F1000 FACULTY CRITIQUE

Severe Sepsis: A Science of Uncertainty [version 1; referees: not peer reviewed]

Jonathan Auerbach, Cameron Dezfulian
Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA

Abstract

This article is included in the Critical care collection.

Corresponding author: Cameron Dezfulian (dezfulianc@upmc.edu)
Competing interests: The authors declare that they have no competing interests.
Grant information: The author(s) declared that no grants were involved in supporting this work.
Copyright: © 2015 Auerbach J and Dezfulian C. This is an open access article distributed under the terms of the Creative Commons Attribution Licence, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
How to cite this article: Auerbach J and Dezfulian C. Severe Sepsis: A Science of Uncertainty [version 1; referees: not peer reviewed] F1000Research 2015, 4:1292 (https://doi.org/10.12688/f1000research.6814.1)
First published: 19 Nov 2015, 4:1292 (https://doi.org/10.12688/f1000research.6814.1)
Critique of:
Citation

Background
Severe sepsis and septic shock are major causes of mortality in intensive care unit (ICU) patients. This study analyzed changes in incidence of severe sepsis and septic shock over time (2000 to 2012) in ICU's across New Zealand and Australia. The study also analyzed mortality rate and discharge to home for these patients. Analysis was made using international consensus conference definitions for severe sepsis, objective definitions of acute organ failure and sensitivity analysis. Authors further used APACHE III scores, treatment facility type and location, age and source and type of infection to further analyze the data.

Methods
The authors studied all patients (101,064) with severe sepsis during the time period from January 1, 2000 through December 31, 2012 in Australia and New Zealand. All hospital outcomes were analyzed including mortality, discharge to rehabilitation, discharge home and discharge to other hospital at 30 days. Subgroup analysis was performed on said patients to include severe sepsis and septic shock, APACHE II or APACHE III scores, operative admission, medical admission, renal failure, respiratory failure, age groups, sepsis with or without shock source urinary in nature and sepsis with or without shock source non-urinary in nature.

Objective
To describe changes in mortality for severe sepsis with and without shock in adult ICU patients. To assess and trend number of severe sepsis cases per year. Subgroup analyses were planned in younger patient’s (<45 yrs), UTI vs. other causes, surgical vs. medical patients and patients by APACHE scores.

Design
Retrospective, observational study.

Setting
Over 90% of adult ICU admissions with severe sepsis in Australia and New Zealand from January 1, 2000 to December 31, 2012.

Subjects
Adult ICU patients, within 24 hours of admission, in Australia and New Zealand obtained via the Australian and New Zealand Intensive Care Society adult ICU patient database. The human research ethics committee of Alfred Hospital provided approval of this study.

Analysis
Logistic regression was used to account for incidence changes of severe sepsis over the studied time period. Further logistic regression was used to associate admission year, APACHE scores and locations with outcomes to ensure that the data was robust over years and locations. Finally, sensitivity analysis was performed to ensure consistency of results by studying a subpopulation of 63 hospitals that had data for the entire time period and showing similarities in outcomes.

Results
Absolute mortality in severe sepsis decreased from 35.0% (95%CI, 33.2%-36.8%; 949/2708) to 18.4% (95% CI, 17.8%-19.0%; 2300/12512; P <0 .001), representing an overall decrease of 16.7% (95% CI, 14.8%-18.6%), an annual rate of absolute decrease of 1.3%, and a relative risk reduction of 47.5% (95% CI, 44.1%-50.8%). After adjusted analysis, mortality decreased throughout the study period with an odds ratio (OR) of 0.49 (95% CI, 0.46-0.52) in 2012, using the year 2000 as the reference (P < .001). The annual decline in mortality did not differ significantly between patients with severe sepsis and those with all other diagnoses (OR, 0.94 [95% CI, 0.94-0.95] vs 0.94 [95% CI, 0.94-0.94]; P = .37). The annual increase in rates of discharge to home was significantly greater in patients with severe sepsis compared with all other diagnoses (OR, 1.03 [95% CI, 1.02-1.03] vs 1.01 [95% CI, 1.01-1.01]; P<0.001). Conversely, the annual increase in the rate of patients discharged to rehabilitation facilities was significantly less in severe sepsis compared with all other diagnoses (OR, 1.08 [95% CI, 1.07-1.09] vs 1.09 [95% CI, 1.09-1.10]; P < .001). In the absence of comorbidities and older age, mortality was less than 5%.

Conclusions
In critically ill patients in Australia and New Zealand with severe sepsis with and without shock, there was a decrease in mortality from 2000 to 2012. These findings were accompanied by changes in the patterns of discharge to home, rehabilitation and other hospitals.

Abstract adapted from the original provided courtesy of PubMed: A service of the National Library of Medicine and the National Institutes of Health.

Commentary
True rates of sepsis and mortality from sepsis have remained elusive. In the past, studies have looked at sepsis incidence, and estimations have been made that there are over 1 million sepsis patients in the US yearly as of 20123. Sepsis rates seem to be increasing based on recent studies1,2, with sepsis being ranked the most expensive reason for hospitalization in the US in 20111. Unfortunately, prior studies were plagued by coding problems and limitations in study population, as data was only partial representation of populations studied. This led to concerns that there were errors in obtaining results and limitations of the data sets, leading to potential confounders.

The data set used in this study comprises over 90% of the ICU admissions in Australia and New Zealand. Admission diagnosis were screened for severe sepsis and studied over a 12-year period from 2000 to 2012. The primary outcomes studied were rates of severe sepsis and all hospital outcomes including mortality, discharge to home, discharge to rehab and discharge to other hospitals. Subgroup analysis was performed to evaluate whether or not patient
For changes in mortality. The accuracy of severe sepsis data collection was also not monitored and the marked increase in severe sepsis rates begs the question whether increasing numbers of less sick patients are being admitted to the ICU. Arguing against this is the APACHE score adjustments which reflect not do reflect a drop in severity. Nonetheless the substantial increase in incidence over such a brief time is surprising and yet to be explained.

The Kaukonen et al. study is the largest, most robust study assessing sepsis incidence and outcomes to date. This study seems to strongly suggest that sepsis mortality is decreasing despite increases in sepsis rates. This would suggest that our care of sepsis is improving from both a diagnostic and therapeutic standpoint. Improved septic patients’ discharge home suggests that severe sepsis patients are also having improved quality of life outcomes. Of note, recent prospective clinical trials in sepsis (ARISE6 and PROCESS7) have noted similar mortality rates to this study, corroborating declining sepsis rates.

**Recommendation**

This is an important epidemiological study that suggests that severe sepsis mortality has decreased significantly over time in the face of increased severe sepsis rates. This study further suggests that all critical care mortality appears to be declining. Patients with severe sepsis do seem to fare better as compared to other critical care illnesses based on increased home discharges. The declining rate of mortality has important implications in the design of future therapeutic trials targeting sepsis.

**Competing interests**

The authors declare that they have no competing interests.

**Grant information**

The author(s) declared that no grants were involved in supporting this work.

**References**

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com