Original Article

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The mortality of patients with sepsis increases in the first month of a new academic year

Running Title: The July effect of sepsis in Korea

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Abstract

Objective: Many studies have examined the July effect. However, little is known regarding the July effect in sepsis. We hypothesized that the July effect would result in worse outcomes in patients with sepsis.

Methods: Prospectively collected patients with sepsis between January 2018 and December 2021 were used. In Korea, the new academic year starts on March 1, so the "July effect" appears in March. The primary outcome was 30-day mortality. Secondary outcomes included adherence to the Surviving Sepsis Campaign bundle. Outcomes were compared between March and other months. Multivariate Cox proportional hazard regression was performed to adjust confounders.

Results: Total 843 patients were included. There were no significant differences in sepsis severity. The 30-day mortality in March was higher (49% vs. 28.5%; $P < 0.001$). However, there was no difference in bundle adherence in March (42.2% vs. 48.0%; $P = 0.264$). Multivariate Cox proportional hazard regression showed that July effect was associated with mortality in patients with sepsis [adjusted hazard ratio, 1.925; 95% confidence interval, 1.405–2.638; $P < 0.001$].

Conclusion: July effect was associated with 30-day mortality in patients with sepsis. However, bundle adherence was not different. These results suggest that the increase in mortality during the turnover period may be related to unmeasured in-hospital management. Intensive supervision and education of residents in care of patients with sepsis is needed in the beginning of training.

Keywords: Sepsis; Medical education; Patient safety; Precision medicine

Capsule summary

(1) What is already known

Many studies have examined the July effect. However, little is known regarding the July effect in sepsis.

(2) What is new in the current study

July effect was associated with 30-day mortality in patients with sepsis. However, bundle adherence was not different. These results suggest that the increase in mortality during the turnover period may be related to unmeasured in-hospital management.

INTRODUCTION

Sepsis is a dysregulated host response to infection that leads to life-threatening organ dysfunction [1]. Sepsis and septic shock have a high mortality rate of approximately 10% and 30%, respectively [2-4]. It is known that initial treatment is important in patients with sepsis, and Surviving Sepsis Campaign (SSC) guidelines specifically recommend antibiotic administration and fluid resuscitation for the initial 1 or 3 h [5]. Improper administration of fluids and delayed administration of antibiotics increase mortality rates [6]. Therefore, it is important to recognize sepsis early and treat it appropriately based on the sepsis bundle.[5] It can be assumed that the prognosis of patients with sepsis will deteriorate if a doctor who lacks experience in the turnover period does not recognize sepsis quickly and proper treatment is delayed.

In teaching hospitals, there is an inevitable transition period during which new residents, fellows, and staff join the front line. During this transitional period, relatively inexperienced doctors enter hospitals. The safety issue that the beginning of a new academic year for residents in training may result in for patients is usually called 'July Effect' in United States of America. Various studies have been conducted on the prognosis of patients who visited hospitals during this period [7]. A study reported an increase in mortality among patients of internal medicine admitted to general ward or intensive care unit(ICU) via the emergency department (ED) on the first Wednesday after the beginning of a new academic year [8]. Another study showed that July effect may be associated with in-hospital cardiac arrest requiring resuscitation attempts [9]. However, there was no increase in mortality among patients admitted to the ICU during the period of beginning of a new academic year [10].

The July effect on emergency physician practice behavior has also been studied. One study reported that less experienced physicians had a longer average time from patient intake to initial evaluation and a longer average time to disposition [11]. However, another study reported consistently longer ED lengths of stay at teaching hospitals than at non-teaching hospitals, but no July effect was observed [12].

Sepsis is a critical condition that requires early recognition and aggressive management [13]. However, the association between the turnover period and the mortality rate of sepsis has rarely been studied.

Given that mortality of medical disease was higher, and the initial evaluation was delayed in July, we hypothesized that the mortality rate of patients with sepsis would be higher in the first month of beginning of a new academic year than during other periods. Additionally, we investigated differences in sepsis bundle adherence during the period.

METHODS

Study Design and Setting

This retrospective observational study used data from a prospectively collected sepsis registry. This research was conducted at the ED of Korea University Ansan Hospital, which is a tertiary teaching hospital with approximately 50,000 ED visits per year.

In South Korea, postgraduate medical education consists of a one-year internship followed by three or four years of residency. Fellowships for one or two years are optional. New trainees and staff members begin their duties on March 1st. Therefore March, not July, is the period of effect referred to so called 'July effect' in Korea. What is usually called the "July Effect" is actually the "March Effect" in Korea. The first month of a new academic year is March but describing it as the July effect or using the unfamiliar word March effect may cause confusion in interpretation, so this study describes it as academic turnover or turnover effect. In our ED, initial assessment and resuscitation were performed by residents under the guidance and supervision of at least one board-certified emergency medicine staff member as per the SSC guidelines. However, consultations with intensivists or board-certified infectious disease experts were generally performed after admission to the ICU or general ward.

Selection of Participants

We used data from adult patients aged ≥18 years from the sepsis registry between January 2018 and December 2021. Every patient who visited the hospital in February were excluded from the analysis because some of their hospitalization period may have overlapped with the turnover period in March. Patients with a Do-Not-Attempt-Resuscitation (DNAR) order before ED presentation were excluded from the analysis as well.

Our institution uses the quick Sepsis Related Organ Failure Assessment [(q)SOFA] as a screening tool for operating the Intelligent Sepsis Management System [14]. The system automatically screens qSOFA-positive patients and informs physicians regarding the possibility of sepsis. The physicians then

confirm the presence of an infection and organ dysfunction. Sepsis-3 criteria, defined as an increase in SOFA scores of two or more from baseline, was used to define organ dysfunction. If the baseline SOFA score was unknown, enrollment was based on a SOFA score of ≥2. Septic shock was also defined based on the Sepsis-3 definition as the need for inotropes and a lactate level of >2 despite adequate fluid resuscitation.

Outcome Measures

The primary outcome measure was the 30-day mortality. Secondary outcomes included SSC bundle adherence, and lengths of ED, hospital, and ICU stays. The 30-day mortality, SSC bundle adherence, and hospitalization days were compared between the turnover and non-turnover periods. Bundle adherence was assessed based on whether each component was completed within 3 h of ED presentation. Antibiotics were assessed for a door-to-administration time within 3 h. Fluid resuscitation was defined as 30 ml/Kg administered within 3 h of door-to-administration if the systolic blood pressure was less than 100 mmHg or lactate was greater than 4 mmol/L. Lactate follow-up was considered adherent if an initial lactate level of ≥2 mmol/L was re-measured within the ED stay. Overall, bundle adherence was considered when all of these were in place.

Statistical Analysis

The normality of the variables was evaluated using the Shapiro–Wilk test. To compare clinical variables, continuous variables were presented as the median and interquartile range (IQR) and compared using the Mann–Whitney U test when variables did not follow normality. If the variables followed normality, we showed the average and standard deviation and compared them using the Student's t-test. Categorical variables were presented as numbers and percentages and compared using either the chi-squared or Fisher's exact test, as appropriate.

The severity was compared by SOFA, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and initial lactate concentration. SOFA is a marker for sepsis diagnosis and severity, indicating

the extent of organ failure. It is based on six organ, each for the respiratory, cardiovascular, liver, bone marrow, kidney, and central nervous systems [15]. APACHE II is one of a severity scoring system for critically ill patients It is applied within 24 hours of hospitalization [16]. It consists of the epidemiologic factors, medical history, vital signs, and laboratory results.

The association between the turnover period and bundle adherence was assessed using logistic regression. Survival was analyzed using Kaplan–Meier curves and log-rank tests for mortality in the turnover and non-turnover periods. To determine the effect of the turnover period on mortality, we used a Cox regression model. Univariate Cox regression modeling was used to identify individual variables that correlated with 30-day mortality. Variables that were statistically significant in the univariate analysis were selected for multivariate Cox regression analysis. This multivariate Cox regression model was used to calculate the adjusted hazard ratio (aHR) of the academic turnover effect after adjusting for confounders.

We calculated the aHR of the turnover effect by performing multivariate Cox regression in each subgroup with the variables identified in the previous multivariate Cox regression model. Subgroup was divided based on presence of septic shock, disposition (ICU or general ward), initial systolic blood pressure, initial lactate concentration, SOFA score and whether mechanical ventilation was applied. Statistical analyses were performed using the SPSS software (version 25.0; IBM, Armonk, NY, USA) and MedCalc for Windows (version 19.8; MedCalc Software, Mariakerke, Belgium).

Ethical Statement

This study was performed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Korea University Ansan Hospital. (IRB number: 2022AS0280). The IRB waived the requirement for informed consent because of the minimal risk of the study design.

RESULTS

Demographic Results

Between 2018 and 2021, 981 patients were enrolled, of whom 87 were excluded because they visited the hospital in February. The 51 patients with sepsis who had documented DNAR orders prior to ED visits were excluded from the analysis. A total of 102 and 741 patients in the turnover and non-turnover periods, respectively, were included in the analysis (Fig. 1). There were no statistically significant differences in sex, age, or comorbidities between the two periods. There was no difference in the rate of septic shock between the two periods. There was also no difference in the Acute Physiology and Chronic Health Evaluation (APACHE) II or SOFA scores. The outcome showed that mortality was significantly higher in the turnover period for 7-day, 14-day, and 30-day mortality. However, there were no significant differences in SSC bundle adherence (Table 1). The lengths of ED stay, hospital, and ICU stays were not significantly different. The logistic regression analysis of SSC bundle adherence during the turnover period showed no statistical significance [odds ratio (OR), 0.788; 95% confidence interval (CI), 0.519–1.198; $P = 0.265$]

The mortality trend by month of patient visit is shown in Fig. 2A. The turnover period (March) had the highest mortality, which was similar for both patients with and without septic shock. However, the monthly SSC bundle adherence rates showed a similar pattern in the turnover and non-turnover periods (Fig. 2B). Survival analysis using a Kaplan–Meier curve and log-rank test between the turnover and non-turnover periods is shown in Fig. 3. In patients with sepsis, a significant turnover effect was observed between the two periods. This was more clearly observed in the patients with septic shock.

Main Results

The results of the univariate Cox hazard regression analysis for each variable associated with 30-day mortality are shown in Table 2. The turnover period was significantly associated with 30-day mortality (aHR, 1.925; 95% CI, 1.405–2.638; $P < 0.001$). Multivariate Cox proportional hazard regression

showed that the turnover period was associated with mortality in patients with sepsis after adjusting for confounders (aHR, 1.990; 95% CI, 1.444–2.743; $P < 0.001$) (Table 3). The results of the subgroup analysis are shown in Fig. 4. When subgroups were analyzed according to shock status, both septic shock and sepsis showed an academic turnover effect in the subgroup with initial systolic blood pressure above 100 and the subgroup with initial systolic blood pressure below 100. However, when the subgroup analysis was performed by disposition, the academic turnover effect was significant in ICU patients but not in general ward patients. The academic turnover effect was significant in the subgroup with lactate concentrations > 4 but not in the subgroup with lactate concentrations < 4. The academic turnover effect was significant in the subgroup with a SOFA score of ≥8 but not in the subgroup with a SOFA score of < 8.

DISCUSSION

In this study, we found that the turnover period was an independent risk factor (HR, 1.925; 95% CI, 1.405–2.638; $P < 0.001$). Academic turnover may play a significant role in the mortality of patients with sepsis. However, no significant differences were observed in SSC bundle adherence. There were also no significant differences in the lengths of ED, hospital, and ICU stay. From October to December, there was a downward trend in the rates of antibiotic administration and overall compliance within 3 h. This was mainly contributted by the fourth wave of the coronavirus disease 2019 (COVID-19) pandemic in 2021..[17] The mortality rate rise sharply and SSC bundle adherence drops sharply in October to December 2021. (Fig. 5.) Owing to the additional quarantine process, triage was time-consuming, antiviral agents were often administered rather than antibiotics. These were main reason of decreased bundle adherence.

We found no academic turnover effect in patients with low-severity sepsis. However, we found an academic turnover effect in patients with higher severity sepsis, although there was no decrease in SCC bundle adherence. There was an academic turnover effect for patients with sepsis of higher severity who required ICU admission, had a high initial serum lactate concentration, and had a multi-organ failure. This suggests that less experienced physicians may be less capable of treating patients with higher severity sepsis after bundle therapy. In addition, the study qualitatively assessed compliance with the bundle. Even if the bundle was adhered to, it is possible that inappropriate treatment was administered to the patient. For example, in the case of fluid resuscitation, if 30 cc/Kg is administered, the bundle is adhered to, but if the patient is dehydrated and should have received more fluid, the bundle adherence may be associated with death, despite the high bundle adherence rate. Therefore, more intense supervision is required during the turnover period.

Our research results contradicted those of previous studies. Academic turnover effect (so-called “July effect”) has been studied in various fields to date. One systematic review reported that 113 studies on the academic turnover effect had been published so far in 2019. Only 21 (18.6%) studies showed a statistically or partially significant academic turnover effect [7].

Few studies have examined the effects of academic turnover in sepsis or critical care. To the best of our knowledge, only one previous study has investigated the effects of academic turnover on sepsis. Saqib et al. attributed a lack of a turnover effect in their study to adherence to protocol-based practice and watchful supervision by senior staff [18]. A limitation of this study is that it performed a subgroup analysis based on pre-morbidity but not based on sepsis severity.

Our institution also had supervision by at least one board-certified emergency medicine staff member in the ED, and the ICUs were staffed by intensivists with day and nighttime duties. The intensivists provide general intensive care to patients. The medical critical care unit is covered by two Postgraduate Year (PGY) 2 internal medicine residents during the day and one PGY2 or higher resident at night. Residents of internal medicine spend their first-year training on the general wards and then begin their first ICU duty in March of their second year. They work 12-hour shifts, and care for critically ill patients under the supervision of attending physicians. There was no significant difference in bundle adherence during the turnover period compared with the non-turnover period. In addition, our institution used an Intelligent Sepsis Management System to warn emergency physicians about the possibility of sepsis, leading to early recognition and increased SSC bundle adherence, resulting in improved survival [14]. As a result, we observed higher bundle adherence even during academic turnover than the overall SSC bundle adherence suggested by a recently published Korean multi-center cohort study [19]. Therefore, the fact that turnover duration was significantly associated with mortality independent of SSC bundle adherence highlights the need to investigate other potential causes of increased mortality.

It is possible that the mortality rate increased because of inadequate detection of clinical deterioration during hospitalization. An observational study on the academic turnover effect in in-hospital cardiac arrest reported an increase in the incidence of in-hospital cardiac arrest during this period [9]. The researchers believed that inexperienced new trainees failed to recognize the preceding signs of cardiac arrest. Patients with sepsis often exhibit rapid deterioration during hospitalization. Delayed recognition of deterioration in patients with sepsis in in-hospital settings may be a cause of increased mortality.

Oh et al. reported no academic turnover effect in the ICU of a tertiary hospital in South Korea,

192 independent of intensivist coverage [10]. This is different from our study, in which the turnover period
193 was associated with higher mortality among patients admitted to the ICU. Oh et al. did not perform
194 subgroup analysis by disease; therefore, time-dependent conditions, such as sepsis, may have been
195 masked by other diseases. Their study also showed a trend toward increased mortality around the time
196 of ICU extension. These results provide indirect evidence that environmental changes are associated
197 with mortality.

198 Increased mortality without changes in adherence to the SSC bundle could be a result of usual care not
199 being covered by the bundle or unmeasured in-hospital management after initial resuscitation in the ED.
200 Further research is required to investigate whether inadequate fluid balance persists after hospitalization,
201 whether nosocomial infections occur, and whether proper nutrition is delivered. In addition, we should
202 consider the possibility that less experienced doctors may not be able to provide individualized
203 treatment that is not specifically stated in the guidelines.

204 There may be an academic turnover effect in certain phenotypes of sepsis or on the composition of the
205 phenotype. Recently, efforts have been made to classify sepsis phenotypes and individualize treatments
206 [20-22]. Seymour et al. classified sepsis into four phenotypes and reconstructed previous sepsis-related
207 randomized trials to show how outcomes differ according to the phenotype composition. The authors
208 simulated the ProCess Trial and showed that early goal-directed therapy improves survival in the alpha
209 type but worsens survival in the delta type [22, 23]. Ma et al. further categorized septic shock into
210 several phenotypes, one of which reported that fluid administration increased mortality [20].

211 The subgroup analysis in our study showed that the academic turnover effect was statistically significant
212 for those with higher lactate concentrations (≥4 mmol/L) and higher SOFA scores (≥8). This is a specific
213 feature of the delta phenotype. In our study, SSC adherence was higher than that reported in other multi-
214 center studies conducted in Korea [19]. However, the mortality rate was rather high in our study. Based
215 on a recent study, it is believed that precision medicine is necessary depending on a patient's condition.
216 Less experienced doctors may not be able to adopt a personalized approach by relying solely on
217 guidelines. For certain phenotypes, SSC bundles may be associated with harmful outcomes; however,

218 further research is required.

219 This study had several limitations. First, because of the retrospective design of our study, complete
220 control over potential confounding factors was difficult to achieve, and we could only show an
221 association, not causation. Vulnerability to selection bias may have also confounded the results. Second,
222 because our study was conducted in a single tertiary teaching hospital, the generalizability of our results,
223 including the composition of sepsis phenotypes, remains uncertain. Third, While the study design
224 cannot completely rule out a seasonal effect, the researchers believe they have ruled it out to some
225 extent by statistically demonstrating that there was no significant difference in suspected infection
226 source, severity (APACHE II, SOFA) between the March and the rest of the year. Increased mortality
227 was observed despite no differences in bundle adherence rates, the reason for which is unknown because
228 the influence of in-hospital interventions has not been investigated. We believe that there are many
229 variables related to post-hospitalization care that may have a significant impact, and further research is
230 needed. Another limitation was that we only included patients with positive qSOFA scores upon
231 admission to the ED. When the sepsis-3 definition was published, screening for sepsis with qSOFA was
232 recommended, which was used in this study; however, the SSC guidelines, revised in 2021, do not
233 recommend screening for sepsis with qSOFA alone. This might have resulted in a selection bias.
234 Nevertheless, this is the first study to report a positive effect of academic turnover in patients with sepsis.
235 Larger multi-center studies are required for external validation.

236 In summary, academic turnover was associated with 30-day mortality in patients with sepsis. However,
237 SSC bundle adherence in the ED did not differ significantly depending on the turnover or non-turnover
238 periods. These results suggest that the increase in mortality during the turnover period may be related
239 to unmeasured in-hospital management.

Ethical statements

This study was performed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Korea University Ansan Hospital. (IRB number: 2022AS0280). The IRB waived the requirement for informed consent because of the minimal risk of the study design.

Conflict of interest statement

None.

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Author Contributions

Sukyo Lee: Methodology, Formal analysis, Investigation, Data Curation, Writing - Original Draft. **Sungjin Kim:** Investigation, Data Curation. **Sejoong Ahn:** Methodology, Formal analysis, Writing - Review & Editing. **Hanjin Cho:** Writing - Review & Editing, Supervision. **Sungwoo Moon:** Writing - Review & Editing, Supervision. **Young Duck Cho:** Writing - Review & Editing. **Jong-Hak Park:** Conceptualization, Methodology, Validation, Writing - Review & Editing, Visualization, Funding acquisition.

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335 **Tables**

336 **Table. 1** Comparison of characteristics of patients with sepsis in turnover and non-turnover periods
337 between 2018 and 2021

Variables	Turnover (n=102)	Non-turnover (n=741)	*P*-value
Male, n (%)	61 (59.8%)	429 (57.9%)	0.714
Age, median (IQR)	77 (68–85)	77 (66–83)	0.286
Underlying disease, n (%)			
Diabetes mellitus	39 (38.2%)	298 (40.2%)	0.702
Hypertension	49 (48.0%)	395 (53.3%)	0.318
Chronic liver diseases	8 (7.8%)	45 (6.1%)	0.490
Chronic kidney disease	12 (11.8%)	90 (12.1%)	0.912
Chronic respiratory disease	16 (15.7%)	131 (17.7%)	0.619
Cardiovascular disease	14 (13.7%)	142 (19.2%)	0.185
Malignancy	24 (23.5%)	162 (21.9%)	0.703
Suspected infection source, n (%)			
Genitourinary infection	36 (35.3%)	280 (37.8%)	0.626
Respiratory infection	63 (61.8%)	485 (65.5%)	0.464
Gastrointestinal infection	12 (11.8%)	63 (8.5%)	0.278
Other infection source	8 (7.8%)	44 (5.9%)	0.453
Multiple infection source	25 (24.5%)	185 (25.0%)	0.920
Presence of shock, n (%)	39 (38.2%)	259 (35.0%)	0.516
Severity, median (IQR)			
APACHE II score	20 (15–24)	19 (15–23)	0.339
SOFA score	9(6–11)	8 (6–11)	0.245

Initial serum lactate (mmol/L)	3.5 (1.9–7.3)	2.9 (1.9–5.5)	0.120
Adherence to SSC bundle, n (%)			
Overall bundle adherence	43 (42.2%)	356 (48.0%)	0.264
Fluid administration in 3 h	68 (66.7%)	512 (69.1%)	0.620
Antibiotics administration in 3 h	73 (71.6%)	576 (77.7%)	0.166
Time to antibiotics, median(min) (IQR)	129 (71–202)	115 (71–181)	0.140
Lactate measurement	101 (99.0%)	741 (99.6%)	0.429
Lactate follow-up	87 (85.3%)	660 (89.1%)	0.248
Time to vasopressor if indicated (min) (IQR)	137 (45.75–293.5)	132 (67.5–240)	0.978
Primary Outcome, n (%)			
7-day mortality	32 (31.4%)	123/736 (16.7%)	< 0.001
14-day mortality	44 (43.1%)	170/727 (23.1%)	< 0.001
30-day mortality	48/98 (49.0%)	202/709 (28.5%)	< 0.001
Secondary Outcome, median (IQR)			
Length of emergency ED stay (min)	689 (488.5–1330.25)	625 (413–1171)	0.114
Length of hospital stay (day)	11 (4–28)	13 (7–23)	0.213
Length of ICU stay (day)	8 (4–14)	9 (4–17)	0.386

IQR, interquartile range; ED, emergency department; ICU, intensive care unit; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sepsis-related Organ Failure Assessment, SSC, Surviving Sepsis Campaign.

341 **Table 2.** Univariable Cox proportional hazard regression analysis of 30-day mortality

Variables	HR (95% CI)	*P*-value
Sex (Reference: men)	1.123 (0.874–1.442)	0.365
Age	1.023 (1.012–1.034)	< 0.001
Underlying disease		
Diabetes Mellitus	1.196 (0.931–1.536)	0.161
Hypertension	1.000 (0.780–1.282)	0.999
Chronic liver diseases	1.325 (0.839–2.092)	0.228
Chronic kidney disease	1.008 (0.692–1.469)	0.967
Chronic respiratory disease	1.242 (0.917–1.682)	0.162
Cardiovascular disease	0.884 (0.638–1.224)	0.457
Malignancy	1.970 (1.516–2.561)	< 0.001
Suspected infection source		0.294
Genitourinary infection	1 (Reference)	
Respiratory infection	1.451 (0.975–2.159)	0.066
Gastrointestinal infection	1.433 (0.750–2.738)	0.277
Other infection sources	1.613 (0.947–2.749)	0.079
Multiple infection sources	1.571 (1.027–-2.403)	0.037
Presence of shock	3.219 (2.506–4.136)	< 0.001
Severity		
APACHE II score	1.088 (1.068–1.109)	< 0.001
SOFA score	1.171 (1.131–1.211)	< 0.001
Initial serum lactate	1.170 (1.139–1.203)	< 0.001
Admission in turnover period	1.925 (1.405–2.638)	< 0.001
Adherence to SSC bundle		
Overall bundle adherence	0.775 (0.603–0.997)	0.047*

Fluid administration in 3hr	0.817 (0.630–1.061)	0.129
Antibiotics administration in 3hr	0.878 (0.661–1.166)	0.369
Lactate follow-up	0.831 (0.568–1.218)	0.343

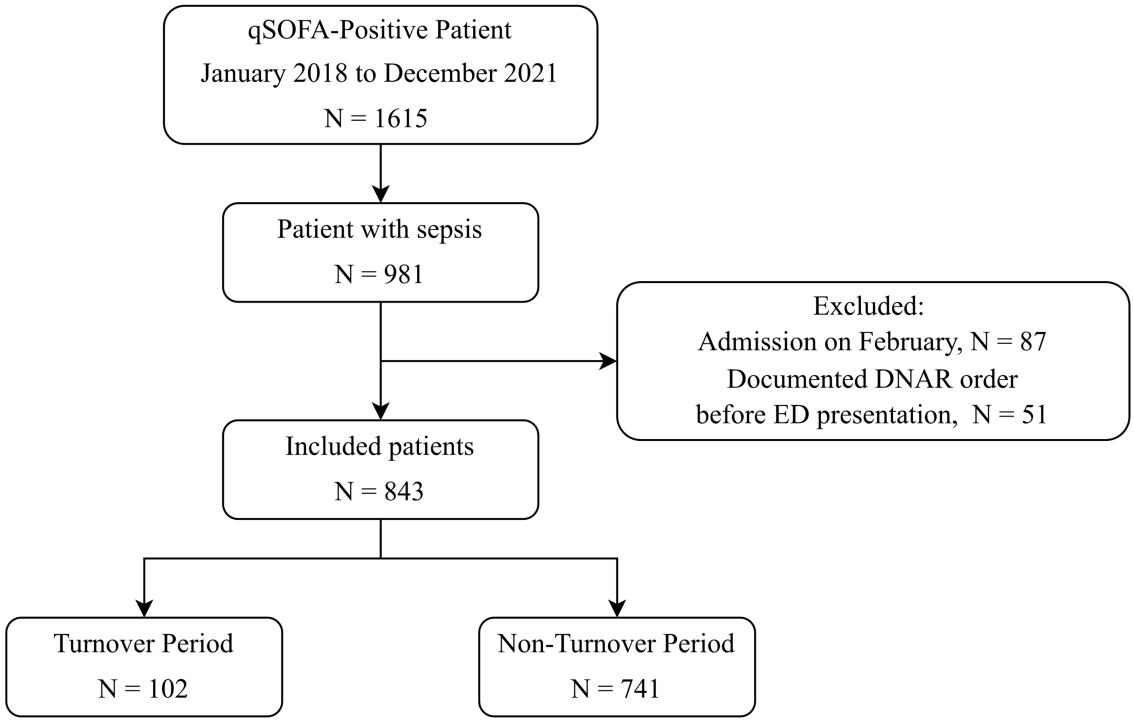
342 APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sepsis-related Organ Failure
343 Assessment; SSC, Surviving Sepsis Campaign.

344 **Table 3.** Multivariate Cox proportional hazard regression analysis of 30-day mortality

Variables	HR (95% CI)	*P*-value
Age	1.026 (1.014–1.037)	< 0.001
Malignancy	1.758 (1.347–2.293)	< 0.001
Presence of shock	1.594 (1.143–2.222)	0.006
SOFA score	1.088 (1.041–1.137)	< 0.001
Initial serum lactate	1.113 (1.077–1.151)	< 0.001
Overall bundle adherence	0.765 (0.592–0.988)	0.040*
Admission in turnover period	1.990 (1.444–2.743)	< 0.001

345 SOFA, Sepsis-related Organ Failure Assessment.

346 **Figure legends**

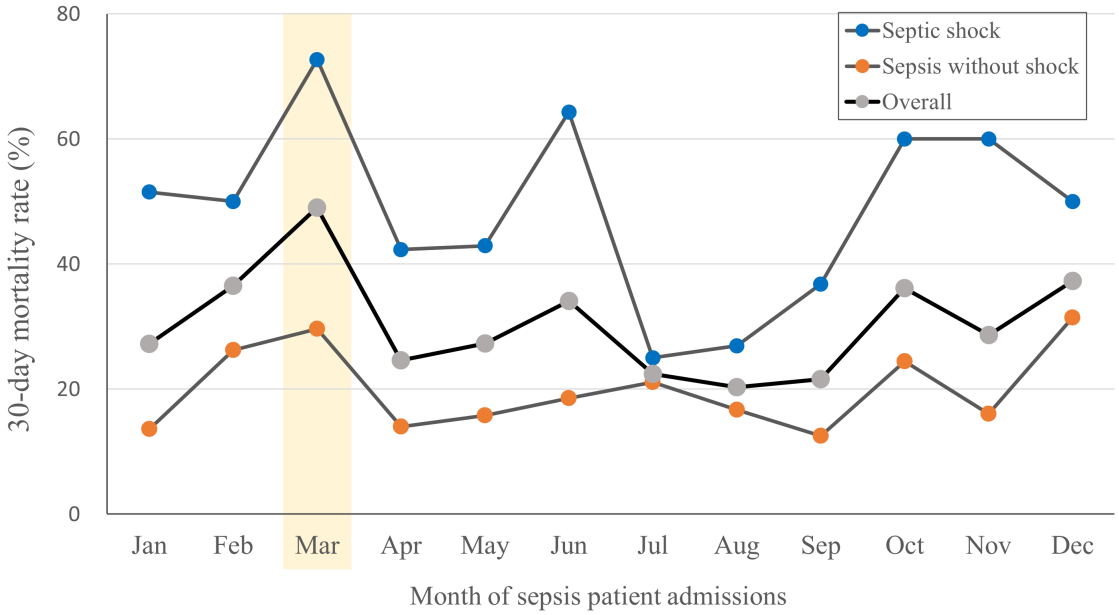


347

348 **Fig. 1.** Flowchart of the number of included and excluded patients.

349 qSOFA, quick Sepsis-related Organ Failure Assessment; ED, emergency department.

350



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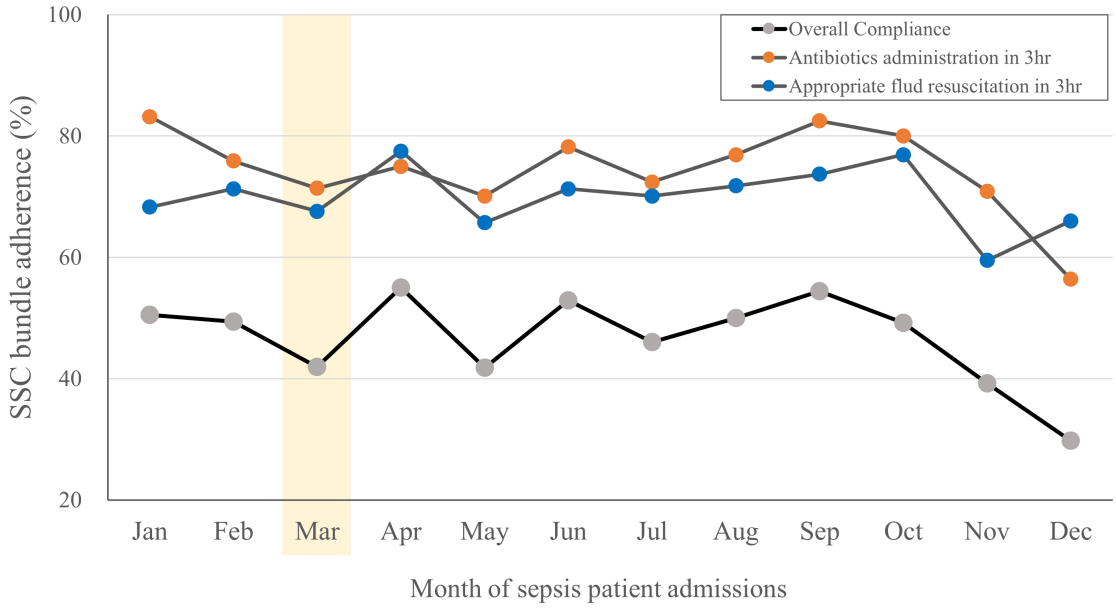
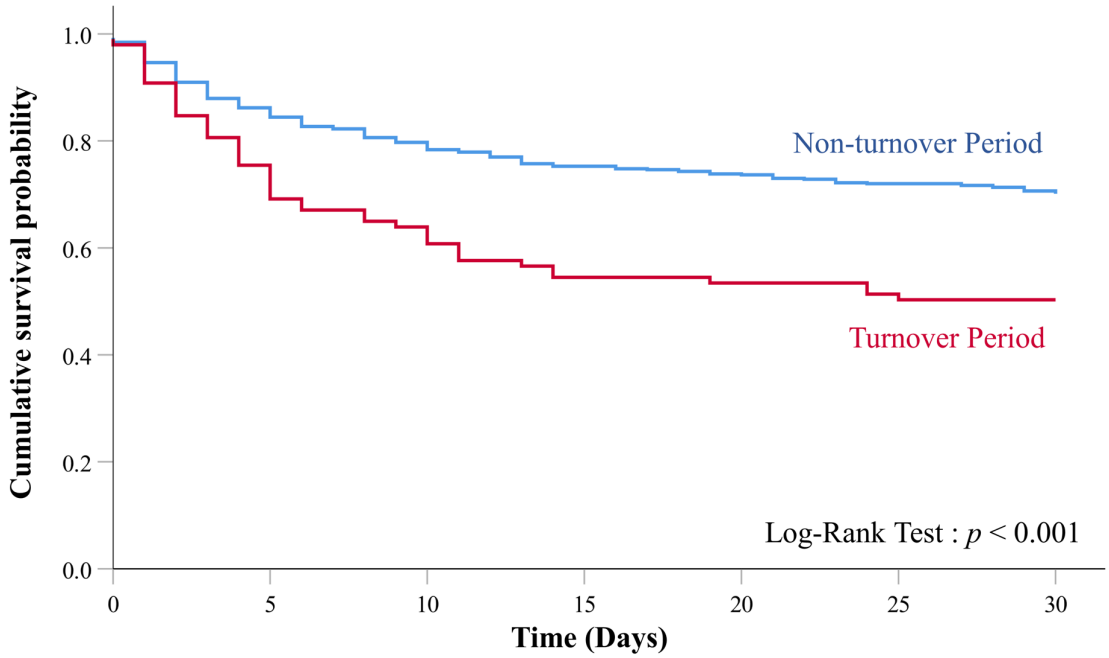


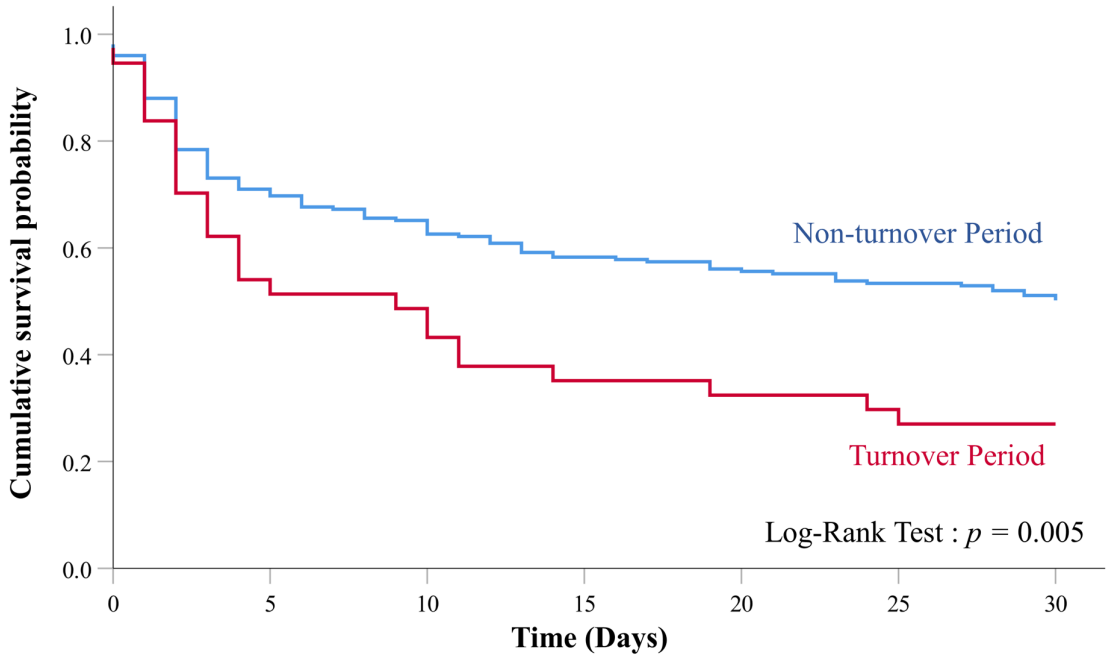
352

353 **Fig. 2.** (A) Monthly trend of 30-day mortality rate of patients with sepsis who visited the hospital
354 between 2018 and 2021. (B) Monthly Surviving Sepsis Campaign (SSC) bundle compliance rate of
355 patients with sepsis who visited the hospital between 2018 and 2021.

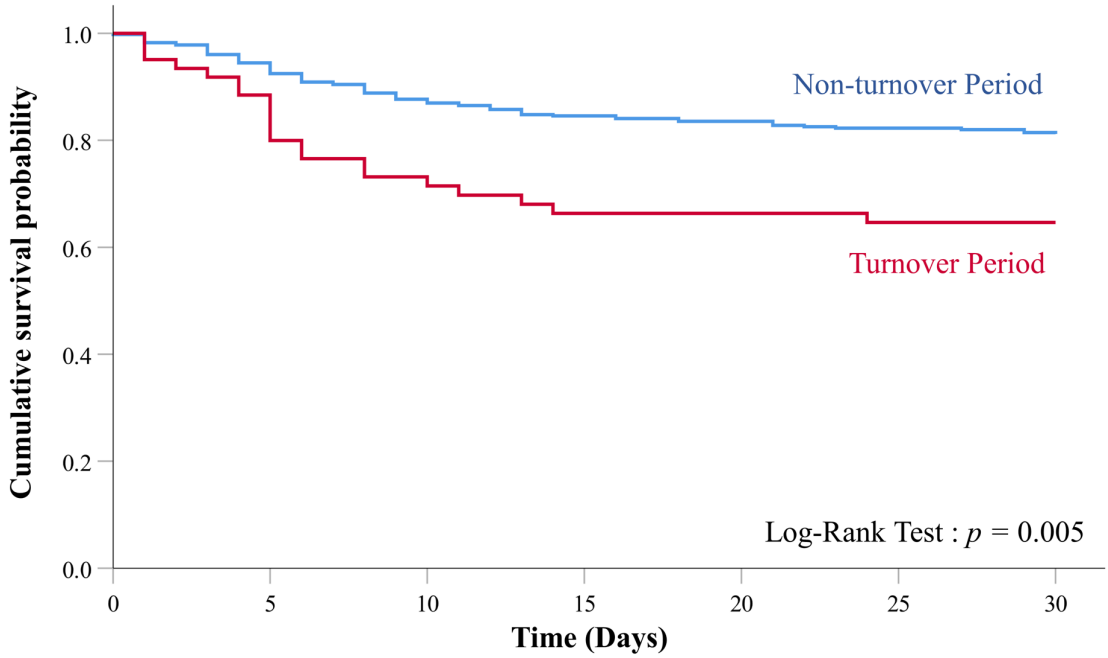
356


Cumulative survival probability
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
30
Time (Days)
Non-turnover Period
Turnover Period
Log-Rank Test : p < 0.001

357


Cumulative survival probability
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
30
Time (Days)
Non-turnover Period
Turnover Period
Log-Rank Test : p = 0.005

358

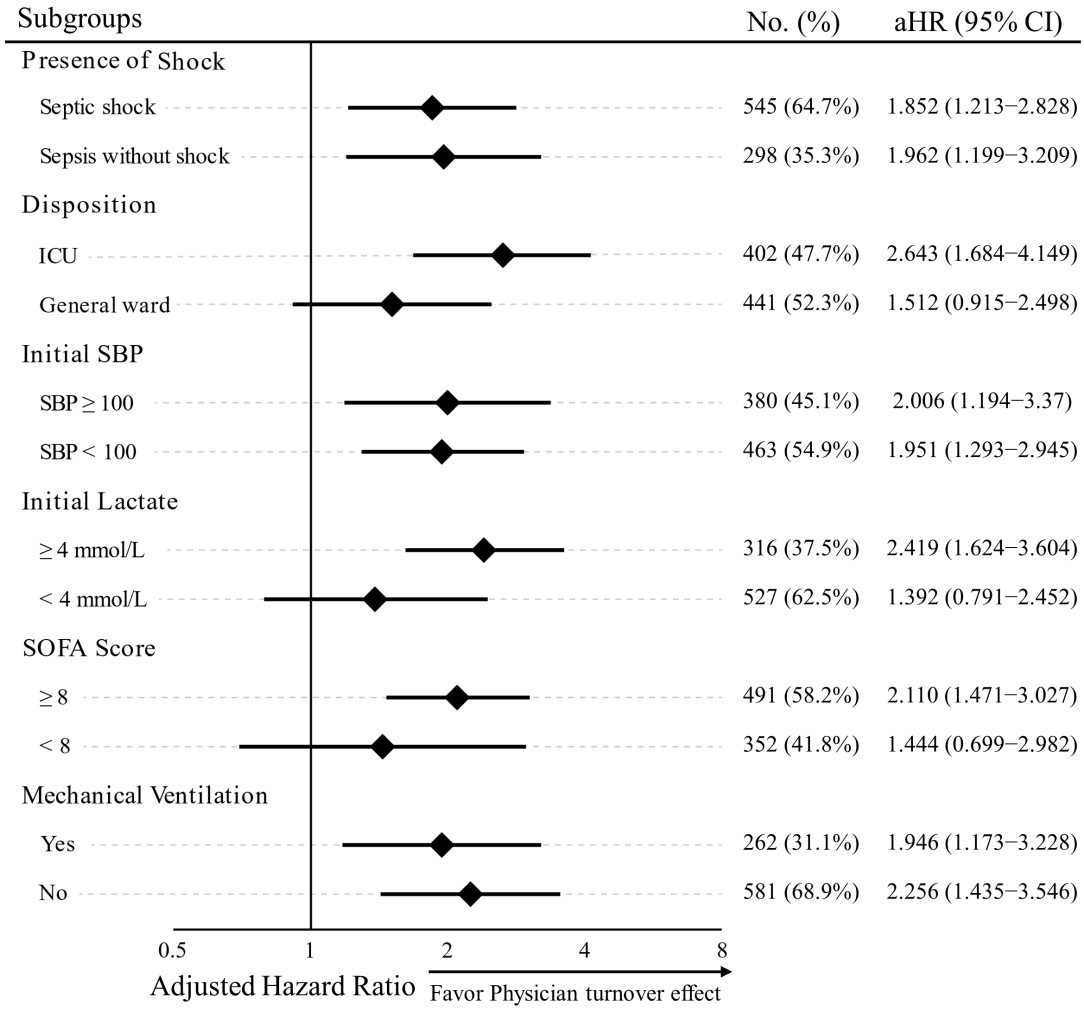


359

360 **Fig. 3.** Kaplan-Meier curve and a log-rank test between the turnover and non-turnover periods.

361 (A) Overall patients with sepsis; (B) Patients with septic shock; (C) Sepsis without shock

362



363

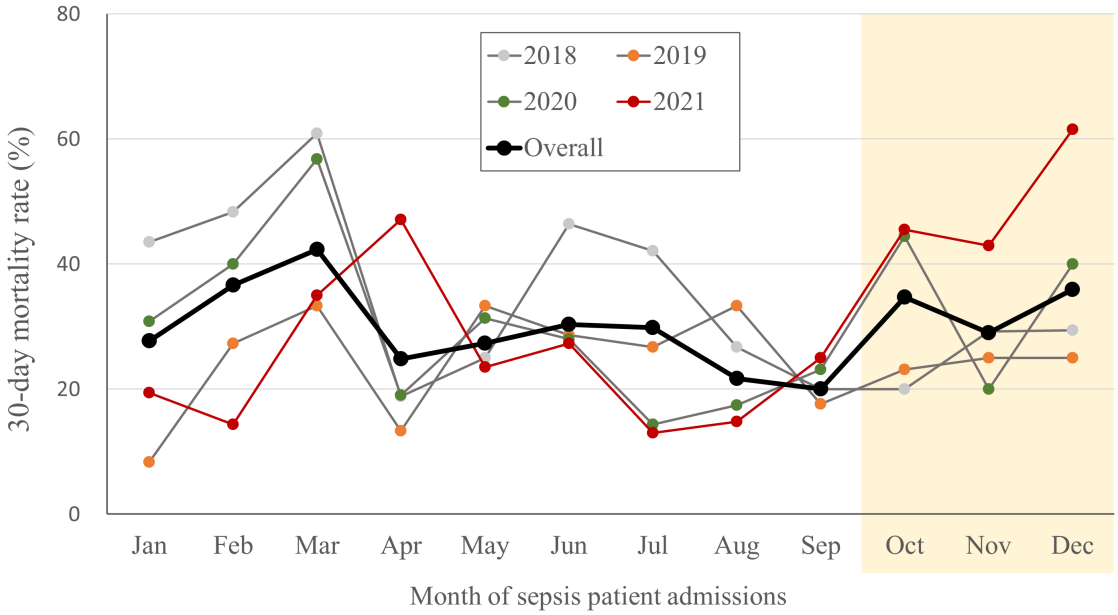
364 **Fig. 4**. Subgroup analysis of adjusted hazard ratio for 30-day mortality in the turnover period.

365 Adjusted confounder was age, malignancy, presence of shock, SOFA score, initial serum lactate, and

366 overall bundle adherence.

367 ICU, intensive care unit; SBP, systolic blood pressure; SOFA, sepsis-related organ failure assessment.

368



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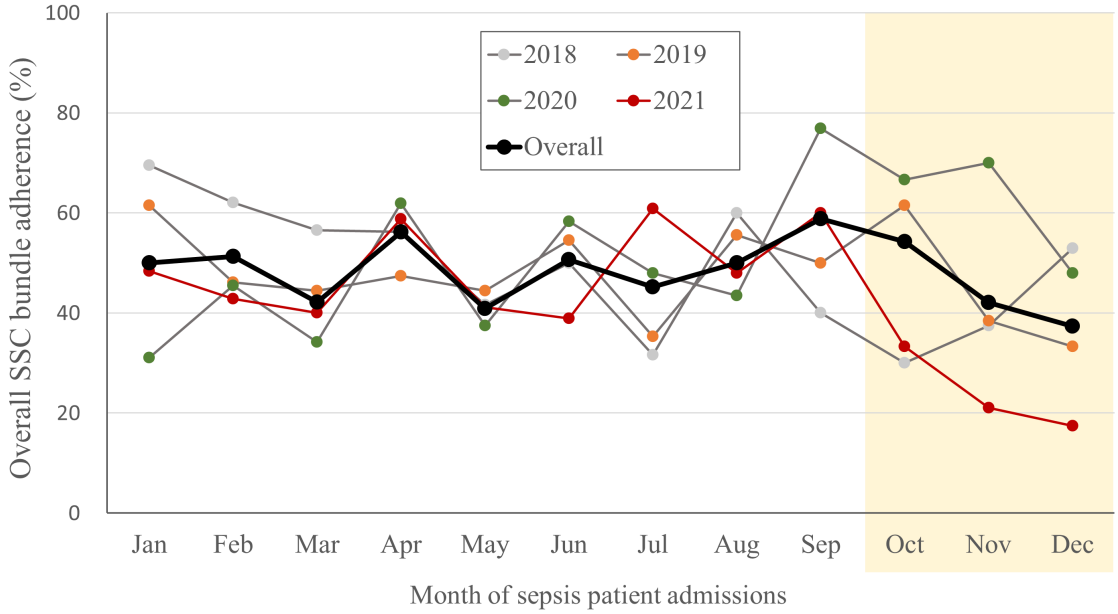

370

371 **Fig. 5.** (A) Monthly trend of 30-day mortality rate of patients with sepsis who visited the hospital by
372 years. (B) Monthly Surviving Sepsis Campaign (SSC) bundle compliance rate of patients with sepsis
373 who visited the hospital by years.