Intensive care unit model and in-hospital mortality among patients with severe sepsis and septic shock

A secondary analysis of a multicenter prospective observational study

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Abstract

We aimed to determine the association between the intensive care unit (ICU) model and in-hospital mortality of patients with severe sepsis and septic shock.

This was a secondary analysis of a multicenter prospective observational study conducted in 59 ICUs in Japan from January 2016 to March 2017. We included adult patients (aged ≥16 years) with severe sepsis and septic shock based on the sepsis-2 criteria who were admitted to an ICU with a 1:2 nurse-to-patient ratio per shift. Patients were categorized into open or closed ICU groups, according to the ICU model. The primary outcome was in-hospital mortality.

A total of 1018 patients from 45 ICUs were included in this study. Patients in the closed ICU group had a higher severity score and higher organ failure incidence than those in the open ICU group. The compliance rate for the sepsis care 3-h bundle was higher in the closed ICU group than in the open ICU group. In-hospital mortality was not significantly different between the closed and open ICU groups in a multilevel logistic regression analysis (odds ratio = 0.83, 95% confidence interval; 0.52–1.32, $P = .43$) and propensity score matching analysis (closed ICU, 21.2%; open ICU, 25.7%, $P = .22$).

In-hospital mortality between the closed and open ICU groups was not significantly different after adjusting for ICU structure and compliance with the sepsis care bundle.

Abbreviations: ADL = activities of daily living, CI = confidence interval, CVP = central venous pressure, FIO2 = fraction of inspired oxygen, FORECAST = Focused Outcomes Research in Emergency Care in Acute Respiratory Distress Syndrome, Sepsis, and Trauma, HR = hazard ratio, ICU = intensive care unit, IQR = interquartile range, LOS = length of hospital stay, MAP = mean arterial pressure, MRSA = methicillin resistant staphylococcus aureus, OR = odds ratio, PaO2 = partial pressure of arterial oxygen, ScvO2 =

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1. Introduction

Sepsis, a common condition in patients admitted to intensive care units (ICU), is a leading cause of death during ICU and hospital stays. The prognosis for patients diagnosed with sepsis has improved, due to early recognition of sepsis and the development of sepsis care bundles, including fluid resuscitation, proper use of antibacterial drugs, and vasopressors. However, recent worldwide prospectively collected data revealed that hospital mortality in patients diagnosed with sepsis when admitted to the ICU was 30.3% (95% confidence interval (CI), 27.1–33.6%) and hospital mortality in patients with septic shock on ICU admission was 43.0% (95% CI, 39.9–46.2%).[1] Sepsis remains to be a burden for ICU patients. Therefore, we need to improve the quality of sepsis management and, consequently, sepsis prognosis.

The quality of medical care was assessed using three Donabedian concepts: structure, process, and outcome.[2] To improve sepsis prognosis, structure, and process are important. Most sepsis and septic shock patients are admitted to the ICU. Thus, the ICU structure might play a role in sepsis prognosis. In the ICU structure, the ICU model has influenced outcome of patients with critical illness and sepsis.[3–7] When considering the process, the proper use of treatments and devices including antibacterial drugs, renal replacement therapy and mechanical ventilation, and compliance with clinical practice guidelines for sepsis and septic shock are important.

Currently, there are only a few studies that focused on the ICU model in the structure when evaluating sepsis care.[7,8] Hence, this study aimed to investigate the association between the ICU model and the prognosis of patients with severe sepsis and septic shock.

2. Materials and methods

2.1. Study design, setting, and participants

In this study, the ICU model and outcome of patients with severe sepsis were evaluated using the database from the Focused Outcomes Research in Emergency Care in Acute Respiratory Distress Syndrome, Sepsis, and Trauma (FORECAST) study. The FORECAST study was a multicenter, prospective observational study that enrolled consecutive patients with acute respiratory distress syndrome, sepsis, and trauma who were admitted to 59 ICUs in Japan from January 2016 to March 2017, and the data was collected by physicians at each ICU. In this study, the sepsis part included adult patients (aged ≥ 16 years) with severe sepsis based on the 2003 sepsis-2 criteria.[9] The inclusion criteria were patients suspected to have or were diagnosed with new-onset infection based on the history of the present illness, patients who met ≥ 2 systemic inflammatory response syndrome criteria, and patients who had at least one occurrence of organ dysfunction. Also, the sepsis-2 criteria included systolic blood pressure < 90 mmHg, mean arterial pressure (MAP) < 65 mmHg, or a decrease in blood pressure > 40 mmHg; serum creatinine > 2.0 mg/dL or diuresis (urine output < 0.5 mL/kg/h); total bilirubin > 2.0 mg/dL; platelet count < 100,000 cells/mm^3; arterial lactate > 2 mmol/L; international normalized ratio > 1.5;

and arterial hypoxemia (partial pressure of arterial oxygen (PaO2)/fraction of inspired oxygen (FIO2) < 200 with pneumonia or PaO2/FIO2 < 250 without pneumonia).[9] The exclusion criteria included the limitation of sustained life care or post-cardiopulmonary arrest resuscitation status at the time of sepsis diagnosis. Details of the FORECAST study were published elsewhere.[10] For this study, patients admitted to ICUs with a 1:2 nurse-to-patient ratio per shift were included. Patients admitted to ICUs with a 1:4 nurse-to-patient ratio per shift were excluded to make ICU characteristics uniform. Patients with missing in-hospital mortality data were also excluded.

The study protocol was reviewed and approved by the ethics committee of all participating institutions in the Japanese Association for Acute Medicine (JAAM) study group (IRB No.014–0306 in Hokkaido University, the representative institution for FORECAST). The need for informed consent from study participants was waived under the approval of the ethics committees.

2.2. Data collection and end point

Data compiled by FORECAST investigators were obtained from the FORECAST database. Facility information included the structure characteristics of the ICU, ICU beds, and the number of certified intensivists. Patient information included the demographic characteristics of the patients, admission source, comorbidities, Charlson comorbidity index score, activities of daily living (ADLs), suspected sites of infection at admission, organ dysfunctions, sepsis-related severity scores, details of antibiotic use, treatment for severe sepsis, septic shock, ICU-free days, ventilator-free days (VFDs), length of hospital stay (LOS), and in-hospital mortality. VFD was defined as the number of days within the first 28 days after enrolment during which a patient was able to breathe without a ventilator. Patients who died during the study period were assigned with a VFD of 0. ICU-free days were calculated in the same manner. In addition, data on compliance with sepsis care bundles proposed in the 2012 Surviving Sepsis Campaign Guidelines (SSCG) were obtained. Compliance was described as evidence that all bundle elements were achieved within the appropriate time frame (i.e., 3 h or 6 h) and were adhered to the indications (i.e., septic shock or lactate level > 4 mmol/L). Data collection was performed as part of the routine clinical workup. The primary outcome was in-hospital mortality.

2.3. Statistical analysis

Patients were categorized into open ICU or closed ICU groups in accordance with the ICU model. Each ICU subjectively described its structure including the ICU model at the initiation of the FORECAST study.

Nonnormally distributed continuous data were presented as medians and interquartile ranges (IQRs) and were compared using the Wilcoxon rank-sum test. Categorical data were summarized as percentages and counts and were compared using Fisher's exact test or χ^2 test. For the primary outcome, a multilevel logistic regression analysis was conducted to adjust for
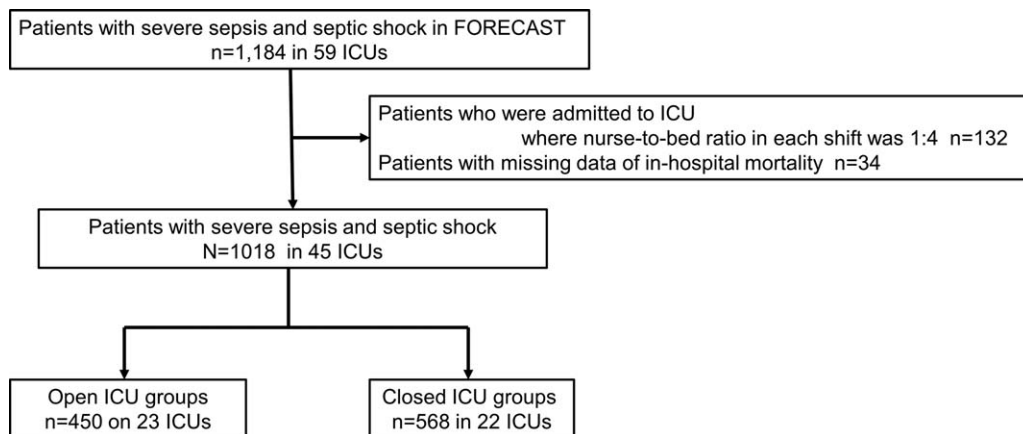
Figure 1. Flow diagram of study participants. FORECAST = Focused Outcomes Research in Emergency Care in Acute Respiratory Distress Syndrome, Sepsis, and Trauma, ICU = Intensive Care Unit.

differences in characteristics of the institutions. The variables applied to the multilevel logistic regression analysis were teaching facility, ICU beds, ICU beds per certified intensivist, age, gender, and BMI of patients, admission source, Charlson comorbidity index score, ADLs, suspected sites of infection, positive blood culture, septic shock, sepsis-related organ failure assessment (SOFA) score, and compliance rate for the entire 3-h bundle. Facility, patient background, and other variables associated with hospital mortality based on previous studies were select-ed.[7,8,11,12] For the sepsis care bundles, only the entire 3-h bundle was selected because the compliance rate of the entire 6-h bundle was very low. Data were presented as odds ratio (OR) with 95% CI. As a sensitivity analysis, a propensity score matching analysis with the same variables as the multilevel logistic regression analysis was performed. For the propensity score matching analysis, calipers of width equal to 0.2 of the standard deviation were used.

P values were two-sided and *P* < .05 was considered statisti-cally significant. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., NC, USA) and STATA 14.0 (StataCorp, TX, USA).

3. Results

Of the 1184 patients registered in the FORECAST study, 132 patients who were admitted to ICUs with a nurse-to-bed ratio of

1:4 per shift and 34 patients with missing in-hospital mortality data were excluded. Thus, 1018 patients in 45 ICUs were included in this study. Among these patients, 450 patients in 23 ICUs were categorized to the open ICU group and 568 patients in 22 ICUs were categorized to the closed ICU group (Fig. 1).

Table 1 shows the characteristics of the study facilities. Teaching facility, the number of ICU beds, ICU patients per year, the number of certified intensivists, and ICU beds per certified intensivist were not statistically different between the two groups. Table 2 shows the baseline characteristics of study patients. All patient demographics, except gender, were not statistically significant between the two groups. The most common suspected site of infection in the closed ICU group was the abdomen, followed by the lung, whereas in the open ICU group, the most common suspected site of infection was the lung, followed by the abdomen. Incidence rates of positive blood culture (60.2 vs. 52.0%, *P* = .008) and septic shock (67.6 vs. 54.7%, *P* < .001) were higher in the closed ICU group than in the open ICU group. Regarding organ dysfunction upon arrival in the ICU, incidence rates of hypotension (53.4 vs. 44.9%, *P* = .007) and thrombocy-topenia (32.9 vs. 24.4%, *P* = .003) were higher in the closed ICU group. As for the severity score, the closed ICU group had a higher SOFA score than the open ICU group (9 vs. 8, *P* = .009).

Table 3 shows the sepsis care bundle, treatment, and outcome of study patients. The compliance rates for the entire 3-h bundle and each item of the 3-h bundle were higher in the closed ICU

Table 1

Characteristics of study facilities.

		Open ICU n = 23	Closed ICU n = 22	*P* value
Teaching facility	no (%)	11 (47.8)	16 (72.7)	.09
ICU beds	Median (IQR)	12 (8–16)	13 (10–18)	.55
ICU beds category				
1–10	no (%)	9 (39.1)	8 (36.4)	.87
11–20	no (%)	12 (52.2)	11 (50.0)	
21 -	no (%)	2 (8.7)	3 (13.6)	
ICU patients per year	Median (IQR)	799 (550–1000)	791 (420–988)	.61
Certified intensivists	Median (IQR)	1 (0–3)	2 (1–3)	.17
ICU beds per a certified intensivist	Median (IQR)	3 (2–14)	5 (2–9)	.08

ICU = intensive care unit, IQR = interquartile range.

Table 2.

Baseline characteristics of study patients (n = 1018).

		Open ICU n = 450	Closed ICU n = 568	P value	Missing
Age	Median (IQR)	73 (65–82)	72 (62–81)	0.05	–
Gender					
male	no (%)	292 (64.9)	334 (58.8)	0.048	–
BMI	Median (IQR)	21.6 (19.0–25.1)	21.8 (19.0–24.4)	0.66	7
Admission source					
Emergency Department	no/total (%)	258/450 (57.3)	297/567 (52.4)	0.06	1
Transfer or other departments	no/total (%)	185/450 (40.0)	240/567 (42.3)		
ICU	no/total (%)	12/450 (2.7)	30/567 (5.3)		
Coexisting conditions					
Myocardial infarction	no (%)	22 (4.9)	29 (5.1)	0.87	–
Congestive heart failure	no (%)	53 (11.8)	56 (9.9)	0.33	–
Cerebrovascular disease	no (%)	49 (10.9)	66 (11.6)	0.71	–
Dementia	no (%)	44 (9.8)	36 (6.3)	0.04	–
Chronic obstructive pulmonary disease	no (%)	31 (6.9)	40 (7.0)	0.92	–
Diabetes mellitus	no (%)	105 (23.3)	138 (24.3)	0.72	–
Chronic kidney disease	no (%)	31 (6.9)	45 (7.9)	0.53	–
Malignancy (solid or blood)	no (%)	72 (16.0)	76 (13.4)	0.23	–
Moderate to severe Liver disease	no (%)	8 (1.8)	15 (2.6)	0.36	–
Charlson comorbidity index	Median (IQR)	1 (0–2)	1 (0–2)	0.40	–
ADL					
dependent	no/total (%)	106/449 (23.6)	140/567 (24.7)	0.69	2
Medication					
Steroids	no (%)	56 (12.4)	77 (13.6)	0.60	–
Immunosuppressant	no (%)	16 (3.6)	23 (4.1)	0.68	–
Suspect site of infection					
Lung	no (%)	177 (39.3)	144 (25.3)	<0.001	–
Abdomen	no (%)	111 (24.7)	161 (28.3)		
Urinary tract	no (%)	73 (16.2)	108 (19.0)		
Blood stream infection/endocardium/Catheter/Implant device	no (%)	11 (2.4)	29 (5.1)		
Central nerve system	no (%)	6 (1.3)	13 (2.3)		
Osteoarticular	no (%)	4 (0.9)	9 (1.6)		
Skin/soft tissue	no (%)	45 (10.0)	59 (10.4)		
Wound	no (%)	3 (0.7)	6 (1.1)		
Other	no (%)	20 (4.5)	39 (6.9)		
Positive blood cultures	no/total (%)	234/450 (52.0)	339/563 (60.2)	0.008	5
Septic shock	no (%)	246 (54.7)	384 (67.6)	<0.001	–
Initial serum lactate	Median (IQR)	3.1 (1.8–5.5)	3.0 (1.9–5.2)	0.59	73
Organ dysfunction on arrival					
Hypotension	no/total (%)	202/450 (44.9)	303/568 (53.4)	0.007	–
Hyperlactatemia (> 2mmol/L)	no/total (%)	291/450 (64.7)	379/568 (66.7)	0.49	–
Acute kidney injury (Creatinine >2.0mg/dl)	no/total (%)	170/450 (37.8)	217/568 (38.2)	0.89	–
Acute lung injury	no/total (%)	54/401 (13.5)	83/536 (15.5)	0.39	–
Hyperbilirubinemia (> 20. Mg/dL)	no/total (%)	74/450 (16.4)	102/568 (18.0)	0.53	–
Thrombocytopenia (< 100,000/μL)	no/total (%)	110/450 (24.4)	187/568 (32.9)	0.003	–
Coagulopathy (PT-INR >1.5)	no/total (%)	77/450 (44.2)	114/568 (20.1)	0.23	–
ARDS	no/total (%)	54/401 (13.5)	83/536 (15.5)	0.39	81
APACHE II score	Median (IQR)	22 (16–29)	23 (17–30)	0.11	108
SOFA score	Median (IQR)	8 (5–11)	9 (6–12)	0.009	160

ADL = Activities of daily living, APACHE = Acute Physiology and Chronic Health Evaluation, BMI = body mass index, ICU = intensive care unit, IQR = interquartile range, PT-INR = Prothrombin Time-International Normalized Ratio, SOFA = Sepsis-related Organ Failure Assessment.

group than in the open ICU group. The compliance rate for the entire 3-h bundle was 71.3% in the closed ICU group and 54.8% in the open ICU group (P < .001). However, the compliance rate for the entire 6-h bundle was very low in both groups because the compliance rates for measurement of central venous pressure (CVP) and central venous oxygen saturation (ScvO2) were low. In contrast, compliance rates for vasopressor use and re-measurement of lactate in the 6-h bundle were high in both groups and the compliance rates were higher in the closed ICU group than in the open ICU group (88.8 vs. 81.5%, P = .001).

Concerning mediations and interventions from diagnosis to within 72 h after diagnosis, the rates of noradrenaline, steroid, and recombinant human-soluble thrombomodulin use were higher in the closed ICU group than in the open ICU group. In contrast, the rates of protease inhibitor and sivelestat sodium use were lower in the closed ICU group than in the open ICU group. With regards to antibacterial drugs, the rates of carbapenem and anti-methicillin-resistant *Staphylococcus aureus* (MRSA) drug use were higher in the closed ICU group than in the open ICU group. ICU-free days, ventilator-free days, and length of hospital

Table 3.

The sepsis care bundle, treatment, and outcome of study patients (n = 1018).

		Open ICU n = 450	Closed ICU n = 568	P value	Missing
Sepsis care bundle					
Compliance with all applicable elements of sepsis 3-h resuscitation bundle					
Serum lactate obtained within 3-h of diagnosis of sepsis	no/total (%)	426/449 (94.9)	563/568 (99.1)	<0.001	1
Broad-spectrum antibiotic given within 3-h of diagnosis of sepsis	no/total (%)	357/448 (79.7)	498/568 (87.7)	<0.001	2
Blood cultures obtained before broad-spectrum antibiotic administration	no/total (%)	388/447 (86.8)	534/568 (94.0)	<0.001	3
For hypotension or lactate concentration >4 mmol/L, 30ml/kg crystalloid fluid bolus delivered within 3-h of diagnosis of sepsis					
Yes	no/total (%)	192/444 (43.2)	346/568 (60.9)	<0.001	6
No	no/total (%)	95/444 (21.4)	88/568 (15.5)		
Not indicated	no/total (%)	157/444 (35.4)	134/568 (23.6)		
Entire 3-h bundle	no/total (%)	246/449 (54.8)	405/568 (71.3)	<0.001	1
Compliance with all applicable elements of sepsis 6-h resuscitation bundle					
Vasopressors use followed initial fluid bolus if needed to maintain MAP ≥ 65 mmHg within 6-h of diagnosis of sepsis (yes/cases with indication)					
Yes	no/total (%)	247/446 (55.4)	391/568 (68.8)	<0.001	4
No	no/total (%)	35/446 (7.8)	45/568 (7.9)		
Not indicated	no/total (%)	164/446 (36.8)	132/568 (23.3)		
Dopamine	no/total (%)	43/247 (17.4)	41/391 (10.5)	0.01	–
Dobutamine	no/total (%)	18/247 (7.3)	51/391 (13.0)	0.02	–
Noradrenaline	no/total (%)	231/247 (93.5)	374/391 (95.7)	0.24	–
For septic shock or lactate >4 mmol/L, CVP measured within 6-h of diagnosis of sepsis (yes/cases with indication)					
Yes	no/total (%)	64/446 (14.4)	103/567 (18.2)	<0.001	5
No	no/total (%)	228/446 (51.1)	330/567 (58.2)		
Not indicated	no/total (%)	154/446 (34.5)	134/567 (23.6)		
For septic shock or lactate >4 mmol/L, ScvO2 measured within 6-h of diagnosis of sepsis (yes/cases with indication)					
Yes	no/total (%)	24/446 (5.4)	13/568 (2.3)	<0.001	4
No	no/total (%)	268/446 (60.1)	420/568 (73.9)		
Not indicated	no/total (%)	154/446 (34.5)	135/568 (23.8)		
Re-measured lactate if initial lactate elevated					
Yes	no/total (%)	309/446 (69.3)	431/563 (76.6)	<0.001	9
No	no/total (%)	54/446 (12.1)	21/563 (3.7)		
Not indicated	no/total (%)	83/446 (18.6)	111/563 (19.7)		
Entire 6-h bundle	no/total (%)	16/358 (4.5)	7/487 (1.4)	0.007	173
Vasopressors use and re-measured lactate in 6-h bundle	no/total (%)	361/443 (81.5)	500/563 (88.8)	0.001	12
Medications and interventions (from diagnosis to within 72 h after diagnosis)					
Time from diagnosis of sepsis to antibiotic use among patients who were given antibiotic within 3 h of diagnosis of sepsis	Median (IQR)	80 (46–118)	71 (34.0–118)	0.15	5
Noradrenaline	no/total (%)	270/450 (60.0)	403/567 (71.1)	<0.001	1
Continuous renal replacement therapy	no/total (%)	118/449 (26.3)	159/565 (28.1)	0.51	4
Intermittent renal replacement therapy	no/total (%)	14/447 (3.1)	21/566 (3.7)	0.62	5
Polymyxin B Hemoperfusion	no/total (%)	43/450 (9.6)	41/567 (7.2)	0.18	1
Protease inhibitor (without sivelestat sodium)	no/total (%)	66/446 (14.8)	6/565 (1.1)	<0.001	7
Sivelestat sodium	no/total (%)	28/447 (6.3)	8/566 (1.4)	<0.001	5
Intravenous immunoglobulin	no/total (%)	86/446 (19.3)	117/564 (20.7)	0.56	8
Selective digestive decontamination	no/total (%)	6/447 (1.3)	3/564 (0.5)	0.17	7
Enteral nutrition	no/total (%)	202/446 (45.3)	276/565 (48.9)	0.26	7
Steroid	no/total (%)	123/448 (27.5)	196/564 (34.8)	0.01	6
Antithrombin	no/total (%)	92/448 (20.5)	125/566 (22.1)	0.55	4
Recombinant human soluble thrombomodulin	no/total (%)	69/448 (15.4)	144/564 (25.5)	<0.001	6
Antibacterial and antifungal drug					
Sulbactam/Ampicillin	no/total (%)	39/450 (8.7)	25/568 (4.4)	0.005	–
Tazobactam/Piperacillin	no/total (%)	101/450 (22.4)	106/568 (18.7)	0.14	–
Ceftriaxone/Cefotaxime	no/total (%)	43/450 (9.6)	34/568 (6.0)	0.03	–
Carbapenem	no/total (%)	199/450 (44.2)	356/568 (62.7)	<0.001	–
Vancomycin	no/total (%)	63/450 (14.0)	123/568 (21.7)	0.002	–
Anti MRSA drug except Vancomycin	no/total (%)	15/450 (3.3)	50/568 (8.8)	<0.001	–
Antifungal drug	no/total (%)	18/450 (4.0)	28/568 (4.9)	0.48	–
ICU-free days	Median (IQR)	19 (10–24)	19 (10–24)	0.48	204
Ventilator-free days	Median (IQR)	20 (0–28)	21 (0–27)	0.22	10
Length of hospital stay	Median (IQR)	23 (12–46)	24 (12–45)	0.82	–
Hospital mortality	no/total (%)	104/450 (23.1)	142/568 (25.0)	0.48	–

CVP = central venous pressure, ICU = intensive care unit, IQR = interquartile range, ScvO2 = Central venous oxygen saturation.

. The multilevel logistic regression analysis for hospital mortality
(n=846).

Variables	Odds ratio (95% CI)	P value
ICU model		
Closed ICU (vs Open)	0.83 (0.52–1.32)	.43
Teaching facility	0.68 (0.40–1.14)	.14
ICU beds category		
1–10	reference	–
11–20	0.54 (0.33–0.91)	.02
21–	0.49 (0.23–1.02)	.06
ICU beds per certified intensivist	1.03 (0.99–1.05)	.07
Age (per year)	1.02 (1.01–1.04)	.003
Gender		
male	0.72 (0.49–1.04)	.08
BMI (per single point)	0.99 (0.96–1.03)	.69
Admission source		
Emergency Department	reference	–
Transfer or other departments	2.36 (0.99–5.59)	.05
ICU	1.22 (0.81–1.83)	.33
Charlson comorbidity index (per single point)	1.20 (1.08–1.34)	<.001
ADL		
Dependent	0.91 (0.58–1.42)	.67
Suspect site of infection		
Lung	reference	–
Abdomen	0.50 (0.31–0.81)	.004
Urinary tract	0.22 (0.11–0.44)	<.001
Blood stream infection/endocardium/ Catheter/Implant device	0.79 (0.32–1.96)	.61
Central nerve system	2.30 (0.72–7.35)	.16
Osteoarticular	0.97 (0.17–5.47)	.97
Skin/soft tissue	0.81 (0.42–1.54)	.52
Wound	0.94 (0.12–7.29)	.95
Other	1.28 (0.61–2.68)	.51
Positive blood culture	1.15 (0.79–1.69)	.46
Septic shock	0.97 (0.61–1.54)	.90
SOFA score	1.19 (1.13–1.26)	<.001
Compliance rate for the entire 3-h bundle	0.97 (0.65–1.45)	.89

ADL = Activities of daily living, BMI = body mass index, CI = confidence interval, ICU = intensive care unit, SOFA = Sepsis-related Organ Failure Assessment.

stays were not significantly different between the two groups. The primary outcome, in-hospital mortality, was 25.0% in the closed ICU group and 23.1% in the open ICU and was not significantly different between the two groups (P=.48).

Table 4 displays the results of the multilevel logistic regression analysis for in-hospital mortality. The OR for in-hospital mortality between the two groups was not statistically significant (OR 0.83 [95% CI: 0.52–1.32] in closed ICU group, reference in open ICU group, P=.43). As a sensitivity analysis, in the propensity score matching analysis, in-hospital mortality between the two groups was not statistically significant (closed ICU

group, 21.2%; open ICU group, 25.7%; P=.22) (Table 5, and see Table S1, Supplemental Digital Content, http://links.lww. com/MD2/A192, which illustrates the comparison for variables between open ICU and closed ICU groups after propensity score matching analysis).

4. Discussion

4.1. Key findings

This study demonstrates that patients in the closed ICU group had a higher severity score and had more incidences of organ failures than patients in the open ICU group. In addition, the closed ICU group had a higher compliance rate for the 3-h bundle than the open ICU group. In-hospital mortality was not significantly different between the closed ICU and the open ICU groups based on the multilevel logistic regression analysis and propensity score matching analysis.

4.2. Relationship to previous studies

Before and after studies and a meta-analysis comparing open and closed ICUs for patients with critical illnesses showed that in-hospital mortality in the closed ICU was lower than that in the open ICU.[3–6,13] A single-center retrospective observational study showed that in-hospital mortality decreased from 25.7% to 15.8% (P=.01) after shifting from the open ICU to the closed ICU.[6] In a meta-analysis, mortality was significantly higher in the open ICU than in the closed ICU (OR 1.31 [95% CI: 1.17–1.48] in open ICU, reference in closed ICU, P<.001).[13] In sepsis patients, a prospective cohort study in Asian ICUs reported that in-hospital mortality was not significantly different between patients cared for in the open ICU versus closed ICU setting (open ICU vs. closed ICU, 42.4% vs. 46.1%; P=.19).[8] A nationwide observational study in Japan showed that in-hospital mortality was significantly lower in the closed ICU than in the open ICU (OR 0.63 [95% CI: 0.55–0.78], P<.001).[7] The study explained that high-quality care, including a high compliance rate to the guidelines, contributed to the lower in-hospital mortality in the closed ICU although there was no data concerning guideline compliance rates.

As for ICU structures, a multicenter prospective observational study conducted in Korea showed that a nurse-to-patient ratio of 1:2 was significantly associated with a lower 28-day mortality (hazard ratio (HR) 0.46 [95% CI: 0.21–0.99], P=.049) but not with in-hospital mortality.[14] Concerning compliance with the 2012 SSCG guidelines, previous studies reported that compliance with the 3-h sepsis bundle and 6-h bundle was statistically associated with lower in-hospital mortality.[11,12,15] This study showed that in-hospital mortality was not significantly different

. Primary outcome between open ICU and closed ICU.

	Open ICU	Closed ICU	P value
Hospital mortality by univariate analysis (n=1018) no/total (%)	104/450 (23.1)	142/568 (25.0)	.48
Hospital mortality by Multilevel logistic regression analysis (n=846) Odds ratio (95% confidence interval)	1.00	0.83 (0.52–1.32)	.43
Hospital mortality by propensity score matching analysis (n=538) no/total (%)	69/269 (25.7)	57/269 (21.2)	.22

ICU = intensive care unit.

in the closed ICU versus open ICU groups after adjusting for the ICU structure and sepsis care bundle compliance. The reason for the difference in our findings compared to previous studies may be due to the rates of compliance with the sepsis care bundle, which were higher in both the closed ICU and open ICU settings compared to previous studies. Moreover, only ICUs with a 1:2 nurse-to-patient ratio per shift were included. Otherwise, each attending physicians in the open ICU might have consulted appropriately with intensivists for sepsis practice. Also, the severity of sepsis among patients admitted to the ICU was high; therefore, patients might have died even if they were treated appropriately.

4.3. Significance and implications

This study showed that in-hospital mortality was not significantly different between the closed and open ICU groups. However, the odds ratio for in-hospital mortality of the closed ICU group was lower (but not significantly different) based on the multilevel logistic regression analysis and propensity score matching analysis. These findings imply that in-hospital mortality in the closed ICU might be better than that in the open ICU.

As for the ICU model, ICU admission, discharge, and triage guidelines revealed that a high-intensity ICU model is recommended.[16] A high-intensity ICU model is characterized by the intensivist being responsible for the day-to-day management of the patient, either in a closed ICU (the intensivist is the patient's primary attending physician) or mandatory critical care consultation (the intensivist is not the patient's primary attending physician, but every patient admitted to the ICU receives a critical care consultation).[16,17] Sufficient human resources are needed to manage a high-intensity ICU. However, there are not enough intensivists in Japan.[18] Hence, the effective utilization of intensivists is important. In low-intensity ICUs, the development of a system that facilitates effective consultation to only a few intensivists and treats patients with them is important. Furthermore, the few intensivists need to educate physicians and ICU nurses about the guidelines for managing critical patients.

4.4. Limitations

This study had several limitations. First, the open ICU and closed ICU settings were not clearly defined in the FORECAST study and each ICU subjectively reported information about their ICU model. Hence, a misclassification bias might have occurred. However, no fundamental definitions of ICU models have been established by any professional intensive care society. Second, this study included only 45 ICUs, which comprise only about one-seventh of the total tertiary emergency facilities in Japan. Thus, sampling bias may have occurred. Furthermore, all ICU structures and processes for the management of sepsis and septic shock could not be investigated. For the ICU structures, the detailed engagement of intensivists in patient treatment in the open ICU, the time coverage (24 h a day or not) of intensivists, and the presence of certified nurses, clinical engineers, and pharmacists were not evaluated. With respect to the process, the compliance to guidelines, such as the ABCDEF bundle[19] and ventilator-associated pneumonia bundle,[20] which might be associated with the prognosis of patients with sepsis and septic shock were not assessed. These factors might have affected the outcomes of this study.

5. Conclusions

This secondary analysis of a multicenter prospective observational study on sepsis in Japan showed that the in-hospital mortality was not statistically different in the closed ICU versus open ICU setting after adjusting for different structure and process elements associated with the management of sepsis. To improve sepsis prognosis, the optimal structure and process for the management of sepsis and septic shock should be explored.

Author contributions

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