Submitted: 22 February, 2021 Accepted: 15 March, 2021 Published: 08 September, 2021 DOI:10.22514/sv.2021.082

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ORIGINAL RESEARCH

Use of quick sequential organ failure assessment score-based sepsis clinical decision support system may be helpful to predict sepsis development

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Abstract

Objectives: A sepsis clinical decision support system (CDSS) can facilitate quicker sepsis detection and treatment and consequently improve outcomes. We developed a qSOFA-based sepsis CDSS and evaluated its impact on compliance with a 3-hour resuscitation bundle for patients with sepsis.

Methods: This before-and-after study included consecutive adult patients with suspected infection and qSOFA scores of $\geq$ 2 at their emergency department (ED) presentation of a tertiary care hospital. Sepsis was defined according to the Sepsis-3 criteria. We evaluated the 3-hour resuscitation bundle compliance rate for control patients from July through August 2016, for patients using the qSOFA-based sepsis CDSS from September through December 2016, and the impact of the system using multivariable logistic regression analysis.

Results: Of 306 patients with suspected infection and positive qSOFA scores at presentation, 265 patients (86.6%) developed sepsis (including 71 patients with septic shock). The 3-hour resuscitation bundle compliance rate did not differ significantly between the patients before and after the routine implementation of the qSOFA-based sepsis CDSS (63.7% vs. 52.6%; $P = 0.071$). Multivariate analysis showed that age (AOR [adjusted odds ratio], 1.033; $P = 0.002$) and body temperature (AOR, 1.677; $P < 0.001$) were associated with bundle compliance.

Conclusions: Among patients with a positive qSOFA score at presentation, sepsis developed in 86.6%, which means the qSOFA-based sepsis CDSS may be helpful; however, it was not associated with improved bundle compliance. Future quality improvement studies with multifactorial, hospital-wide approaches using sepsis CDSS tools are warranted.

Keywords

Quick SOFA; Compliance; Resuscitation bundle; Clinical decision support system; Sepsis

1. Introduction

Despite recent medical advances, the morbidity and mortality rates associated with sepsis remain high. Early recognition and timely management of sepsis are key factors for improving outcomes [1, 2]. In 2016, as part of the efforts to enhance the early recognition and timely intervention of sepsis management, a joint Society for Critical Care Medicine (SCCM) and European Society of Intensive Care Medicine (ESICM) task force newly defined sepsis as life-threatening organ dysfunction due to a dysregulated response, i.e., an increase of at least 2 points in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score [1, 2]. Additionally, the quick Sequential Organ Failure Assessment (qSOFA) score, using respiratory rate, blood pressure, and mental status, was announced as a rapid bedside assessment tool for screening patients at risk of sepsis development [1, 2].

Surviving Sepsis Campaign (SSC) guidelines have also emphasised immediate resuscitation, in the form of 3-hour and 6-hour resuscitation bundles, and timely and aggressive resuscitation, achieved by compliance with 3-hour resuscitation bundles for every patient at risk of sepsis would improve outcomes [3–5].

A clinical decision support system (CDSS) offers systematic applications of health-related knowledge and analysis of available data directly to the clinician, facilitating key performance goals and adherence to best practices [6–8]. A study from the United States about electronic surveillance for systemic inflammatory response syndrome criteria and hypotension demonstrated the effectiveness of provider alerts for improving early goal-directed therapy [9]; however, there

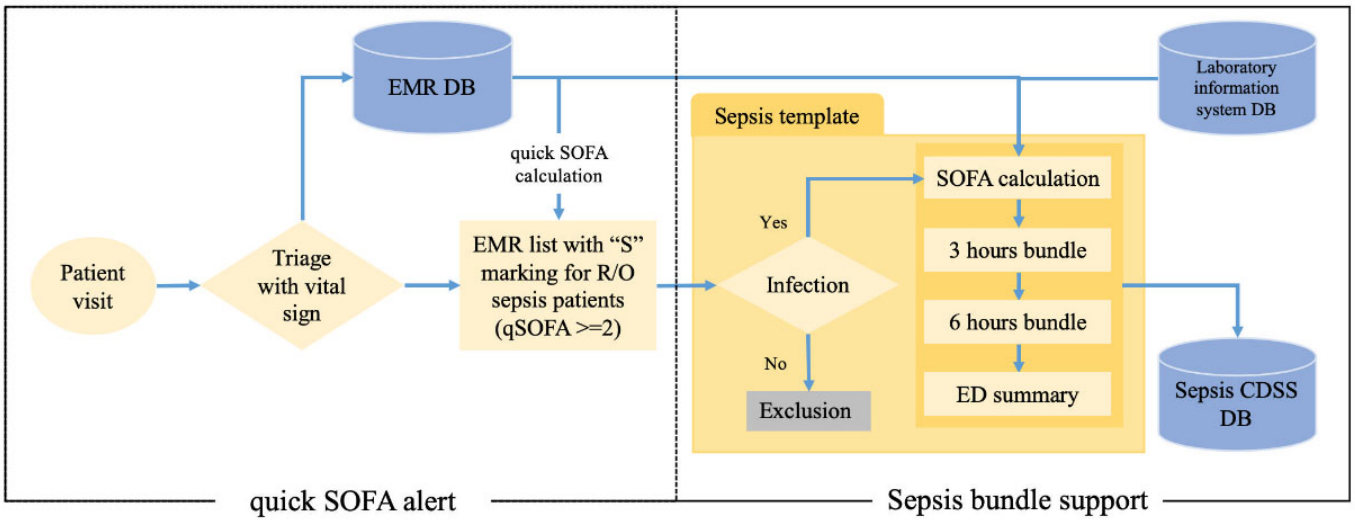

FIGURE 1. Timeline of the quick Sequential Organ Failure Assessment (qSOFA) score-based sepsis clinical decision support system. CDSS, clinical decision support system; DB, data base; EMR, electronic medical records; qSOFA, quick Sequential Organ Failure Assessment.

is a paucity of sepsis CDSS data regarding to the new sepsis definition. Therefore, we developed a qSOFA score-based sepsis CDSS to help ED physicians and nurses promptly detect patients at high risk of sepsis and enhance compliance with 3-hour resuscitation bundles. In this before-and-after study, we evaluated the rate of sepsis and septic shock development among patients with qSOFA scores ≥ 2 and the impact of the qSOFA score-based sepsis CDSS on compliance with a 3-hour resuscitation bundle for sepsis patients admitted to our ED. We hypothesised that the early recognition of patients at risk of sepsis development at the time of emergency department (ED) presentation would facilitate the implementation of 3-hour resuscitation bundles.

2. Methods

Asan Medical Center's institutional review board approved the study (Study No. 2016-0818) and waived the requirement for informed consent because the study involved the analysis of a case registry. The research is in accordance with the Helsinki Declaration of 1975, as revised in 2010.

2.1 Introduction to the qSOFA-based sepsis CDSS

A team of emergency medicine and information medicine doctors and a technician from the medical information office developed a qSOFA score-based sepsis CDSS for ED physicians and nurses between January and July 2016. The system automatically calculated the qSOFA score using every patient's vital signs at ED presentation, and when the patients had a qSOFA score ≥ 2, this was indicated with a label of "S" beside their names in the list of electronic medical records (EMRs) (Fig. 1). In addition to a systolic blood pressure ≤ 100 mmHg and a respiratory rate ≥ 2 breaths/min, mental status at ED presentation was assessed according to the Alert/responsive, Voice/responsive, Pain/responsive, Unresponsive (AVPU) scale; unalert patients were considered to have an altered mental status [1, 10]. The ED physicians were advised to evaluate the "S" patients as soon as possible, whether or not the patient was suspected of having an infection. The sepsis CDSS template was provided after the physician confirmed "suspected infection". The template contained the positive component of the qSOFA score, a semi-automatic calculation of the SOFA score, and a checklist for the 3-hour and 6-hour resuscitation bundles for sepsis (Supplementary Fig. 1). Lactic acid levels were checked using point-of-care blood gas analysis with the GEM PremierTM 3000 (Instrumentation Laboratory, Lexington, MA, USA) and recorded automatically in the CDSS template. The timing of accomplishment for each bundle element was recorded to enhance resuscitation bundle compliance. This system was finally adopted for our EMR system from September 2016 onwards.

2.2 Study design and population

This retrospective before-and-after study was performed at the ED of a tertiary referral hospital in Seoul, Korea, with 110,000 annual ED visits. Our hospital treated the patients with sepsis and septic shock using the SSC's 3-hour and 6-hour resuscitation bundle guidelines [3, 11]. Asan Medical Center's institutional review board approved the study (Study No. 2016-0818) and waived the requirement for informed consent because the study involved the analysis of a case registry.

The patients with positive qSOFA scores enrolled from September through December 2016 were considered the treatment group (for whom the qSOFA-based CDSS was used), whereas the patients enrolled from July through August 2016 were considered the control group (for whom the qSOFA-based CDSS was not used). The qSOFA score-based sepsis CDSS prospectively screened all consecutive adult patients (aged > 18 years) with qSOFA scores ≥ 2 at ED presentation, and an ED physician on duty confirmed if patients were suspected of having an infection or not. Patients with suspected infection and positive qSOFA scores were automatically regis-

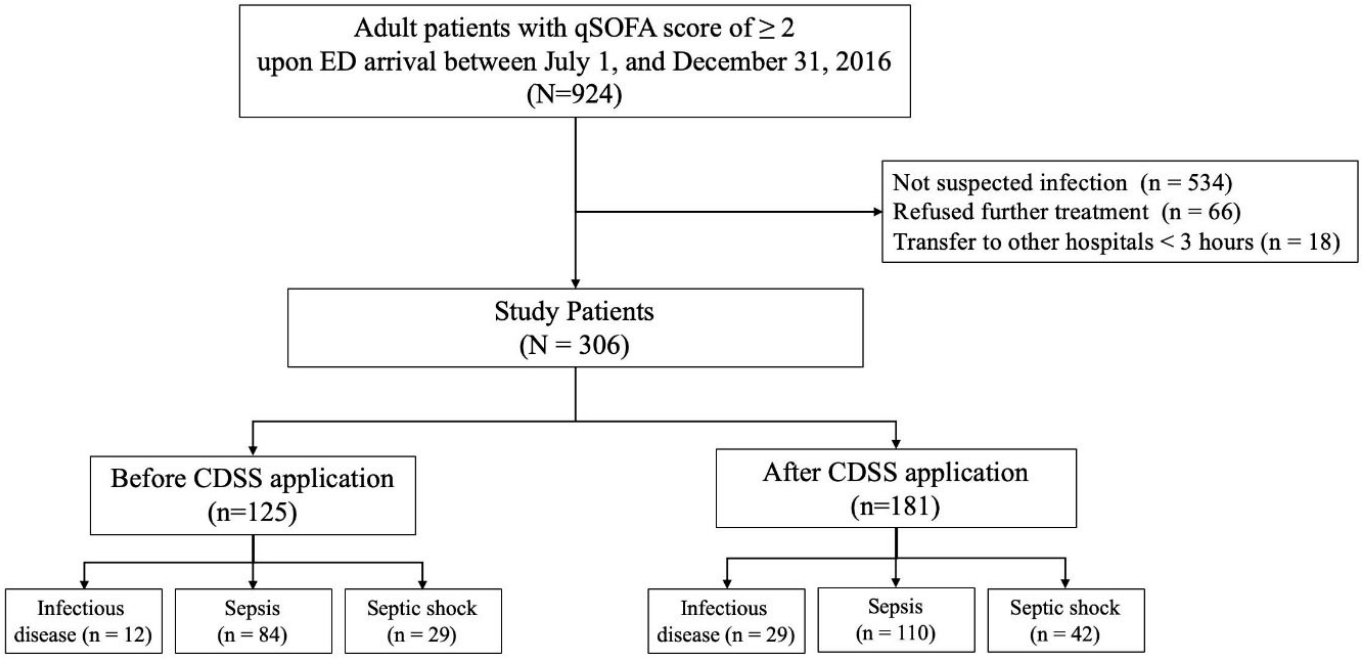

FIGURE 2. Patient flow diagram. CDSS, clinical decision support system; ED, emergency department; qSOFA, quick Sequential Organ Failure Assessment.

tered in the qSOFA score-based sepsis CDSS patient list. We retrieved the data of patients with positive qSOFA scores for the control group, and an investigator (YJK) retrospectively reviewed and recorded their clinical data using the CDSS.

The study included all consecutive adult patients (≥18 years) with qSOFA scores ≥ 2 at ED presentation with suspected or confirmed infection between July 1 and December 31, 2016. Patients were excluded from this study if they refused further examination and treatment; consented to a "do not resuscitate" order; or were directly transferred to another hospital from the ED within 3 hours. According to the Third International Consensus for sepsis and septic shock (Sepsis-3), we diagnosed the patients as having infectious disease, sepsis, and septic shock [2]. Patients with an acute increase of ≥2 SOFA points were diagnosed with sepsis, and those who had persistent hypotension requiring vasopressors and serum lactate concentrations > 2 mmol/L after adequate fluid administration were diagnosed with septic shock [2].

The primary outcome was the completion of all 3-hour resuscitation bundle compliance for patients diagnosed with sepsis or septic shock during ED stay. The 3-hour resuscitation bundle includes (1) measuring lactate level; (2) obtaining blood cultures before antibiotic administration; (3) administering broad-spectrum antimicrobial agents; and (4) rapidly administering at least 30 mL/kg of intravenous crystalloid for hypotension or lactate ≥ 4 mmol/L within 180 minutes after ED presentation. Our institution recommended administering the bolus of 200 to 300 mL crystalloid with close monitoring for patients with heart failure or end-stage renal disease, and 20 mL/kg of intravenous crystalloid administration was recommended for those patients.

2.3 Data collection

For each patient, we captured the demographic information, vital signs at ED presentation, suspected or confirmed infection focus, baseline SOFA score, SOFA score at ED presentation, delta SOFA score, initial lactic acid, outcome, and the timing of 3-hour resuscitation bundle implementation recorded in the CDSS.

'Time zero' was defined as the ED presentation time, as listed on each patient's EMR [12]. The timing was recorded on the CDSS when each element of the resuscitation bundle was completed. In addition to the data retrieved from CDSS, the Charlson Comorbidity Index (CCI) and the mean ED occupancy rate for 3 hours after ED presentation were calculated; both of these values can affect compliance and outcomes [13, 14]. The CCI was used to assess the burden of chronic disease [13]. The ED occupancy rate was calculated as the total number of patients in our ED's critical care zone at each hour divided by the number of beds in the zone [14, 15]. All of the patients were followed for 30 days after ED presentation.

2.4 Statistics

Continuous variables are expressed as means with standard deviation or medians with interquartile ranges due to their distribution, determined using the Kolmogorov-Smirnov test. Categorical data are presented as absolute numbers and percent frequencies. Student's *t*-test was used to compare the values of normally distributed continuous variables. The Kruskal-Wallis rank test for 3 groups or the Mann-Whitney U test for 2 groups was used to compare skewed distributed continuous variables' values. Differences between categorical variables were analysed using the chi-square test or Fisher's exact test, as appropriate. The associations of the baseline characteristics and CDSS implementation with the 3-hour resuscitation

TABLE 1. The baseline characteristics of the study patients according to disease severity.

Characteristic	Total (n = 306)	Infectious disease (n = 41)	Sepsis (n = 194)	Septic shock (n = 71)	*P*-value
Age, years	68.0 (57.0–77.0)	60.0 (41.5–76.0)	68.5 (56.0–77.0)	69.0 (61.0–78.0)	0.04
Male	174 (56.9%)	18 (43.9%)	115 (59.3%)	41 (57.7%)	0.19
Charlson Comorbidity Index	5.0 (3.0–7.0)	4.0 (2.0–7.0)	5.5 (3.0–7.0)	5.0 (4.0–7.0)	0.14
qSOFA score					0.003
2	271 (88.6%)	39 (95.1%)	177 (91.2%)	55 (77.5%)	
3	35 (11.4%)	2 (4.9%)	17 (8.8%)	16 (22.5%)	
qSOFA component					
Respiratory rate ≥ 22/min	262 (85.6%)	40 (97.6%)	170 (87.6%)	52 (73.2%)	0.001
Systolic blood pressure < 100 mmHg	231 (75.5%)	30 (73.2%)	135 (69.6%)	66 (93.0%)	< 0.001
Altered mentation	155 (50.7%)	14 (34.1%)	100 (51.5%)	41 (57.7%)	0.05
Baseline SOFA	0.0 (0.0–0.0)	0.0 (0.0–1.5)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.08
SOFA	5.0 (3.0–8.0)	1.0 (0.5–2.5)	5.0 (3.0–7.0)	9.0 (7.0–11.0)	< 0.001
Delta SOFA	5.0 (2.0–8.0)	1.0 (0.0–1.0)	4.0 (3.0–7.0)	9.0 (7.0–10.0)	< 0.001
Focus of infection					0.01
Respiratory	133 (43.5%)	18 (43.9%)	97 (50.0%)	18 (25.4%)	
Hepatobiliary	52 (17.0%)	3 (7.3%)	31 (16.0%)	18 (25.4%)	
Gastrointestinal	32 (10.5%)	7 (17.1%)	16 (8.2%)	9 (12.7%)	
Urinary	24 (7.8%)	3 (7.3%)	16 (8.2%)	5 (7.0%)	
Others	65 (21.2%)	10 (24.4%)	34 (17.5%)	21 (29.6%)	
Initial vital signs					
Systolic blood pressure, mmHg	93.0 (83.0–100.0)	98.0 (93.0–103.0)	95.0 (85.8–111.3)	83.0 (70.0–92.0)	< 0.001
Diastolic blood pressure, mmHg	59.0 (50.0–67.0)	63.0 (55.5–70.5)	60.0 (52.8–68.3)	51.0 (38.0–57.0)	< 0.001
Respiratory rate, breaths/min	24.0 (22.0–26.0)	24.0 (22.0–28.0)	24.0 (22.0–26.0)	24.0 (22.0–28.0)	0.38
Pulse rate, beats/min	106.5 (26.6)	101.8 (31.7)	105.2 (24.6)	112.6 (27.9)	0.07
Body temperature, ºC	37.5 (36.6–38.5)	37.8 (36.8–38.7)	37.4 (36.6–38.4)	37.5 (36.5–38.6)	0.76
Initial lactic acid, mmol/L	2.0 (1.1–3.5)	1.4 (1.0–2.4)	1.6 (1.0–2.5)	4.2 (2.6–6.8)	< 0.001
Time to the bundle implementation					
Serum lactate measurement, min	14.5 (11.0–25.0)	15.0 (12.0–28.0)	15.0 (11.0–25.0)	13.0 (9.0–20.0)	0.02
Blood cultures, min	78.0 (46.0–146.0)	80.0 (41.0–169.0)	83.0 (49.0–162.5)	61.0 (35.0–107.0)	0.01
Broad-spectrum antibiotics	143.0 (88.0–236.0)	190.5 (128.8–350.0)	151.0 (89.5–263.8)	108.0 (78.5–147.0)	< 0.001
3-hour bundle compliance	165 (53.9)	13 (31.7)	96 (49.5)	56 (78.9)	< 0.001
30-day mortality	71 (23.2)	5 (12.2)	43 (22.2)	23 (32.4)	0.04

All values are presented as median (interquartile range), mean (standard deviation) or number (percent), as appropriate. qSOFA, quick sequential organ failure assessment; SOFA, sequential organ failure assessment.

bundle compliance were analysed using univariable logistic regression. The variables with entry-level *P*-values < 0.10 in the univariable analysis were selected for multivariable stepwise logistic regression analysis with the backward elimination method. The results of the logistic regression analysis are presented as odds ratios (ORs) and 95% confidence intervals (CIs). Models were tested for goodness of fit using the Hosmer-Lemeshow method. Two-sided *P*-values < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS Statistics for Macintosh, version 20.0 (IBM Corp., Armonk, NY, USA). Assuming the baseline 3-hour bundle compliance rate before CDSS of 40%, a sample

TABLE 2. Comparison of baseline characteristics between the sepsis patients before and after the routine implementation of the qSOFA-based sepsis decision support system.

Characteristic	Overall (n = 265)	CDSS group (n = 152)	Control group (n = 113)	*P*-value
Age, years	69.0 (58.0–77.0)	70.0 (60.0–78.8)	66.0 (55.0–76.0)	0.08
Male	156 (58.9%)	91 (59.9%)	65 (57.5%)	0.70
Charlson Comorbidity Index	5.0 (4.0–7.0)	5.0 (4.0–7.0)	6.0 (3.5–8.0)	0.17
qSOFA				0.47
2	232 (87.5%)	135 (88.8%)	97 (85.8%)	
3	33 (12.5%)	17 (11.2%)	16 (14.2%)	
qSOFA component				
Respiratory rate ≥ 22/min	223 (84.2%)	123 (80.9%)	100 (88.5%)	0.10
Systolic blood pressure < 100 mmHg	201 (75.8%)	112 (73.7%)	89 (78.8%)	0.34
Altered mentation	141 (53.2%)	87 (57.2%)	54 (47.8%)	0.13
Baseline SOFA	0.0 (0.0–0.0)	0.0 (0.0–0.8)	0.0 (0.0–0.0)	0.06
SOFA	6.0 (4.0–9.0)	6.0 (4.0–9.0)	6.0 (4.0–8.0)	0.30
Delta SOFA	6.0 (3.0–8.0)	6.0 (3.0–9.0)	5.0 (4.0–8.0)	0.53
Focus of infection				0.71
Respiratory	115 (43.4%)	65 (42.8%)	50 (44.2%)	
Hepatobiliary	49 (18.5%)	26 (17.1%)	23 (20.4%)	
Gastrointestinal	25 (9.4%)	14 (9.2%)	11 (9.7%)	
Urinary	21 (7.9%)	15 (9.9%)	6 (5.3%)	
Others	55 (20.8%)	32 (21.1%)	23 (20.4%)	
Initial vital signs				
Systolic blood pressure, mmHg	92.0 (81.0–100.0)	92.5 (81.3–104.8)	91.0 (81.0–100.0)	0.66
Diastolic blood pressure, mmHg	58.0 (49.5–66.5)	58.0 (50.0–67.8)	58.0 (49.0–65.5)	0.58
Respiratory rate, breaths/min	24.0 (22.0–26.0)	24.0 (22.0–26.0)	24.0 (22.0–26.0)	0.82
Pulse rate, beats/min	107.2 (25.7)	105.8 (27.7)	109.1 (22.6)	0.30
Body temperature, ºC	37.4 (36.6–38.5)	37.3 (36.5–38.2)	37.5 (36.8–38.7)	0.15
ED occupancy rate, %	133.3 (106.9–162.8)	123.9 (98.9–143.5)	156.2 (131.1–175.2)	< 0.001
Initial lactic acid, mmol/L				0.18
< 2	125 (47.2%)	79 (52.0%)	46 (40.7%)	
2–4	82 (30.9%)	44 (28.9%)	38 (33.6%)	
> 4	58 (21.9%)	29 (19.1%)	29 (25.7%)	
Disease severity				0.72
Sepsis	194 (73.2%)	110 (72.4%)	84 (74.3%)	
Septic shock	71 (26.8%)	42 (27.6%)	29 (35.7%)	
Culture-positive sepsis	62 (24.2%), n = 256	39 (27.1%), n = 144	23 (20.5%), n = 112	0.23
Time to the bundle implementation				
Serum lactate measurement, min	14.0 (11.0–23.0), n = 264	14.0 (11.0–22.0), n = 151	14.0 (10.0–25.0), n = 113	0.95
Blood cultures, min	77.5 (46.0–141.8), n = 256	77.5 (44.5–139.8), n = 144	76.5 (46.5–145.5), n = 112	0.90
Broad-spectrum antibiotics, min	136.0 (85.0–230.0), n = 255	139.0 (90.5–257.0), n = 144	132.0 (84.0-208.0), n = 111	0.22
Gap time from blood culture to antibiotics. min	34.0 (5.3–85.0), n = 248	40.0 (11.8–91.3), n = 138	20.0 (2.8–71.8), n = 110	0.008

TABLE 2. Continued.

Characteristic	Overall (n = 265)	CDSS group (n = 152)	Control group (n = 113)	*P*-value
Compliance with bundle				
Serum lactate measurement	260 (98.1%)	150 (98.7%)	110 (97.3%)	0.65
Blood cultures	214 (80.8%)	119 (78.3%)	95 (84.1%)	0.24
Broad-spectrum antibiotics	163 (61.5%)	89 (58.6%)	74 (65.5%)	0.25
Fluid administration*	265 (100%)	152 (100%)	113 (100%)	-
All compliance	152 (57.4%)	80 (52.6%)	72 (63.7%)	0.07
30-day mortality	66 (24.9%)	41 (27.0%)	25 (22.1%)	0.37

All values are presented as median (interquartile range), mean (standard deviation) or number (percent), as appropriate.
** The 25 patients with severe heart failure or end-stage renal disease were administered 20 mL/kg of intravenous crystalloid and were categorized in the completion of the fluid administration.*
CDSS, clinical decision support system; qSOFA, quick sequential organ failure assessment; SOFA, sequential organ failure assessment.

size of 190 patients with sepsis was calculated based on 80% power, 0.05 alpha, and a 0.20 proportional increase.

3. Results

Between July 1 and December 31, 2016, there were 924 adult patients with qSOFA scores $\geq$ 2 upon arrival at our ED (Fig. 2). Of these cases, 618 were excluded from the study because the patients either were not suspected of having an infectious disease (n = 534), refused further examination and treatment (including those with "do not resuscitate" orders) (n = 66), or were directly transferred to another hospital from the ED within 3 hours (n = 18). A total of 306 cases were finally included in this study and grouped according to disease severity: infectious disease (n = 41, 13.4%), sepsis (n = 194, 63.4%), and septic shock (n = 71, 23.2%).

Table 1 summarises the baseline clinical characteristics and outcomes of the patients according to the severity of the infection. The study patients predominantly had qSOFA scores of 2 (85.6%), whereas the proportion of patients with qSOFA scores of 3 was significantly higher among patients in the septic shock group (22.5%). As disease severity increased (from infectious disease to septic shock), the SOFA score, serum lactic acid level, and 3-hour resuscitation bundle compliance rate significantly increased, whereas the time to bundle implementation time decreased.

The baseline characteristics and comparisons of the before-and-after CDSS analysis for patients with sepsis and septic shock development are presented in Table 2. There were no statistically significant differences between the CDSS and control groups in terms of suspected infection focus, disease severity, SOFA score or culture-positive sepsis. The median ED occupancy rate during the study period was 133.3% (IQR, 106.9%–162.8%), and it was significantly higher in the control group (median, 123.9% vs. 156.2%; $P < 0.001$). The 3-hour resuscitation bundle compliance for all 4 components was 57.4%, with no significant difference between the groups.

Among the 62 culture-positive patients, *Escherichia coli* (n = 26, 9.8%) was most frequently identified microorganism in blood culture, followed by and *Klebsiella pneumoniae* (n = 14, 5.3%) and *Staphylococcus aureus* (n = 6, 2.3%) (Supplement Table 1). The broad-spectrum antimicrobial agent was administered for 255 patients during ED stay. Piperacillin/tazobactam (n = 86, 33.7%) and ceftriaxone (n = 54, 21.2%) were the most frequently administered antibiotics in our study (Supplement Table 2).

In the univariable analysis, 3-hour resuscitation bundle compliance was significantly more likely with increases in patient age (OR, 1.024; 95% CI, 1.006–1.042; $P = 0.009$), respiratory rate (OR, 1.063; 95% CI, 1.010–1.118; $P = 0.019$), pulse rate (OR, 1.010; 95% CI, 1.001–1.020; $P = 0.038$), and body temperature (OR, 1.611; 95% CI, 1.306–1.987; $P < 0.001$). SOFA score, ED occupancy rate, and the presence of the CDSS were not significantly associated with 3-hour resuscitation bundle compliance (Table 3). The multivariable logistic regression analysis indicated that age (AOR [adjusted odds ratio], 1.033; 95% CI, 1.012–1.053; $P = 0.002$) and body temperature (AOR, 1.677; 95% CI, 1.339–2.100; $P < 0.001$) were independently associated with 3-hour resuscitation bundle compliance among sepsis and septic shock patients with qSOFA scores $\geq$ 2 upon arrival at our ED. The CDSS did not affect the compliance with the 3-hour resuscitation bundle standard (AOR, 0.591; 95% CI, 0.342–1.021; $P = 0.059$).

4. Discussion

We found that qSOFA score-based sepsis CDSS did not affect 3-hour resuscitation bundle compliance for the patients with qSOFA scores $\geq$ 2 upon arrival at our ED who developed sepsis and septic shock while in the ED. Among the patients with qSOFA scores $\geq$ 2 upon arrival at our ED, who were suspected of having an infectious disease, 86.6% (265/306) developed sepsis and septic shock while in the ED. For patients who developed sepsis or septic shock, the 3-hour resuscitation bundle compliance rate was 61.5%, and administering broad-spectrum intravenous antibiotics was the main barrier to bundle compliance among the bundle elements. Age and body temperature at ED arrival were the only independent factors that significantly influenced 3-hour resuscitation bundle compliance, while ED occupancy rate did not affect 3-hour resuscitation

TABLE 3. Univariable and multivariable logistic regression analyses of 3-hour resuscitation bundle compliance for sepsis patients with positive qSOFA scores upon emergency department admission.

	Univariable analysis			Multivariable analysis		
	Odds ratio	95% Confidence interval	*P*-value	Adjusted odds ratio	95% Confidence interval	*P*-value
Age, years	1.02	1.01–1.04	0.009	1.03	1.01–1.05	0.002
Male	0.97	0.59–1.59	0.90			
Charlson Comorbidity Index	1.06	0.97–1.17	0.21			
qSOFA score						
2	Reference					
3	1.57	0.73–3.39	0.25			
qSOFA component						
Respiratory rate ≥ 22/min	1.13	0.58–2.20	0.71			
Systolic blood pressure < 100 mmHg	0.90	0.51–1.59	0.71			
Altered mentation	1.21	0.75–1.98	0.44			
Baseline SOFA	0.99	0.79–1.24	0.92			
SOFA	1.06	0.98–1.14	0.13			
Delta SOFA	1.07	0.99–1.15	0.09	1.08	0.99–1.17	0.09
Focus of infection						
Respiratory	Reference					
Hepatobiliary	1.01	0.52–2.04	0.85			
Gastrointestinal	1.75	0.70–4.39	0.23			
Urinary	1.65	0.62–4.39	0.32			
Others	1.07	0.56–2.04	0.85			
Initial vital signs						
Systolic blood pressure, mmHg	1.00	0.99–1.01	0.99			
Diastolic blood pressure, mmHg	1.00	0.98–1.01	0.73			
Respiratory rate, breaths/min	1.06	1.01–1.12	0.02	1.06	1.00–1.12	0.05
Pulse rate, beats/min	1.01	1.00–1.02	0.04			
Body temperature, ºC	1.61	1.31–1.99	< 0.001	1.68	1.34–2.10	< 0.001
ED occupancy rate, %	1.00	0.99-1.00	0.29			
Initial lactic acid, mmol/L						
< 2	Reference					
2–4	1.96	1.10–3.49	0.02			
> 4	1.66	0.88–3.14	0.12			
qSOFA score-based decision system	0.63	0.38–1.04	0.07	0.59	0.34–1.02	0.06

SOFA, sequential organ failure assessment; qSOFA, quick sequential organ failure assessment.

bundle compliance.

Sepsis and septic shock are time-dependent diseases, for which early recognition and treatment, represented by 3-hour and 6-hour sepsis resuscitation bundles, are associated with improved outcomes [5, 12, 13]. However, bundle compliance rates for sepsis patients have generally been dismal in clinical practice, with estimates ranging from 7% to 27% [4, 12–14]. The main barriers to bundle compliance are delayed recognition by inexperienced physicians or ED resource shortages due to overcrowded ED environments [4, 12–14]. During the study period, the median ED occupancy rate was 133.3%, which is generally recognised as overcrowding [14, 15]. However, our ED's 3-hour bundle compliance rate was 57.4%, with the administration of broad-spectrum antibiotics within 3 hours

being accomplished for 61.5% of the patients. Consistent with previous studies, a delay in the administration of broad-spectrum antibiotics was the main obstacle [4, 12, 14]. The implementation of an automated dispensing cabinet in the ED would be a component of the multifaceted, hospital-wide approach to achieving prompt antibiotic administration for sepsis patients [16, 17].

Despite some controversy regarding the prognostic value of the qSOFA score [18–21], 86.6% of patients with qSOFA scores ≥ 2 at ED presentation developed sepsis or septic shock while in the ED. Our findings suggest that qSOFA score when patients arrive at the ED may be a reliable screening strategy for identifying patients at risk of sepsis, and ED physicians and nurses should act promptly for patients with qSOFA scores ≥ 2. However, our qSOFA-based CDSS was not associated with an improvement in bundle compliance in this study. Some limitations of our system would contribute to this unimprovement. Firstly, the system only consisted of displaying of an "S" beside the patient's name, 3-hour and 6-hour bundle checklists, and a SOFA score calculator to minimise alert fatigue and clinician workflow interruptions. However, this non-interrupting alert system might fail to arouse physicians' attention and consequently fail to improve bundle compliance. Also, the ED physicians would be highly likely to identify the patients with qSOFA scores ≥ 2 as high acuity patients without the CDSS. Secondly, the clinicians and nurses could recognise patients with qSOFA scores ≥ 2 via the ED patient list, but clinicians are required to open the program to view the checklist and be required to manually input some laboratory and clinical values to use the SOFA score calculator. Thirdly, the bundle compliance rate in our ED was higher (57.4%) than previously reported rates (<30%), and the possible positive impact could be obscured.

We found that older age and higher body temperature at ED arrival were associated with 3-hour bundle compliance. Other vital signs, ED crowding, or the application of a qSOFA score-based CDSS showed no significant association with bundle compliance in the multivariable logistic regression analysis. Elderly patients or those with higher body temperatures were given high priority among those with a high risk of developing sepsis upon ED arrival, regardless of ED overcrowding or the presence of the CDSS program. These results suggest that physicians and nurses gave priority to the patients who seemed to have a higher risk of deterioration. Many artificial intelligence-based early warning systems and prediction models are developed in critical care medicine, including sepsis, acute respiratory distress syndrome, heart failure, and in-hospital cardiac [22–24], which demonstrated the outperformance compared to conventional methods in prediction. A more precise early warning system identifying the patients in order of the risk of deterioration due to sepsis in ED and an automated alarm system would improve the sepsis management and patients' outcome. Also, it would enhance accurate decision-making and efficacy in allocations of medical resources.

Our study had several limitations. Firstly, we developed and applied the system at a single medical centre and included a small number of patients during a short study period. This limits our findings' generalisability to other institutions or patient populations, and our results should be cautiously interpreted, especially when considering EDs with low levels of crowding. Secondly, although we prospectively collected the data after the routine implementation of the CDSS, we also retrospectively collected the data from before the CDSS implementation. Thirdly, all clinicians treated patients according to the SSC guidelines, but we could not adjust for all potential inter-clinician variability and the effects of unobserved biases. Finally, we only determined qSOFA scores at ED arrival instead of using real-time bedside monitoring.

5. Conclusions

In conclusion, we developed a qSOFA-based sepsis CDSS to improve the early recognition and timely treatment of sepsis, represented by 3-hour bundle compliance, but the system was not associated with improved bundle compliance. We believe that the relatively high rate of bundle compliance and overcrowding in our ED might have blunted the potential benefits of the qSOFA-based CDSS, and multifactorial, hospital-wide approaches are warranted to improve the care of patients with sepsis.

AUTHOR CONTRIBUTIONS

YJK and JHL designed the study. YJK, JHL and SWL collected the data. YJK and WYK analyzed the data. YJK analyzed the results and drafted the manuscript. All authors contributed substantially to the revision.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Asan Medical Center's institutional review board approved the study (Study No. 2016-0818) and waived the requirement for informed consent because the study involved the analysis of a case registry. The research is in accordance with the Helsinki Declaration of 1975, as revised in 2010.

ACKNOWLEDGMENT

The authors would like to express our gratitude to all those who helped me during the writing of this manuscript, and we thank to all the peer reviewers for their opinions and suggestions.

FUNDING

This research was supported by the Basic Science Research Program, through the National Research Foundation of Korea (NRF), funded by the Ministry of Education (No. NRF-2015R1D1A1A01057091).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/1391673656692621312/attachment/Supplementary%20material.rar.

DATA AVAILABILITY

The data used to support the findings of this study are available from the corresponding author upon request.

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How to cite this article: Youn-Jung Kim, Jae-Ho Lee, Sang-Wook Lee, Won Young Kim. Use of quick sequential organ failure assessment score-based sepsis clinical decision support system may be helpful to predict sepsis development. Signa Vitae. 2021;17(5):86-94. doi:10.22514/sv.2021.082.