

Model for Predicting Short-Term Mortality of Severe Sepsis

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Severe sepsis remains a leading cause of death in industrialized countries, and the number of deaths caused by sepsis is increasing despite improved survival rates. The objective of this study was to design a prognostic model for predicting death within 14 days of severe sepsis onset at any time during the first 28 days of the ICU stay. The model was to be based on variables collected at admission and on the day the sepsis episode was diagnosed. Up to four sepsis episodes per patient were included. We compared our model with other, widely used scores. Our model may prove useful for designing future studies.

We conducted a prospective observational study using data entered into a multicenter database from November 1996 to April 2007. The database contains data on admission features and diagnosis, daily disease severity, iatrogenic events, nosocomial infections and vital status. Data were collected daily by senior physicians in the participating ICUs. For each patient, the data were entered into an electronic case-report form. Severity of illness was evaluated on the first ICU day using the Simplified Acute Physiology Score (SAPS II), Logistic Organ Dysfunction (LOD) score, Sequential Organ Failure Assessment (SOFA) score, Mortality Probability models II score (MPM0 II score), and Acute Physiologic and Chronic Health Evaluation (APACHE) II score. Patients were followed until the end of the hospital stay in order to record the vital status 14 days after sepsis onset. Severe sepsis was defined as sepsis associated with at least one [major] organ dysfunction, and septic shock was defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation together with organ dysfunction. The outcome variable of interest was death within 14 days after the diagnosis of an episode of severe sepsis (up to four) acquired in the community, hospital or ICU.

Results

Among the 7,719 patients in the base, 2,268 experienced 2,737 episodes of severe sepsis, including 674 patients who had 793 episodes of septic shock. Of the 2,268 patients, 1,458 patients with 1,716 episodes of severe sepsis were included in the training cohort and 810 patients with 1,021 episodes of severe sepsis were included in the validation cohort. Factors that were significantly associated with early death included worse SAPS II and LOD scores at ICU admission, septic shock (eg requiring

either inotropic therapy or vasoactive agent support), multiple organ failure (which showed the strongest association) and comorbidities (immunodeficiency, chronic heart failure, chronic hepatic failure, acute respiratory failure and acute heart failure). On the day of the diagnosis of severe sepsis, factors significantly associated with early death included the use of invasive procedures and a need for vasoactive agents and/or inotropic support. *Escherichia coli*, *Pseudomonas* species, methicillin-resistant *Staphylococcus aureus*, *Candida* species, bacteremia and multiple sources of infection were also associated with early death in the univariate analysis.

We found that predicting death within 14 days after the onset of severe sepsis during the first 28 days in the ICU was feasible in patients with no to three previous episodes of severe sepsis. By adjusting for confounders, we were able to build a predictive model in a training cohort that performed well in the validation cohort. If used in randomized trials, this prognostic model might help to include patients with similar disease severity and to improve adjustment for confounders. We chose to study short-term mortality, despite the current trend among researchers to focus on long-term mortality. Most studies of sepsis used 28-day all-cause mortality as the primary end-point. However, life-limiting disease is a common risk factor for sepsis and may cause death shortly after successful treatment of the septic episode. Sepsis is an acute event and its main manifestation, acute organ dysfunction, does not seem to be associated with long-term mortality in patients who survive the original insults. Furthermore, many studies failed to adjust appropriately for treatment-limitation decisions such as DNR given less than two days or later during the ICU stay. Moreover, treatment-limitation decisions were found to be independently associated with ICU deaths.

Severe infections per se are associated with a decrease in life expectancy. Short-term survival may need to be viewed as a surrogate measure, because it is desirable only when followed by long-term survival with an acceptable quality of life. On the other hand, focusing on very long-term mortality, which is extremely relevant to healthcare-cost issues, may mask beneficial effects of drugs used to treat sepsis if the patient dies later on as a result of an underlying chronic illness associated with a risk of sepsis. High death rates due to underlying diseases may explain why many therapeutic trials in patients with severe sepsis failed to detect benefits related to the experimental treatments. Therefore, when designing large trials of treatments for severe

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