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, MPM₀, MPM₂₄, MPM-II₀, MPM-II₂₄, 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 (MPM₀-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 |
| and the state of t | (2) Age (years) | Continuous variable |
| | (3) Hospital admission | Scheduled*, Emergency |
| | | After scheduled surgery*, |
| | (4) Reason for entering ICU | After emergency surgery, |
| | | Internal medical disease |
| | (5) Time between admission and entry into ICU | Direct, after 1 day, |
| | (days) | after 2-4 days*, after > 4 days |
| Anytime | (6) Use of fresh frozen plasma or platelet preparation | Yes=1, No=0 |
| ICU | (7) Mechanical ventilation | Yes=1, No=0 |
| admission | (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 | Validation dataset | D volve |
|--|----------------------|----------------------|-----------|
| | (n = 3,505) | (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 (%) | |
| nfection | 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 | 0.000 | |
| Female | 43.7 | 8.6 | 0.088 | |
| (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 | ZO 001 | |
| Emergency | 51.2 | 16.2 | < 0.001 | |
| (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 Io | CU entry (days) | | | |
| Direct | 30.5 | 15.3 | | |
| After 1 day | 18.2 | 4.7 | <0.001 | |
| After 2-4 days | 25.3 | 3.5 | < 0.001 | |
| After > 4 days | 25.9 | 12.2 | | |
| (6) Use of fresh frozen plasm | a or platelet preparation | 1 | | |
| Yes | 9.2 | 20.4 | <0.001 | |
| No | 90.8 | 8.5 | < 0.001 | |
| (7) Mechanical ventilation | | | | |
| Yes | 14.4 | 32.9 | <0.001 | |
| No | 85.6 | 5.7 | < 0.001 | |
| (8) Dialysis | | | | |
| Yes | 3.7 | 45.3 | ∠0.001 | |
| No | 96.3 | 8.2 | < 0.001 | |
| (9) Pressors/vasoconstrictors | | | | |
| Yes | 41.3 | 13.8 | ∠0.001 | |
| No | 58.7 | 6.6 | < 0.001 | |

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

| Variable | В | SE | Wald | P | OR | OR |
|---|-------|------|-------|---------|------|-----------|
| Valiable | | | | | | 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 | 0.45 | 0.19 | 5.5 | 0.019 | 1.57 | 1.08-2.29 |
| preparation | 0.43 | 0.19 | 5.5 | 0.019 | 1.57 | 1.00-2.29 |
| (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-sui | Total | |
|----------|-----------|----------|----------|----------|-------|
| Decile _ | Observed | Expected | Observed | Expected | Total |
| 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

| D-44 | N I1 | N 44 - 114 | Hosmer-Lemeshow | Ъ | ROC AUC |
|--------------------------|-------------|------------|-----------------|------|-----------|
| Dataset | Number | Mortality | χ-square | P | (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 |
|-------------|------------|--------------|-----------|---------------|----------------|
| (%) | | | Survivors | Non-survivors | ratio (%) |
| 20 | | Survivor | 2395 | 412 | 83.7 |
| 20 | | Non-survivor | 117 | 329 | 03.7 |
| | | Survivor | 2717 | 90 | 88.7 |
| 50 | Observed N | Non-survivor | 276 | 170 | 86.7 |
| =0 | _ | Survivor | 2786 | 21 | 88.2 |
| 70 | | Non-survivor | 362 | 84 | 00.2 |

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.

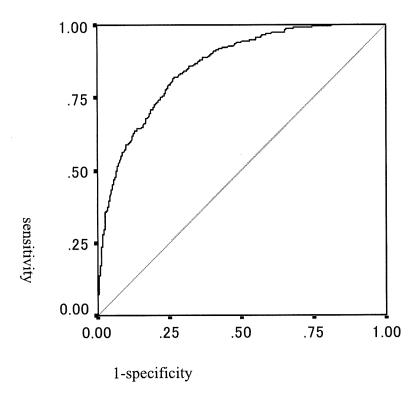
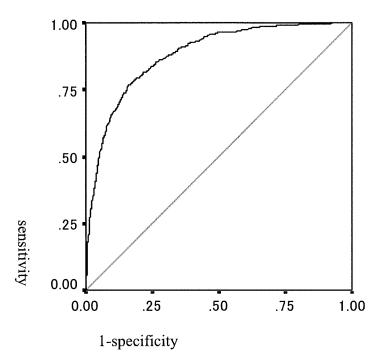


Figure 2.



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.

\$ 1,750, *p* < 0.01).

Conclusions: In the current study, the severity of sepsis did not correlate with ICU costs. Moreover, ICU staffing patterns were not associated with healthcare costs and daily costs for patients with sepsis in critical care units. Compared to lack of CCPs, allocation of a CCP might reduce these costs in patients with sepsis, irrespective of the level of intensivist care. Therefore, further research is necessary to determine the effect of CCPs on ICU costs for patients with sepsis.