Critical care medicine: insights from the American Thoracic Society 2016 Annual Meeting

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The American Thoracic Society 2016 Annual Meeting featured exciting research studies in critical care medicine. Recently, researchers tried to answer the question about the appropriate timing of renal replacement therapy (RRT) in the ICU and we saw an exponential growth of interest in long-term outcomes of ICU survivors. We discuss five of the studies discussed at ATS and their impact on critical care management.

RRT in the ICU: is there an optimal time to start?

Gaudry *et al*. recently published a 31-center trial in France that randomized 620 patients with acute kidney injury to receive either early RRT or delayed RRT and measured 60-day mortality as their primary outcome (1). Inclusion criteria were patients who required mechanical ventilation, and/or catecholamine infusion with concomitant severe acute kidney injury (defined as stage 3 acute kidney injury from the Kidney Disease: Improving Global Outcomes (KDIGO) classification). Patients meeting inclusion criteria were either started within 6 h on RRT or started on RRT if they had severe hyperkalemia, acidosis, pulmonary edema, blood urea nitrogen greater than 112 mg per deciliter, or oliguria more than 72 h. The results—contrary to prior observational trials—showed no difference in mortality at 60 days (48.5% *vs*. 49.7%, P=0.79) and half of the patients in the delayed group did not receive RRT (2,3). Of note, there was a 50-hour delay in initiation of RRT in the delayed group; 55% of patients were started on intermittent hemodialysis (IHD); and the delayed group also had less blood-stream infections (5% *vs*. 10%, P=0.03).

Zarbock *et al*. also recently published a paper investigating this same question (4). While similar in design to the above trial, patients were enrolled if they developed KDIGO stage 2 acute kidney injury, had evidence of at least severe sepsis, and/or use of vasoactive medications, and a plasma neutrophil gelatinase associated lipocalin (NGAL) >150 ng/mL. In contrast to Gaudry's trial, all patients had RRT initiated using continuous veno-venous hemodiafiltration. The primary outcome in this single-center trial with 231 patients was 90-day mortality. There was a clear mortality benefit in the early RRT group (39.3% *vs*. 54.7%, P<0.03) at 90 days, but also improved renal recovery and a decrease in time in the hospital. Although these studies provide some insight into optimal timing of RRT in the critically ill, the debate has not been settled and it seems patient characteristics should guide initiation of RRT (5).

Do patients admitted in the ICU suffer from greater bone turn over and decreased bone mineral density (BMD) compared to the general population?

Patients with critical illness face increased risk of fragility fracture; however, there is no prospective evidence describing the relationship between critical illness and long-term bone loss (6). Orford *et al*. conducted a long-term prospective observational cohort analysis comparing 66 patients who were admitted to the ICU with mechanical ventilation for at least 24 h with population-based control subjects from the Geelong Osteoporosis study (7). Investigators examined patient demographics, ICU interventions, osteoporosis risk factors, serum bone

formation and resorption markers, and BMD at three intervals: ICU baseline, post ICU discharge, and 1 year post ICU discharge. The ICU cohort had significantly greater BMD decrease (anterior-posterior spine, –1.59%; 95% CI, –2.18% to –1.01%; P<0.001, femoral neck –1.20%; 95% CI, –1.69% to –0.70%; P<0.001) and increased estimated 10-year fracture risk for all major fractures (4.85 *vs.* 5.5, P<0.001). This study provides evidence that BMD loss and increased fracture risk occurs in ICU patients and offers a new area for further intervention and investigation.

Do long-term data indicate that patients admitted with sepsis suffer from increased all-cause mortality and cardiovascular mortality?

Ou *et al.* utilized the Taiwan National Health Insurance Research Database (NHIRD) to conduct a retrospective large-scale study investigating hazard ratios (HR) for all-cause mortality and cardiovascular adverse events associated with a sepsis hospitalization (8). Patients with age >20 years and an ICD-9 code for sepsis were included. Two control groups were included: a population control cohort and a group of non-septic hospitalized patients and 93,862 patients were enrolled. The HR associated with all-cause mortality with sepsis admission was 5.58 (95% CI, 5.37–5.80, P<0.001) and 2.09 (95% CI, 2.03–2.14, P<0.001) compared to population matched controls at one and five years respectively and 3.31 (95% CI, 3.17–3.46, P<0.001) and 2.03 (95% CI, 1.95–2.10, P<0.001) when matched with the non-septic hospitalized cohort at one and five years, respectively. The HR associated with adverse cardiovascular events was 2.33 (95% CI, 2.19–2.48, P<0.001) and 1.40 (95% CI, 1.35–1.47, P<0.001) for the population control cohort at one and five years respectively and 1.89 (95% CI, 1.74–2.06, P<0.001) and 1.35 (95% CI, 1.26–1.42, P<0.001) for the non-septic hospitalized patient cohort. These data demonstrate that patients with sepsis have increased all-cause mortality and increased cardiovascular adverse events that peak within the first year of discharge but persist up to five years after discharge compared to population controls and hospitalized non-sepsis controls.

Does intensive physical therapy (PT) provide improved outcomes for patients with acute respiratory failure?

The optimal PT regimen for the critically ill is uncertain. Moss *et al.* conducted a randomized controlled trial to investigate the effectiveness of an intensive PT program compared to standard care using the Continuous Scale Physical Functional Performance Test (CS-PFP-10) as outcomes at 1, 3, and 6 months (9). Patients were recruited from five medical centers and included in the study if they were older than 18 years and had mechanical ventilation for four days or more. A total of 120 patients were randomized to either intensive PT (a total of 408±261 minutes of therapy) or standard of care PT (86±63 minutes of therapy). In both groups, physical function improved through the course of the six months and no statistical difference was identified between the total CS-PFP-10 scores. The results suggest that standard PT may be sufficient for some patients in the ICU. Regardless, further investigation is needed in this area.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Gaudry S, Hajage D, Schortgen F, et al. Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit. N Engl J Med 2016;375:122-33.
2. Schneider AG, Uchino S, Bellomo R. Severe acute kidney injury not treated with renal replacement therapy: characteristics and outcome. Nephrol Dial Transplant 2012;27:947-52.
3. Elseviers MM, Lins RL, Van der Niepen P, et al. Renal replacement therapy is an independent risk factor for mortality in critically ill patients with acute kidney injury. Crit Care 2010;14:R221.
4. Zarbock A, Kellum JA, Schmidt C, et al. Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury: The ELAIN Randomized Clinical Trial. JAMA 2016;315:2190-9.
5. Macedo E, Mehta RL. Timing of dialysis initiation in acute kidney injury and acute-on-chronic renal failure. Semin Dial 2013;26:675-81.
6. Orford NR, Saunders K, Merriman E, et al. Skeletal morbidity among survivors of critical illness. Crit Care

Med 2011;39:1295-300.

7. Orford NR, Lane SE, Bailey M, et al. Changes in Bone Mineral Density in the Year after Critical Illness. Am J Respir Crit Care Med 2016;193:736-44.

8. Ou SM, Chu H, Chao PW, et al. Long-term Mortality and Major Adverse Cardiovascular Events in Sepsis Survivors:

A Nationwide Population-based Study. Am J Respir Crit Care Med 2016;194:209-17.

9. Moss M, Nordon-Craft A, Malone D, et al. A Randomized Trial of an Intensive Physical Therapy Program for Patients with Acute Respiratory Failure. Am J Respir Crit Care Med 2016;193:1101-10.