Trauma Cases and Reviews

Association between Sequential Organ Failure Assessment Score and In-hospital Deaths of Surgical, Critically Ill Patients with Sepsis

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Abstract

Purpose: This study was designed to identify factors prognostic of in-hospital deaths of surgical, critically ill patients with sepsis and to evaluate the effects of treatments for sepsis on in-hospital deaths.

Methods: This retrospective cohort study involved 103 patients with sepsis who were hospitalized in the surgical intensive care units of 20 hospitals. Clinical, microbiologic, and laboratory factors, as well as treatments, were compared between patients who survived hospitalization and those who died in-hospital.

Results: The in-hospital mortality and septic shock rates were 24.3% and 19.4%, respectively. Multivariate logistic regression analysis showed that Sequential Organ Assessment (SOFA) score was the only independent predictor of in-hospital death (P = 0.027). Receiver operating characteristic curve analysis of in-hospital death showed that the optimal SOFA score cutoff at admission to the surgical intensive care unit was 8, with in-hospital death rate being significantly higher in the 22 patients with SOFA score > 8 than in the 81 patients with SOFA score ≤ 8 (P = 0.0039). Cox regression analyses by inverse probability treatment weighting to control for selection bias showed that in-hospital death rates were not significantly altered by treatment with intravenous immunoglobulins, renal replacement therapy, or endotoxin-absorbing therapy using polymyxin B.

Conclusions: SOFA score may be prognostic of in-hospital deaths of surgical critically ill patients with sepsis. SOFA score > 8 was associated with a significantly higher in-hospital death rate and should be regarded as a cut-off for intensive treatment in surgical patients with sepsis.

Introduction

Sepsis, defined as infection-induced systemic inflammatory response syndrome (SIRS), is the leading cause of death in non-cardiac critically ill patients [1]. In the United States, nearly 200,000 deaths per year are attributed to sepsis [2]. Worldwide, as many as 20 million people may experience sepsis annually, with a mortality rate of about 35% [3]. Sepsis involves multiple mechanisms, including the release of cytokines and the activation of the complement, coagulation and fibrinolytic systems [4].

The first internationally accepted guidelines to improve outcomes in patients with severe sepsis and septic shock were adopted in 2004 [5,6] and updated in 2008 [7] and 2012 [8,9]. Current guidelines recommend a specific anatomical diagnosis of infection as rapidly as possible, with intervention for source control started within the first 12 hours after diagnosis, if feasible [8,9].

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Few studies to date have described the treatment of surgical, critically ill patients with sepsis [10,11,12]. The results of treatments of sepsis in surgical patients requiring other types of treatment, including burn care, catheter drainage of the source of infection and abdominal surgery under general anesthesia, remain unclear. It is therefore of interest to clarify factors prognostic of survival in surgical, critically ill patients with sepsis.

Moreover, although adjunctive therapies, including intravenous immunoglobulins (IVIG) [13,14], renal replacement therapy [15,16], and endotoxin-absorbing therapy using polymyxin B (PMX) [17], have been reported to reduce the risks of death in septic patients, these treatments have not been universally accepted. Inverse probability of treatment weighting (IPTW) was therefore used to balance the underlying distributive covariates among patients who did and did not receive each adjunctive therapy. IPTW weights the samples using propensity score to reduce the confounding that frequently occurs in cohort studies of the effects of treatment on outcome, and enables estimation of marginal or population-average treatment effects [18].

This study was therefore designed to identify factors prognostic of in-hospital deaths in surgical, critically ill patients with sepsis and to evaluate the effects of treatment of sepsis on patient survival.

Materials and Methods

This retrospective cohort study involved 110 patients who were hospitalized with sepsis in the surgical intensive care units of 20 hospitals affiliated with the Department of Surgery and Medical Science, Graduate School of Medical Sciences, Kyushu University, between January 2012 and December 2013 (Supplemental Table 1). Patients lacking adequate clinical data were excluded.

Sepsis was defined as an infection with SIRS, defined as the occurrence of at least two of the following criteria: (1) body temperature > 38˚C or < 36˚C, (2) heart rate > 90 beats per minute, (3) respiratory rate > 20 breaths a minute or $PaCO_2$ < 32 mmHg, and (4) white blood cell count > 12,000/ mm³ or < 4000/mm³ or < 10 % immature forms [4]. Blood samples were drawn when patients first fulfilled the criteria for SIRS. Septic shock was defined as sepsis-induced hypotension, consisting of systolic blood pressure below 90 mmHg, which persisted despite adequate fluid resuscitation [8]. Ileus was defined as any impairment, arrest, or reversal of the normal flow of intestinal contents toward the anal canal.

All patients diagnosed with sepsis and admitted to the surgical intensive care unit before and after surgery were enrolled in this study. Demographic and clinical data retrieved from their medical records included sex, age, underlying disease, location of the primary infection, bacterial species, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Assessment (SOFA) score, blood pressure, heart rate, hematocrit, white blood cell (WBC) count, platelet count, C-reactive protein (CRP), total bilirubin, serum creatinine, fibrinogen, prothrombin activity, fibrinogen degradation products (FDP), D-dimer, and type of surgical intervention for sepsis, including removal or drainage of sites of infection.

Treatment of sepsis, including surgical intervention and antimicrobial therapy, was initiated as soon as possible according to the Surviving Sepsis Campaign guidelines [8,9]. If primary antibiotics were not effective, as determined by WBC count, CRP concentration, and clinical signs such as high fever, IVIG (5 g/kg body weight) was administered for 3 days along with antibiotics [13,14]. Patients with septic shock who experienced acute renal failure, defined as anuria and/or serum creatinine concentration > 4.0 mg/dl, were administered renal replacement therapy, including continuous hemodiafiltration (CHDF) or intermittent hemodialysis, to protect renal function and remove inflammatory cytokines [15,16]. If hemodynamic stability could not be restored by adequate fluid resuscitation and vasopressor therapy, patients were administered PMX [16]. In addition, mechanical ventilation was administered to patients with sepsis-induced acute lung injury (ALI)/acute respiratory distress syndrome (ARDS). Fluid resuscitation and catecholamine were administered to maintain circulation in patients with septic shock, thus preventing the development of a more critical condition that could result in multiple organ failure (MOF) and death [8,9].

Statistical Analysis

For continuous variables, nonparametric analyses were performed using Wilcoxon rank-sum tests. Categorical variables were compared using chi-squared or Fisher's exact tests. The Kaplan-Meier method was used to construct cumulative survival curves. To identify factors independently predictive of in-hospital death, the factors found to be significant on univariate analysis were assessed by multivariate logistic regression analyses. The SOFA score cut-off value for in-hospital death was calculated using the receiver operator characteristic (ROC) curve method [19].

IPTW analysis was performed to overcome possible biases from differences in distribution among patients who did and did not receive each treatment [18,20]. Propensity scores by IPTW were calculated using a Cox regression model to predict the probability of each patient receiving each treatment on the basis of eight clinical variables: age; sex; APACHE II score; SOFA score; positive (vs. negative) blood culture; and treatment including IVIG, renal replacement therapy, and PMX. Following balancing by IPTW, the between group differences in in-hospital death rates were evaluated by the log-rank test. Statistical analyses were performed using the R statistical programming environment (the Comprehensive R Archive Network, http://cran.md.tsukuba.ac.jp) and JMP 9.0 software (SAS Institute, Cary, NC). Four basic R programming packages were used for IPTW analyses: Rcmdr, survival, RcmdrPlugin, survival, and Epi. Statistical significance was defined as a P value < 0.05.

Results

Of the 110 patients enrolled initially, seven were excluded owing to uncertainties about initial recognition of SIRS. The primary causes of sepsis in the 103 analyzed patients included acute peritonitis (n = 50), acute cholecystitis (n = 17), acute cholangitis (n = 9), ileus (n = 7), gangrene of the lower limbs (n = 4), liver abscess (n = 2), postoperative catheter infection (n = 2), postoperative acute enteritis (n =2), postoperative pneumonitis (n = 2), postoperative urinary tract infection (n = 2), postoperative infectious endocarditis (n = 1), extensive burn (n = 1), abdominal compartment syndrome (n = 1), esophageal perforation (n = 1), postoperative leakage of esophageal anastomosis (n = 1), and postoperative pancreas fistula (n = 1). Table 1 shows the relationships between the primary cause of sepsis and surgical treatment in these patients. Of the 103 patients, 60 (58.3%) underwent surgery under general anesthesia, and 24 (23.3%) underwent surgical drainage under local anesthesia. Adjunctive

Supplemental Table 1: Hospitals included in this Study

National Hospital Organization Kyushu Cancer Center
Kyushu Central Hospital of the Mutual Aid Association of Public School Teachers
Saiseikai General Hospital
Fukuoka City Hospital
Fukuoka Higashi Medical Center
Social Insurance Nakabaru Hospital
Munakata Medical Association Hospital
Saiseikai Yahata General Hospital
Steel Memorial Yahata Hospital
Shinnakama Hospital
Aso Iizuka Hospital
Tagawa Municipal Hospital
Onga Hospital
Oita Red Cross Hospital
Oita Prefectural Hospital
Nakatsu Municipal Hospital
Saiseikai Karatsu
Imari Arita Kyoritsu Hospital
Hiroshima Red Cross Hospital and Atomic Bomb Survivors Hospital
Matsuyama Red Cross Hospital

Table 1: Causes of sepsis and types of treatment in surgical critically ill patients with sepsis

Cause of sepsis	Patients	Primary therapy		Adjunctive therapy		
		Surgery	Drainage	IVIG	RRT	PMX
	(n = 103)	(n = 60)	(n = 24)	(n = 33)	(n = 18)	(n = 21)
Acute peritonitis	50	42	4	19	11	15
Acute cholecystitis	17	5	10	4	1	1
Acute cholangitis	9	0	4	3	1	0
Ileus	7	6	1	1	1	0
Lower limbs gangrene	4	4	0	2	1	1
Liver abscess	2	0	2	0	0	0
Postop. catheter infection	2	0	2	0	0	0
Postop. acute enteritis	2	0	0	1	1	1
Postop. Pneumonitis	2	0	0	1	0	1
Postop. UTI	2	0	1	0	0	0
Postop. infectious endocarditis	1	0	0	0	0	0
Extensive burn	1	1	0	1	1	1
Abd. compartment syndrome	1	1	0	1	1	1
Esophageal perforation	1	1	0	0	0	0
Postop. leakage of esophageal Anastomosis	1	0	0	0	0	0
Postoperative pancreas fistula	1	0	0	0	0	0

Abbreviations: IVIG: intravenous immunoglobulins; RRT: renal replacement therapy; PMX: endotoxin-absorbing therapy using polymyxin B; UTI: urinary tract infection; Postop: postoperative; Abd: abdominal.

Table 2: Univariate analysis of risk factors for in-hospital deaths among surgical, critically ill patients with sepsis Results reported as mean ± standard error

Variables	Hospital Survivors (n = 78)	Hospital Non-survivors (n = 25)	P-value
Age (years)	72.5 ± 1.4	71.7 ± 2.3	0.869
Gender (Male)	47 (60.3%)	18 (72.0%)	0.347
Body weight (kg)	52.1 ± 1.3	57.0 ± 3.6	0.299
Comorbidities			
Diabetes mellitus	11 (14.1%)	4 (16.0%)	0.755
Hypertension	18 (23.1%)	3 (12.0%)	0.271
Heart failure	4 (5.1%)	5 (20.0%)	0.036
Chronic renal failure	9 (11.5%)	0 (0.0%)	0.109
Neoplasm	21 (26.9%)	9 (36.0%)	0.450
Positive blood culture	30 (38.5%)	7 (28.0%)	0.473
Localization of infection			
Respiratory	2 (2.6%)	0 (0.0%)	1.000
Heart	1 (1.3%)	0 (0.0%)	1.000
Upper digestive tract	11 (14.1%)	2 (8.0%)	0.730
Hepatobiliary-pancreas	25 (32.0%)	8 (32.0%)	1.000
Lower digestive tract	32 (41.0%)	13 (52.0%)	0.362
Urinary tract	1 (1.3%)	1 (4.0%)	0.428
Soft tissue	6 (7.7%)	1 (4.0%)	1.000
APACHE II score (points)	14.0 ± 0.8	20.4 ± 2.0	0.002
SOFA score (points)	5.0 ± 0.4	8.8 ± 0.8	< 0.0001
Body temperature (centigrade)	37.6 ± 0.2	37.0 ± 0.3	0.145
Heart rate (/minute)	101.8 ± 2.0	106.6 ± 4.9	0.508
Hematocrit (%)	33.6 ± 0.8	35.1 ± 1.6	0.263
White blood cell count (/mm³)	13920 ± 1184	15296 ± 9968	0.661
Platelet (×10⁴/mm³)	20.4 ± 1.3	17.2 ± 2.4	0.162
C-reactive protein (mg/dl)	16.2 ± 1.3	14.4 ± 3.2	0.222
Total bilirubin (mg/dl)	1.3 ± 0.1	2.3 ± 0.8	0.205
Serum creatinine (mg/dl)	1.7 ± 0.2	1.9 ± 0.3	0.147
Fibrinogen (mg/dl)	476.9 ± 30.9	351.0 ± 72.2	0.054
Prothrombin activity (%)	66.6 ± 2.7	55.2 ± 3.4	0.006
FDP (µg/ml)	24.9 ± 3.7	62.2 ± 34.0	0.983
D-dimer (µg/ml)	10.6 ± 1.5	17.4 ± 7.5	0.480
Surgical intervention	66 (84.6%)	18 (72.0%)	0.234

Abbreviations: APACHE II: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; FDP: fibrinogen degradation products

Table 3: Multivariate analysis of risk factors for in-hospital deaths among surgical, critically ill patients with sepsis

Variables	Multiple logistic regression analysis		
	Odds ratio	95% Confidence Interval	P-value
Heart failure	1.71	0.25-11.9	0.575
APACHE II score (points)	1.02	0.94-1.11	0.617
SOFA score (points)	1.24	1.03-1.52	0.023
Prothrombin activity (%)	0.99	0.96-1.02	0.521

Abbreviations: APACHE II: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment

hospital stay was 36.7 ± 2.5 days (range, 2-100 days). The mean APACHE II and SOFA scores at admission were 15.5 ± 0.8 and 5.9 ± 0.4, respectively.
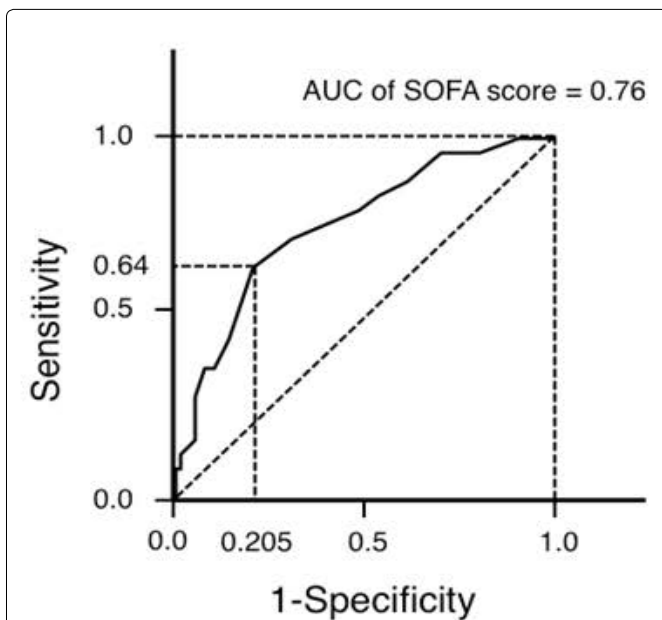
Univariate analysis identified four variables as risk factors for in-hospital deaths in these patients: heart failure as a comorbidity (P = 0.036), APACHE II score (P = 0.002), SOFA score (P < 0.0001), and prothrombin activity (P = 0.006). Of the 78 in-hospital survivors, nine had chronic renal failure, including two on hemodialysis, with no differences in rates of chronic renal failure between survivors and non-survivors (P = 0.109). Multivariate logistic regression analysis showed that SOFA score was the only independent predictor of in-hospital death (P = 0.027, odds ratio 1.24; 95% confidence interval 1.03-1.52, Table 2 and Table 3).

ROC curve analysis and determination of the area under the ROC curve (AUC) showed that SOFA score was effective in distinguishing surgical, critically ill patients with sepsis who did and did not survive in-hospital. The AUC of SOFA score was 0.76. ROC curve analysis for in-hospital deaths showed that the optimal SOFA score cutoff at admission to the surgical intensive care unit was 8 (sensitivity; 0.64, 1-specificity; 0.25, Figure 1). The in-hospital death rate was significantly higher in the 22 patients with SOFA score > 8 than in the 81 patients with SOFA score ≤ 8 (P = 0.0039, Figure 2).
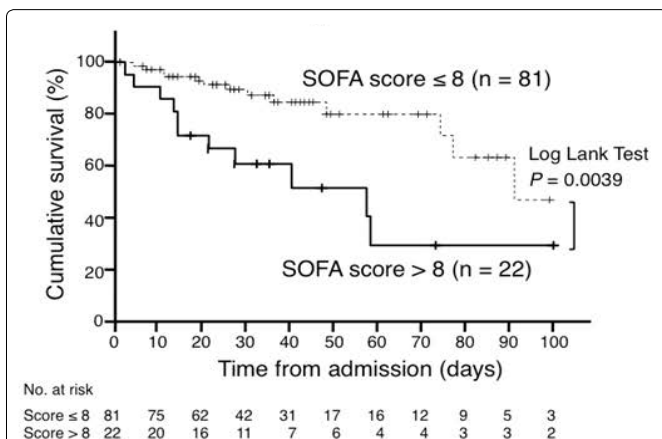
The microorganisms isolated from these patients are shown in table 4. Gram-positive microorganisms were cultured from 37.9 % of these patients; Gram-negative organisms from 34.0 %; and Candida species from 2.9%. In-hospital deaths were not associated with either Gram-positive or Gram-negative organisms. Escherichia coli was associated with the main source of infection in patients with septic shock (P = 0.021), but not with in-hospital deaths. None of the other microorganisms was associated with either septic shock or in-hospital death rate. Antimicrobial treatment was administered to all patients. Only six patients (7.8%) received inadequate antimicrobial treatment, but this was not related to in-hospital mortality (P = 0.620). Of these six patients, three were infected with methicillin-resistant

treatments included IVIG therapy in 33 patients (32.0%), renal replacement therapy in 18 (17.5%), and PMX in 21 (20.4%).

The mean age of the 103 patients (65 men and 38 women) was 72.3 ± 1.2 years (range, 37-99 years). Twenty-five (24.3 %) patients died in-hospital and 20 (19.4 %) experienced septic shock. The mean

Table 4: Microorganisms associated with in-hospital deaths among surgical, critically ill patients with sepsis

Variables	Hospital Survivors (n = 78)	Hospital Non-survivors (n = 25)	P-value	Septic shock (n = 20)	P-value
Gram positive	31	8	0.344	5	0.211
Enterococcus species	10	3	1	1	0.454
Staphylococcus aureus	10	2	0.726	1	0.453
Streptococcus species	7	1	0.676	2	0.651
Clostridium species	2	1	0.57	1	0.481
Staphylococcus epidermidis	1	0	1	1	0.454
Bacillus species	1	0	1	0	1
Corynebacterium species	0	1	1	0	1
Gram negative	25	10	0.476	10	0.116
Escherichia coli	11	6	0.352	7	0.021
Bacteroides species	6	1	1	1	0.454
Klebsiella pneumoniae	2	2	1	1	1
Pseudomonas aeruginosa	2	1	0.57	1	0.481
Enterobacter cloacae	2	0	1	0	1
Citrobacter freundii	1	0	1	0	1
Proteus vulgaris	1	0	1	0	1
Candida species	2	1	0.57	0	1
Unknown	20	6	-	5	-

Figure 1: Receiver operating characteristic (ROC) curve analysis of SOFA score distinguishing in-hospital survivors and non-survivors among surgical, critically ill patients with sepsis. The area under the ROC curve (AUC) was 0.76.

Figure 2: Kaplan-Meier survival curves of surgical, critically ill patients with sepsis having SOFA scores ≤ 8 and > 8. The 22 patients with SOFA score > 8 had a significantly higher in-hospital death rate than the 81 patients with SOFA score ≤ 8 (P = 0.0039).

Table 5: Analyses of the effects of adjunctive treatments of surgical, critically ill patients with sepsis by inverse probability of treatment weighting

Treatments	Multiple Cox regression analyses for in-hospital death			
	n	Adjusted HR	95% CI	P-value
Intravenous immunoglobulins	33	2.834	1.085-7.404	0.059
Renal replacement therapy	18	0.855	0.361-2.025	0.733
PMX	21	2.356	0.872-6.371	0.229

Abbreviations: HR: hazard ratio; CI: confidence interval; PMX: endotoxin-absorbing therapy using polymyxin B.

Staphylococcus aureus (MRSA), two with Candida glabrata, and one with Enterococcus faecium; four (67%) of these patients received empirical treatment with carbapenems.

We also assessed the effects of adjunctive treatment with IVIG, renal replacement therapy, and PMX in patients with sepsis. Following IPTW using eight variables: age, sex, positive blood culture, APACHE score, SOFA score, and treatment with IVIG, renal replacement therapy, and PMX, we found that the weighted in-hospital death rates were similar in patients who did and did not receive each treatment (Table 5).

Discussion

Sepsis is the leading cause of death of surgical patients pre- and postoperatively [21-23]. Once the sources of infection are identified, surgical intervention plus antibiotics are recommended as treatment [8,9]. However, the in-hospital death rate remains high, even following these guidelines [8,9]. The mortality rate in surgical patients with sepsis was reported to be 25.5%, similar to the rate in our study (24.3%) [22]. However, the effectiveness of adjunctive treatments, such as IVIG, renal replacement therapy, and PMX, remains unclear. Moreover, few reports have assessed surgical treatments associated with sepsis, risk factors associated with mortality of surgical, critically ill patients, and microbes associated with sepsis [23]. Although epidemiology and outcomes before and after admission to the surgical intensive care unit have been analyzed [10,11], prognostic factors and treatment results in septic surgical patients remain unclear. The duration of SIRS has been reported to be significantly prognostic of sepsis in medical and surgical units (P = 0.015) [22]. Our study showed that SOFA score may be potentially prognostic of in-hospital deaths in surgical, critically ill patients with sepsis. These results are in accordance with a study that found an association between SOFA score and outcomes in patients admitted to the intensive care unit [24]. Serial measurements of SOFA score during the first week were very useful in predicting the outcome of sepsis, whereas APACHE II scores on the day of admission were not reliable in predicting mortality [25].

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SOFA score is simple and objective, allowing the calculation of the number of dysfunctional organ systems and their severity among six organ systems (respiratory, coagulatory, liver, cardiovascular, renal, and neurologic) [26]. Moreover, SOFA score can measure dysfunction of individual and aggregate organs [27]. SOFA score has been used to evaluate patients with multiple organ dysfunction syndromes (MODS) and their survival [26]. Organ failure may worsen outcomes in surgical critically ill patients with sepsis. Indeed, we found that in-hospital death rates were significantly higher in patients with SOFA scores > 8 than ≤ 8 at admission. SOFA score at admission may therefore suggest the type of primary treatment, including adjunctive therapy. In surgical patients, organ dysfunction at sites other than that of surgery may be more strongly associated with death than transient vital signs and serum chemistry included in the APACHE II score on admission [28].

Although our univariate analysis found that APACHE II score was prognostic of in-hospital deaths, this finding was not observed on from multivariate analyses. APACHE II score is used in intensive care units to assess disease severity. However, SOFA score may be superior to APACHE II score in predicting in-hospital deaths of surgical, critically ill patients with sepsis, because SOFA score, which includes platelet count, may objectively evaluate failure of individual and aggregate organs [26]. Coagulopathy, such as low platelet count, has been associated with sepsis-induced disseminated intravascular coagulation (DIC) [29] and may lead to a severe disease condition or in-hospital death. A prospective survey in Japan also demonstrated that SOFA and DIC scores were consistently higher in nonsurvivors than survivors on the day of admission and 3 days later [23].

Microbial assessment found that E. coli infection was frequently associated with septic shock, including in patients with community-acquired bloodstream infection [30]. Because none of the other microorganisms assayed was associated with septic shock or in-hospital death and only 7.8% of patients received inadequate antimicrobial treatment, surgical, critically ill patients with sepsis should be treated with a broad empirical antimicrobial agent such as a carbapenem. Infections with MRSA and Candida species are of particular concern. The frequency of invasive fungal infections in developed countries has increased because of advances in medical management [31]. Although invasive Candidiasis is frequently intraabdominal in critically ill surgical patients, prompt antifungal therapy and adequate source control may yield good outcomes [32]. Resistance to azoles, particularly fluconazole, should be considered when starting an empirical treatment [32].

Although we attempted to assess the effects of adjunctive treatment, including IVIG, renal replacement therapy, and PMX, in patients with sepsis by IPTW analysis, we found that none had a significantly positive effect on this patient population. However, our study had several limitations. First, relatively few patients received each type of adjunctive treatment. Second, this was a retrospective cohort study assessing the causes of sepsis in Japanese patients. Thus, the results were not externally validated and were limited to patients of Japanese ethnicity. Third, we could not plan a prospective study to clarify the effectiveness of each adjunctive therapy in surgical critically ill patients with sepsis. However, well-designed randomized controlled studies and/or meta-analyses may result in external validity, as well as assessing these adjunctive treatments in patients of varying ethnicity.

In conclusion, this study found that SOFA score may be prognostic of in-hospital deaths of surgical, critically ill patients with sepsis. SOFA > 8 was associated with significantly higher in-hospital death rate and may be a cut-off for the necessity of intensive treatment in these patients.

Conflict of Interest

All authors declare no conflicts of interest.

Compliance with Ethical Requirements

The study protocol was approved by the ethics committees of all participating hospitals, and study information was disclosed to the patients or their survivors by members of the Department of Surgery and Medical Science, Graduate School of Medical Sciences, Kyushu University.

References

1. Rangel-Frausto MS, Pittet D, Costigan M, Hwang T, Davis CS, et al. (1995) The natural history of the systemic inflammatory response syndrome (SIRS). A prospective study. JAMA 273: 117-123.

2. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, et al. (2001) Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med 29: 1303-1310.

3. Daniels R (2011) Surviving the first hours in sepsis: getting the basics right (an intensivist's perspective). J Antimicrob Chemother 66 Suppl 2: ii11-23.

4. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, et al. (2003) 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med 31: 1250-1256.

5. Dellinger RP, Carlet JM, Ramsay G, Zimmerman JL, Vincent JL, et al. (2004) Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 32: 858-873.

6. Dellinger RP, Carlet JM, Ramsay G, Zimmerman JL, Vincent JL, et al. (2014) Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Intensive Care Med 30: 536-555.

7. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, et al. (2008) Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med 34: 17-60.

8. Dellinger RP, Levy MM, Webb SA, Beale RJ, Vincent JL, et al. (2013) Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 41(2): 580-637.

9. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, et al. (2013) Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med 39: 165-228.

10. Rhodes A, Moreno RP, Metnitz B, Hochrieser H, Bauer P, et al. (2011) Epidemiology and outcome following post-surgical admission to critical care. Intensive Care Med 37: 1466-1472.

11. Elias AC, Matsuo T, Grion CM, Cardoso LT, Verri PH (2012) Incidence and risk factors for sepsis in surgical patients: a cohort study. J Crit Care 27: 159-166.

12. De Waele J, De Bus L (2014) How to treat infections in a surgical intensive care unit. BMC Infect Dis 14: 193.

13. Alejandria MM, Lansang MA, Dans LF, Mantaring JB (2002) Intravenous immunoglobulin for treating sepsis and septic shock. Cochrane Database Syst Rev CD001090.

14. Turgeon AF, Hutton B, Fergusson DA, McIntyre L, Tinmouth AA, et al. (2007) Meta-analysis: intravenous immunoglobulin in critically ill adult patients with sepsis. Ann Intern Med 146: 193-203.

15. Mehta RL, McDonald B, Gabbai FB, Pascual MT, Farkas A, et al. (2001) A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. Kidney Int 60: 1154-1163.

16. Ronco C, Bellomo R, Homel P, Dan M, Piccinni P, et al. (2000) Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial. Lancet 356: 26-30.

17. Cruz DN, Perazella MA, Bellomo R, de Cal M, Polanco N, et al. (2007) Effectiveness of polymyxin B-immobilized fiber column in sepsis: a systematic review. Crit Care 11: R47.

18. Austin PC (2013) The performance of different propensity score methods for estimating marginal hazard ratios. Stat Med 32: 2837-2849.

19. Lusted LB (1971) Signal detectability and medical decision-making. Science 171: 1217-1219.

20. Harada N, Shirabe K, Maeda T, Kayashima H, Ishida T, et al. (2015) Blood transfusion is associated with recurrence of hepatocellular carcinoma after hepatectomy in Child-Pugh class A patients. World J Surg 39: 1044-1051.

21. Doklestic SK, Bajec DD, Djukic RV, Bumbasirevic V, Detanac AD, et al. (2014) Secondary peritonitis - evaluation of 204 cases and literature review. J Med Life 7: 132-138.

22. Sugita H, Kinoshita Y, Baba H (2012) The duration of SIRS before organ failure is a significant prognostic factor of sepsis. Int J Emerg Med 5: 44.

23. Ogura H, Gando S, Saitoh D, Takeyama N, Yamashita N, et al. (2014) Epidemiology of severe sepsis in Japanese intensive care units: a prospective multicenter study. J Infect Chemother 20: 157-162.

24. Routsi C, Pratikaki M, Sotiropoulou C, Platsouka E, Markaki V, et al. (2007) Application of the sequential organ failure assessment (SOFA) score to bacteremic ICU patients. Infection 35: 240-244.

25. Desai S, Lakhani JD (2013) Utility of SOFA and APACHE II score in sepsis in rural set up MICU. J Assoc Physicians India 61: 608-611.

26. Vincent JL, Moreno R, Takala J, Reinhart CK, Suter PM, et al. (1996) The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 22: 707-710.

27. Artero A, Zaragoza R, Camarena JJ, Sancho S, González R, et al. (2010) Prognostic factors of mortality in patients with community-acquired bloodstream infection with severe sepsis and septic shock. J Crit Care 25: 276-281.

28. Vincent JL, Nelson DR, Williams MD (2011) Is worsening multiple organ failure the cause of death in patients with severe sepsis? Crit Care Med 39: 1050-1055.

29. Gando S, Saitoh D, Ishikura H, Mashiko K, Tsubota T, et al. (2013) A randomized, controlled, multicenter trial of the effects of antithrombin on disseminated intravascular coagulation in patients with sepsis. Crit Care 7: R297

30. de Ruiter J, Weel J, Manusama E, Kingma WP, van der Voort PH (2009) The epidemiology of intra-abdominal flora in critically ill patients with secondary and tertiary abdominal sepsis. Infection 37: 522-527.

31. Aki K, Okubo Y, Nanjo H, Ishiwatari T, Masuda H, et al. (2015) Genomic Analysis of Single Nucleotide Polymorphisms Asp299Gly and Thr399Ile in Japanese Patients with Invasive Aspergillosis. Jpn J Infect Dis 68: 330-332.

32. Aguilar G, Delgado C, Corrales I, Izquierdo A, Gracia E, et al. (2015) Epidemiology of invasive candidiasis in a surgical intensive care unit: an observational study. BMC Res Notes 8: 491.

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