switched to an antibiotic with a spectrum as narrow as possible according to the targeted pathogens. The companion drug (aminoglycoside or fluoroquinolone or macrolide) was stopped at day 3. The choice of antibiotics was based on international guidelines. The empirical antibiotics directed against methicillin-resistant Staphylococcus aureus (MRSA) were stopped if MRSA was not identified in microbiological cultures. For the purpose of this study, de-escalation was considered if the pivotal antibiotic was switched for an antibiotic with a narrower spectrum than the empirical treatment, according to a ranking of molecules provided in Electronic Supplementary Material Table 2. The companion drug and the antibiotic used against MRSA were eliminated after inclusion.

Continuation strategy

After randomization, the pivotal antibiotic of the empirical treatment was continued for the entire duration of the treatment, independently of microbiological results (although the treatment should be active against the identified pathogen). For prolonged treatment (>15 days), the physician had the choice of de-escalating after 8–15 days of treatment. The companion antibiotic (aminoglycoside or fluoroquinolone or macrolide) was stopped between day 3 and day 5. Empirical antibiotics directed against MRSA were used according to international guidelines.
Purpose: Risk factors for β-lactam antibiotic underdosing in critically ill patients have not been described in large-scale studies. The objective of this study was to describe pharmacokinetic/pharmacodynamic (PK/PD) target non-attainment envisioning empirical dosing in critically ill patients and considering a worst-case scenario as well as to identify patient characteristics that are associated with target non-attainment.

Methods: This analysis uses data from the DALI study, a prospective, multi-centre pharmacokinetic point-prevalence study. For this analysis, we assumed that these were the concentrations that would be reached during empirical dosing, and calculated target attainment using a hypothetical target minimum inhibitory concentration (MIC), namely the susceptibility breakpoint of the least susceptible organism for which that antibiotic is commonly used. PK/PD targets were free drug concentration maintained above the MIC of the suspected pathogen for at least 50% and 100% of the dosing interval respectively ($fT_{\geq MIC}$). Multivariable analysis was performed to identify factors associated with inadequate antibiotic exposure.
Results: A total of 343 critically ill patients receiving eight different β-lactam antibiotics were included. The median (interquartile range) age was 60 (47–73) years, APACHE II score was 18 (13–24). In the hypothetical situation of empirical dosing, antibiotic concentrations remained below the MIC during 50% and 100% of the dosing interval in 66 (19.2%) and 142 (41.4%) patients respectively. The use of intermittent infusion was significantly associated with increased risk of non-attainment for both targets; creatinine clearance was independently associated with not reaching the 100% \( fT_{>MIC} \) target.

Conclusions: This study found that—in empirical dosing and considering a worst-case scenario—19% and 41% of the patients would not achieve antibiotic concentrations above the MIC during 50% and 100% of the dosing interval. The use of intermittent infusion (compared to extended and continuous infusion) was the main determinant of non-attainment for both targets; increasing creatinine clearance was also associated with not attaining concentrations above the MIC for the whole dosing interval. In the light of this study from 68 ICUs across ten countries, we believe current empiric dosing recommendations for ICU patients are inadequate to effectively cover a broad range of susceptible organisms and need to be reconsidered.
A data-driven approach to optimized medication dosing: a focus on heparin

Methods: We identified available clinical features which impact patient response to heparin and extracted 1,511 patients from the multi-parameter intelligent monitoring in intensive care II database which met our inclusion criteria. These were used to develop two multivariate logistic regressions, modeling sub- and supra-therapeutic activated partial thromboplastin time (aPTT) as a function of clinical features. We combined information from these models to estimate an initial heparin dose that would, on a per-patient basis, maximize the probability of a therapeutic aPTT within 4–8 h of the initial infusion. We tested our model’s ability to classifying therapeutic outcomes on a withheld dataset and compared performance to a weight-alone alternative using volume under surface (VUS) (a multiclass version of AUC).

Results: We observed statistically significant associations between sub- and supra-therapeutic aPTT, race, ICU type, gender, heparin dose, age and Sequential Organ Failure Assessment scores with mean validation AUC of 0.78 and 0.79 respectively. Our final model improved outcome classification over the weight-alone alternative, with VUS values of 0.48 vs. 0.42.

Conclusions: This work represents an important step in the secondary use of health data in developing models to optimize drug dosing. The next step would be evaluating whether this approach indeed achieves target aPTT more reliably than the current weight-based heparin dosing in a randomized controlled trial.
Methods: This nationwide, population-based, propensity score-matched analysis used data from the linked administrative databases of Taiwan’s National Health Insurance program. Patients were hospitalized for sepsis between 2000 and 2010. All-cause mortality and major adverse consequences of sepsis, such as in-hospital death, intensive care unit admission, shock events, and the use of mechanical ventilation, were assessed. Patients were divided into high-potency statin users (at least 10 mg rosvuastatin, at least 20 mg atorvastatin, or at least 40 mg simvastatin), low-potency statin users (all other statin treatments), and non-users.

Results: A propensity score-matched cohort of 27,792 statin users and 27,792 non-users was included. Of 27,792 statin users, 9,785 (35.2%) were treated with high-potency statins and 18,007 (64.8%) were treated with low-potency statins. The 1-year mortality risk was significantly lower among both low-potency [adjusted hazard ratio (aHR) 0.89, 95% confidence interval (CI) 0.85–0.93] and high-potency (aHR 0.80, 95% CI 0.75–0.86) statin users compared with non-users. The risks of mortality and adverse consequences of sepsis were lower among high-potency than among low-potency statin users.

Conclusions

High-potency statin use is associated with a lower risk of sepsis-related mortality compared with low-potency statin use.
Dexamethasone pretreatment for 24 h versus 6 h for prevention of postextubation airway obstruction in children: a randomized double-blind trial

Methods: Hundred twenty-four children (3 months to 12 years) intubated for ≥48 h and planned to have extubation during next 24 h were randomized to receive 24hPD (0.5 mg/kg/dose, q6h, total of six doses; n = 66) or 6hPD (total of three doses; n = 58). Patients with preexistent upper airway conditions, chronic respiratory diseases, steroid therapy in last 7 days, gastrointestinal bleeding, hypertension, and hyperglycemia and those likely to have poor airway reflexes were excluded.

Results: The two groups were similar at baseline. 24hPD reduced the incidence of PEAO (43/66 versus 48/58; p = 0.027) with absolute risk reduction of 17 %. It also reduced the incidence of reintubation, though nonsignificantly, by half [5/61 versus 9/58; relative risk (RR), 1.09; 95 % confidence interval (CI), 0.96–1.25]. Time to recovery from PEAO among non-reintubated patients was shorter among 24hPD patients (p = 0.016). No adverse event was noted with dexamethasone use. Intubation duration >7 days and cuffed tracheal tubes were found to be independent risk factors for PEAO (odds ratio 6 and 3.12, respectively).

Conclusions

24-h pretreatment with multidose dexamethasone reduced the incidence of PEAO and the time to recover from it. 24hPD should be considered for high-risk children intubated for >48 h in the study setting. Further studies with larger sample size from different socioeconomic background are desirable to validate these findings.
Pediatric cancer type predicts infection rate, need for critical care intervention, and mortality in the pediatric intensive care unit

Methods: We performed a retrospective multicenter analysis of 10,365 PICU admissions of cancer patients no greater than 21 years old among 112 PICUs between 1 January 2009 and 30 June 2012. We evaluated the effect of cancer type, age, gender, genetic syndrome, stem cell transplantation, PRISM3 score, infections, and critical care interventions on PICU mortality.

Results: After excluding scheduled perioperative admissions, cancer patients represented 4.2 % of all PICU admissions (10,365/246,346), had overall mortality of 6.8 % (708/10,365) vs. 2.4 % (5,485/230,548) in the general PICU population (RR = 2.9, 95 % CI 2.7–3.1, p < 0.001), and accounted for 11.4 % of all PICU deaths (708/6,215). Hematologic cancer patients had greater median PRISM3 score (8 vs 2, p < 0.001), rates of sepsis (27 vs 9 %, RR = 2.9, 95 % CI 2.6–3.1, p < 0.001), and mortality (9.6 vs 4.5 %, RR = 2.1, 95 % CI 1.8–2.5, p < 0.001) compared to solid cancer patients. Among hematologic cancer patients, stem cell transplantation, diagnosis of acute myeloid leukemia, PRISM3 score, and infection were all independently associated with PICU mortality.

Conclusions: Children with cancer account for 4.2 % of PICU admissions and 11.4 % of PICU deaths. Hematologic cancer patients have significantly higher admission illness severity, rates of infections, and PICU mortality than solid cancer patients. These data may be useful in risk stratification for closer monitoring and patient counseling.
Validation of the KDIGO acute kidney injury criteria in a pediatric critical care population

- **Purpose:** Acute kidney injury (AKI) occurs commonly in critically ill children and has been associated with increased mortality of up to 50%. The Kidney Disease: Improving Global Outcomes (KDIGO) AKI working group has proposed a standardized definition of AKI. Utilizing routinely available clinical data, we evaluated the KDIGO AKI criteria and the relationship of AKI with relevant outcomes in a single center tertiary pediatric intensive care (PICU) and cardiac intensive care unit (CICU) population.

- **Methods:** The University of Michigan Pediatric Critical Care Database was probed for all discharges from the pediatric intensive care and cardiac intensive care units between July 2011 and October 2013 ($N = 4,645$). The KDIGO serum creatinine (SCr)-based criteria staged AKI with the modification that a minimum SCr of greater than 0.5 mg/dL was required to be classified as AKI. Exclusion: end-stage renal disease, new renal transplant, missing PRISM III data, or no measured Cr during intensive care unit (ICU) admission ($N = 1,636$).

- **Results:** AKI occurred in 737 (24.5%, stage I = 193, stage II = 189, and stage III = 355) of 3,009 discharges (PICU $N = 1,870$, CICU $N = 1,139$) that included 2,415 patients. In multivariate analysis AKI was associated with increased ICU length of stay (LOS) in hours (I $\beta = 42.2$, $p = 0.024$, II $\beta = 74.1$, $p = 0.003$, III $\beta = 215.8$, $p < 0.001$). Multivariate analysis showed that AKI was associated with increased odds of ICU mortality (OR 3.4, 95% CI 2.0–6.0) and increased length of mechanical ventilation among those requiring mechanical ventilation ($\beta = 2.3$ days, $p < 0.001$).

- **Conclusions:** Using the KDIGO criteria to define AKI, we observed a high prevalence of AKI among critically ill children. Worsening stages of AKI were associated with increased ICU LOS, and AKI was independently associated with prolonged mechanical ventilation and increased mortality. The KDIGO criteria describe clinically relevant AKI in a broad pediatric critical care population.

**Purpose** To analyze trends in incidence and mortality of candidemia in intensive care units (ICUs) vs. non-ICU hospitalized patients and to determine risk factors for infection by specific species and for death.

**Results**

Among 2,507 adult cases included, 2,571 Candida isolates were collected and species were *C. albicans* (56%), *C. glabrata* (18.6%), *C. parapsilosis* (11.5%), *C. tropicalis* (9.3%), *C. krusei* (2.9%), and *C. kefyr* (1.8%). Candidemia occurred in ICU in 1,206 patients (48.1%). When comparing ICU vs. non-ICU patients, the former had significantly more frequent surgery during the past 30 days, were more often preexposed to fluconazole and treated with echinocandin, and were less frequently infected with *C. parapsilosis*. Risk factors and age remained unchanged during the study period. A significant increased incidence in the overall population and ICU was found. The odds of being infected with a given species in ICU was influenced by risk factors and preexposure to fluconazole and caspofungin. *Echinocandins initial therapy* increased over time in ICU (4.6% first year of study, to 48.5% last year of study, \( p < 0.0001 \)). ICU patients had a higher day-30 death rate than non-ICU patients (odds ratio [OR] 2.12; 95% confidence interval [CI] 1.66–2.72; \( p < 0.0001 \)). The day-30 and early (<day 8) death rates increased over time in ICU (from 41.5% the first to 56.9% the last year of study (\( p = 0.001 \)) and 28.7–38.8% (\( p = 0.0292 \), respectively). Independent risk factors for day-30 death in ICU were age, arterial catheter, *Candida* species, preexposure to caspofungin, and lack of antifungal therapy at the time of blood cultures results (\( p < 0.05 \)).

**Conclusions:** The availability of new antifungals and the publication of numerous guidelines did not prevent an increase of candidemia and death in ICU patients in the Paris area.
Methods: This study was a retrospective analysis of 1,392 episodes of candidemia in 647 adult ICU patients from 22 Brazilian hospitals. The characteristics of candidemia in these ICU patients were compared in two periods (2003–2007, period 1; 2008–2012, period 2), and the predictors of 30-day mortality were assessed.

Results: The proportion of patients who developed candidemia while in the ICU increased from 44 % in period 1 to 50.9 % in period 2 ($p = 0.01$). Prior exposure to fluconazole before candidemia (22.3 vs. 11.6 %, $p < 0.001$) and fungemia due to *Candida glabrata* (13.1 vs. 7.8 %, $p = 0.03$) were more frequent in period 2, as was the proportion of patients receiving an echinocandin as primary therapy (18.0 vs. 5.9 %, $p < 0.001$). The 30-day mortality rate decreased from 76.4 % in period 1 to 60.8 % in period 2 ($p < 0.001$). Predictors of 30-day mortality by multivariate analysis were older age, period 1, treatment with corticosteroids and higher APACHE II score, while treatment with an echinocandin were associated with a higher probability of survival.

Conclusions

We found a clear change in the epidemiology and clinical management of candidemia in ICU patients over the 9-year period of the study. The use of echinocandins as primary therapy for candidemia appears to be associated with better outcomes.
Candida in the respiratory tract secretions of critically ill patients and the impact of antifungal treatment: a randomized placebo controlled pilot trial (CANTREAT study)

Methods: We conducted a double-blind, placebo-controlled, multicenter pilot randomized trial of antifungal therapy in critically ill patients with a clinical suspicion of ventilator-associated pneumonia with positive airway secretion specimens for Candida spp. We also included an observational group without Candida spp. in their airway secretions. We measured recruitment rate, inflammatory and innate immune function profiles over time, and clinical outcomes.

Results: We recruited 60 patients into the randomized trial and 29 patients into the observational study. Markers of inflammation and all clinical outcomes were comparable between placebo and antifungal treatment group at baseline and over time. At baseline, plasma TNF-α levels were higher in patients with VAP and Candida compared to the observational group (mean ± SD) (21.8 ± 23.1 versus 12.4 ± 9.3 pg/ml, p = 0.02) and these patients had lower innate immune function as evidenced by reduced whole blood ex vivo LPS-induced TNF-α production capacity (854.8 ± 855.2 versus 1,559.4 ± 1,290.6 pg/ml, p = 0.01).

Conclusions: This study does not provide evidence to support a larger trial examining the efficacy of empiric antifungal treatment in patients with a clinical suspicion of ventilator-associated pneumonia and Candida in the endotracheal secretions. The presence of Candida in the lung may be associated with persistent inflammation and immunosuppression.
Introduction: For decades, clinicians dealing with immunocompromised and critically ill patients have perceived a link between Candida colonization and subsequent infection. However, the pathophysiological progression from colonization to infection was clearly established only through the formal description of the colonization index (CI) in critically ill patients. Unfortunately, the literature reflects intense confusion about the pathophysiology of invasive candidiasis and specific associated risk factors.

Methods: We review the contribution of the CI in the field of Candida infection and its development in the 20 years following its original description in 1994. The development of the CI enabled an improved understanding of the pathogenesis of invasive candidiasis and the use of targeted empirical antifungal therapy in subgroups of patients at increased risk for infection.

Results: The recognition of specific characteristics among underlying conditions, such as neutropenia, solid organ transplantation, and surgical and nonsurgical critical illness, has enabled the description of distinct epidemiological patterns in the development of invasive candidiasis.

Conclusions: Despite its limited bedside practicality and before confirmation of potentially more accurate predictors, such as specific biomarkers, the CI remains an important way to characterize the dynamics of colonization, which increases early in patients who develop invasive candidiasis.
Semi-quantification of pneumothorax volume by lung ultrasound

**Background:** Lung ultrasound (LUS) may accurately diagnose pneumothorax. However, there is uncertainty about its usefulness in the quantification of pneumothorax size. To determine the ability of LUS in the semi-quantification of pneumothorax volume, we compared the projection of the lung point (LP) with the pneumothorax volume measured by computerized tomography (CT) and the interpleural distance on chest radiography (CXR).

**Methods:** We performed LUS in patients with pneumothorax and all the LP located on the chest wall were compared to CXR and CT studies. The primary outcome of the study was the ability of LP to grade pneumothorax volumes measured by CT. The secondary outcome was the accuracy of LP to predict small and large pneumothorax according to the societal guidelines based on CXR reading.

**Results:** A total of 124 patients with pneumothorax were enrolled (76 spontaneous, 20 traumatic and 28 post-procedural). Ninety-four CXR and 58 CT were available for the analysis. An LP posterior to the mid axillary line corresponded to three different CXR criteria for large pneumothorax with sensitivity from 81.4 to 88.2 % and specificity from 64.7 to 72.6 %. The mid axillary line also represented the limit for predicting greater than 15 % of lung collapse when volume is measured at CT, with sensitivity 83.3 % and specificity 82.4 %.

**Conclusions:** LUS-targeted assessment of LP was a useful predictor of pneumothorax volume in this research study setting. LUS reliably classified pneumothorax size when compared to criteria based on CXR reading, particularly the small sized pneumothorax. However, LUS greatly outperformed conventional CXR reading for a graded quantification of the percentage of lung collapse.
Early lung ultrasonography predicts the occurrence of acute respiratory distress syndrome in blunt trauma patients

**Methods:** Forty-five blunt trauma patients were prospectively studied. Clinical examination, chest radiography, and LUS were performed on arrival at the emergency room. Lung contusion extent was quantified using a LUS score and compared to CT scan measurements. The ability of the LUS score to predict ARDS was tested using the area under the receiver operating characteristic curve (AUC-ROC). The diagnostic accuracy of LUS was compared to that of combined clinical examination and chest radiography for pneumothorax, lung contusion, and hemothorax, with thoracic CT scan as reference.

**Results:** Lung contusion extent assessed by LUS on admission was predictive of the occurrence of ARDS within 72 h (AUC-ROC = 0.78 [95% CI 0.64–0.92]). The extent of lung contusion on LUS correlated well with CT scan measurements (Spearman’s coefficient = 0.82). A LUS score of 6 out of 16 was the best threshold to predict ARDS, with a 58% [95% CI 36–77] sensitivity and a 96% [95% CI 76–100] specificity. The diagnostic accuracy of LUS was higher than that of combined clinical examination and chest radiography: (AUC-ROC) 0.81 [95% CI 0.50–1.00] vs. 0.74 [0.48–1.00] ($p = 0.24$) for pneumothorax, 0.88 [0.76–1.00] vs. 0.69 [0.47–0.92] ($p < 0.05$) for lung contusion, and 0.84 [0.59–1.00] vs. 0.73 [0.51–0.94] ($p < 0.05$) for hemothorax.

**Conclusions**

LUS on admission identifies patients at risk of developing ARDS after blunt trauma. In addition, LUS allows rapid and accurate diagnosis of common traumatic thoracic injuries.
Ultrasonic identification and semiquantitative assessment of uniloculated pleural effusions in critically ill patients by residents after a focused training

- **Purpose:** Chest ultrasonography is currently a required element to achieve competence in general critical care ultrasound (GCCUS) which should be part of the training of every intensivist. We sought to assess the ability of resident novices in ultrasonography to identify and quantify uniloculated pleural effusions in ICU patients after a limited training program.

- **Methods:** A total of 147 patients (mean age, 62 ± 17 years; simplified acute physiology score II, 35 ± 15; 78 % ventilated) with a suspected pleural effusion underwent a thoracic ultrasonography performed successively by a recently trained resident novice in ultrasound and by an experienced intensivist with expertise in GCCUS, considered as reference. Ultrasonographic examinations were performed randomly and independently. In the presence of a pleural effusion, the maximal interpleural distance was measured at the thoracic base.

- **Results:** Residents performed a mean of 15 ± 9 examinations. Agreement between residents and experienced intensivists for the diagnosis of left- and right-sided pleural effusions was good to excellent [kappa 0.74 (95 % CI 0.63–0.85) and 0.86 (95 % CI 0.78–0.94), respectively]. Agreement for the measurement of left and right maximal interpleural distance was excellent (intraclass concordance coefficient, 0.86 [95 % CI 0.77–0.91] and 0.85 [95 % CI 0.75–0.90], respectively). Mean bias for left and right interpleural distance was −0.3 mm (95 % CI −2.4, 1.8 mm) and −1.2 mm (95 % CI −3.4, 1.1 mm), respectively.

- **Conclusions:** After a focused training program, resident novices in ultrasound identify and quantify uniloculated pleural effusions in ICU patients using chest ultrasonography with a good agreement with experts.
The association of targeted temperature management at 33 and 36 °C with outcome in patients with moderate shock on admission after out-of-hospital cardiac arrest: a post hoc analysis of the Target Temperature Management trial

- **Methods**
  - Shock was defined as a systolic blood pressure of <90 mm Hg for >30 min or the need of supportive measures to maintain a blood pressure ≥90 mmHg and/or clinical signs of end-organ hypoperfusion.
  - In this post hoc analysis reported here, we further analyzed the 139 patients with shock at admission; all had been randomized to receive intervention at 33 °C (TTM33; n = 71) or 36 °C (TTM36; n = 68).
  - Severity of circulatory shock assessed by mean arterial pressure, serum lactate, fluid balance and the extended Sequential Organ Failure assessment (SOFA) score.

- **Results**
  - There was no significance difference between targeted temperature management at 33 °C or 36 °C on 180-day mortality [log-rank test, \( p = 0.17 \), hazard ratio 1.33, 95% confidence interval (CI) 0.88–1.98] or ICU mortality (61 vs. 44 %, \( p = 0.06 \); relative risk 1.37, 95 % CI 0.99–1.91). Serum lactate and the extended cardiovascular SOFA score were higher in the TTM33 group (\( p < 0.01 \)).

- **Conclusions**
  - We found no benefit in survival or severity of circulatory shock with targeted temperature management at 33 °C as compared to 36 °C in patients with shock on admission after OHCA.
Trends in admission prevalence, illness severity and survival of haematological patients treated in Dutch intensive care units

Methods: A total of 1,741 haematological and 60,954 non-haematological patients admitted to the medical ICU were analysed.

Results

The proportion of haematological patients among all medical ICU patients increased over time [odds ratio (OR) 1.06; 95% confidence interval (CI) 1.03–1.10 per year; p < 0.001]. Risk-adjusted mortality was significantly higher for haematological patients admitted to the ICU with white blood cell (WBC) counts of <1.0 × 10⁹/L (47%; 95% CI 41–54%) and ≥1.0 × 10⁹/L (45%; 95% CI 42–49%), respectively, than for patients admitted with chronic heart failure (27%; 95% CI 26–28%) and with chronic liver cirrhosis (38%; 95% CI 35–42%), but was not significantly different from patients admitted with solid tumours (40%; 95% CI 36–45%). Over the years, the risk-adjusted hospital mortality rate significantly decreased in both the haematological and non-haematological group with an OR of 0.93 (95% CI 0.92–0.95) per year. After correction for case-mix using the APACHE-II score (with WBC omitted), a WBC <1.0 × 10⁹/L was not a predictor of mortality in haematological patients (OR 0.86; 95% CI 0.46–1.64; p = 0.65). We found no case–volume effect on mortality for haematological ICU patients.
**Survival in solid cancer patients following intensive care unit admission**

- **Purpose:** One in seven patients admitted to intensive care units (ICU) has a cancer diagnosis but evidence on their expected outcomes after admission has not been synthesised.

- **Methods:** Systematic literature review of solid cancer adult patients admitted to ICU from 2000 onwards using EMBASE and MEDLINE electronic databases.

- **Results**
  - There were 48 papers identified that reported survival in ICU patients with solid cancers. ICU mortality was reported in 35 studies comprising a total sample of 25,339 patients and ranging from 4.5 to 85%. The average mortality of the distribution of reported mortality rates within ICU was 31.2% (95% CI 24.0–39.0%). Hospital mortality was reported in 31 studies across a total sample of 74,061 patients. The average hospital mortality was 38.2% (33.8–42.7%) and ranged from 4.6 to 76.8%. **Poorer physiological score, invasive mechanical ventilation and poor functional status** were associated with higher mortality.

- **Conclusions**
  - Several factors have been associated with poor survival in ICU cancer patients; however, primary research is still needed to describe outcomes in cancer patients with sufficient case mix and treatment details to be of prognostic value to clinicians.
Introduction: After-hours discharge from the intensive care unit (ICU) is associated with adverse patient outcomes including increased ICU readmissions and mortality. Since Australian and New Zealand data were last published, overall ICU patient mortality has decreased; however it is unknown whether changes in discharge practices have contributed to these improved outcomes. Our aim was to examine trends over time in discharge timing and the contemporary associations with mortality and ICU readmission.

Methods: Retrospective cohort study using data from the Australian and New Zealand Intensive Care Society Adult Patient Database (ANZICS APD) for patients admitted to Australian and New Zealand ICUs between January 2005 and December 2012. Data collected included patient characteristics, time of ICU discharge, hospital mortality and ICU readmissions.

Results: Between 1 January 2005 and 31 December 2012, there were 710,535 patients available for analysis, of whom 109,384 (15.4 %) were discharged after-hours (1800–0600 hours). There were no changes in timing of ICU discharge over the 8 years of the study. Patients discharged after-hours had a higher hospital mortality (6.4 versus 3.6 %; P < 0.001) and more ICU readmissions (5.1 versus 4.5 %; P < 0.001) than patients discharged in-hours. Although post-ICU mortality for all patients declined during the study period, the risk associated with after-hours discharge remained elevated throughout (odds ratio 1.34, 95 % confidence intervals 1.30–1.38).

Conclusions

After-hours discharge remains an important independent predictor of hospital mortality and readmission to ICU. Despite widespread dissemination this evidence has not translated into fewer after-hours discharges or reduction in risk in Australian and New Zealand hospitals.
Eligibility for organ donation following end-of-life decisions: a study performed in 43 French intensive care units

- **Purpose:** A persistent shortage of available organs for transplantation has driven French medical authorities to focus on organ retrieval from patients who die following the withdrawal of life-sustaining therapy. This study was designed to assess the theoretical eligibility of patients who have died in French intensive care units (ICUs) after a decision to withhold or withdraw life-sustaining therapy to organ donation.

- **Methods:** This was an observational multi-center study in which data were collected on all consecutive patients admitted to any of the 43 participating ICUs during the study period who qualified for a withholding/withdrawal procedure according to French law. The theoretical organ donor eligibility of the patients once deceased was determined a posteriori according to current medical criteria for graft selection, as well as according to the withholding/withdrawal measures implemented and their impact on the time of death.

- **Results:** A total of 5,589 patients were admitted to the ICU during the study period, of whom 777 (14 %) underwent withholding/withdrawal measures. Of the 557 patients who died following a foreseeable circulatory arrest, 278 (50 %) presented a contraindication ruling out organ retrieval. Of the 279 patients who would have been eligible as organ donors regardless of measures implemented, cardiopulmonary support was withdrawn in only 154 of these patients, 70 of whom died within 120 min of the withdrawal of life-sustaining treatment. Brain-injured patients accounted for 29 % of all patients who qualified for the withholding/withdrawal of treatment, and 57 % of those died within 120 min of the withdrawal/withholding of treatment.

- **Conclusion**

A significant number of patients who died during the study period in French ICUs under withholding/withdrawal conditions would have been eligible for organ donation. Brain-injured patients were more likely to die in circumstances which would have been compatible with such practice.
Purpose: The response of the hypothalamic–pituitary–adrenal (HPA) axis to the sustained stress of sepsis has been the focus of study in recent years because the early phase of sepsis is known to be dominated by major alterations in the HPA axis. This prospective observational study aimed at assessing the predictive values of copeptin and HPA hormones in determining sepsis progression and mortality in the emergency department (ED).

Methods: Serum arginine vasopressin (AVP) and copeptin concentrations were measured upon ED admission. Baseline levels of total and free cortisol and adrenocorticotropic hormone (ACTH) were measured within 24 h of ED admission. Mortality in Emergency Department Sepsis (MEDS) score was calculated at enrollment.

Results: Our findings demonstrated that serum copeptin, baseline total cortisol, baseline free cortisol and baseline ACTH concentrations gradually increased, based upon the increasing severity of the disease ($p < 0.001$). Multivariate logistic regression analysis showed that copeptin and total cortisol baseline concentrations were independent predictors of septic shock (odds ratio = 1.034 and 1.355, respectively) and 28-day mortality (odds ratio = 1.039 and 1.499, respectively). The areas under the receiver operating characteristic curve (AUC) for copeptin level in prediction of septic shock was 0.856 and 28-day mortality was 0.826. Importantly, AUC analysis of the combination of copeptin, total cortisol baseline, MEDS score, and procalcitonin level resulted in a more significant prognostic ability than analysis of each parameter alone ($p < 0.001$).

Conclusions: Increased copeptin and HPA hormones baseline levels may provide crucial information for risk stratification in a variety of septic states in the ED. Furthermore, measurements of copeptin level and serum baseline cortisol concentration are promising independent prognostic markers for mortality in patients with severe sepsis or septic shock.
Impact of fluid balance on outcome of adult patients treated with extracorporeal membrane oxygenation

- **Design**: Retrospective observational study.

- **Patients**: 115 patients treated with ECMO for refractory heart failure and 57 patients treated with ECMO for refractory respiratory failure.

- **Methods**: We analysed the association between early daily FB versus hospital and 90-day mortality using multivariable logistic regression model, Cox proportional-hazards model and propensity score.

- **Results**: Fifty-seven per cent of patients had acute kidney injury (AKI) at ECMO initiation, and 60% (n = 103) of patients received continuous renal replacement therapy (CRRT) during ECMO course, beginning at a median of 1 (0–3.5) days after ECMO initiation. Overall 90-day mortality was 24%. Survivors exhibited lower daily FB from day 3 to day 5. After adjustments, Acute Physiology and Chronic Health Evaluation (APACHE) III, CRRT during the first 3 days, major bleeding event at day 1 and positive FB on day 3 were independent predictors of 90-day mortality. **Positive FB at ECMO day 3 remained an independent predictor of hospital and 90-day mortality, regardless of the statistical model used or the inclusion of a propensity score to have positive FB.**

- **Conclusions**: Positive FB at ECMO day 3 is an independent predictor of 90-day mortality. Further interventional studies aimed at testing the value of strategy of tight control of FB during the early ECMO period are now warranted.
Purpose: Assess the relationship between optic nerve sheath diameter (ONSD) measured on bedside portable computed tomography (CT) scans and simultaneously measured intracranial pressure (ICP) in patients with severe traumatic brain injury.

Methods: Retrospective cohort study of 57 patients admitted between 2009 and 2013. Linear and logistic regression were used to model the correlation and discrimination between ONSD and ICP or intracranial hypertension, respectively.

Results: The cohort had a mean age of 40 years (SD 16) and a median admission Glasgow coma score of 7 (IQR 4–10). The between-rater agreement by intraclass coefficient was 0.89 (95% CI 0.83–0.93, \(P<0.001\)). The mean ONSD was 6.7 mm (SD 0.75) and the mean ICP during CT was 21.3 mmHg (SD 8.4). Using linear regression, there was a strong correlation between ICP and ONSD (\(r = 0.74, P<0.001\)). ONSD had an area under the curve to discriminate elevated ICP (≥20 mmHg vs. <20 mmHg) of 0.83 (95% CI 0.73–0.94). Using a cutoff of 6.0 mm, ONSD had a sensitivity of 97%, specificity of 42%, positive predictive value of 67%, and a negative predictive value of 92%. Comparing linear regression models, ONSD was a much stronger predictor of ICP (\(R^2\) of 0.56) compared to other CT features (\(R^2\) of 0.21).

Conclusions

Simultaneous measurement of ONSD on CT and ICP were strongly correlated and ONSD was discriminative for intracranial hypertension. ONSD was much more predictive of ICP than other CT features. There was excellent agreement between raters in measuring ONSD.
Secretoneurin as a marker for hypoxic brain injury after cardiopulmonary resuscitation

**Methods:** This was a prospective observational clinical study. All patients admitted to a tertiary medical intensive care unit after successful CPR with expected survival of at least 24 h were consecutively enrolled from September 2008 to April 2013. Serum SN and neuron-specific enolase were determined in 24 h intervals starting with the day of CPR for 7 days. Neurological outcome was assessed with the Cerebral Performance Categories Scale (CPC) at hospital discharge.

**Results:** A total of 134 patients were included with 49 % surviving to good neurological outcome (CPC 1–2). SN serum levels peaked within the first 24 h showing on average a sixfold increase above normal. SN levels were significantly higher in patients with poor (CPC 3–5) than in patients with good neurological outcome [0–24 h: 75 (43–111) vs. 38 (23–68) fmol/ml, p < 0.001; 24–48 h: 45 (24–77) vs. 23 (16–39) fmol/ml, p < 0.001]. SN determined within the first 48 h showed a receiver operating characteristic (ROC) area under the curve (AUC) of 0.753 (0.665–0.841). NSE in the first 72 h had a ROC-AUC of 0.881 (0.815–0.946). When combining the two biomarkers an AUC of 0.925 (0.878–0.972) for outcome prediction could be reached.

**Conclusions**

SN is a promising early biomarker for hypoxic brain injury. Further studies will be required for confirmation of these results.
Thanks for listening!