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Original Article

Association between APACHE II Score and Nosocomial Infections in Intensive Care Unit Patients: A Multicenter Cohort Study

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Abstract

Objective: To examine whether nosocomial infection risk increases with APACHE II score, which is an index of severity-of-illness, in intensive care unit (ICU) patients.

Methods: Using the Japanese Nosocomial Infection Surveillance database, 8,587 patients admitted to 34 participating ICUs between July 2000 and May 2002, aged 16 years or older, who had stayed in the ICU for 2 days or longer, had not transferred to another ICU, and had not been infected within 2 days after ICU admission, were followed until ICU discharge, Day 14 after ICU admission, or the development of nosocomial infection. Adjusted odds ratios with their 95% confidence intervals for nosocomial infections were calculated using logistic regression models, which incorporated sex, age, operation, ventilator, central venous catheter, and APACHE II score (0–5, 6–10, 11–15, 16–20, 21–25, 26–30, and 31+).

Results: There were 683 patients with nosocomial infections. Adjusted odds ratios for nosocomial infections gradually increased with APACHE II score. Women and elective operation showed significantly low odds ratios, while urgent operation, ventilator, and central venous catheter showed significantly high odds ratios. Age had no significant effect on the development of nosocomial infection.

Conclusions: Nosocomial infection risk increases with APACHE II score. APACHE II score may be a good predictor of nosocomial infections in ICU patients.

Key words: multicenter cohort study, ICU, APACHE II score, nosocomial infection

Introduction

In July 2000, the Japanese Ministry of Health, Labour, and Welfare started the Japanese Nosocomial Infection Surveillance (JANIS) System, which consists of three components, intensive care unit (ICU), laboratory, and hospitalwide surveillance (1–3). In the ICU component, all of the patients admitted to the participating ICUs are followed until hospital discharge. Patient data, including characteristics, physical and laboratory findings, and treatment, are collected using specific database-oriented software in the standardized forms.

Severity-of-illness scoring systems have been developed for predicting the outcome of ICU patients. APACHE II is a well-known severity-of-illness scoring system, which uses a point score based on initial values of 12 routine physiological measurements, age, and previous health status to provide a general measure of severity-of-illness (4). The JANIS System has incorporated the APACHE II score. Previous studies have examined the association between APACHE II score and nosocomial infections in ICU patients (5–10). To be expected, those who are in poor condition (i.e., those who have a high APACHE II score) may be susceptible to nosocomial infections, but the findings of the previous studies were not always in agreement. Using the large cohort database of the JANIS System, we examined whether nosocomial infection risk increases with APACHE II score in ICU patients.

Subjects and Methods

A large cohort database was accumulated from the JANIS System (11). Details of data collections and definitions in the JANIS System have been described elsewhere (1, 11, 12). For all of the patients admitted to 34 participating ICUs (mostly from national university hospitals) between July 2000 and May 2002, the following patient data were collected using specific database-

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oriented software in the standardized forms: sex, age, underlying disease, severity-of-illness (APACHE II score (4)), ICU admission and discharge (date, time, and route), operation (elective and urgent), device use (ventilator, urinary catheter, and central venous catheter), infection (pneumonia, urinary tract infection, catheter-related bloodstream infection, sepsis, wound infection, and others), and hospital discharge (date and outcome). All types of infection were diagnosed according to the JANIS criteria (13).

The study subjects were 8,587 eligible patients (5,509 men and 3,078 women), aged 16 years or older, who had stayed in the ICU for 2 days or longer, had not transferred to another ICU, and had not been infected within 2 days after ICU admission. Their mean (standard deviation) age was 62.6 (15.6) years. From a preliminary analysis, we found that 90% of patients with nosocomial infections had been infected within 14 days after ICU admission. Therefore, the 8,587 patients were followed until ICU discharge, Day 14 after ICU admission, or the development of nosocomial infection. Nosocomial infection was defined as a newly developed infection at least 2 days after ICU admission (14).

We observed the guidelines for epidemiological studies by the Japanese Ministry of Health, Labour, and Welfare and the Japanese Ministry of Education, Culture, Sports, Science, and Technology. We paid special attention to the protection of the anonymity and confidentiality of the available data.

Statistical analyses

Statistical analyses were performed with the Statistical Analysis Systems (SAS, version 8.2). Nosocomial infection rates were calculated as the number of patients with nosocomial infections per 100 ICU admissions. Adjusted odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) for nosocomial infections were calculated using logistic regression models, which incorporated sex (men, women), age (–44, 45–64, 65–74, and 75+; as dummy variables), operation (no, elective, urgent; as dummy variables), ventilator (no, yes), central venous catheter (no, yes), and APACHE II score. APACHE II score was categorized into the following seven classes: 0–5, 6–10, 11–15, 16–20, 21–25, 26–30, and 31+. The class of 0–5 was set aside as reference, and the other classes were incorporated into the model as dummy variables.

Results

There were 683 patients with nosocomial infections. Of the 683 patients, 386 (56.5%), 164 (24.0%), 89 (13.0%), and 44 (6.4%) were infected on Days 3–5, 6–8, 9–11, and 12–14 after ICU admission, respectively.

Table 1 shows nosocomial infection rates by sex, age, operation, ventilator, and central venous catheter, respectively. Nosocomial infection rates were significantly higher in those

Table 1 Nosocomial infection rates (%) and their corresponding 95% confidence intervals

	N	APACHE II score						
		0–5 (n=1139)	6–10 (n=2367)	11–15 (n=2118)	16–20 (n=1408)	21–25 (n=819)	26–30 (n=468)	31+ (n=268)
All	8587	2.6 (1.9–3.7)	4.1 (3.3–4.9)	7.1 (6.1–8.3)	10.7 (9.1–12.4)	15.6 (13.3–18.3)	15.6 (12.6–19.2)	20.9 (16.5–26.2)
Sex								
Men	5509	2.6 (1.7–4.0)	5.0 (4.0–6.2)	8.6 (7.2–10.2)	10.9 (9.1–13.2)	17.3 (14.3–20.9)	15.5 (11.7–20.2)	19.4 (14.1–26.1)
Women	3078	2.7 (1.4–5.0)	2.2 (1.4–3.5)	4.7 (3.4–6.3)	10.2 (7.8–13.1)	12.7 (9.5–16.9)	15.8 (11.3–21.6)	23.3 (16.2–32.3)
Age, y.o.								
16–44	1057	2.2 (1.1–4.3)	5.4 (3.2–8.8)	7.2 (4.3–12.0)	15.0 (9.7–22.5)	19.0 (11.2–30.4)	19.1 (10.4–32.5)	33.3 (18.6–52.2)
45–54	1170	2.3 (1.1–4.9)	3.8 (2.2–6.4)	7.1 (4.6–11.0)	10.3 (6.4–16.0)	15.2 (8.9–24.7)	26.0 (15.9–39.6)	16.1 (7.1–32.6)
55–64	1807	3.4 (1.9–6.0)	4.2 (2.8–6.3)	7.2 (5.1–10.1)	8.6 (5.8–12.5)	16.3 (11.2–23.1)	16.5 (9.9–26.1)	16.7 (9.0–28.7)
65–74	2664	2.6 (1.1–5.8)	4.4 (3.2–6.1)	7.7 (6.0–9.8)	12.0 (9.4–15.3)	15.9 (12.2–20.6)	13.0 (8.5–19.4)	23.5 (15.6–33.8)
75+	1889	0.0 (0.0–79.3)	2.8 (1.7–4.7)	6.1 (4.4–8.4)	9.2 (6.7–12.5)	14.1 (10.3–19.1)	13.0 (8.5–19.4)	18.7 (11.5–28.9)
Operation								
None	3459	1.4 (0.7–3.1)	3.3 (2.3–4.7)	6.3 (4.8–8.3)	11.2 (9.0–14.0)	13.2 (10.3–16.8)	13.6 (10.0–18.4)	17.1 (12.1–23.4)
Elective operation	3060	3.8 (2.4–5.9)	4.0 (3.0–5.3)	6.1 (4.7–7.9)	9.2 (6.7–12.5)	12.8 (8.7–18.4)	11.7 (6.3–20.7)	44.0 (26.7–62.9)
Urgent operation	2068	2.5 (1.1–5.3)	5.6 (3.9–8.0)	9.8 (7.5–12.7)	11.1 (8.5–14.5)	22.4 (17.4–28.3)	21.6 (15.5–29.4)	21.9 (14.0–32.7)
Ventilator								
Non-user	2747	0.9 (0.4–2.1)	1.7 (1.1–2.7)	4.3 (3.0–6.1)	6.0 (3.8–9.3)	8.1 (4.4–14.2)	15.2 (7.6–28.2)	8.0 (2.2–25.0)
User	5840	4.3 (2.9–6.3)	5.9 (4.7–7.2)	8.3 (7.0–9.9)	11.9 (10.1–14.0)	17.0 (14.4–19.9)	15.6 (12.5–19.4)	22.2 (17.5–27.9)
Central venous catheter								
Non-user	2059	0.3 (0.0–1.5)	2.3 (1.4–3.7)	4.0 (2.5–6.2)	7.8 (5.3–11.5)	8.9 (5.3–14.6)	14.1 (7.8–24.0)	10.3 (3.6–26.4)
User	6528	3.8 (2.7–5.4)	4.8 (3.9–5.9)	7.9 (6.7–9.3)	11.4 (9.7–13.4)	17.1 (14.4–20.1)	15.9 (12.6–19.8)	22.2 (17.4–27.9)

Table 2 Adjusted odds ratios and their corresponding 95% confidence intervals for nosocomial infections

	Odds ratio	95% confidence interval (lower–upper)
APACHE II score		
0–5	1.00	(reference)
6–10	1.57	(1.03–2.40)
11–15	2.55	(1.70–3.85)
16–20	3.62	(2.39–5.49)
21–25	5.38	(3.50–8.27)
26–30	5.14	(3.23–8.16)
31+	7.09	(4.34–11.59)
Sex		
Men	1.00	(reference)
Women	0.74	(0.62–0.88)
Age, y.o.		
16–44	1.00	(reference)
45–54	0.83	(0.60–1.15)
55–64	0.83	(0.62–1.12)
65–74	0.89	(0.68–1.18)
75+	0.75	(0.56–1.00)
Elective operation	0.78	(0.63–0.98)
Urgent operation	1.22	(1.00–1.49)
Ventilator	2.11	(1.62–2.76)
Central venous catheter	1.48	(1.14–1.93)

who had a higher APACHE II score ($p<0.001$ with Cochran-Armitage test for trend); crude ORs (95%CIs) for nosocomial infection in the classes of 6–10, 11–15, 16–20, 21–25, 26–30, and 31+ were 1.56 (1.20–2.03), 2.82 (2.23–3.57), 4.41 (3.60–5.39), 6.85 (5.76–8.14), 6.83 (5.77–8.09), and 9.76 (8.31–11.47), respectively. The association between APACHE II score and nosocomial infections was significant even when stratified by sex, age, operation, ventilator, and central venous catheter, respectively ($p<0.001$ with Cochrane-Mantel-Haentzel test). Women had lower rates than men in every class of APACHE II score, except for the higher score classes (26–30 and 31+). Urgent operation had higher rates than none and elective operation. Elective operation of the highest score class showed a rather higher rate, but there was no significant difference between the rates of elective and urgent operations. Ventilator and central venous catheter were associated with higher rates in every class of APACHE II score. Meanwhile, age was not associated with lower or higher rates in any score classes.

Table 2 shows adjusted ORs and their corresponding 95% CI for nosocomial infections. Adjusted ORs for nosocomial infections gradually increased with APACHE II score. Women and elective operation showed significantly low ORs, while urgent operation, ventilator, and central venous catheter showed significantly high ORs. Age had no significant effect on the development of nosocomial infection.

Discussion

Using the large cohort database of the JANIS System, we examined whether nosocomial infection risk increases with APACHE II score in ICU patients. To our knowledge, this is the first study investigating the details of the association between APACHE II score and nosocomial infections in ICU patients in Japan.

Nosocomial infection rates were significantly higher in those who had a higher APACHE II score, and the association between APACHE II score and nosocomial infections was significant even when stratified by sex, age, operation, ventilator, and central venous catheter, respectively. In the multivariate analysis, adjusted ORs for nosocomial infections gradually increased with APACHE II score. These results suggest that nosocomial infection risk increases with APACHE II score in ICU patients.

We calculated both crude and adjusted ORs for nosocomial infection related to APACHE II score and found that the crude values were higher than the adjusted values. The difference between crude and adjusted values probably indicates the effect of confounding factors. It is worth pointing out that inadequate adjustment for confounding factors can lead to under- or over-estimation of nosocomial infection risk related to APACHE II score. Risk factors of nosocomial infections can be intrinsic (e.g., immunosupression) or extrinsic (e.g., invasive interventions) (15). APACHE II score represents the patient's intrinsic risk factors. Those who have an increased APACHE II score might have also extrinsic risk factors. However, because of adjustment for major extrinsic risk factors (operation, ventilator, and central venous catheter), the nosocomial infection risk increase with APACHE II score in this study is less likely to suggest the effect of extrinsic risk factors.

Overall, the findings of this study suggest that APACHE II score may be a good predictor of nosocomial infections in ICU patients. Those who have an increased APACHE II score may be at high risk for nosocomial infections. In previous studies, the following three studies showed that APACHE II score was predictive for nosocomial infections. Fernandez-Crehuet et al., in a prospective study of 944 patients, reported that APACHE II score had a hazard ratio of 1.04 (95%CI: 1.01–1.06) for the development of nosocomial infection (7). Chevret et al. conducted a multicenter cohort study on nosocomial pneumonia (107 ICUs, 996 patients) and found that APACHE II score of 16 or higher was significantly associated with nosocomial pneumonia (6). Sofianou et al. reported a significant association between APACHE II score and nosocomial pneumonia, but they included only patients requiring mechanical ventilation and did not adjust for confounding factors (9). Other studies have shown that APACHE II score was not predictive for nosocomial infections (5, 8, 10), nor was APACHE III score (16, 17). Bueno-Cavanillas et al., in a prospective study of 448 patients, reported that APACHE II score was not significantly incorporated into a stepwise logistic regression model for nosocomial infection (5). Hurr et al., in a retrospective chart review of 113 trauma patients, reported that APACHE II score had an odds ratio of 1.01 (95%CI: 0.97–1.05) for the development of nosocomial infection (8). Laupland et al. conducted a multicenter cohort study on nosocomial urinary tract infection (3 ICUs, 1158 patients) and found no significant association between APACHE II score and nosocomial urinary tract infection (10). Because of differences in settings, subjects, and outcome (all or site-specific infections), it is difficult to compare the findings of the previous studies and those of this study. In the future, we will examine the association between APACHE II score and nosocomial infections by infection site.

The JANIS System attempts to provide a uniform approach of data collection and definitions to participating ICUs. Data are collected using specific database-oriented software in the standardized forms. All types of infection are diagnosed according to the JANIS criteria. WIth the JANIS database, we may further obtain reliable findings from standardized data. However, most of the participating ICUs are in national university hospitals, where the levels of hospital infection control are likely to be higher in Japan. The findings of this study may not represent the average for Japanese hospitals. The multicenter cohort study has the advantage of collecting much patient data. On the other hand, ICUs are likely to have different organizational characteristics (e.g., medical or surgical ICU, criteria for ICU admission and ICU discharge, and treatment strategies). It is uncertain whether the association between APACHE II score and nosocomial infections varies between ICUs. Further studies may be required to confirm the findings of this study in other hospitals, taking account of organizational characteristics.

In conclusion, nosocomial infection risk increases with APACHE II score. APACHE II score may be a good predictor of nosocomial infections in ICU patients. Nosocomial infections are one of the most important determinants for the outcome of ICU patients. Many researchers have conducted epidemiological surveys to elucidate risk factors of nosocomial infections in ICU patients. Studies should pay attention to the association between APACHE II score and nosocomial infections, and add some measure of severity-of-illness to the model. Nosocomial infection rates are regarded as an indicator of quality of care, and are often used by hospitals for external comparisons (18). It is worth pointing out that nosocomial infection rates adjusted for APACHE II score may be a more meaningful indicator of quality of care.

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