Title: Risk factors of sepsis among patients with qSOFA<2 in the emergency department

Running head: Risk factors of sepsis among patients with qSOFA<2.

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Author's Contributors

JS, IO, and TG conceived and designed the study. JS, IO, HI, and TG performed the statistical analyses. JS, IO, and TG drafted the initial manuscript. TS, KH, KN, and TG supervised the study. All authors interpreted the data, critically revised the manuscript for important intellectual content, and approved the final manuscript.

Declaration of Interest statement

Dr. Sonoo is the Chief Executive Officer of TXP Medical Co. Ltd. and reports grants from AI Hospital Research grant from Japan Cabinet Office. Dr. Goto is the Chief Scientific Officer of TXP Medical Co., Ltd. Dr. Hara is a researcher at TXP Medical Co. Ltd.

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Sepsis, qSOFA, emergency department, triage, vital signs

ABSTRACT (342 words; maximum 350 words)

Objective: Studies have suggested that qSOFA can be used for early detection of sepsis immediately upon arrival at the emergency department (ED). Despite this, little is known about the risk factors associated with the subsequent diagnosis of sepsis among patients with qSOFA<2 in the ED.

Methods: This is a retrospective cohort study using ED data from a large tertiary medical center in Japan, 2018-2020. We included adult patients (aged ≥18 years) presenting to the ED with suspected infection (e.g., having a fever) and qSOFA<2. We identified patients who developed sepsis based on the Sepsis-3 criteria, and compared patient characteristics (e.g., demographics, vital signs upon the initial triage, chief complaint, and comorbidities) between patients who developed sepsis or not. Additionally, we identified the potential risk factors of sepsis among patients with qSOFA<2 using a multivariable logistic regression model.

Results: We identified 151 (7%) patients who developed sepsis among 2,025 adult patients with suspected infection and qSOFA<2. Compared with patients who did not develop sepsis, patients who developed sepsis were likely to be older and have vital signs suggestive of imminent sepsis (e.g., high respiratory rate). In the multivariable logistic regression model, the potential risk factors of sepsis among patients with qSOFA<2 were older age (adjusted OR, 1.92 [95%CI 1.19-3.19]), vital signs suggestive of imminent sepsis (e.g., adjusted OR of altered mental status, 3.50 [95%CI 2.25-5.50]), receipt of oxygen therapy upon arrival at the ED (adjusted OR, 1.91 [95%CI 1.38-2.26]), chief complaint of sore throat (adjusted OR, 2.15 [95%CI 1.08-4.13]), and the presence of comorbid diabetes mellitus, ischemic heart disease, and chronic kidney disease (e.g., adjusted OR of diabetes mellitus, 1.47 [95%CI 1.10-1.96]). On the contrary, chief complaint of abdominal and chest pain were associated with a lower risk of sepsis (e.g., adjusted OR of abdominal pain, 0.26 [95%CI 0.14-0.45]).

Conclusions: We found that older age, vital signs prognosticating sepsis, and the presence of some comorbidities were the potential risk factors of sepsis in patients with qSOFA<2. These potential risk factors could be useful to efficiently recognize patients who might develop sepsis in the ED.

Key words:

Sepsis, qSOFA, emergency department, triage, vital signs

INTRODUCTION

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] In 2017, approximately 49 million cases of sepsis occurred worldwide, and 11 million people died of sepsis-related diseases.[2] In the emergency department (ED), physicians need to rapidly identify patients with sepsis and initiate appropriate treatment based on the Surviving Sepsis Campaign bundle to reduce mortality.[3,4]

For screening patients with sepsis, the Sepsis-3 Task Force introduced the quick Sequential Organ Failure Assessment (qSOFA) score, which consists of three criteria: altered mental status (Glasgow Coma Scale [GCS] $\leq$ 14), respiratory rate (RR) $\geq$ 22/min, and systolic blood pressure (sBP) $\leq$ 100mmHg.[5] The cutoff of qSOFA$\geq$2 has been proposed for early detection of sepsis among patients with suspected infection in the ED.[6-8] Nevertheless, some patients with suspected of sepsis may not be well-detected at a threshold of qSOFA$\geq$2 due to the suboptimal sensitivity of qSOFA$\geq$2 in screening for sepsis, which is reported to be 0.30 to 0.60 in previous studies.[9-11] Indeed, Wang et al. showed that 79 % of all patients with sepsis initially had qSOFA<2 on arrival at the ED in the US over 2009-2011.[12] Thus, understanding the potential risk factors of sepsis among patients with qSOFA<2 is beneficial for earlier detection of patients who should be prioritized for targeted treatment without underestimating the patient's risk of exacerbation. Despite this, little is known about the characteristics of patients with qSOFA<2 in the ED who later develop sepsis based on the Sepsis-3 criteria.

To address this knowledge gap in the literature, we aimed to compare the characteristics of ED patients with suspected infection and qSOFA<2 who were ultimately diagnosed with sepsis based on the Sepsis-3 criteria versus those without sepsis. Additionally, we investigated the risk factors associated with development of sepsis among patients with suspected infection and qSOFA<2 in the ED.

METHODS

Study design and setting

We retrospectively analyzed data from the ED of Hitachi General Hospital from April 1, 2018 to March 31, 2020. Hitachi General Hospital is one of the largest tertiary medical centers in Japan, located in a city with about 3 million people, and has approximately 20,000 annual ED visits. The ED of Hitachi General Hospital is staffed by emergency attending physicians and has affiliations with transitional and emergency medicine (EM) residency training programs. The medical charts are structured through an electronic medical record system, which supports healthcare workers input clinical information as structured data.[13] The study protocol was approved by the Ethics Committee of Hitachi General Hospital, and the requirement for informed consent was waived due to the retrospective nature of the study.

Study participants

We included adult patients (aged ≥18 years) presenting with suspected infection and qSOFA<2 to the ED who were initially treated by emergency medicine physicians. At Hitachi General Hospital, almost all patients who visit via the ED are first admitted to the ICU and then stepped down depending on their medical condition. Our system is designed so that all patients with sepsis admitted via the ED are treated in the ICU. For these reasons, we targeted only patients admitted to the ICU. Suspected infection was defined based on the chief complaint of fever, increased body temperature (≥ 37.5 °C), or diagnosis of infection (e.g., pneumonia, urinary tract infection, cellulitis, pharyngitis, and meningitis) at the ED. As for the diagnosis of infection, we referred to each patient's clinical diagnosis on arrival at the ED, which was routinely recorded by emergency physicians at Hitachi General Hospital and automatically converted to ICD-10 codes by the original algorithm of the NEXT Stage ER system.[13] We excluded patients who died immediately upon arrival at the ED, had trauma or cardiac arrest, were transported to other hospitals after ED arrival, or had at least five of seven missing vital sign parameters (systolic blood pressure [sBP], diastolic blood pressure [dBP], heart rate [HR], respiratory rate [RR], body temperature [BT], Glasgow coma scale [GCS], and O2 saturation level [SpO2]) upon ED arrival (**Figure 1**).

NEXT Stage ER system

Hitachi General Hospital used the NEXT Stage ER system, an electronic medical record system that supports healthcare workers input clinical information as structured data. By using the system as an EMR software, we were able to retrospectively use all the data on demographics, vital signs, chief complaints, present illness, medical history, physical assessment, and physician's ED diagnoses for each patient's ED visit as well-structured and coded information (e.g., medical history based on ICD10 codes and medication data based on the WHO's Anatomical Therapeutic Chemical Classification System [ATC]).

Measurements

For each enrolled patient, we collected patient demographics (age and sex), vital signs at initial triage (sBP, dBP, HR, RR, BT, GCS, and SpO_2), receipt of oxygen therapy upon arrival at the ED, chief complaints (abdominal pain, back pain, chest pain, chills, cough, diarrhea, fever, headache, nausea, malaise, shortness of breath, and sore throat), comorbidities (hypertension, diabetes mellitus [DM], malignancy, stroke, heart failure [HF], ischemic heart disease [IHD], chronic lung disease [CLD], and chronic kidney disease [CKD]), and disposition (discharge from the ED, hospital admission, ICU admission, and in-hospital mortality). For patients admitted to the ICU, we also collected all data on laboratory tests (e.g., serum creatinine, total bilirubin, platelet count, and serum lactate level), microbiological blood culture tests, and the use of medications (e.g., antibiotics and vasopressors) and mechanical ventilators to determine the presence of sepsis based on the sepsis clinical surveillance definition (**Table 2**).[14-16]

Candidate risk factors

We selected patient demographics (age and sex), initial triage vital signs (sBP, HR, RR, BT, altered mental status [GCS ≤14], and SpO_2), receipt of oxygen therapy upon arrival at the ED, chief complaints (abdominal pain, back pain, chest pain, chills, cough, diarrhea, fever, headache, nausea, malaise, shortness of breath, and sore throat), and comorbidities (hypertension, DM, malignancy, stroke, HF, IHD, CLD, and CKD) as candidate risk factors of sepsis obtainable from the patients' clinical presentation (shown in **Table 3**). We selected 12 major chief complaints and 8 major comorbidities as potential risk factors based on some previous studies. However, we included all patients with suspected infection and qSOFA<2 in our analysis, regardless of patients' chief complaints and comorbidities (e.g., we analyzed the data on patients with seizure, which was not selected in 12 chief complaints as potential risk factors).[17-19] However, we included patients without the 12 chief complaints and 8 comorbidities in our analysis.

Outcome measures

We identified patients who developed sepsis based on the Sepsis-3 criteria. The primary outcome was a diagnosis of sepsis according to the Sepsis-3 criteria. Given that we have difficulty in identifying patients with sepsis accurately based on the Sepsis-3 criteria (i.e., ≥2 points increase in SOFA score) in the current retrospective study, we used the modified sepsis clinical surveillance definition (shown in **Table 2**) instead of using the original Sepsis-3 criteria. Our sepsis definition was developed based on the criteria initially proposed by Rhee et al., which was to define sepsis based on the Sepsis-3 criteria in the setting of retrospective studies. [14-16]

Statistical analyses

To minimize the selection bias induced by the missing data, we applied the random forest method to impute all the missing vital signs data (as shown in Table 1) using the following variables: age, sex, vital signs, qSOFA (routinely calculated by medical staff at the ED for patients with any suspected infectious diseases at the triage), and disposition (i.e., ICU admission and in-hospital mortality).[20-22] We then used summary statistics to delineate the characteristics of patients presenting to the ED with suspected infection and qSOFA<2 and compared each variable between patients who develop sepsis or not. Second, to identify risk factors of sepsis among ED patients with suspected infection and qSOFA<2, we developed a multivariable logistic regression model using the following candidate risk factors: patient demographics (age and sex), initial triage vital signs (sBP, HR, RR, BT, altered mental status [GCS ≤14], and SpO2), receipt of oxygen therapy upon arrival at the ED, chief complaints (abdominal pain, back pain, chest pain, chills, cough, diarrhea, fever, headache, nausea, malaise, shortness of breath, and sore throat), and comorbidities (hypertension, DM, malignancy, stroke, HF, IHD, CLD, and

CKD). In the logistic regression, we divided the age of individuals into three categories (i.e., young [18-39 years], middle-aged [40-64 years], and elderly patients [≥65 years]), and used vital signs data in the following forms: sBP [per 10 mmHg], HR [per 10/min], RR [/min], BT [°C], altered mental status [GCS ≤14], and 100-SpO2 [%].

Furthermore, as a sensitivity analysis, we excluded the three qSOFA items (i.e., sBP, RR, and altered mental status) from all candidate risk factors and developed a logistic regression model to identify risk factors of sepsis among ED patients with suspected infection and qSOFA <2.

All analyses were conducted using R version 3.6.1 (R Foundation, Vienna, Austria).[23] A P-value of <0.05 was considered statistically significant.

RESULTS

Patient characteristics

We identified 2,025 adult patients presenting with suspected infection and qSOFA<2 in the ED of Hitachi General Hospital from April 2018 to March 2020. Flow chart of selection of study participants is shown in **Figure 1**. The median (IQR) age was 73 (54-82) years, and 1,156 (57%) were male. Of these, we identified 151 (7%) as patients who developed sepsis and 1,874 (93%) as patients who did not develop sepsis (**Table 3**).

Comparison between patients who developed sepsis or not

Patients who developed sepsis were likely to be older (median age: 80 vs. 72; **Table 3**). As for vital signs, patients who developed sepsis tended to have higher HR (102 vs. 93 per min), higher RR (21 vs. 20 per min), altered mental status (the proportion of patients with altered mental status: 17% vs. 5%), and lower SpO_2 (95% vs. 97%). In addition, patients with sepsis were more likely to have received oxygen therapy upon arrival at the ED (44% vs. 16%), have chief complaints of chills and shortness of breath (e.g., the proportion of patients with shortness of breath: 17% vs. 11%), and have hypertension, DM, stroke, and CKD (e.g., the proportion of patients with DM: 22% vs. 15%) compared to patients who did not develop sepsis. By contrast, patients who developed sepsis were less likely to have abdominal or chest pain (e.g., the proportion of patients with abdominal pain: 1% vs. 12%).

Risk factors of sepsis among patients with qSOFA<2

As shown in Figure 2, the potential risk factors of sepsis among patients with qSOFA<2 were older age (e.g., elderly patients compared to younger patients, 2.86 [95%CI 1.83-4.60]), higher RR, higher BT, altered mental status, and lower SpO2 (e.g., adjusted OR of RR, 1.03 [95%CI 1.01-1.06] and adjusted OR of altered mental status, 3.50 [95%CI 2.25-5.50]), adjusted OR of receipt of oxygen therapy upon ED arrival, 1.91 [95% CI 1.38-2.66], adjusted OR of chief complaint of sore throat, 2.15 [95%CI 1.08-4.13], and having comorbidities of DM, IHD, and CKD (e.g., adjusted OR of DM, 1.47 [95%CI 1.10-1.96]). There was no significant association between hypertension and sepsis (adjusted OR, 0.99 [95%CI 0.77-1.26]; P=0.93). By contrast, high sBP and chief complaint of abdominal or chest pain were negatively associated with sepsis (e.g., adjusted OR of sBP, 0.93 [95%CI 0.89-0.97]); adjusted OR of abdominal pain, 0.26 [95%CI 0.14-0.45]). The logistic regression model using all candidate factors excluding qSOFA items as a sensitivity analysis showed results that were overall consistent with the primary analysis **(Figure 3)**.

DISCUSSION

In this retrospective study of 2,025 adult patients presenting with suspected infection and qSOFA<2 to the ED of a tertiary medical center, we found that the potential risk factors of sepsis among patients with suspected infection and qSOFA<2 were older age, vital signs prognosticating sepsis (i.e., high HR, high RR, altered mental status, and low SpO_2), receipt of oxygen therapy upon arrival at the ED, and a chief complaint of sore throat, and specific comorbidities (e.g., DM, IHD, and CKD). By contrast, high sBP and chief complaints of abdominal or chest pain had negative associations with sepsis.

Since qSOFA was originally developed as a prognostic tool for patients with suspected infection using three vital signs prognosticating sepsis (i.e., altered mental status, high RR, and low sBP), physicians cannot rule out the possibility of sepsis just because a patient does not have a qSOFA ≥ 2 upon ED arrival. A previous study showed that 75% of patients who were subsequently diagnosed with sepsis based on the Sepsis-3 criteria did not initially meet qSOFA≥2 upon presentation at the ED.[24] Therefore, since patients with risk factors elucidated in the current study (e.g., high HR and RR) are at increased risk of developing sepsis over the next few days, clinicians should carefully monitor them with serial qSOFA calculations to make sure that they can initiate the Surviving Sepsis Campaign Bundle for patients with suspected sepsis at the right time.

Older age and comorbidities such as DM, IHD, and CKD, all of which are associated with impairment of the immune system and systemic organ damage, were risk factors of sepsis.[25-29] Patients with these factors may have decreased systemic response to infections, resulting in longer time to reach a qSOFA≥2. The association between sore throat and sepsis could be attributable to life-threatening infections, such as epiglottitis and peritonsillar abscesses.[30] In addition, given that patients with sore throat caused by life-threatening infection (e.g., epiglottis) are often prophylactically intubated and carefully followed up in the ICU, such patients could meet our sepsis clinical surveillance criteria even if they did not have respiratory failure. Interestingly, some chief complaints (i.e., abdominal and chest pain) were negatively associated with sepsis. This could be attributed to the nature of the chief complaint: some chief complaints are mostly related to non-infectious diseases.

Considering patients' chief complaints and comorbidities as well as vital signs at triage could be helpful for physicians in identifying patients at high risk of sepsis among ED visitors with qSOFA<2. Moreover, absolute values of each vital sign, which are lost when calculating the criteria (e.g., patients with 20/min and 12/min of respiratory rate are considered as at the same risk in qSOFA criteria), would be useful for risk assessment in patients with qSOFA<2 at the ED. Taken together, to make the most of qSOFA for triage patients likely to develop sepsis, emergency physicians should closely monitor vital signs and carefully listen to patients' chief complaints and past medical histories to effectively pick up patients at higher risk of developing sepsis.

LIMITATIONS

Our study has several limitations. First, in our dataset, there were some patients (3.7% of all ED visitors) with many missing vital signs and other patients with missing data (2%-20% of continuous variables), which could be a potential source of bias. However, we believe this issue was minimized by using random forest imputation after excluding patients whose vital signs were largely missing.[20-22] Second, all the data on the ED visits were retrospectively collected, which could result in misclassification. However, all the data we used were well-structured and coded by the NEXT Stage ER system with a sensitivity and specificity of >90% for most of the data (e.g., chief complaints, comorbidities, medications, and physician diagnoses).[13] Third, due to the retrospective nature of the study, we were not able to identify patients with sepsis accurately based on the Sepsis-3 criteria (i.e., ≥2 points increase in SOFA score). Meanwhile, we identified patients who developed sepsis by using the modified sepsis clinical surveillance definition based on the modified Sepsis-3 criteria proposed by Rhee et al., which has been broadly used to identify sepsis patients in retrospective studies.[14-16] Lastly, our findings may have limited generalizability because this study was retrospectively conducted in a single center. To verify our findings, larger multicenter population-based studies are warranted.

CONCLUSIONS

We found that older age, vital signs prognosticating sepsis, and comorbidities such as DM, IHD, and CKD were potential risk factors of sepsis in ED patients with qSOFA<2. To efficiently recognize patients who might develop sepsis in the ED, we should treat patients with qSOFA<2 more cautiously if they have any risk factors prognosticating sepsis.

Footnotes

Ethics approval and Patient consent for participate

This study protocol was approved by the Ethics Committee of Hitachi General Hospital. Due to the retrospective nature of the study, the requirement for informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed in the current study are not publicly available because the sharing of the data is not approved by the Ethics Committee.

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FIGURE LEGENDS

Figure 1. Flow chart of patient selection

Abbreviations: qSOFA, the quick Sequential Organ Failure Assessment; ED, emergency department

Figure 2. Odds ratios of candidate risk factors obtained using multivariable logistic regression model.

We examined the association between the selected candidate risk factors and sepsis among patients presenting to the ED with suspected infection and qSOFA<2. Points and error bars indicate the odds ratio and 95% confidence interval of the variables, respectively.

Abbreviations: OR, odds ratio; CI, confidential interval; ED, emergency department

Figure 3. Odds ratios of candidate risk factors excluding qSOFA items obtained using a multivariable logistic regression model

We examined the association between the selected candidate risk factors and sepsis among patients presenting to the ED with suspected infection and qSOFA<2. In this logistic regression model, the three items of qSOFA, systolic blood pressure, respiratory rate, and altered mental status were excluded from the model used in Fig. 2. Other conditions were the same as the model in Fig. 2. Points and error bars indicate the odds ratio and 95% confidence interval of variables, respectively.

Table 1. The proportion of missingness of variables in 8,983 patients

Vital signs	Missing, n (%)*
Systolic blood pressure	472 (5)
Diastolic blood pressure	577 (6)
Heart rate	151 (2)
Respiratory rate	1824 (20)
Body temperature	1772 (20)
Glasgow Coma Scale score	1046 (12)
O_2 saturation	1772 (20)

Abbreviations: ICU, Intensive Care Unit

*All missing data were substituted by the random forest method using the following variables: age, sex, vital signs, qSOFA (routinely calculated by medical staff at the for patients who have any suspected infectious diseases at the triage), and dispositions (i.e., ICU admission and in-hospital mortality). For our analyses, we recalculated all qSOFA using all vital signs data after the multiple imputation

Table 2. The modified sepsis clinical surveillance definition

1. Presumed serious infection:

・Blood culture obtained (regardless of results), AND

・New antibiotics administration started within ± 2 days of blood culture collection

AND

2. ICU admission

AND

3. Acute organ dysfunction (any one of the following criteria within ± 2 days of blood culture collection):

・Initiation of vasopressors (norepinephrine, dopamine, epinephrine, phenylephrine, or vasopressin)

・Initiation of mechanical ventilation

・Doubling in serum creatinine level compared to baseline*

・Total bilirubin level ≥2.0 mg/dL and doubling in total bilirubin from baseline*

・Platelet count $<100 \times 10^3$ /μL and ≥50% decline from baseline (baseline must be $\geq 100 \times 10^3$ /μL)

・Serum lactate ≥2.0 mmol/L

* Baseline laboratory values are defined as the lowest values for creatinine and total bilirubin and highest values for platelet count during hospitalization.

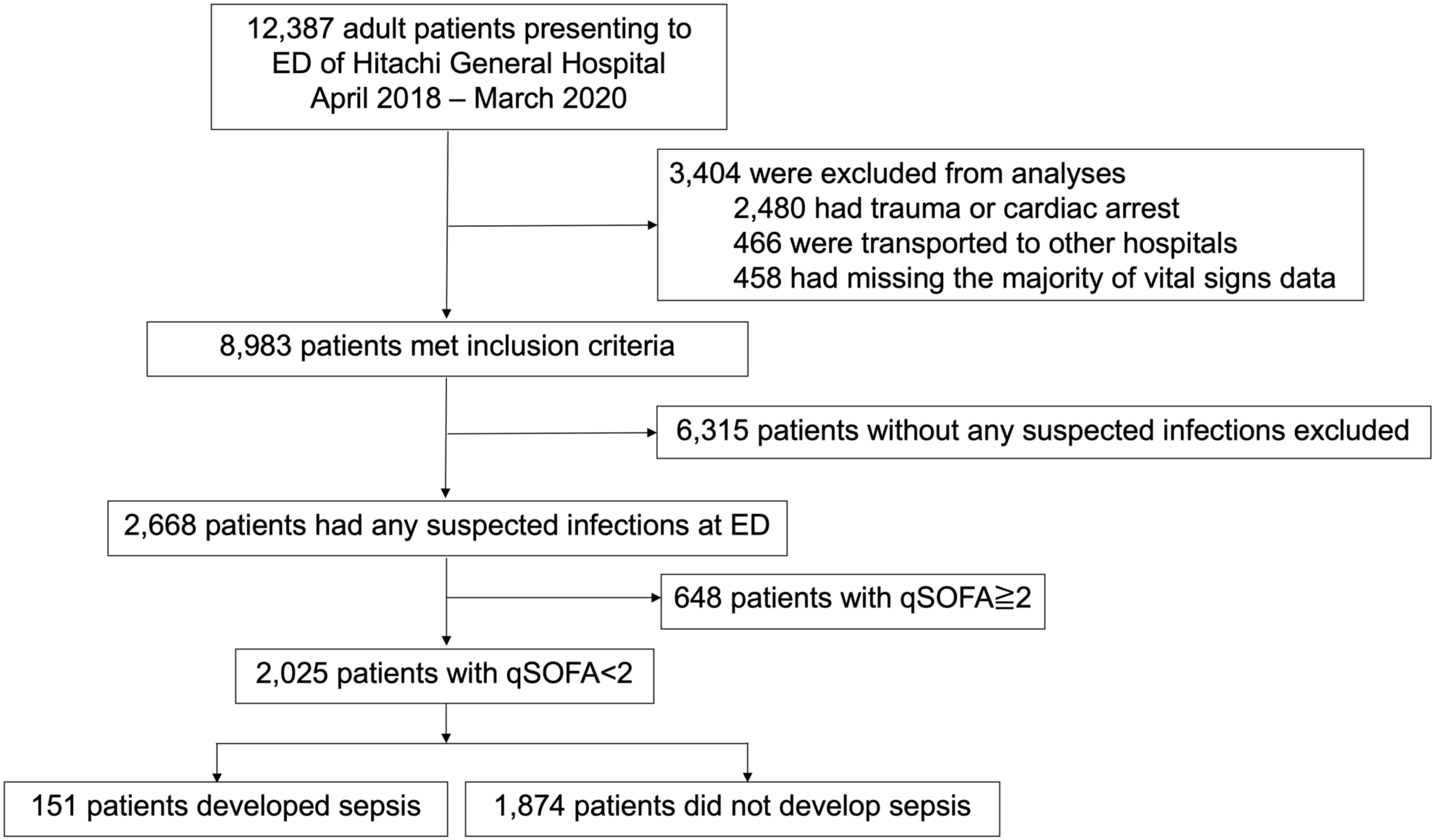
According to the Sepsis-3 criteria, sepsis is defined as infection-induced life-threatening organ dysfunction, which is estimated based on ≥ 2-point increase in the Sequential Organ Failure Assessment (SOFA) score. Since this assessment is not accurately available in the setting of retrospective studies, Rhee C et al. proposed a new definition for retrospective surveillance using electrical health records. Using the definition by Rhee C et al., we created a modified sepsis clinical surveillance criteria to identify the incidence of sepsis among patients presenting to the emergency department with suspected infection.

Table 3. Characteristics of all, patients who did or did not develop sepsis with suspected infection and qSOFA<2

Characteristics	**All patients with qSOFA<2 (n= 2,025)**	**Patients who developed sepsis with qSOFA<2 (n=151)**	**Patients who did not develop sepsis with qSOFA<2 (n=1,874)**	**P value**
Age (year), median (IQR)	73 (54-82)	80 (68-86)	72 (53-82)	<0.001
Male sex, No. (%)	1,156 (57)	90 (60)	1,066 (57)	0.57
Vital signs				
Systolic blood pressure (mmHg), median (IQR)	137 (120-155)	136 (119-153)	137 (121-155)	0.46
Heart rate (/min), median (IQR)	93 (80-108)	102 (87-117)	93 (80-107)	<0.001
Respiratory rate (/min), median (IQR)	20 (18-24)	21 (19-24)	20 (18-24)	<0.001
Body temperature (°C), median (IQR)	37.5 (36.7-38.2)	37.5 (36.8-38.7)	37.5 (36.7-38.1)	0.01
Altered mental status, No. (%)	111 (5)	25 (17)	86 (5)	<0.001
SpO2 (%), median (IQR)	97 (95-98)	95 (90-97)	97 (95-98)	<0.001
Treatment, No. (%)				
Receipt of oxygen therapy upon arrival at the ED	356 (18)	66 (44)	290 (16)	<0.001
Chief complaints, No. (%)				
Abdominal pain	217 (11)	1 (1)	216 (12)	<0.001
Back pain	86 (4)	6 (4)	80 (4)	0.99
Chest pain	50 (2)	3 (2)	47 (3)	0.90
Chills	31 (2)	6 (4)	25 (1)	0.03
Cough	53 (3)	3 (2)	50 (3)	0.81
Diarrhea	58 (3)	2 (1)	56 (3)	0.36
Fever	553 (27)	48 (32)	505 (27)	0.23
Headache	65 (3)	3 (2)	62 (3)	0.52
Nausea	128 (6)	9 (6)	119 (6)	0.99
Malaise	113 (6)	9 (6)	104 (6)	0.98
Shortness of breath	221 (11)	25 (17)	196 (11)	0.03
Sore throat	55 (3)	6 (4)	49 (3)	0.47
Selected comorbidities, No. (%)				
Hypertension	565 (28)	60 (40)	505 (27)	0.01
Diabetes mellitus	321 (16)	33 (22)	288 (15)	0.047
Malignancy	267 (13)	16 (11)	251 (13)	0.39
Stroke	152 (8)	18 (12)	134 (7)	0.049
Heart failure	177 (9)	18 (12)	159 (9)	0.20
Ischemic heart disease	75 (4)	10 (7)	65 (4)	0.08
Chronic lung disease	119 (6)	7 (5)	112 (6)	0.62
Chronic kidney disease	59 (3)	9 (6)	50 (3)	0.04
Outcomes, No. (%)				
Sepsis	151 (7)	-	-	-
Admission to the intensive care unit	580 (29)	151 (100)	429 (23)	-

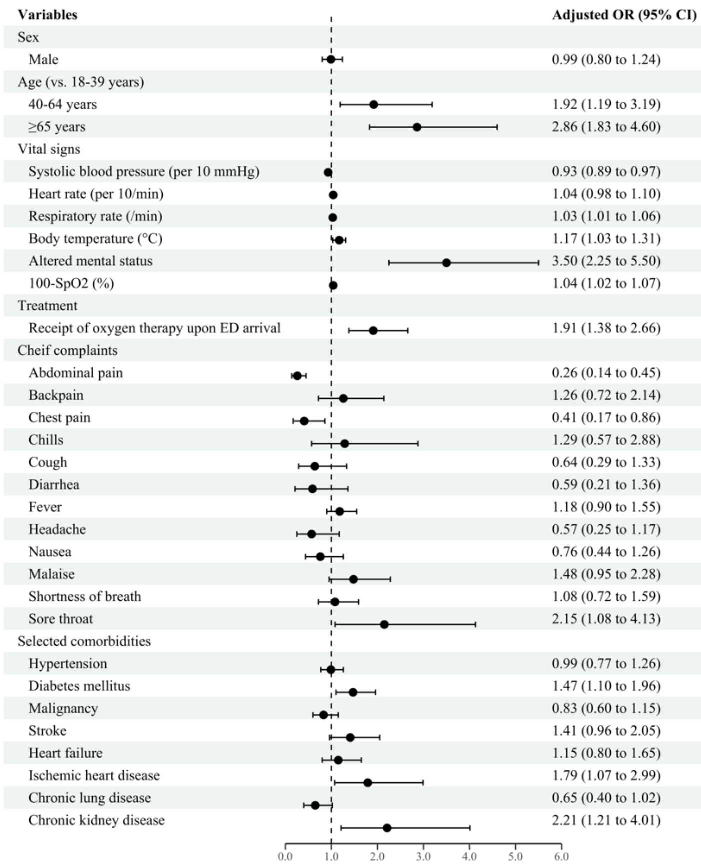
Abbreviations: qSOFA, the quick Sequential Organ Failure Assessment; IQR, interquartile range; ED, emergency department

Figure 1. Flow chart of patient selection



Abbreviations: qSOFA, the quick Sequential Organ Failure Assessment; ED, emergency department

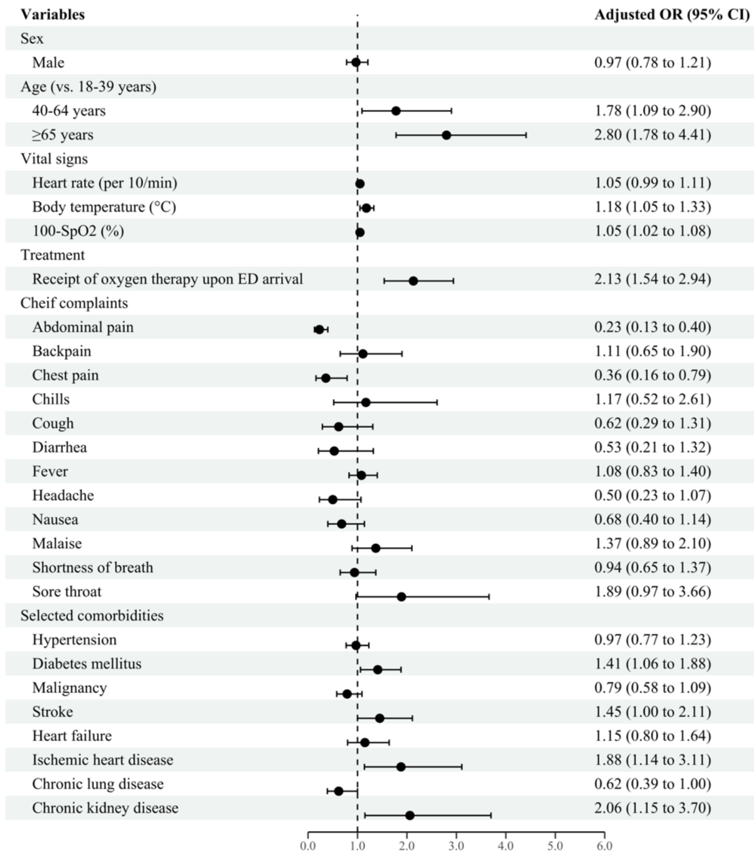
Figure 2. Odds ratios of candidate risk factors obtained using multivariable logistic regression model



Legend: We examined the association between the selected candidate risk factors and sepsis among patients presenting to the ED with suspected infection and qSOFA<2. For this logistic regression model, all the variables listed in the **Table 1** were used as covariates, and the objective variable was the categorical variable of whether the patient was diagnosed with sepsis. Points and error bars indicate the odds ratio and 95% confidence interval of variables, respectively.

Abbreviations: OR, odds ratio; CI, confidential interval; ED, emergency department

Figure 3. Odds ratios of candidate risk factors excluding qSOFA items obtained using a multivariable logistic regression model



Legend: We examined the association between the selected candidate risk factors and sepsis among patients presenting to the ED with suspected infection and qSOFA<2. In this logistic regression model, the three items of qSOFA, systolic blood pressure, respiratory rate, and altered mental status were excluded from the model used in Fig. 2. Other conditions were the same as the model in Fig. 2. Points and error bars indicate the odds ratio and 95% confidence interval of variables, respectively.

Abbreviations: OR, odds ratio; CI, confidential interval; ED, emergency department