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Original article

A multicenter, prospective evaluation of quality of care and mortality in Japan based on the Surviving Sepsis Campaign guidelines

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ABSTRACT

To elucidate the standard Surviving Sepsis Campaign (SSC) guidelines-based quality of care and mortality related to severe sepsis in Japan, we conducted a multicenter, prospective, observational study using a new web-based database between June 1, 2010, and December 31, 2011. A total of 1104 patients with severe sepsis were enrolled from 39 Japanese emergency and critical care centers. All-cause hospital mortality was 29.3% in patients with severe sepsis and 40.7% in patients with septic shock. Pulmonary, renal, hepatic, and hematological dysfunctions were associated with significantly higher mortality, and hematological dysfunction, especially coagulopathy, was associated with the highest odds ratio for mortality. Compliance with severe sepsis bundles in our study was generally low compared with that in a previous international sepsis registry study, and glycemic control was associated with lowest odds ratio for mortality. Despite higher complication rates of multiple organ dysfunction syndrome and low compliance with severe sepsis bundles on the whole, mortality in our study was similar to that in the international sepsis registry study. From these results, we concluded that our prospective multicenter study was successful in evaluating SSC guidelines-based standard quality of care and mortality related to severe sepsis in Japan. Although mortality in Japan was equivalent to that reported worldwide in the above-mentioned international sepsis registry study, compliance with severe sepsis bundles was low. Thus, there is scope for improvement in the initial treatment of severe sepsis and septic shock in Japanese emergency and critical care centers.

1. Introduction

Sepsis is prevalent among hospitalized patients worldwide. In fact, severe sepsis and septic shock are the major cause of admission and mortality in intensive care units (ICUs). However, mortality rates vary among countries and regions, depending on medical resources available. Japan has government health insurance and emergency medical systems but is also at the forefront of countries with an aging population; therefore, morbidity and mortality statistics may not be comparable with those of other countries in which sepsis epidemiology has been demonstrated on a multicenter basis. A Japanese retrospective study examined incidence in a single emergency room and found that 4.5% of patients met the criteria for sepsis, 2.5% for severe sepsis, and 2.1% for septic shock [1]. In another retrospective study using Japan Nosocomial Infection Surveillances (JANIS), the incidence of sepsis was reported to be 2.1% among patients admitted to ICUs [2]; however, this value is very low compared with that observed in previous multicenter cohort studies, and it does not appear to be generalizable to nationwide ICUs accepting patients from emergency

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rooms, including our facilities. Prospective, multicenter-based, epidemiological studies of sepsis should have been conducted in Japan in order to advance the development of institutional and governmental strategies aimed at tackling this critical illness.

In response to an increasing demand for a systematic approach to sepsis, the Society of Critical Care Medicine, the European Society of Intensive Care Medicine, and the International Sepsis Forum launched the Surviving Sepsis Campaign (SSC) in the hope of decreasing mortality [3]. Updated versions of guidelines developed by SSC were published in 2008 and 2013, in which the Japanese Association for Acute Medicine (JAAM) evolved as an organization comprising various professional societies. In accordance with SSC, a set of interventions, referred to as severe sepsis bundles, was introduced to change bedside behavior, and chart review database software was freely distributed in several languages to evaluate the quality of care in each hospital and to register patients worldwide [4]. However, because this software was not available in a Japanese version, almost no Japanese patients were included in the international sepsis registry; therefore, quality of care standards and mortality associated with severe sepsis and septic shock remain poorly clarified in Japan.

The present study aimed to elucidate the epidemiology of severe sepsis and examine the SSC guidelines-based standard quality of care related to severe sepsis in Japan. To the best of our knowledge, this is the first report examining severe sepsis in Japan on the basis of a multicenter observational study.

2. Patients and methods

This multicenter, prospective, observational study was registered at the University Hospital Medical Information Network Clinical Trial Registry (UMIN-CTR ID: UMIN000008195). Patients fulfilling the original and revised definition of severe sepsis or septic shock according to the American College of Chest Physicians/Society of Critical Care Medicine consensus conference were registered [5,6].

JAAM established a sepsis registry (SR) interim committee in 2007. The committee developed a web-based database in collaboration with the Internet Data and Information Center for Medical Research, a division of the University Hospital Medical Information Network. Since the JAAM SR database used in this study was equipped with functions equivalent to the SSC chart review database, it was capable of collecting the data necessary for evaluating quality indicators at individual institutes and sending anonymous patient data to the SSC office [4,7]. Data collected in this study were exactly the same as data collected in the international sepsis registry database and thus did not include information regarding parameters such as age, gender, comorbidities, Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, or treatments other than severe sepsis bundles. Data regarding blood glucose, median BG values and times of hypoglycemic episodes during the initial 24 h were collected. This secure database is accessible through the Internet. Quality indicators were programmed to be calculated automatically as soon as data input from patients was completed, and included Q1: blood lactate measurement; Q2: blood culture; Q3: early antibiotic use; Q4: fluid resuscitation and vasopressors; Q5: achievement of CVP $>$ 8 mmHg; Q6: achievement of $ScvO_2 > 70\%$; Q7: all resuscitation bundles (Q1–Q6); Q8: following glucocorticoid policy; Q9: following activated protein C (APC) policy (not evaluated in this study); Q10: glycemic control; Q11: low inspiratory plateau pressure; and Q12: all management bundles (Q8, 10, 11).

In addition to the 18 core JAAM SR committee institutes, we recruited JAAM board-approved hospitals that could register patients in the database. All institutes and hospitals obtained approval from their ethics committees and recruited patients for 365 sequential days. Multiple organ dysfunction syndrome (MODS) was defined according to the SSC severe sepsis screening table [4]. Incidence of individual organ dysfunction in MODS, quality indicators, and their correlation with all-cause hospital mortality were evaluated. To evaluate the effect of organ dysfunction in MODS and compliance with individual severe sepsis bundles on mortality, univariate analysis was used. We also applied multivariate logistic regression analysis to MODS and two sets of quality indicators were applied to the same denominator, i.e., Q1, Q2, Q3, and Q10 in patients with severe sepsis and Q1, Q2, Q3, Q4, Q5, Q6, Q8, and Q10 in patients with septic shock. Simultaneous test procedures were used for analysis of MODS, and the stepwise backward elimination method (likelihood ratio) was used for evaluation of MODS subcategories and quality indicators. To compare values between two groups, Pearson's chi-square test was used. To evaluate the effect of the total number of dysfunctional organs and systems on mortality, univariate analysis was used. Survival between two groups was compared using Kaplan–Meier survival curves with a log-rank significance test. All statistical analyses were performed using IBM SPSS statistics (V20) software (International Business Machines Corp., NY, USA), and the level of significance was set at $P < 0.05$.

3. Results

Using the JAAM SR database, 1104 patients with severe sepsis from 39 hospitals were registered between June 1, 2010, and December 31, 2011 (information of participated sites is shown in a supplementary table). Overall sepsis-related hospital mortality was 29.3%. Patients with septic shock had a significantly higher mortality (n = 484, 40.7%) than those without (n = 620, 20.3%, $P < 0.0005$). When our results were compared with the 30.8% mortality rate of 509 patients included in the final quarter of the SSC international sepsis registry study, the difference was not significant according to Pearson's chi-square test ($P = 0.517$) [7].

Table 1 shows patient demographics in our study. The emergency department was the most common route of admission, followed by the general ward. Pneumonia or empyema was the most common type of infection, followed by acute abdominal infection, urinary tract infection, and skin/soft tissue infection. Among MODS, hemodynamic dysfunction was the most frequent, followed by hematological, renal, pulmonary, and hepatic dysfunction. The average number of dysfunctional organs and systems reported in our study was 2.16 ± 1.06 (mean ± standard deviation), which was significantly higher than that (1.94 ± 1.01) reported in the international sepsis registry study, according to chi-square test mean scores with modified ridit scores ($P < 0.0001$). The incidence of individual organ dysfunction in our study was equivalent to or greater than that reported in previous studies, indicating a similar or higher severity of illness.

We next analyzed the effects of MODS on mortality (Table 2). Existence of pulmonary, renal, hepatic, and hematological dysfunction was associated with significantly higher mortality. The mortality in patients with one, two, three, four, and five MODS was 19.7%, 28.0%, 34.7%, 48.0%, and 53.6%, respectively, and each additional MODS was associated with an approximately 1.5-fold increase in mortality (Table 2). We also assessed the effect of the following MODS subcategory abnormalities on mortality: hypotension, hyperlactatemia, acute lung injury, thrombocytopenia, and coagulopathy. Hypotension, thrombocytopenia, and coagulopathy were associated with higher mortality. We further performed multivariate logistic regression analysis. When the effects of individual organ dysfunction and system in MODS were analyzed, pulmonary, renal, and hematological dysfunction were extracted as significant parameters (Table 3A), and when MODS subcategory abnormalities in addition to renal and hepatic dysfunction were