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### Research News

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#### Severe Sepsis: Are Outcomes Better if Hospitals Treat a High Volume of Patients?

A study from the Boston University School of Medicine, published recently in the American Journal of Respiratory and Critical Care Medicine, looked at the associations between hospital sepsis caseload and outcomes, and found that academic hospitals with higher severe sepsis case volume have lower severe sepsis hospital mortality without higher costs.

Using data from US academic hospitals the researchers identified 56,997 patients with severe sepsis admitted to 124 US academic hospitals during 2011. Hospitals admitted  $460 \pm 216$  patients with severe sepsis, with median length of stay 12.5 days (IQR 11.1-14.2), median direct costs \$26,304 (IQR \$21,900-32,090), and average hospital mortality  $25.6 \pm 5.3\%$ . The analysis showed that higher severe sepsis case volume was associated with lower unadjusted severe sepsis mortality ratio ( $R^2=0.10$ ,  $p=0.01$ ) and risk-adjusted severe sepsis mortality ( $R^2=0.21$ ,  $p<0.001$ ).

After adjustment, hospitals in the highest severe sepsis case volume quartile had an absolute 7% (95% CI 2.4-11.6%) lower hospital mortality than hospitals in the lowest quartile. The authors did not identify associations between case volume and resource utilisation.

Lead author, Allan J. Walkey, assistant professor of medicine, BUSM, and attending physician, pulmonary, critical care and allergy medicine, Boston Medical Centre states, "We wanted to adjust for potential confounding variables in the association between case volume and outcomes. We adjusted for patient-level severity of illness by using a standardised mortality ratio and then adjusted for hospital-level factors that were either associated with severe sepsis case volume (eg., # of beds) or associated with mortality (eg, geography, long term acute care referral practices)."

Walkey pointed out, "In patients with severe sepsis the only therapies that have thus far been shown to improve outcomes are those that are basically processes of care: for example early sepsis recognition, early administration of appropriate antibiotics, early goal directed fluid resuscitation. We hypothesised that 'practice makes perfect' when it comes to treatment of patients with severe sepsis and that outcomes would be better as high severe sepsis volume hospitals."

ICU Management asked Dr. Walkey about the implications for changing the processes of care in those hospitals which do not have a high sepsis caseload. He said, "There are a few possibilities for addressing the differences in outcome based on case volume. One is studying whether simulation training in severe sepsis may be a way to improve processes and outcomes at low volume centres. Also, we need to study more thoroughly the way severe sepsis care is implemented in high volume hospitals, and how this care may differ from the lower volume centres. For example: Are high sepsis volume centres more likely to have checklists or protocols? Do high volume hospitals recognise patients with sepsis sooner and is time to antibiotics shorter or use of lung protective ventilation more frequent? How are transfers between services accomplished? If disparities in sepsis outcomes can't be closed, then the last alternative is that 'centres of excellence' be created whereby patients are shunted to centres with more experience/better outcomes. More research obviously needs to be done to address these questions."

Walkey added, "We chose to restrict our analysis only to academic hospitals to eliminate potential confounding by hospital teaching status. Whether recognition of sepsis differs by hospital case volume is worthy of further study."

#### Reference

Walkey AJ, Wiener RS (2014) Hospital case volume and outcomes among patients hospitalized with severe sepsis. *Am J Respir Crit Care Med*, 189(5): 548-55.

#### ICU Patients with Kidney Injury Show High Mortality and Elevated Urinary Protein

Follow up over four years of 1,464 participants in the randomised controlled trial Randomised Evaluation of Normal vs. Augmented Levels of RRT (RENAL) study found that patients with acute kidney injury (AKI) in an intensive care unit who require renal replacement therapy (RRT; haemodialysis combined with haemofiltration) do not benefit from higher intensity RRT.

At a median of 43.9 months follow up, mortality (63% in the low intensity and 63% in the high intensity group), as well as quality of life among those who survived, were the same in both groups. Albuminuria (elevated protein levels in urine, signifying persistent kidney injury) was common among survivors and with equal rates in both groups (40% in the low intensity and 44% in the high intensity group).

The authors explain, "Our study highlights the increased longterm risk of death associated with AKI treated with RRT in an ICU. Only one third of randomised patients were alive 3.5 years later, a lower survival than seen in recognised high mortality conditions such as acute respiratory distress syndrome. Although, in our patients the risk of subsequent maintenance dialysis dependence is low, almost half have evidence of significant proteinuria, portending further risk in the years to come. These findings support the view that survivors of AKI are at increased risk and that closer surveillance may be justified. In addition, our findings suggest that chronic proteinuria reduction strategies, which have shown benefit in some patient groups with proteinuria, may warrant investigation as a therapeutic intervention."

Limitations of the study are that the patients were enrolled in a randomised trial and did not represent patients in ICUs with AKI in general, and not all patients agreed to long term follow up.

The authors conclude, "In a large cohort of patients with acute kidney injury randomised to differing doses of continuous renal replacement therapy in the ICU, the increased risk of death continues well beyond hospital discharge and is not altered by increased intensity of dialysis. The proportion of patients entering a maintenance dialysis program is small but there is a high prevalence of proteinuria amongst survivors, suggesting significant ongoing risk of chronic kidney disease and mortality."

#### Reference

Gallagher M, Alan Cass A, Rinaldo Bellomo R et al. (2014) Longterm survival and dialysis dependency following acute kidney injury in intensive care: extended follow-up of a randomized controlled trial. PLoS Medicine, 11 (2).

#### Statin Use Reduces Delirium in Critically Ill Patients

Continued use of statins may help prevent delirium in critically ill patients who received statins before hospital admission, according to a study of 470 intensive care patients in the UK published online in the American Journal of Respiratory and Critical Care Medicine.

"This is the first study using a validated delirium screening tool, the Confusion Assessment Method-ICU (CAM-ICU), to show that the administration of statins reduces delirium in these patients," said lead author Dr. Valerie J. Page, of the Watford General Hospital in Watford, UK. "This benefit may be mediated by a reduction in systemic inflammation."

151 of the 470 patients included in the study received statins. Statins were only administered to patients who had received statins prior to admission.

After adjustment for age, sex and illness severity, administration of statins the previous evening was associated with a significantly lower risk of delirium and a concomitant reduction in serum C-reactive protein (CRP), a marker of systemic inflammation, the following day. The strength of the relationship between statin use and a lower risk of delirium was reduced when CRP was adjusted for.

"Although the pathogenesis of delirium is not fully understood, these data are consistent with a neuro-inflammatory cause and suggest that the anti-inflammatory effects of statins may contribute to the effects of statin treatment on delirium," said Dr. Page. "Our study on statin use and the risk of delirium in critically ill subjects included extensive data on a large, broadly representative population of consecutive intensive care patients, increasing its strength."

Study limitations include the possibility that not all potential confounding factors were adjusted for and the limits of cognitive assessment tools in critically ill patients.

"Our findings suggest that statin treatment should be continued to help prevent delirium in critically ill patients who received statins before being admitted," said Dr. Page.

"The relationship between statin therapy and delirium and the mechanisms underlying this relationship are the subject of an ongoing randomised, placebo-controlled study in critically ill ventilated patients."

#### Reference

Page VJ, Davis D, Zhao XB et al. (2014) Statin use and risk of delirium in the critically ill. Am J Respir Crit Care Med, Jan 13. [Epub ahead of time] © For personal and private use only. Reproduction must be permitted by the copyright holder. Email to [copyright@mindbyte.eu](mailto:copyright@mindbyte.eu).

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#### **Wise Choices in Critical Care for Doctors and Patients**

The Critical Care Societies Collaborative, comprising the American Association of Critical-Care Nurses, the American College of Chest Physicians, the American Thoracic Society and the Society of Critical Care Medicine has published a list of "Five Things Physicians and Patients Should Question" in critical care as part of the Choosing Wisely® campaign, led by the ABIM Foundation.

The list is five targeted, evidence-based recommendations that can support physicians and patients in making wise choices about their care:

1. Don't order diagnostic tests at regular intervals (such as every day), but rather in response to specific clinical questions.
2. Don't transfuse red blood cells in haemodynamically stable, non-bleeding ICU patients with a haemoglobin concentration greater than 7 mg/dL.
3. Don't use parenteral nutrition in adequately nourished critically ill patients within the first seven days of an ICU stay.
4. Don't deeply sedate mechanically ventilated patients without a specific indication and without daily attempts to lighten sedation.
5. Don't continue life support for patients at high risk for death or severely impaired functional recovery without offering patients and their families the alternative of care focused entirely on comfort.

The list is the first Choosing Wisely list to include collaboration with a nursing organisation and only the second that's a product of collaboration instead of being issued by a sole medical society

#### **Reference**

<http://www.choosingwisely.org/doctor-patient-lists/critical-caresocieties-collaborative-critical-care/>

#### **Erasmus Hospital Celebrates Significant Milestone**

Erasmus Hospital in Brussels, Belgium, recently admitted its 100,000th patient since its establishment in 1978. The service was set up by the late Professor Robert Kahn as a full service, with no distinction between medical and surgical patients. Kahn also had the nous to install the unit in the basement of the hospital, which had large areas that nobody wanted for obvious reasons of lack of light. Sadly Professor Kahn died in September 1996. He was succeeded by Professor Jean- Louis Vincent as acting Head of Department, who was confirmed in office a few months later.

The excellent reputation of the Department of Intensive Care is due to several factors. The medical team is very high level. However, the quality of intensive care depends as much on the other members of the team: nurses, physiotherapists, biotechnologists, psychologists and others. With a team of 200 people, the Department of Intensive Care is the largest department in the hospital.

Communication is essential. The service has established procedures for structured presentations during morning rounds (with the three doctors who hand over), late morning (at the bedside of each patient) and evening with the three doctors beginning their care. Nurses and other members of the healthcare team are actively encouraged to contribute actively to discussions.

The quality of care is closely linked to the quality of the research performed. The Department of Intensive Care has the highest scientific production per doctor at the institution. The department is also involved in early trials of new treatments and the provision of new advanced equipment. The trainees see their training as full, somewhat stressful, but very informative, and are eager to return.

These qualities of clinical practice, research and education also attract many foreign doctors from all continents. The service has strong links with Brazil in particular (more than 100 Brazilian doctors have been trained to date), Italy (known today almost as much Italian as French in the service) and Spain.

The ICU is known for organising ISICEM, the annual symposium of intensive care and emergency medicine, which has become the largest in the world in the area, attracting 6000 participants from around the world.

Responding to the needs of patients and their families is another priority. Thanks to a special fund to help patients and their families, the service was able to add a psychologist to the team as well as accommodation for relatives

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