most frequent among the surgery cases (38.4% and 30.6 %, respectively) and infection was most frequent in the internal medical disease cases. There were significant differences in the rates of neoplastic, metabolic, gastrointestinal, respiratory and neuromuscular disease in the internal medical disease cases and in cerebral surgery, abdominal surgery, lung or mediastinal surgery, and orthopedic surgery in the patients who underwent surgery. The results of univariate analysis are shown in Table 3. The overall mortality rate was 9.8%. The strongest association with mortality was found for use of dialysis (45.3%), followed by mechanical ventilation (32.9 %). Gender was not a significant factor ($p = 0.489$) ($p > 0.25$). Excluding gender, the remaining 8 variables were subjected to multiple logistic analysis (stepwise backward selection method) to construct the model.

In the validation data set, coefficients of the prediction model variables, odds ratios, 95% confidence intervals, and the final equation are shown in Table 4. The most influential factor was use of dialysis (OR = 4.85, 95 % CI = 3013-7.5). A Hosmer-Lemeshow contingency table for the validation dataset is presented in Table 5. For validation of the prediction model, the Hosmer-Lemeshow χ-square, p value, and the area under the ROC curve (95% CI) are shown in Table 6. The Hosmer-Lemeshow statistic (a measure of the discrepancy between the observed and predicted risk) was 13.45 ($p = 0.1$) and 3.08 ($p = 0.93$) in the test and validation datasets, respectively, indicating good calibration of the model. The calibration was also shown to be better than that of the COPE model. Cases in the internal medical disease, emergency surgery, and scheduled surgery categories also showed good Hosmer-Lemeshow χ-square values indicating good calibration (7.61, 8.54, and 7.53, respectively). The different levels of probability in the validation dataset are shown in Table 7. The discrimination ratio was 88.7% for 50% probability. The C statistic for the test dataset was 0.86 (Figure 1) and that for the validation dataset was 0.88 (Figure 2), indicating good discrimination.

DISCUSSION

The different versions of APACHE, MPM and SAPS are widely used in the intensive care field [3-14]. These approaches mainly depend on organ scores that require physiological data such as serum creatinine, serum bilirubin, heart rate, platelet count and partial oxygen pressure. Areas under the ROC curves for APACHE-II, APACHE-III, MPM_0, MPM_{24}, MPM-II_0, MPM-II_{24}, SAPS, and SAPS-II in previous studies have been summarized by Ohno-Machado et al. [3] Excluding SAPS, this area was ≥ 0.8 for all scoring systems. Duke et al. [2] derived the Critical care Outcome Prediction Equation (COPE) model using administrative data and simple variables. The COPE model is favored because it has an area under the ROC curve of 0.83-0.84 and relatively few variables, and is currently the only model based on administrative data alone. Only mechanical ventilation is evaluated as therapy for the intensive-care patients in this model, and not other life support interventions such as dialysis and pressors/vasoconstrictors. The Hosmer-Lemeshow χ-square statistic suggested that calibration of the COPE model was no better than that of APACHE-III. Compared with the COPE model, our model has a better Hosmer-Lemeshow χ-square value and area under the ROC curve, which suggests that improved calibration might be achieved by inclusion of information on use of dialysis and pressors/vasoconstrictors.

The model developed in this study has several advantages over existing models. First, the variables depend on information that can be obtained from administrative data based on a systematic input form. These variables can be input by doctors and nurses in a timely manner, rather than at or after discharge, which improves the reliability of the data. In addition, the model uses only 8 variables, which facilitates its generalization and application. Second, the model is independent of the primary diagnosis, which avoids the problems of difficulty in identification of the disease in critical care patients. Since patients with various diseases are treated in intensive care, including primary disease and aggravated concomitant diseases, development of a model capable of

uniform evaluation of all ICU cases is important.

The Project IMPACT study published in 2007 [15] used a combination of a Mortality Probability Model (MPM_0-II) to assess clinical performance and a new Weighted Hospital Days scale (WHD) model to assess resource utilization for benchmarking ICUs. Our QIP study and the Project IMPACT study have similar uncertainty regarding the clinical course after discharge. A 90-day mortality rate may be a better measure of outcome than vital status at hospital discharge, but there is difficulty with collection of data after discharge [16]. Therefore, we considered hospital mortality as an endpoint in the present study. We note that administrative data in Japan includes all daily orders and health care costs.

There are several limitations in the present study. First, we did not compare our model with other scoring systems using physiological data. Therefore, we cannot state whether the accuracy of the model is high or low compared to other systems. In addition, the accuracy of the model might not have been fully investigated since our data did not include a predicted mortality score as a gold standard. However, compared to the COPE model, our model has better calibration and discrimination, and the COPE model has no better calibration and discrimination than the APACHE III model. Second, the administrative data include information given on a "calendar day" basis, rather than an hourly basis, and therefore the first ICU day was defined by a calendar day and this provides no distinction regarding the use of dialysis and pressors/vasoconstrictors before or after ICU entry on the first ICU day. However, these resources are mostly used under monitoring in the ICU. Third, the indications for mechanical ventilation, dialysis, and pressors/vasoconstrictors varied among the hospitals in the study, which may have produced therapeutic bias in the model. Fourth, the administrative data do not indicate if renal replacement therapy was given for chronic or acute renal failure or for a non-renal indication; if mechanical ventilation was used for acute respiratory failure or postoperative weaning; and if pressors/vasoconstrictors were used to treat hypovolemic or

septic shock. Finally, except for the reason for ICU entry and the time from admission to ICU entry, the variables used in the model were not ICU-specific, and different admission criteria among the ICUs could have produced a selection bias that affected hospital mortality at discharge, making the prediction model less ICU-specific.

Among the candidate variables, gender was not a significant variable, which is consistent with the other scoring systems. Age is a variable used by all scoring systems, but the inadequacy of using age alone for mortality prediction has been reported [16]. The COPE model [2] has a high discrimination based on administrative data alone, and the area under the ROC curve for our model was ≥ 0.8 for the validation datasets, suggesting that the predictive ability of our model is comparable to or higher than that of other models. The lack of use of physiological data has a large handicap since clinical diagnosis is not possible, but the model is advantageous in using routine daily administrative data collected for a large population (all discharged patients) and for the accuracy of the clinical record. Comparison of the performance of ICUs is currently being attempted using administrative data, and our model establishes a method for evaluation of severity of illness in these studies. However, since the present study included only 9% of acute care hospitals that use the DPC system, further verification and modification of the model is required in a larger sample of patients and ICUs.

CONCLUSIONS

We prepared a hospital mortality prediction model for adult intensive care that is based only on administrative data, is independent of primary diagnosis, and uses a relatively small number of variables that are easily collected. This model can be used to evaluate the severity of a patient's condition in the ICU based on administrative data and may be applicable to critical care studies.

Conflict of Interest and Declarations

All authors declare no conflicts of interest. The design, data collection and analysis, and the writing of the manuscript were performed by all four authors. The corresponding author takes full responsibility for the validity of the data.

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Table 1. Candidate variables used in development of the hospital mortality prediction model.

	Candidate variables	Category
	(1) Gender	Male, Female
	(2) Age (years)	Continuous variable
	(3) Hospital admission	Scheduled*, Emergency
	(4) Reason for entering ICU	After scheduled surgery*, After emergency surgery, Internal medical disease
Anytime during ICU admission	(5) Time between admission and entry into ICU (days)	Direct, after 1 day, after 2-4 days*, after > 4 days
	(6) Use of fresh frozen plasma or platelet preparation	Yes=1, No=0
	(7) Mechanical ventilation	Yes=1, No=0
	(8) Dialysis	Yes=1, No=0
	(9) Pressor/vasoconstrictor	Yes=1, No=0

*: Reference

Table 2. Demographic data for the test and validation datasets

	Test dataset (n = 3,505)	Validation dataset (n = 3,253)	*P* value
Number of hospital	16	17	
Number of beds	541.7 ± 189.3	566.7 ± 258.4	0.768
Number of ICU beds	7.4 ± 4.5	7.8 ± 2.7	0.802
Number of admissions (per year)	10767.9 ± 5199.7	11816.0 ± 6937.5	0.688
Number of ICU admissions (per year)	512.3 ± 317.6	543.2 ± 279.6	0.807
Length of stay (days)	13.6 ± 1.8	13.9 ± 1.8	0.721
Length of ICU stay (days)	3.6 ± 4.8	4.4 ± 7.4	< 0.001**
Primary diagnosis on admission in patients with internal medical disease	Frequency (%)	Frequency (%)	
Infection	6.4	6.6	
Toxin	1.2	0.9	
Neoplastic†	2.2	4.2	
Metabolic†	1.2	0.6	
Hematologic and Immunologic	0.8	0.8	
Gastrointestinal†	2.9	2.2	
Renal	1.5	1.4	
Respiratory†	5.9	6.4	
Neuromuscular†	1.1	2.8	
Others	1.0	1.1	
Surgical procedure in patients with scheduled or emergency surgery	Frequency (%)	Frequency (%)	
Cerebral surgery†	11.6	16.7	
Abdominal surgery†	38.4	30.6	
Lung or mediastinal surgery†	9.2	12.0	
Orthopedic surgery†	7.4	5.2	
Others†	9.1	8.5	

†: Significant difference between the two datasets by Pearson's or Fisher's exact chi-square test

Table 3. Frequency and mortality of individual variables in the test model

Variable	Frequency (%)	Mortality (%)	P
(1) Gender			
Male	56.3	10.3	0.088
Female	43.7	8.6	
(2) Age			
20-44	9.8	3.5	
45-54	9.0	5.1	
55-64	18.8	6.4	<0.001
65-74	26.0	9.5	
75+	36.3	14.1	
(3) Admission category			
Scheduled	48.8	2.7	<0.001
Emergency	51.2	16.2	
(4) Reason for entering ICU			
After scheduled surgery	46.4	6.1	
After emergency surgery	29.4	7.0	<0.001
Medical disease	24.3	19.4	
(5) Time from admission to ICU entry (days)			
Direct	30.5	15.3	
After 1 day	18.2	4.7	<0.001
After 2-4 days	25.3	3.5	
After > 4 days	25.9	12.2	
(6) Use of fresh frozen plasma or platelet preparation			
Yes	9.2	20.4	<0.001
No	90.8	8.5	
(7) Mechanical ventilation			
Yes	14.4	32.9	<0.001
No	85.6	5.7	
(8) Dialysis			
Yes	3.7	45.3	<0.001
No	96.3	8.2	
(9) Pressors/vasoconstrictors			
Yes	41.3	13.8	<0.001
No	58.7	6.6	

Table 4. Coefficients in the hospital mortality prediction model developed using the test data set.

Variable	B	SE	Wald	P	OR	OR 95% CI
(2) Age	0.03	0.01	39.6	< 0.001	1.03	1.02-1.04
(3) Admission category (Emergency)	1.35	0.18	54.8	< 0.001	3.86	2.7-5.53
(4) Reason for entering ICU						
(i) Medical disease	0.69	0.15	21.8	< 0.001	2	1.49-2.67
(5) Time from admission to ICU entry (days)						
(i) after > 4 days	0.78	0.15	26.4	< 0.001	2.18	1.62-2.94
(6) Use of fresh frozen plasma or platelet preparation	0.45	0.19	5.5	0.019	1.57	1.08-2.29
(7) Mechanical ventilation	1.57	0.14	125.6	< 0.001	4.79	3.65-6.31
(8) Dialysis	1.58	0.22	50	< 0.001	4.85	3.13-7.5
(9) Pressors/vasoconstrictors	1.14	0.14	70.2	< 0.001	3.11	2.39-4.06
Constant	-6.92	0.4	305.1	< 0.001		

OR = Odds Ratio; CI = confidence interval

Predicted mortality risk = $e^y / (e^y + 1)$, where y = 0.03 * (2) + 1.35 * (3) + 0.69 * (4-i) + 0.78 * (5-i) + 0.45 * (6) + 1.57 * (7) + 1.58 * (8) + 1.14 * (9) – 6.92.

(3), (4-i), (5-i), (6), (7), (8), and (9) = 1 if variables applicable and 0 if variables not applicable.

Table 5. Contingency table for the Hosmer-Lemeshow test in the validation dataset

Decile	Survivors		Non-survivors		Total
	Observed	Expected	Observed	Expected	
1	316	315	1	2	317
2	324	323	2	3	326
3	322	320	3	5	325
4	321	322	9	8	330
5	313	314	13	12	326
6	301	305	24	20	325
7	295	293	30	32	325
8	271	269	54	56	325
9	220	223	105	102	325
10	124	121	205	208	329

Table 6. Validation of the prediction model

Dataset	Number	Mortality	Hosmer-Lemeshow χ-square	P	ROC AUC (95% CI)
Test	3,505	9.6	13.45	0.1	0.84-0.88
Validation	3,253	13.7	3.08	0.93	0.87-0.9
COPE model	3,253	13.7	18.64	0.02	0.8-0.84
Internal medical disease	877	28.2	7.61	0.47	0.8-0.86
Emergent surgery	854	9.8	8.54	0.38	0.88-0.94
Scheduled surgery	1,522	7.6	7.53	0.48	0.83-0.89

Table 7. Contingency table for different levels of probability in the validation dataset

Probability (%)			Expected		Discrimination ratio (%)
			Survivors	Non-survivors	
20	Observed	Survivor	2395	412	83.7
		Non-survivor	117	329	
50		Survivor	2717	90	88.7
		Non-survivor	276	170	
70		Survivor	2786	21	88.2
		Non-survivor	362	84	

FIGURE LEGENDS

Figure 1. Area under the ROC curve for the test dataset (AUC = 0.86)

Figure 2. Area under the ROC curve for the validation dataset (AUC = 0.88)

Figure 1.

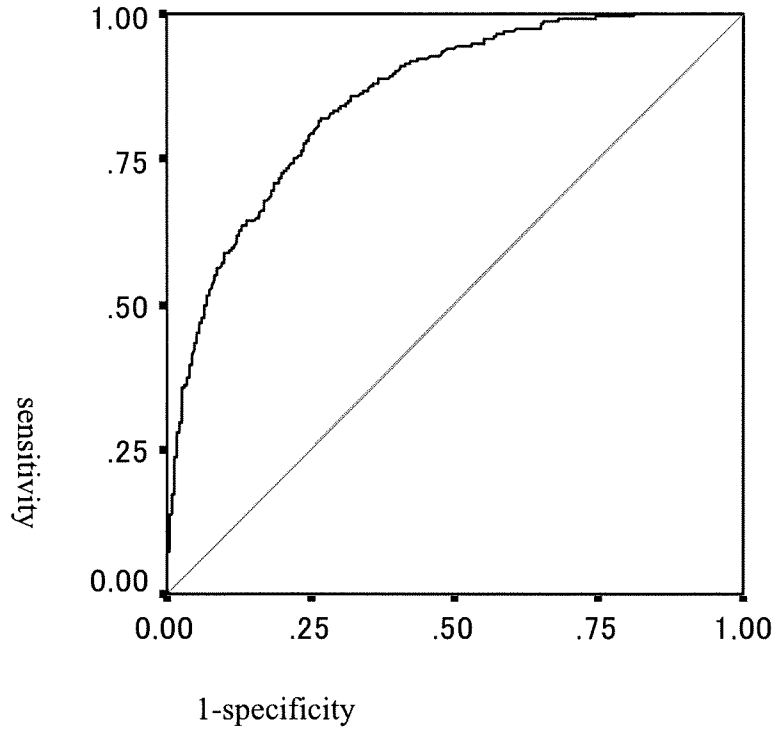
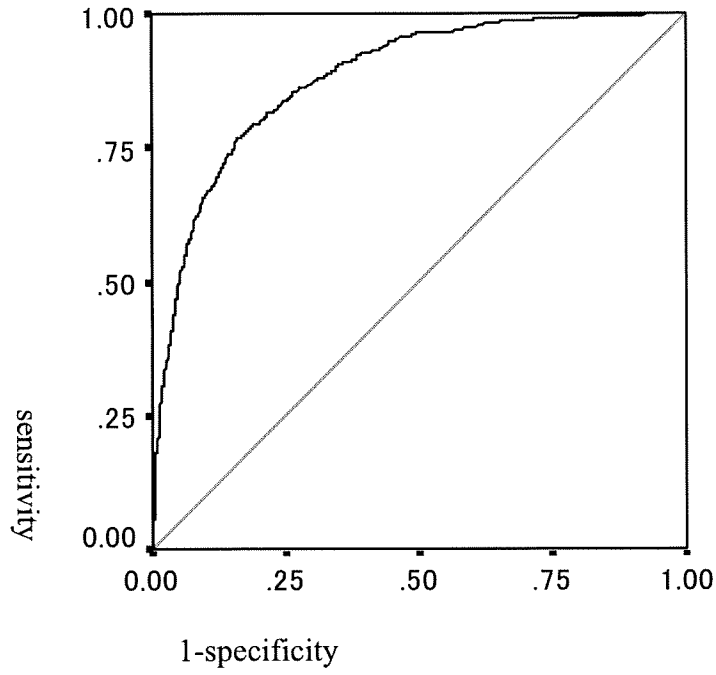


Figure 2.



Physician Staffing Patterns and Costs for Septic Patients in Intensive Care Units

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Key Words: healthcare costs; intensive care units; economics; sepsis; multicenter study

ABSTRACT

Objective: Sepsis is a serious disease, from both clinical and economical perspectives. From 2002, the Surviving Sepsis Campaign attempted to achieve better clinical outcomes. Nevertheless, high mortality in patients with sepsis remains an issue. For instance, approximately 9,300 patients per 100,000 population in Japan died of sepsis in 2007. In addition to the challenge of further improving clinical outcomes in patients with sepsis, the cost of sepsis is a serious burden for the healthcare system. Costs of intensive care unit (ICU) stays are associated with both the underlying disease and the high incidence of severe sepsis in critical care patients. As healthcare costs vary between hospitals, the difference in hospital or ICU costs at various institutions is unknown. In the present study, we utilized patient classification systems data to evaluate the relationship between physician staffing patterns and healthcare costs for patients with sepsis in ICUs in Japan.

Design: An observational cross-sectional study was performed between January 1, 2007, and December 31, 2008. The Institutional Review Board of the Faculty of Medicine at the Graduate School of Medicine of Kyoto University, Kyoto, Japan approved this study.

Setting: 49 ICUs in 49 acute-care hospitals in Japan.

Patients: All cases identified as sepsis were obtained from administrative data in Japan. For the identification of patients with sepsis, we used the International Classification of Diseases, 10th version. Sepsis was defined as the coding series related to bacterial, fungal, viral, and obstetric sepsis. Patients less than 20 years of age were excluded from our analysis. For the present study, 786 cases with a diagnosis of sepsis were analyzed.

Interventions: None.

Measurements and Main Results: To assess healthcare costs and daily costs in the ICU, administrative data from the Quality Indicator/Improvement Project database enabled us to collect data from a large population in a short period of time. The data, which was based on Diagnosis Procedure Combination data with detailed claims data, included information on medical care, daily resource use, and health care costs. Based on ICU staffing patterns, the 49 ICUs were classified into either high-intensity ICUs, in which critical care physicians (CCPs) had primary responsibility or mandatory consult, or low-intensity ICUs, in which CCPs had optional consult or were not involved. Of the 18 high-intensity ICUs, 303 cases were analyzed; of the 31 low-intensity ICUs, 483 cases were analyzed. Age, gender, and reason for admission were not significantly different between the two ICU groups. Most patients with ≥3 organ failures had stays in high-intensity ICUs. Healthcare costs during ICU stays (termed total ICU costs) were calculated from ICU admission to ICU discharge. Daily ICU costs were calculated by dividing the total ICU cost by the ICU length of stay (in days). All costs were converted to US dollars at the 2008 exchange rate (¥102=US $1). For overall cases, correlation of ICU costs and predicted mortality rate calculated using the Critical Care Outcome Prediction Equation (COPE) model without physiological data was not presented. In the low-intensity and high-intensity ICU groups, no significant differences in healthcare costs ($ 9,937 vs. $ 10,264; $p = 0.987$) or daily costs in the ICU ($ 1,761 vs. $ 1,688; $p = 0.461$) were observed. Subgroup analysis in the low-intensity ICU group, however, showed that healthcare costs and daily costs of the no-CCP group, which included only 19 cases from 3 ICUs, were significantly more expensive than those of the optional consult group (healthcare costs, $ 35,730 vs. $ 9,853, $p < 0.05$) (daily costs, $ 3,970 vs.