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Sepsis and organ system failure are major determinants of post–intensive care unit mortality

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on behalf of the Sepsis Occurrence in Acutely Ill Patients Investigators[1]

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Abstract

Purpose: The aim of the study was to investigate predictors of post–intensive care unit (ICU) in-hospital mortality with special emphasis on the impact of sepsis and organ system failure.

Methods: This study is a subanalysis of the database from the observational Sepsis Occurrence in Acutely Ill Patients study conducted in 198 ICUs in 24 European countries between May 1 and May 15, 2002. Potential predictors of post-ICU mortality were considered at 3 levels: admission status, procedures and therapy during the ICU stay, and status at ICU discharge.

Results: Of the 3147 patients included in the Sepsis Occurrence in Acutely Ill Patients study, 1729 (54.9%) were discharged to the general floor (study group) and 125 of these died (overall post-ICU hospital mortality rate, 4%); 26 (20.8%) died already the first day on the floor. Nonsurvivors were older, had higher incidence of hematologic cancer and cirrhosis, and greater Simplified Acute Physiology Score II and Sequential Organ Failure Assessment score on ICU admission; they were also more likely to have been admitted for medical reasons than survivors. In a multivariate forward stepwise logistic regression analysis, age, hematologic cancer, cirrhosis, simplified acute physiology score II on admission, medical admission, sepsis at any time during ICU stay, and organ dysfunction at ICU discharge were all independently associated with a greater risk of post-ICU death.

Conclusions: This large international study identified not only age, medical admission, and preexisting comorbidities on ICU admission but also sepsis and organ system failure as important independent risk factors for in-hospital post-ICU death.

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1. Introduction

Mortality after discharge from the intensive care unit (ICU) remains a major concern in critically ill patients and has been reported to range from 6% to 31% [1-9]. Many prognostic factors for post-ICU mortality have been identified, including preadmission events [9-12], severity of illness and comorbidities on admission to the ICU [7-9], and residual organ dysfunction/failure at ICU discharge [7-9]. A task force of the American College of Critical Care Medicine [13] has provided guidelines for ICU admission, discharge, and triage. However, this publication, provides relatively broad and nonspecific discharge criteria provided because of a lack of sufficient relevant data. Identifying the determinants of post-ICU death may, consequently, influence decision-making at ICU discharge, and hence may reduce mortality after ICU discharge by reducing inappropriate early discharge [14].

Factors related to therapy and evolution of the underlying disease process during the ICU stay may play an important role in determining post-ICU mortality. Sepsis syndromes are one such factor, not only because of their common occurrence in the ICU setting [15-17] but also because they are a major determinant of organ dysfunction/failure and of worse outcomes in critically ill patients [15,17]. The aim of our study was, therefore, to investigate the predictors of post-ICU in-hospital mortality with special emphasis on the impact of sepsis syndromes and organ system failure.

2. Methods

This study is a subanalysis of the database from a prospective, multicenter, observational study, the Sepsis Occurrence in Acutely Ill Patients (SOAP) study, which was designed to evaluate the epidemiology of sepsis among ICU patients in European countries. Recruitment, data collection, and management are detailed elsewhere [17]; briefly, all patients older than 15 years admitted to the 198 participating centers (see the Appendix 1 for a list of participating countries and centers) between May 1 and May 15, 2002 were included. We excluded patients who stayed in the ICU for less than 24 hours for routine postoperative observation. Patients were followed up until death, hospital discharge, or for 60 days. Study approval was sought from all participating centers before patient enrollment and received in the form of a waiver or expedited approval because of the observational nature of the SOAP study; informed consent was not required.

Data were collected prospectively using preprinted case report forms. Data collection on admission included demographic data and comorbidities. Clinical and laboratory data for the Simplified Acute Physiology Score II (SAPS II) [18] were reported as the worst value within 24 hours after admission. Microbiologic and clinical infections were reported daily as well as the antibiotics administered. A daily evaluation of organ function according to the Sequential Organ Failure Assessment (SOFA) score [19] was performed, with the most abnormal value for each of the 6 organ systems (respiratory, renal, cardiovascular, hepatic, coagulation, and neurologic) being collected on admission and every 24 hours thereafter. Data were encoded centrally in the organizing center by medical personnel (Department of Intensive Care, Erasme Hospital; Brussels, Belgium), and a number of quality control measures were carried out to ensure the consistency of data and the quality of data entry [17]. All variables were defined a priori and were available on an Internet-based Web site throughout the study period.

Sepsis was defined according to the consensus conference definitions [20]. Organ failure was defined as a SOFA score higher than 2 for the organ in question [21]. Severe sepsis was defined by sepsis plus at least one organ failure. Daily fluid balance was calculated as the total fluid balance during the ICU stay divided by the duration of ICU stay in days. Intensive care unit–acquired sepsis was defined as sepsis occurring after 48 hours of ICU admission. The day of ICU discharge was defined as the 24 hours (from 8:00 to 8:00) preceding discharge.

2.1. Statistical methods

Data were analyzed using SPSS 13.0 for Windows (SPSS Inc, Chicago, Ill). Descriptive statistics were computed for all study variables. The Kolmogorov-Smirnov test was used to verify the normality of distribution of continuous variables. Nonparametric tests of comparison were used for variables evaluated as not normally distributed. Difference testing between groups was performed using the 2-tailed *t* test, Mann-Whitney *U* test, χ^2 test, and Fisher exact test as appropriate. To identify the factors associated with increased risk of post-ICU death, we performed a multivariate logistic regression analysis, forward stepwise, with post-ICU mortality as the dependent factor in patients discharged to the general floor (n = 1729). Covariates were selected and entered in the model if they attained a $P < .2$ on a univariate basis, and included source and type of admission, age, sex, comorbidities on admission, SAPS II on admission, and the daily fluid balance. The degree of organ failure assessed by the SOFA score, procedures (mechanical ventilation and pulmonary artery catheter), the presence of sepsis syndromes during the ICU stay, the type of hospital (university- vs community-affiliated hospital) and number of ICU beds (<15, 16-30, and >30 beds), and the ICU length of stay were also included as independent variables. The presence of residual sepsis, systemic inflammatory response syndrome (SIRS), albumin administration, and the individual SOFA scores at ICU discharge were inserted in the final model. Colinearity between variables was tested before modeling by computing the correlation of estimates, with $R^2 > 0.7$ considered to be significant [22]. A Hosmer and Lemeshow goodness-of-fit test was performed, and odds ratios (95% confidence interval) were computed. The country effect was tested, with the country with the lowest mortality and a