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Original Contributions

EXTERNAL VALIDATION OF THE QSOFA SCORE IN EMERGENCY DEPARTMENT PATIENTS WITH PNEUMONIA

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☐ **Abstract—Background: Pneumonia is the leading cause of sepsis. In 2016, the 3rd International Consensus Conference for Sepsis released the Quick Sepsis-Related Organ Failure Assessment (qSOFA) to identify risk for poor outcomes in sepsis. Objective: We sought to externally validate qSOFA in emergency department (ED) patients with pneumonia and compare the accuracy of qSOFA to systemic inflammatory response syndrome score (SIRS), Confusion, Respiratory Rate and Blood Pressure (CRB), Confusion, Respiratory Rate, Blood Pressure and Age (CRB-65), and DS CRB-65, which is based on the CRB-65 score and includes two additional items—presence of underlying comorbid disease and blood oxygen saturation. Methods: A subgroup analysis of U.S. Critical Illness and Injury Trials Group (USCIITG–Lung Injury Prevention Study [LIPS]; ClinicalTrials.gov ID: NCT00889772) prospective cohort. The primary outcome was in-hospital mortality. Secondary outcomes were measures of intensive care unit (ICU) utilization. Sensitivity, specificity, and area under the curve (AUC) were reported. Results: From March to August 2009, 5584 patients were enrolled; 713 met inclusion criteria. Median age was 61 years (interquartile range 49–75 years). SIRS criteria had the highest sensitivity for death (89%) and lowest specificity (25%), while CRB had the highest specificity (88%) and lowest sensitivity (31%), followed by qSOFA (80% and 53%, respectively). This trend was maintained for the secondary outcomes. There was no significant difference in the AUC for death using qSOFA (AUC 0.75; 95% confidence interval [CI] 0.66–0.84), SIRS (AUC 0.70; 95% CI 0.61–0.78), CRB (AUC 0.71; 95% CI 0.62–0.80), CRB-65 (AUC 0.71; 95% CI 0.63–0.80), and DS CRB-65 (AUC 0.73; 95% CI 0.64–0.82). Conclusions: In this multicenter observational study of ED patients hospitalized with pneumonia, we found no significant differences between qSOFA and SIRS for predicting in-hospital death. In addition, several popular pneumonia-specific severity scores performed nearly identically to qSOFA score in predicting death and ICU utilization. Validation is needed in a larger sample.**

☐ **Keywords—pneumonia; sepsis; qSOFA; CRB; CRB-65; mortality; emergency department**

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INTRODUCTION

Community-acquired pneumonia (CAP), defined as an acute infection of the pulmonary parenchyma acquired in a community setting, is a common cause of sepsis (1–3). CAP results in nearly 1 million hospitalizations annually, and is estimated to cost more than $9.5 billion annually (4). CAP is responsible for nearly 60,000 deaths per year in the United States and was the eighth-leading cause of mortality in 2014 (5). Despite advances in medical care of pneumonia, it remains the leading cause of sepsis. The mortality rate for pneumonia-related sepsis exceeds 50% (6). Accurate stratification of patients with high-risk CAP is key to reducing mortality and allocating health care resources.

The identification of emergency department (ED) patients with CAP who are at risk for a poor outcome remains an important challenge for clinicians. Substantial effort has been invested toward the development of a scoring system to predict both severity of illness and mortality among patients with CAP. The Pneumonia Severity Index (PSI) is perhaps the most widely studied and validated system; however, with more than 20 parameters, each with different scoring weights, the PSI is overly burdensome for use in the fast-paced ED (7). The Confusion, Respiratory Rate and Blood Pressure (CRB) score and the Confusion, Respiratory Rate, Blood Pressure and Age (CRB-65) score have since been developed as alternatives to PSI (8–10). These scores emphasize simplicity and ease of use, and are well validated and only slightly less accurate than the PSI (11–16). The DS CRB-65 is based on the CRB-65 score and includes two additional items—presence of underlying comorbid disease and blood oxygen saturation—both of which have been shown to independently predict mortality in CAP (7,17). In a Swedish cohort of patients with CAP, the DS CRB-65 score was found to be more accurate than the CRB-65 (area under the curve [AUC] 0.83 vs. 0.77; $p = 0.01$) and similar to that of PSI (AUC 0.84) (17).

In 2016, the 3rd International Consensus Conference for Sepsis Task Force proposed a novel screening tool to identify patients at risk for death from sepsis, the Quick Sepsis-Related Organ Failure Assessment (qSOFA). The overlying objective was for qSOFA to replace the systemic inflammatory response syndrome score (SIRS), which had been in use for decades and was unanimously considered by the task force to be ineffective (18).

qSOFA is purported to be superior to SIRS in predicting sepsis patients with ≥10% risk of mortality; however, validation of the performance of the qSOFA vs. SIRS score, and qSOFA vs. the CRB, CRB-65, and DS CRB-65 scores, is lacking (18–21).

Importance

While the promise of enhanced accuracy of qSOFA over SIRS for identification of sepsis makes qSOFA an attractive tool, evidence supporting the superiority of qSOFA over SIRS among ED patients with pneumonia is limited to small, single-center cohorts, in non-U.S. populations (22–27). There are no multicenter studies externally validating the performance of qSOFA in pneumonia among U.S. ED patients. Comparisons of the accuracy of qSOFA vs. pneumonia-specific scores, such as CRB, CRB-65, and DS CRB-65, are even sparser, similarly limited to single-center, non-U.S. cohorts, which fail to show superiority of qSOFA (23–28).

Understanding the relative performance of qSOFA, SIRS, CRB, and CRB-65 in the ED setting is critical to improving the care of pneumonia patients. We compared the performance of qSOFA, to SIRS, CRB, CRB-65, and DS CRB-65 to predict clinically important outcomes in a multicenter cohort of patients with pneumonia who presented to U.S. EDs.

MATERIALS AND METHODS

Study Design

We conducted a secondary analysis of a multicenter, prospective, observational cohort study—the U.S. Critical Injury and Illness Trial Group–Lung Injury Prevention Study 1 (USCIITG-LIPS 1) (29). The study received approval from each of the respective local Institutional Review Boards. This sub-study was accepted by the LIPS ancillary study committee from full Institutional Review Board review.

Study Setting

The USCIITG-LIPS 1 study enrolled patients at 20 U S. and 2 non-U.S. academic and community hospitals during a 6-month period from March 2009 through August 2009. Details of the original study population have been reported previously (29). Briefly, adult (aged >18 years) patients were enrolled prospectively in USCIITG-LIPS 1 cohort if they were admitted from the ED or hospitalized with at least one or more a priori major risk factors predisposing to acute lung injury. The USCIITG-LIPS investigators included a diagnosis of pneumonia, aspiration, sepsis, shock, pancreatitis, high-risk trauma, or high-risk surgery as major risk factors for acute lung injury. Efforts to ensure validity of data in the original prospective study included electronic range checks of numerical values and validation rules to eliminate erroneous data and data artifacts. Hospital admissions logs were

reviewed to minimize misclassification of patients. Study investigators and coordinators at each site participated in online training for all data collection elements and were responsible for the quality control of data collection and entry (29).

Selection of Participants

We considered subjects from the USCIITG-LIPS 1 cohort appropriate for inclusion if they were admitted to a U.S. hospital from the ED with suspected infection, had initial vital signs and Glasgow Coma Scale (GCS) score recorded, and were diagnosed with pneumonia according to the USCIITG-LIPS criteria. Pneumonia was defined in the original cohort if patients were included if chest radiographs demonstrated a new or progressive infiltrate, consolidation, cavitation, or pleural effusion, and either presence of new-onset or change in character of purulent sputum. Positive cultures were used when available. Patients admitted who were do not intubate (DNI), hospice, or comfort measures only status were excluded in the LIPS cohort. A study flow diagram is illustrated in Figure 1.

Data Collection and Processing

Baseline characteristics, including demographics, comorbidities, and clinical variables, were collected during the first 6 h of the ED evaluation. Vital signs from the first 6 h represent the most aberrant values recorded. The SIRS definition of sepsis was applied and recorded as part of the original study criteria. Prior to study initiation at each site, investigators and study coordinators received structured training. The principal investigators from each site were responsible for data collection, data entry, and quality control. The qSOFA score is comprised of three simple physiological variables that can be readily obtained during a bedside clinical assessment: systolic blood pressure $\leq$ 100 mm Hg, respiratory rate $\geq$ 22 breaths/min, and GCS score < 15. We applied the qSOFA score retrospectively to all patients with suspected or diagnosed pneumonia. We calculated the CRB, CRB-65, and DS CRB-65 scores retrospectively according to the original publications (9,10,17).

Outcome Measures

The primary outcome was in-hospital mortality among patients with pneumonia. Secondary outcomes were determined a priori and included composite of in-hospital mortality or intensive care unit (ICU) length of stay (LOS) $\geq$ 3 days, ICU LOS $\geq$ 3 days alone, ICU utilization of any duration, invasive mechanical ventilation, non-invasive ventilation, vasopressor use, and hemodialysis secondary to acute renal failure. Composite outcome

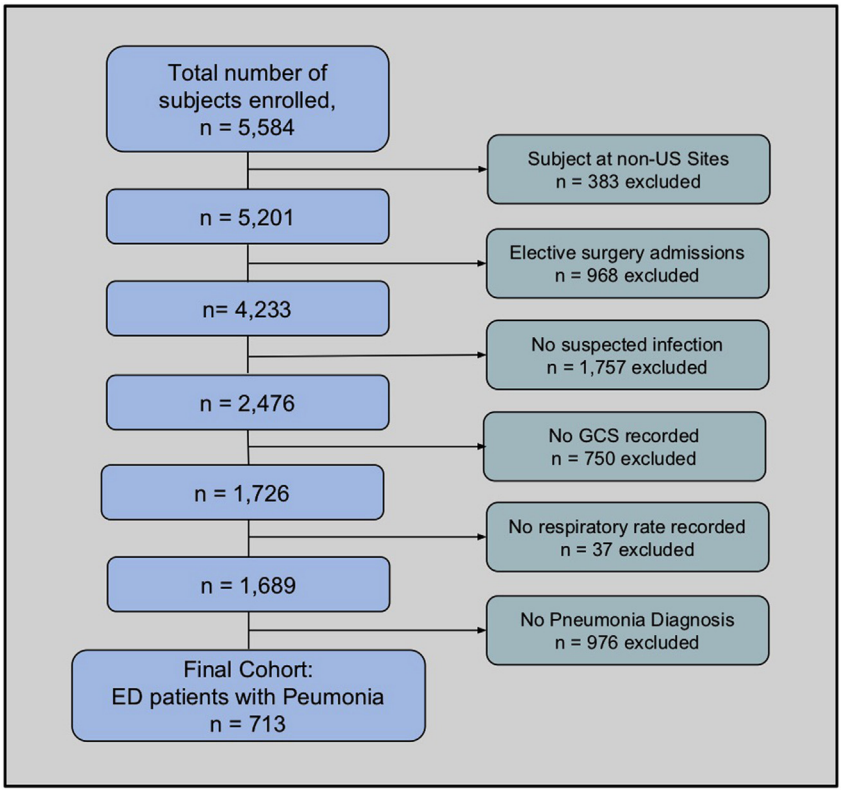

Figure 1. Flow diagram. ED = emergency department; GCS = Glascow Coma Scale; US = United States.

of ICU LOS ≥ 3 days or death was chosen in accordance with the 3rd International Consensus Conference on sepsis. The other secondary outcomes were chosen, given that these interventions represent a high level of severity of illness. Additionally, each of the interventions commonly requires ICU level of care and thus the predictive ability of the screening tool for these outcomes may be considered clinically relevant in determining resource utilization.

Statistical Analysis

We followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines in the design and reporting of this observational study (30). Baseline demographics and clinical characteristics were examined using one-way analysis of variance and Kruskal-Wallis tests for normally and non-normally distributed continuous variables, respectively, and χ^2 or Fisher's exact tests for categorical variables. We assessed the association between qSOFA ≥ 2, SIRS ≥ 2, CRB ≥ 2, CRB-65 ≥ 2, DS CRB-65 ≥ 3 for each clinical outcome using generalized linear mixed-effects regression models, accounting for the correlation among ED patients from the same study site, adding study site as the random effect. For each criteria (qSOFA, SIRS, CRB, CRB-65, and DS CRB-65) the cutoff value of ≥ 2 (and ≥ 3 in the case of DS CRB-65) was determined by both literature review for recommended cutoff values, and reflect the cutoff values in the 3rd International Consensus Conference, thus these values are the most relevant to current clinical practice.

Additionally, we assessed the prognostic performance of qSOFA ≥ 2, SIRS ≥ 2, CRB ≥ 2, CRB-65 ≥ 2, and DS CRB-65 ≥ 3 criteria to predict the primary and secondary clinical outcomes using area under the receiver operating characteristic curve (AUROC). We reported sensitivity, specificity, and AUROC, along with their 95% confidence interval (CI). Additionally, we calculated odds ratios (ORs), positive predictive values, and negative predictive values for each cutoff. All significance tests were two-sided, with a p value < 0.05 considered statistically significant. All statistical analyses were performed using Statistical Analysis Software, version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

General Characteristics of the Study Cohort

From March to August 2009, 5584 patients were enrolled in the USCIITG-LIPS 1 cohort. Among these patients, 713 patients met inclusion criteria (diagnoses of pneumonia with all variables for qSOFA documented). Males comprised 51.9%. Median age of the study cohort was 61 years (interquartile range 49–75 years); patients who met qSOFA ≥ 2 or SIRS ≥ 2 criteria were approximately 10 years younger than those who met the CRB ≥ 2, CRB-65 ≥ 2, and DS CRB-65 ≥ 3 criteria. The distribution of patients who met qSOFA ≥ 2, SIRS ≥ 2, CRB ≥ 2, CRB-65 ≥ 2, and DS CRB-65 ≥ 3 in the cohort was 22.2%, 76.2%, 13.3%, 29.7%, and 25.7% respectively (Table 1). Distribution of clinical and laboratory markers found in each cohort are detailed in Appendix A.

Outcomes

The overall in-hospital mortality for the cohort was 5.1%. There was a significant difference in the frequency of the primary outcome (in-hospital mortality) across all of the scoring systems among those meeting qSOFA ≥ 2, CRB ≥ 2, CRB-65 ≥ 2, and DS CRB-65 ≥ 3 criteria vs. those who did not, except for SIRS criteria (Appendix B).

The OR for in-hospital mortality was largest for qSOFA ≥ 2 vs. < 2 (OR 4.39; 95% CI 2.19–8.79), whereas there was no evidence of statistical difference in the odds of in-hospital mortality for those with SIRS ≥ 2 compared to those with SIRS < 2 (OR 2.48;

Table 1. Patient Demographic Characteristics and Comorbidities Stratified by Score

Characteristics	All
n (%)	713 (100)
Demographic	
Age ≥ 65 years, n (%)	
Age, years, median (25th, 75th)	61 (49, 75)
Sex, male, n (%)	370 (51.9)
Caucasian, n (%)	401 (58.5)
African American, n (%)	237 (34.6)
Hispanic ethnicity, n (%)	54 (9.3)
Clinical	
Smoking, n (%)	277 (41.3)
Alcohol use, n (%)	185 (28.2)
Systemic steroids, n (%)	98 (13.7)
ACE inhibitors, n (%)	165 (23.1)
Shock, n (%)	42 (5.9)
APACHE II median (25^{th}, 75^{th})	11 (7, 15)
Comorbidities	
Metastatic solid cancer, n (%)	46 (6.5)
Immunosuppression, n (%)	102 (14.3)
COPD, n (%)	152 (21.3)
Asthma, n (%)	101 (14.2)
CHF NYHA Class IV, n (%)	37 (5.2)
Chronic hemodialysis, n (%)	47 (6.6)
Cirrhosis, n (%)	10 (1.4)
Diabetes mellitus, n (%)	208 (29.2)
Body mass index (kg/m^2) (25^{th}, 75^{th})	25.7 (21.6, 30.2)

ACE = angiotensin-converting-enzyme inhibitor; APACHE = Acute Physiology and Chronic Health Evaluation; CHF = chronic heart failure; COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association.

Table 2. Association Between Each Score and Outcomes

Outcome	qSOFA ≥ 2 (vs. < 2)	SIRS ≥ 2 (vs. < 2)	CRB ≥ 2 (vs. < 2)	CRB-65 ≥ 2 (vs. < 2)	DS CRB-65 ≥ 3 (vs. < 3)
Death	4.39 (2.19–8.79)*	2.48 (0.86–7.16)	3.19 (1.49–6.82)*	2.92 (1.47–5.81)*	3.54 (1.78–7.02)*
Death/ICU LOS ≥ 3 days	5.31 (3.42–8.22)*	2.40 (1.39–4.16)*	5.22 (3.16–8.62)*	3.63 (2.40–5.47)*	3.30 (2.19–4.98)*
ICU LOS ≥ 3 days	5.03 (3.22–7.87)*	2.45 (1.38–4.35)*	4.96 (2.98–8.24)*	3.28 (2.15–5.00)*	2.79 (1.83–4.25)*
ICU utilization	5.70 (3.70–8.78)*	3.34 (1.95–5.70)*	5.8 (3.46–9.60)*	3.64 (2.46–5.40)*	3.73 (2.51–5.55)*
Invasive ventilation	4.25 (2.64–6.84)*	2.36 (1.24–4.50)*	4.47 (2.62–7.64)*	2.76 (1.76–4.34)*	2.99 (1.90–4.70)*
Vasopressors	5.99 (3.19–11.24)*	2.34 (0.96–5.71)	7.56 (3.92–14.59)*	5.70 (2.99–10.85)*	2.55 (1.53–4.27)*
Non-invasive ventilation	1.72 (0.99–3.02)	1.96 (0.97–3.97)	2.11 (1.14–3.92)*	2.13 (1.27–3.55)*	5.37 (2.89–9.96)*
Hemodialysis	1.50 (0.69–3.26)	2.39 (0.82–6.93)	2.07 (0.90–4.76)	1.51 (0.73–3.09)	2.08 (1.02–4.22)*

Data are odds ratio (95% confidence interval).
CRB = Confusion, Respiratory Rate and Blood Pressure; CRB-65 = Confusion, Respiratory Rate, Blood Pressure, and Age; DS CRB-65 = Confusion, Respiratory Rate, Blood Pressure, Age, and presence of underlying comorbid disease and blood oxygen saturation; ICU = intensive care unit; LOS = length of stay; qSOFA = Quick Sepsis-Related Organ Failure Assessment; SIRS = systemic inflammatory response syndrome score.
* $p < 0.05$ when compared to group with criteria value < 2 (<3 for DS CRB-65).

95% CI 0.86–7.16) (Table 2). Odds ratios for patients meeting vs. not meeting criteria of each of the five scores and each of the secondary outcomes are found in Table 2.

Predictive Performance

For the primary outcome of in-hospital mortality, the discriminative ability of qSOFA ≥ 2 compared to qSOFA < 2 demonstrated the strongest predictive ability when compared with SIRS, CRB ≥ 2, CRB-65, and DS CRB-65 (AUROC 0.75; 95% CI 0.66–0.84), compared to 0.70 (95% CI 0.61–0.78), 0.71 (95% CI 0.62–0.80), 0.71 (95% CI 0.63–0.80), and 0.73 (95% CI 0.64–0.82, respectively) (Table 3). However, there was large overlap of 95% CIs for nearly all measures. Overall, there was no statistically significant difference in the AUROC between the different scores for the primary outcome of death (Table 4).

As compared to SIRS score, qSOFA showed better performance in discriminating secondary outcome of death/ICU LOS ≥ 3 days (AUROC 0.80; 95% CI 0.76–0.84) vs. 0.74 (95% CI 0.70–0.79; $p = 0.006$), ICU LOS ≥ 3 days (AUROC 0.80; 95% CI 0.76–0.85) vs. 0.75 (95% CI 0.70–0.80; $p = 0.006$), and ICU utilization (AUROC 0.80; 95% CI 0.76–0.84) vs. 0.76 (95% CI 0.72–0.80; $p = 0.024$). While several other significant differences were in secondary outcomes between the various scores, the effect sizes were largely unremarkable, with considerable overlap of the 95% CIs (Table 4).

SIRS ≥ 2 was by far the most sensitive for all outcomes measured, exhibiting twice the sensitivity of qSOFA ≥ 2 and CRB-65 ≥ 2 and, three times that of CRB ≥ 2. High sensitivity values for SIRS ≥ 2 indicate that about 85–90% of those who had primary and secondary outcomes satisfied SIRS ≥ 2 criteria. In contrast, CRB ≥ 2 was the most specific, with approximately four times the specificity for SIRS ≥ 2 and 6–9% greater than qSOFA ≥ 2 and 15–17% greater than CRB-65 ≥ 2 for all outcomes. Specificity for CRB ≥ 2 ranged from 87% to 93%, indicating that among those who did not have adverse outcomes, about 90% had CRB <2. (Table 5).

DISCUSSION

In 2016, the 3rd International Consensus Conference for Sepsis Task Force released updated guidelines for sepsis

Table 3. Discriminative Ability of Each Score to Predict Outcomes

Outcome	qSOFA ≥ 2 (vs. < 2)	SIRS ≥ 2 (vs. < 2)	CRB ≥ 2 (vs. < 2)	CRB-65 ≥ 2 (vs. < 2)	DS CRB-65 ≥ 3 (vs. < 3)
Death	0.75 (0.66–0.84)	0.70 (0.61–0.78)	0.71 (0.62–0.80)	0.71 (0.63–0.80)	0.73 (0.64–0.82)
Death/ICU LOS ≥ 3 days	0.80 (0.76–0.84)	0.74 (0.70–0.79)	0.78 (0.74–0.83)	0.78 (0.74–0.82)	0.77 (0.73–0.82)
ICU LOS ≥ 3 days	0.80 (0.76–0.85)	0.75 (0.70–0.80)	0.79 (0.75–0.83)	0.78 (0.73–0.82)	0.77 (0.72–0.81)
ICU utilization	0.80 (0.76–0.84)	0.76 (0.72–0.80)	0.78 (0.74–0.82)	0.78 (0.74–0.82)	0.78 (0.74–0.82)
Invasive ventilation	0.76 (0.71–0.81)	0.72 (0.66v0.77)	0.77 (0.72–0.81)	0.74 (0.69–0.80)	0.75 (0.70–0.80)
Vasopressors	0.79 (0.72–0.86)	0.73 (0.66–0.80)	0.80 (0.73–0.86)	0.79 (0.72–0.86)	0.78 (0.71–0.85)
Non-invasive ventilation	0.68 (0.61–0.75)	0.69 (0.62–0.76)	0.68 (0.61–0.75)	0.69 (0.62–0.76)	0.69 (0.62–0.76)
Hemodialysis	0.66 (0.57–0.76)	0.70 (0.61–0.80)	0.68 (0.58–0.77)	0.66 (0.57–0.76)	0.68 (0.59–0.78)

Data represents area under the receiver operating characteristics curve (95% confidence interval).
CRB = Confusion, Respiratory Rate and Blood Pressure; CRB-65 = Confusion, Respiratory Rate, Blood Pressure, and Age; DS CRB-65 = Confusion, Respiratory Rate, Blood Pressure, Age, and presence of underlying comorbid disease and blood oxygen saturation; ICU = intensive care unit; LOS = length of stay; qSOFA = Quick Sepsis-Related Organ Failure Assessment; SIRS = systemic inflammatory response syndrome score.

Table 4. Comparison of Discriminating Performance of Each Score

Outcome	Death	Death ICU LOS ≥ 3 days	ICU LOS ≥ 3 days	ICU Utilization	Invasive Ventilation	Vasopressors	Non-Invasive Ventilation	Hemodialysis
qSOFA vs. SIRS	0.278	0.006*	0.006*	0.024*	0.057	0.098	0.532	0.347
qSOFA vs. CRB	0.23	0.323	0.332	0.199	0.821	0.836	0.918	0.739
qSOFA vs. CRB-65	0.474	0.295	0.137	0.222	0.376	0.975	0.802	0.982
qSOFA vs. DS CRB-65	0.715	0.16	0.048*	0.233	0.558	0.707	0.596	0.669
SIRS vs. CRB	0.799	0.026*	0.027*	0.162	0.035*	0.087	0.523	0.542
SIRS vs. CRB-65	0.739	0.076	0.145	0.242	0.224	0.147	0.837	0.46
SIRS vs. DS CRB-65	0.503	0.12	0.281	0.24	0.131	0.233	0.951	0.717
CRB vs. CRB-65	0.83	0.727	0.346	0.867	0.097	0.778	0.722	0.708
CRB vs. DS CRB-65	0.531	0.418	0.13	0.852	0.322	0.515	0.548	0.803
CRB-65 vs. DS CRB-65	0.52	0.485	0.351	0.961	0.73	0.541	0.68	0.195

Data represent *p* values for testing differences between area under the receiver operating characteristics curve for models using each score.
CRB = Confusion, Respiratory Rate and Blood Pressure; CRB-65 = Confusion, Respiratory Rate, Blood Pressure, and Age; DS CRB-65 = Confusion, Respiratory Rate, Blood Pressure, Age, and presence of underlying comorbid disease and blood oxygen saturation; ICU = intensive care unit; LOS = length of stay; qSOFA = Quick Sepsis-Related Organ Failure Assessment; SIRS = systemic inflammatory response syndrome score.
* $p < 0.05$.

(Sepsis-3), which advised the use of a novel mortality prediction score, the qSOFA criteria, in lieu of the SIRS criteria (18). However, in this observational study of ED patients hospitalized with sepsis due to pneumonia, we found that qSOFA was no more accurate than SIRS for predicting in-hospital death. qSOFA was more accurate at predicting the composite outcome of hospital mortality and ICU stay ≥ 3 days. Additionally, we found that several popular pneumonia-specific severity scores—CRB score, CRB-65 score, and DS CRB-65 score—performed nearly identically to qSOFA score in terms of predicting death and markers of ICU utilization. Absence of significant differences between the scores in predicting the primary outcome may be due in part to the low frequency of death in this cohort. Future studies may benefit from a larger sample.

The SIRS criteria were originally proposed to describe the inflammatory process of a clinical response arising from infection, often complicated by organ dysfunction. As the number of SIRS criteria increases, mortality increased (31,32). Hence, it has been used to assess illness severity in sepsis and identify risk for poor outcomes. The SIRS criteria were not originally proposed to define/diagnose sepsis itself. Yet, in practice, the difference between a severity score and diagnostic criteria is frequently obscured and too often the presence of SIRS criteria was conflated with the diagnosis of sepsis. The conflation of SIRS with sepsis is a central limitation to the comparative study of SIRS criteria vs. other mortality prediction tools in sepsis. This study is unique because it focused solely on patients with pneumonia—thus affording the opportunity to evaluate for sepsis independently of the presence or absence SIRS criteria. In this cohort, SIRS re-demonstrated its superior sensitivity over qSOFA ≥ 2, while qSOFA ≥ 2 had much stronger specificity. However, qSOFA did not demonstrate statistically significant superiority in terms of accuracy in predicting death. These results differ from the findings of multiple previous reports comparing SIRS and qSOFA (33–39). Given the relatively low mortality rate in this sample, equivalence between the scores may be due in part to underpowering of the sample.

Sepsis is a clinical syndrome comprised of a heterogeneous group of infectious diseases, each with distinct pathophysiology (e.g., pneumosepsis, urosepsis). It is plausible that disease-specific mortality prediction scores, such as CRB or CRB-65, may be more accurate than generalized sepsis scores (qSOFA and SIRS). Few investigators have compared the accuracy of disease-specific mortality prediction among sepsis mortality scores (such as qSOFA, SIRS, and CRB) or assessed the relative predictive performance of these scoring tools (23–28). Chen and colleagues were the first to compare the accuracy of qSOFA to CRB and CRB-65 among ED patients in China (25). The authors looked at patients with pneumonia in a single-center referral hospital in Beijing, and demonstrated that qSOFA, CRB, and CRB-65 all had similar predictive performance. The study had multiple limitations, including but not limited to a 54% overall mortality rate, which reduced the generalizability of their findings. Müller et al. performed a retrospective analysis comparing the performance of qSOFA, SIRS, and CRB-65 in 527 pneumonia patients in a Swiss ED (23). While the overall mortality rate was approximately 13.3% higher in the Swiss group, the odds of in-hospital mortality and ICU utilization were comparable to the findings reported here (2.6; 95% CI 1.4–4.7; $p < 0.001$ and 3.5; 95% CI, 2.0–5.8; $p < 0.001$, respectively). Additionally, the prediction scores did not differ significantly in their prognostication of in-hospital mortality. In a similar study, Ranzani et al. performed a large

Table 5. Predictive Performance of Each Score

Outcome	Score	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %
Death	qSOFA ≥ 2	53	80	12	97
	SIRS ≥ 2	89	25	6	98
	CRB ≥ 2	31	88	12	96
	CRB-65 ≥ 2	53	71	9	97
	DS CRB-65 ≥ 3	53	76	10	97
Death/ICU LOS ≥ 3 days	qSOFA ≥ 2	46	85	49	84
	SIRS ≥ 2	89	28	27	89
	CRB ≥ 2	31	92	54	81
	CRB-65 ≥ 2	51	77	40	84
	DS CRB-65 ≥ 3	45	80	40	83
ICU LOS ≥ 3 days	qSOFA ≥ 2	47	85	46	85
	SIRS ≥ 2	89	27	25	90
	CRB ≥ 2	31	92	51	83
	CRB-65 ≥ 2	50	76	36	85
	DS CRB-65 ≥ 3	43	79	36	83
ICU utilization	qSOFA ≥ 2	43	87	58	78
	SIRS ≥ 2	90	30	36	87
	CRB ≥ 2	28	93	64	75
	CRB-65 ≥ 2	48	78	49	78
	DS CRB-65 ≥ 3	43	82	51	77
Invasive ventilation	qSOFA ≥ 2	46	82	31	90
	SIRS ≥ 2	89	26	17	93
	CRB ≥ 2	31	90	35	88
	CRB-65 ≥ 2	48	73	24	89
	DS CRB-65 ≥ 3	45	78	26	89
Vasopressors	qSOFA ≥ 2	57	80	18	96
	SIRS ≥ 2	88	25	8	96
	CRB ≥ 2	45	89	23	96
	CRB-65 ≥ 2	65	73	15	97
	DS CRB-65 ≥ 3	61	77	16	96
Non-invasive ventilation	qSOFA ≥ 2	34	79	16	91
	SIRS ≥ 2	86	25	12	94
	CRB ≥ 2	26	88	20	91
	CRB-65 ≥ 2	47	72	17	92
	DS CRB-65 ≥ 3	46	77	19	92
Hemodialysis	qSOFA ≥ 2	29	78	6	96
	SIRS ≥ 2	85	28	6	97
	CRB ≥ 2	24	87	8	96
	CRB-65 ≥ 2	38	71	6	96
	DS CRB-65 ≥ 3	41	75	8	96

CRB = Confusion, Respiratory Rate and Blood Pressure; CRB-65 = Confusion, Respiratory Rate, Blood Pressure, and Age; DS CRB-65 = Confusion, Respiratory Rate, Blood Pressure, Age, and presence of underlying comorbid disease and blood oxygen saturation; ICU = intensive care unit; LOS = length of stay; qSOFA = Quick Sepsis-Related Organ Failure Assessment; SIRS = systemic inflammatory response syndrome score.

retrospective trial of two Spanish EDs comparing qSOFA, CRB, CRB-65, and PSI among pneumonia patients, again reporting similar findings (24).

In this study, we evaluated several common pneumonia mortality prediction scores and compared them to qSOFA and SIRS among a cohort of U.S. ED patients with pneumonia. We found a trend toward increased accuracy of both qSOFA ≥ 2 and CRB ≥ 2 vs. SIRS ≥ 2 for nearly all outcomes, however, with broad overlap in CIs, few outcomes reached significance. Importantly, when examining hospital mortality alone, no single score was superior to another. The addition of SpO_2 threshold and underlying comorbidity to the CRB scores (i.e., DS CRB-65) did not enhance predictive ability.

Interestingly, there was increased specificity for all outcomes using CRB ≥ 2 compared to qSOFA ≥ 2, while the opposite was true for sensitivity. Tradeoffs in sensitivity and specificity between scores are of considerable concern from an ED perspective: low sensitivity of qSOFA criteria may result in poor or delayed detection of sepsis, while lack of specificity in SIRS criteria threaten to overwhelm hospital and ICU resources. The well-demonstrated strengths and weaknesses of these two scoring systems (SIRS superior sensitivity and qSOFA superior specificity), lends support to the idea of employing a two-step process whereby SIRS (or a similarly sensitive tool) is used to initiate identification into the presence of sepsis during initial ED triage and management, then a second tool (such as CRB or qSOFA) is commissioned to stratify patients based on risk of poor outcomes once the diagnosis has been (preliminarily) made. Alternatively, recently investigations have shown

that qSOFA ≥ 1 has superior sensitivity for mortality than SIRS ≥ 2 in sepsis (40). Future research could focus on using qSOFA in a stepwise pattern (qSOFA ≥ 1 for recognition, qSOFA ≥ 2 for disposition) to improve outcomes for ED patients.

Limitations

Our study has several limitations. This cohort was relatively small compared to previous studies of qSOFA, and the primary outcome of death was not common, thus reducing our power to detect relevant outcomes. However, this is one of the largest to look at qSOFA in pneumonia patients. Furthermore, our results are similar to others' findings in the literature.

Absence of complete data on GCS led to exclusion of 716 patients from the cohort. This may have contributed to selection bias and reduced power. Additionally, data from the LIPS cohort is from 2009; secular trends in the care of pneumonia patients could potentially lead to improved outcomes compared to 2009. However, evidence from large cohorts has not demonstrated significant improvements in survival over the past 20 years (41).

Data regarding time to outcome were not available; thus, it is not possible to know which scoring system would provide earliest detection. Though this may be relevant to the ED setting, there is not a detectable mortality difference. Given that ICU utilization itself is an outcome, lack of standardization across sites for criteria for ICU admission is a limitation. The effect of any potential differences in ICU admission patterns across sites was likely small, given that the analysis of differences in accuracy across the scores for other measures associated with ICU level of care (such as intubation and vasopressors) were not substantially different. Given that our dataset only spans a single year (2009), we were not about to account for secular trends in pneumonia treatment. Finally, patients with DNI orders or hospice/comfort measures only status were excluded from the original LIPS study cohort, thus limiting extrapolation of our findings in this population.

CONCLUSIONS

Among this cohort of ED patients with pneumonia, qSOFA was no more accurate than SIRS for predicting in-hospital death, however, qSOFA was more accurate at predicting the composite outcome of hospital mortality and ICU stay ≥ 3 days. Several popular pneumonia-specific severity scores—CRB score, CRB-65 score, and DS CRB-65 score—performed nearly identically to qSOFA score in terms of predicting death and markers of ICU utilization. Given that the primary outcome of mortality was uncommon in this cohort, future research should focus on validating the scores with a larger sample size.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jemermed.2019.08.043.

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ARTICLE SUMMARY

1. Why is this topic important?

Pneumonia is the leading cause of sepsis and a frequent contributor to mortality. The Quick Sepsis-Related Organ Failure Assessment (qSOFA) score was developed to identify risk for mortality in sepsis; however, the accuracy of the qSOFA score among emergency department (ED) patients with pneumonia is not known.

2. What does this study attempt to show?

This study compares the test characteristics of the qSOFA score to the accuracy of existing pneumonia severity scores, including systemic inflammatory response syndrome score (SIRS), Confusion, Respiratory Rate and Blood Pressure (CRB), Confusion, Respiratory Rate, Blood Pressure and Age (CRB-65), and DS CRB-65, which is based on the CRB-65 score and includes two additional items—presence of underlying comorbid disease and blood oxygen saturation—for predicting mortality among ED patients with pneumonia.

3. What are the key findings?

The SIRS criteria had the highest sensitivity for death, but the lowest specificity, while CRB and qSOFA had the highest specificity for mortality but the lowest sensitivity. Overall, there was no significant difference in accuracy between any of the scores.

4. How is patient care impacted?

The qSOFA score requires no laboratory values for calculation and is the simplest of the five pneumonia severity scores evaluated. This study provides further support for ED clinicians who elect to use the qSOFA score. These findings may help to simplify the increasingly crowded and complex landscape of illness severity scores for ED clinicians.