Prolonged length of stay in the emergency department and increased risk of hospital mortality in patients with sepsis requiring ICU admission

Zhongheng Zhang,1 Faran Bokhari,2 Yizhan Guo,3 Hemant Goyal4

ABSTRACT

Background and objectives Delayed patient admission to the intensive care unit (ICU) from the ED is common in China. Patients with severe sepsis or septic shock requiring ICU admission are in need of specialised monitoring and tailored treatment. Delayed admission to the ICU might be associated with adverse clinical outcomes for patients with sepsis.

Methods Patients with sepsis admitted to the ICU from the ED January 2010 to April 2018 were retrospectively identified from a clinical data warehouse. The primary endpoint was in-hospital mortality. Length of stay in ED (EDLOS) was compared between survivors and non-survivors. A multivariable regression model was employed to adjust for potential confounding due to patient clinical condition.

Results A total of 1997 patients, including 473 non-survivors and 1524 survivors, were included. The crude mortality rate for patients with EDLOS <6 hours was 21.4%, which was significantly lower than patients with EDLOS of 12–24 hours (31.9%), and those with EDLOS >24 hours (31.8%). After adjusting for PaO2/FiO2, serum creatinine, age, Sequential Organ Failure Assessment, body mass index, lactate, comorbidities and infection site, EDLOS continued to be independently associated with increased risk of hospital mortality. Compared with the group with EDLOS <6 hours, those with EDLOS between 12 and 24 hours (OR 1.82, 95% CI 1.27 to 2.52) and EDLOS >24 hours (OR 1.79, 95% CI 1.27 to 2.52) showed a significantly increased risk of death.

Conclusions Our study shows that prolonged EDLOS is independently associated with increased risk of hospital mortality in patients with sepsis requiring ICU admission.

INTRODUCTION

Sepsis is a leading cause of morbidity and mortality among hospitalised patients. A substantial number of patients with sepsis require intensive care unit (ICU) admission for close monitoring and supportive therapy. Close monitoring of conditions such as unstable vitals and circulatory haemodynamics, oxygen supply and demand, and respiratory dysfunction are key components in the successful treatment of severe sepsis and septic shock. Patients with sepsis typically have organ failure that requires supportive treatment, including mechanical ventilation, renal replacement therapy, vasopressors or even extracorporeal membrane oxygenation. ICUs have a high ratio of doctors and nurses per patient and are well equipped to manage patients with critical illness with sepsis.

Key messages

What is already known on this subject
► Prolonged length of stay in the ED is common in Chinese hospitals.
► Prolonged stay in ED has been found to be associated with worse outcome in heterogeneous patients with critical illness.

What this study adds
► Prolonged length of stay in ED is independently associated with increased risk of hospital mortality in patients with critical illness with sepsis.
► In multivariable model, the length of stay in ED and severity score are independently associated with mortality outcome.

However, critical care resources are extremely limited in China. A recent study conducted in China showed that the number of ICU beds per 100 000 population was only 3.69, which was far lower than that in European countries (11 per 100 000 population) and the USA (34 per 100 000 population). Therefore, it is common to have ICU congestion in Chinese tertiary care hospitals resulting in patients remaining in the ED for prolonged periods of time while waiting for an ICU bed. Because the ED is not designed to function as a specialised inpatient unit, medical care in the ED may be suboptimal compared with the ICU.

In previous studies conducted elsewhere than China, delayed admission (eg, delayed transferring of patient from the ED to the ICU after the patient has been designated as needing an ICU bed) was found to be associated with poorer outcomes in ICU patients with different diagnoses. Such an association was not replicated in other studies. There are no data specifically for patients with sepsis, nor from Chinese hospitals. To address these knowledge deficits, we aimed to investigate the association of the length of stay in ED (EDLOS) and in-hospital mortality for patients with sepsis who were admitted to ICU. We hypothesised that the prolonged stay in ED was associated with higher risk of mortality.

METHODS AND MATERIALS

Study design and setting

This was a retrospective medical record evaluation of patients with sepsis who transferred from the ED to the ICU of Sir Run Run Shaw Hospital (a...
tertiary care university-affiliated hospital) in Hangzhou, China, from January 2010 to April 2018. Informed consent was waived due to the retrospective design of the study.

**Data source**

Data for this study were abstracted from the clinical data warehouse which has been created as a collaboration between the department of information technology (IT) of Sir Run Run Shaw Hospital and Lejiu Health (Shanghai, China). Core elements of the data warehouse were deidentified so that all queries and analytics could be carried out without exposing private health information.

**Participants**

Adult (≥18 years old) patients admitted from the ED to the ICU with a diagnosis of sepsis during the study period. Sepsis was defined as a diagnosis of infection plus acute organ dysfunction.\(^8^\)\(^9^\) The definition was proposed by Angus et al.,\(^10^\) and was subsequently used in identifying patients with sepsis from electronic health record (EHR).\(^11^\)\(^12^\) The identification of sepsis cases was made collaboratively by the clinical investigators and engineers from the IT department.

We determined infection by use of the International Classification of Diseases, Ninth Revision (ICD-9) code for the ED diagnosis of pneumonia, infections of the urinary tract infection, skin or soft tissue, bloodstream, central nervous system, gastrointestinal tract or other organs; cholangitis; or peritonitis. Patients were deemed to have end-organ damage if the ICD-9 code for their ED visit included any of the following: hypotension, shock without mention of trauma, secondary thrombocytopenia, encephalopathy and acute kidney failure (detailed codes for extracting this information can be found in online supplementary material S1). Patients were also considered to have acute organ failure if there was an acute rise in the ED in the Sequential Organ Failure Assessment (SOFA) score of ≥2.\(^11^\)\(^3\) SOFA score was calculated by retrospective chart review and variables were collected on the first ED visit. If a variable such as the Glasgow Coma Scale was missing in ED, the first recorded value on ED admission was used. The data were abstracted by IT engineer from the database and verified by a senior researcher. Patients were excluded if their EDLOS >72 hours; this criterion was used because some patients were not critically ill enough to meet the ICU entry criteria at the initial presentation to ED, and they became more critically ill after 2–3 days while remaining in the ED awaiting an inpatient bed. Other exclusions were: age ≤18, missing data on survival outcomes; duplicated registration in the ED; and admissions from other hospitals or other parts of our hospital, such as transfers from inpatient medicine wards. This last exclusion criterion was employed to exclude sepsis caused by nosocomial infections. A subsample of 100 patients was verified manually by two authors for the diagnosis of sepsis. The Cohen's kappa coefficient was 0.96.

**Variables assessed as predictors of survival**

The primary outcome was the association of EDLOS and hospital mortality. EDLOS was defined as the hours between ED arrival time and the ICU admission time. We included all ED visits for which patients were admitted to the ICU. Thus, if patients visited the ED more than once during the study, all visits in which they were admitted to the ICU were included. Patients were categorized into four groups based on EDLOS duration: <6 hours, 6–12 hours, 12–24 hours and >24 hours.\(^8^\)\(^9^\)

Patient variables abstracted from the clinical data warehouse were demographic characteristics (age, gender), body mass index (BMI), comorbidities, infection site, BP, RR, HR, blood glucose and temperature as measured and recorded on presentation to the ED. Laboratory variables extracted were serum creatinine, procalcitonin, C-reactive protein (CRP), PaO\(_2\)/FiO\(_2\), total bilirubin and platelet count as measured during the ED stay. If there were two or more laboratory measurements obtained during the ED stay, the first measurement on ED admission was used for analysis. The use of vasopressors was also extracted. Vasopressor use was defined as norepinephrine, epinephrine, phenylephrine and dopamine (when administered >5 mcg/kg/min).

**Missing values**

Single imputation by mean was performed for variables with missing values of less than 5%.\(^8^\)\(^9^\) For missing values greater than 5%, multiple imputation was used. A multivariable regression model was fit by using the variable to be imputed as the response variable, and other variables (gender, BMI, temperature, HR, RR, BP, age, infection site, comorbidity, blood glucose, platelet, creatinine, P/F ratio, bilirubin, lactate, procalcitonin, CRP, use of vasopressor and SOFA) as covariates. Five imputed data sets were generated to account for the uncertainty induced by imputation.\(^14^\)\(^3\) The procedure was performed on the whole data set.

**Statistical methods**

The primary outcome was in-hospital mortality, which was defined as survival after ICU admission and during hospitalisation; patients who died in ED were not included. The secondary outcome was hospital LOS, which was defined as time elapsed from transfer to the ICU bed to discharge. Time spent in the ED was not included for hospital LOS. Patients were divided into survivors and non-survivors based on in-hospital vital status and the variables of interest in predicting mortality were compared according to these two groups. Continuous variables were tested for normality using the Shapiro-Wilk test. Normally, distributed data are expressed as means and SDs, and compared between survivors and non-survivors by using Student's t-test. Non-normally distributed data are expressed as medians and IQRs, and compared using the Mann-Whitney test. Categorical variables are expressed as the number and proportion, and compared by using the \(\chi^2\) test or Fisher’s exact test, as appropriate. The R package \texttt{CBCgrps} was employed for these statistical descriptions and bivariate comparisons.\(^15^\)

Logistic regression was used to assess the relationship of EDLOS and in-hospital mortality. Predictor variables with a \(p\) value ≤0.05 in univariable analyses were entered into the multivariable regression model. We also included variables (eg, kidney failure, liver failure, vasopressor use and BMI) considered by subject knowledge or literature to be associated with mortality.\(^16^\)

Collinearity among explanatory variables was judged by the use of variance inflation factors (VIF). Higher VIF indicates higher collinearity. VIF values above 5 were used to define high collinearity (online supplementary table S1).\(^17^\) Principle component analysis would be used if there was high collinearity among variables.

All statistical analyses were performed using R software (V3.4.3). A two-tailed \(p\) value ≤0.05 was considered as indicative of statistical significance.

**RESULTS**

**Participants**

An initial search of the clinical data warehouse identified 8079 ICU admissions from the ED. Of these, 2870 fulfilled the diagnosis of sepsis and were further screened for potential eligibility.
Figure 1  Flow chart of patient selection. ER, emergency room; LOS, length of stay.

After application of exclusion criteria, a total of 1997 patients were finally included for the analysis (figure 1).

Comparison of clinical characteristics between the survivors and non-survivors
Survivors were younger, with a higher BMI, lower HR, higher temperature and lower SOFA scores than non-survivors (table 1). Infection sites were different between the two groups; survivors were more likely to have abdominal infections, while non-survivors were more likely to have lung infections. Serum creatinine and lactate levels were higher in the non-survivors. There were no differences between survivors and non-survivors in gender, RR, diastolic BP, hypertension and renal failure.

In-hospital mortality and length of ED stay
Median EDLOS was significantly higher in non-survivors (3.9 vs 3.3 days, p=0.003). There was no difference in mortality for patients with EDLOS <6 hours and those with EDLOS of 6–12 hours. Mortality in patients with EDLOS <12 hours was 21%, and 32% in those with EDLOS of 12–24 hours and those with EDLOS >24 hours (table 2). In the multivariable logistic regression model, EDLOS continued to be associated with mortality outcome (table 3). By including EDLOS as continuous variable, each 1 hour delay was associated with a 1.015-fold increase in the odds of death (OR 1.015; 95% CI 1.007 to 1.024). The relationship between increasing EDLOS and increased predicted probability of hospital death is shown in figure 2. As compared with patients who stayed for less than 6 hours, those stayed more than 12 hours had a 1.82-fold increase in the odds of death, and those stayed more than 24 hours had 1.79-fold increase in the odds of death. Other variables including age, PaO2/FiO2, temperature, HR, lactate, heart failure and malignancy were independently associated with mortality (table 3).

DISCUSSION
The findings from this study suggest that prolonged EDLOS is independently associated with higher in-hospital mortality among patients with sepsis who require ICU admission in China. Although early ICU admission is ideal for patients with critical illness with sepsis, this is not always possible due to limited medical resources, particularly in China. Further evaluation is necessary to determine what additional resources might be needed to allow outcomes similar to those with shorter times to ICU transfer.

Previous researchers have examined the relationship of EDLOS and mortality with similar results to ours. Chalfin and colleagues observed that delayed transfer from ED to ICU (>6 hours ED boarding) was associated with prolonged hospital stay (7 vs 6 days; p<0.001) and higher mortality (17.4% vs 12.9%; p<0.001) among patients with critical illness with various diagnoses in a US ED. A single-centre cohort study conducted in Brazil also observed that each hour of delay to admission was independently associated with a 1.5% increased risk of ICU death (HR 1.015; 95% CI 1.006 to 1.02). Hsieh et al evaluated patients with acute respiratory failure presenting to the ED and found that patients who remained in the ED more than 1 hour before ICU admission had greater mortality than those with ED stay less than 1 hour. Similar findings that prolonged stay in ED was associated with worse clinical outcome have also been found in other subgroups of patients such as those requiring mechanical ventilation, surgery and neurologic care.

In contrast, Khan and colleagues failed to identify differences in mortality between patients who stayed less than or more than...
Table 1  Clinical characteristics in survivors, non-survivors and the overall patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall (n=1997)</th>
<th>Survivors (n=1524)</th>
<th>Non-survivors (n=473)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male (%)</td>
<td>1282 (64.2)</td>
<td>992 (65.1)</td>
<td>290 (61.3)</td>
<td>0.149</td>
</tr>
<tr>
<td>BMI (kg/m²) (mean (SD))</td>
<td>22.74 (4.35)</td>
<td>22.85 (4.26)</td>
<td>22.39 (4.61)</td>
<td>0.045</td>
</tr>
<tr>
<td>Temperature (mean (SD))</td>
<td>36.86 (1.02)</td>
<td>36.90 (0.99)</td>
<td>36.72 (1.09)</td>
<td>0.001</td>
</tr>
<tr>
<td>HR (mean (SD))</td>
<td>94.94 (22.21)</td>
<td>94.16 (21.59)</td>
<td>97.48 (23.92)</td>
<td>0.004</td>
</tr>
<tr>
<td>RR (mean (SD))</td>
<td>20.18 (6.15)</td>
<td>20.09 (6.16)</td>
<td>20.49 (6.12)</td>
<td>0.210</td>
</tr>
<tr>
<td>Systolic BP (mean (SD))</td>
<td>130.36 (28.11)</td>
<td>130.93 (27.21)</td>
<td>128.49 (30.78)</td>
<td>0.099</td>
</tr>
<tr>
<td>Diastolic BP (mean (SD))</td>
<td>72.44 (16.63)</td>
<td>72.58 (16.24)</td>
<td>71.99 (17.87)</td>
<td>0.499</td>
</tr>
<tr>
<td>Age (years) (mean (SD))</td>
<td>63.81 (17.33)</td>
<td>62.12 (17.42)</td>
<td>69.24 (15.86)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Infection site, n (%)<0.001
- Abdomen 345 (17.3) 279 (18.3) 66 (14.0)
- Biliary system 193 (9.7) 171 (11.2) 22 (4.7)
- Bloodstream 18 (0.9) 14 (0.9) 4 (0.8)
- CNS 46 (2.3) 35 (2.3) 11 (2.3)
- GI tract 24 (1.2) 20 (1.3) 4 (0.8)
- Lung 722 (36.2) 529 (34.7) 193 (40.8)
- Others 105 (5.3) 77 (5.1) 28 (5.9)
- Skin and soft tissue 32 (1.6) 26 (1.7) 6 (1.3)
- Urinary tract 512 (25.6) 373 (24.5) 139 (29.4)

Comorbidities, n (%) 0.430
- Hypertension, n (%) 870 (43.6) 656 (43.0) 214 (45.2)
- Diabetes mellitus, n (%) 382 (19.1) 278 (18.2) 104 (22.0)
- Liver failure, n (%) 106 (5.3) 88 (5.8) 18 (3.8)
- Renal failure, n (%) 27 (1.4) 17 (1.1) 10 (2.1)
- Heart failure, n (%) 251 (12.6) 160 (10.5) 91 (19.2)
- Malignancy, n (%) 216 (10.8) 139 (9.1) 77 (16.3)

Hospital LOS (days) (median [IQR]) 14.03 [7.74, 24.48] 14.67 [8.42, 24.78] 12.73 [5.89, 22.97] <0.001

Laboratory tests
- Blood glucose (mmol/L) (mean (SD)) 10.47 (37.03) 9.32 (22.50) 14.18 (64.41) 0.012
- Platelet (×10⁹/L) 177.11 (92.98) 178.32 (94.57) 173.15 (102.13) 0.290
- Serum creatinine (mmol/L) 119.61 (176.93) 117.32 (184.43) 126.96 (150.21) 0.301
- Total bilirubin (μmol/L) 31.90 (47.34) 31.73 (46.76) 32.44 (49.19) 0.778
- Lactate (mmol/L) 3.69 (3.56) 3.49 (3.32) 4.33 (4.18) <0.001
- Procalcitonin (ng/mL) 19.11 (34.60) 19.15 (34.10) 18.97 (36.21) 0.920
- C-reactive protein (mg/L) 82.48 (95.91) 81.41 (96.19) 85.92 (95.05) 0.373
- Use of vasopressor, n (%) 299 (15.0) 189 (12.4) 110 (23.3) <0.001
- SOFA (median [IQR]) 4.00 [2.00, 6.00] 4.00 [2.00, 6.00] 5.00 [3.00, 7.00] <0.001
- Year of admission after 2015, n (%) 1668 (83.5) 1301 (85.4) 367 (77.6) <0.001
- EDLOS (hours) (median [IQR]) 3.47 [1.53, 10.00] 3.33 [1.48, 8.42] 3.90 [1.72, 16.93] 0.003

Continuous variables were expressed as median and IQR; or mean and SD as appropriate; and categorical data were expressed as number and proportion.

BMI, body mass index; CNS, central nervous system; EDLOS, length of stay in ED; GI, gastrointestinal; LOS, length of stay; SOFA, Sequential Organ Failure Assessment.

Table 2  Outcomes of patients according to length of stay in ED

<table>
<thead>
<tr>
<th>EDLOS</th>
<th>&lt;6 hours (n=1306)</th>
<th>6–12 (n=223)</th>
<th>12–24 (n=216)</th>
<th>&gt;24 (n=236)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, n (%)</td>
<td>280 (21.4)</td>
<td>46 (20.6)</td>
<td>69 (31.9)</td>
<td>75 (31.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

6 hours.9 A study conducted in a level I trauma centre showed that non-delayed group had significantly higher risk of death than delayed group (18% vs 2.3%). This might be explained by the fact that more severely ill trauma patients were transferred with priority without delay.23 In another study by Agustin et al, the authors found no difference in mortality outcome between patients with sepsis with and without prolonged ED stay.24 Probably, these studies were underpowered due to limited sample size.

Our study showed increased in-hospitality mortality when ICU patients stayed longer in the ED, although we detected a statistically significant difference only after EDLOS was greater than 12 hours. The difference between this study and Chalfin is that we measured the total LOS (which would include workup...
time and boarding) while Chalfin’s study only looked at the time elapsed from the decision to admit to an ICU and transfer (ie, boarding). However, similar to Chalfin’s study, the study conducted in Brazil showed that the mortality did increase with each hour of delay (HR 1.015; 95% CI 1.006 to 1.02). Our patients were potentially more critically ill than Chalfin’s study, as reflected by our patients’ higher mortality rate (30% vs 17%). Also in our study, we evaluated patient severity of illness based on clinical data from the ED study, while Chalfin’s study adjusted for Acute Physiology and Chronic Health Evaluation II as obtained after ICU admission.

Several limitations must be acknowledged in the present study. First, the study was retrospective and suffered from inherent limitations of this design. We were unable to determine when the decision to admit to the ICU occurred, and thus cannot be sure that the time in the ED represents a delay after admission, or evaluation and management time. However, given that we adjusted for illness severity, it seems unlikely that the difference is due to the patients with prolonged stays having longer evaluations. Second, selection bias was possible because some patients were transferred to other nearby hospitals when there was no ICU bed available in our hospital. However, there were less than 10 such patients during the study period. Many variables had missing values, which may introduce potential bias. To minimise such kind of bias, we used the multiple imputation method to handle missing values. This method minimises information loss caused by casewise deletion (eg, an observation would be excluded from multivariate regression model if it contained missing value in one or more variables), and accounts for the uncertainty caused by imputation. Third, the clinical definition of sepsis was revised several times during the study period. In earlier years, sepsis was defined as inflammatory systemic response syndrome plus suspected or documented infection; while the third sepsis definition defined sepsis as infection plus organ dysfunction. The third sepsis definition is actually consistent with the severe sepsis in the old definition. Thus, the mortality can be higher with the updated third definition. In our study, we used the definition proposed by Angus et al., which was subsequently used in identifying patients with sepsis from EHR. Patients identified in this way were generally consistent with the third sepsis definition. Fourth, our study did not compare the time to treatment between groups with different EDLOS. It has been shown that the time to treatment (eg, initiation of antibiotics, fluids and lactate measurement) has a significant impact on mortality. Unfortunately, the time for the administration of antibiotics and fluid was not recorded in the EHR. Fifth, our study was basically looking at the patient’s time in the ED, not whether they were stabilised and then there was a delay for a bed. Several reasons may result in delayed ICU admission: (1) the decision made by ED clinician considering a patient for ICU admission is delayed (ie, more the fault of the ED clinician); (2) ICU consultant delays in seeing the patient or approving an ICU admission; and (3) delays in getting a bed in the ICU because none were available or because of bureaucratic delays in transferring the patient to the ICU. Different reasons may have different impact on the mortality outcome, but we cannot explore this issue by using EHR. Finally, the association noted in our study is probably affected by clinician behaviour. The clinicians might aggressively manage younger and healthier patients, but let elderly patients with multiple comorbidities stay in ED. Although we have tried to adjust for age and severity of illness in multivariate analysis, we are unable to adjust for clinician belief and practice.

In conclusion, our study showed that prolonged EDLOS was independently associated with increased risk of hospital mortality in patients with sepsis requiring ICU admission. While the ultimate

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Adjusted OR for variables associated with mortality</th>
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<tbody>
<tr>
<td>Variables</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>PaO2/FiO2 (for 50%)</td>
<td>0.87 (0.82 to 0.92)</td>
</tr>
<tr>
<td>Serum creatinine (for 60%)</td>
<td>0.98 (0.93 to 1.02)</td>
</tr>
<tr>
<td>Age (for 10 years)</td>
<td>1.22 (1.13 to 1.31)</td>
</tr>
<tr>
<td>EDLOS (&lt;6 hours as reference)</td>
<td></td>
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<tr>
<td>6–12 hours</td>
<td>1.15 (0.78 to 1.66)</td>
</tr>
<tr>
<td>12–24 hours</td>
<td>1.82 (1.28 to 2.58)</td>
</tr>
<tr>
<td>&gt;24 hours</td>
<td>1.79 (1.27 to 2.52)</td>
</tr>
<tr>
<td>SOFA (for 1 unit)</td>
<td>1.07 (1.1 to 1.14)</td>
</tr>
<tr>
<td>BMI</td>
<td>1.0 (0.97 to 1.02)</td>
</tr>
<tr>
<td>Temperature</td>
<td>0.87 (0.78 to 0.97)</td>
</tr>
<tr>
<td>HR (for 101)</td>
<td>1.06 (1.10 to 1.11)</td>
</tr>
<tr>
<td>Lactate</td>
<td>1.06 (1.03 to 1.09)</td>
</tr>
<tr>
<td>Primary infection site (abdomen as reference)</td>
<td></td>
</tr>
<tr>
<td>Biliary system</td>
<td>0.59 (0.33 to 0.93)</td>
</tr>
<tr>
<td>Bloodstream</td>
<td>0.99 (0.24 to 3.27)</td>
</tr>
<tr>
<td>CNS</td>
<td>1.56 (0.69 to 3.3)</td>
</tr>
<tr>
<td>GI tract</td>
<td>0.72 (0.2 to 2.1)</td>
</tr>
<tr>
<td>Lung</td>
<td>1.31 (0.93 to 1.86)</td>
</tr>
<tr>
<td>Skin and soft tissue</td>
<td>1.05 (0.35 to 2.74)</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>1.22 (0.85 to 1.77)</td>
</tr>
<tr>
<td>Others</td>
<td>1.31 (0.74 to 2.28)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1.47 (1.06 to 2.01)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>2.07 (1.47 to 2.9)</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>1.78 (0.7 to 4.36)</td>
</tr>
<tr>
<td>Liver failure</td>
<td>0.79 (0.43 to 1.36)</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>1.22 (0.84 to 1.78)</td>
</tr>
<tr>
<td>Annual volume (with each 10,000 admissions increase)</td>
<td>0.85 (0.80 to 0.90)</td>
</tr>
<tr>
<td>Admission year after 2015 versus before 2015</td>
<td>1.46 (0.94 to 2.27)</td>
</tr>
</tbody>
</table>

A mixed-effects generalised linear regression model was fit by using treating physician as the random-effects term. 1 indicates the increase in respective number of unit. For example, the OR for PaO2/FiO2 was for each 50-unit increase. BMI, body mass index; CNS, central nervous system; EDLOS, length of stay in ED; GI, gastrointestinal; SOFA, Sequential Organ Failure Assessment.

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**Figure 2**  Adjusted probability of hospital mortality against length of stay in ED.
goal is to improve timely access to the ICU for patients with sepsis, further prospective studies are needed to identify potentially modifiable risk factors for patients who must remain in the ED.

**Contributors** ZZ conceived the study. ZZ and YG carried out data entry, data check and interpretation. ZZ performed statistical analysis and drafted the manuscript. FB and HG helped review and interpret the results. All authors read and approved the final manuscript.

**Funding** ZZ received funding from the Public Welfare Research Project of Zhejiang Province (LG18H150005) and the scientific research project of Zhejiang Education Commission (Y201737841).

**Patient consent for publication** Not required.

**Ethics approval** The study was approved by the Ethics Committee of Sir Run Run Shaw Hospital, Zhejiang University School of Medicine.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**REFERENCES**