

# Comparison of Predictive Scoring Systems in Assessing Risk for Intensive Care Unit Admission and In-Hospital Mortality in Patients with Urinary Tract Infections

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**Cite this article as:** Bae SJ, Lee JH, Choi YH. Comparison of Predictive Scoring Systems in Assessing Risk for Intensive Care Unit Admission and In-Hospital Mortality in Patients with Urinary Tract Infections. J Crit Intensive Care 2022;13:25–31

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**Received:** Dec 17, 2021

**Accepted:** Dec 24, 2021

**Available online:** Feb 10, 2022

## ABSTRACT

**Objective:** We aimed to investigate the effectiveness of confusion, respiratory rate, blood pressure (CRB), CRB-65, and quick sequential organ failure assessment (qSOFA) in predicting intensive care unit (ICU) admission and in-hospital mortality of patients with urinary tract infections (UTI) compared with Systemic Inflammatory Response Syndrome (SIRS).

**Methods:** Data of patients with UTI who visited the emergency department of a single centre between February 2018 and March 2020 were retrospectively analysed. Baseline characteristics were compared with the prevalence of ICU admission and in-hospital mortality. The effectiveness of CRB, CRB-65, qSOFA, and SIRS as indicators of ICU admission and in-hospital mortality were evaluated using the area under the receiver operating characteristic (AUROC) curve.

**Results:** Overall, 1151 patients were included, of whom 132 (11.5%) were admitted to the ICU and 30 (2.6%) succumbed to in-hospital mortality. AUROC values of CRB, CRB-65, and qSOFA as predictors of ICU admission and in-hospital mortality were similar. CRB score  $\geq 1$  had a sensitivity and specificity of 71.3% and 73.5%, respectively, for ICU admission; 66.7% and 69.2%, respectively, for in-hospital mortality. CRB-65 score  $\geq 2$  had a sensitivity and specificity of 61.2% and 80.9%, respectively, for ICU admissions; 60% and 76.9%, respectively, for in-hospital mortality. A qSOFA score  $\geq 1$  had a sensitivity and specificity of 71.3% and 79.6%, respectively, for ICU admission; 66.7% and 74.8%, respectively, for in-hospital mortality. AUROC values of SIRS were 0.580 and 0.617 respectively for ICU admission and in-hospital mortality, which showed lower predictive performance than those of the other three scoring systems.

**Conclusion:** In ICU admission, CRB, CRB-65, and qSOFA have better predictive performance than SIRS. CRB-65 and qSOFA have superior performance compared to CRB and SIRS in predicting mortality.

**Keywords:** Emergency Departments, In-hospital Mortality, Intensive Care Units, Risk Assessments, Urinary Tract Infections

## Introduction

A systematic response to infection is termed sepsis, which can lead to life-threatening organ dysfunction (1, 2). Early recognition of sepsis is critical for improving patient outcomes. In approximately 20%–30% of patients, sepsis resulted from urinary tract infection (UTI). In 1992, the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) gave recommendations to better define sepsis (3). This definition was revised and expanded in 2001, and the most recent update was made by the Sepsis-3 task force in 2016 (4, 5). The task force proposed the use of sequential (sepsis-related) organ failure assessment (Sequential Organ Failure Assessment [SOFA]) score as a measure of organ dysfunction. In addition, they proposed the quick

SOFA (qSOFA), which is a simplified version of the SOFA that comprises only three variants (altered mental status, systolic blood pressure,  $\leq 100$  mmHg, and respiratory rate,  $\geq 22$ /min) (5, 6). In addition, many severity scoring systems have been developed to identify critically ill patients, such as the Acute Physiology and Chronic Health Evaluation (APACHE) and the Multiple Organ Dysfunction Score (MODS) (7). However, these scoring systems are difficult to apply in the early phase of treatment in the emergency department (ED) because the results of some parameters are based on laboratory tests. On the other hand, CRB and CRB-65 scoring systems, which were designed primarily to predict mortality in patients with pneumonia as a simplified system of CURB-65 (confusion, urea  $> 7$  mmol/L, respiratory rate  $\geq 30$ /minute, low systolic [ $< 90$  mmHg] or diastolic [ $\leq 60$



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mmHg] blood pressure, age  $\geq 65$  years), contain only a few simple variables. The CRB scoring criteria are similar to those of qSOFA and include only clinical features available from a clinical assessment without laboratory tests (8). Moreover, qSOFA is used as a tool for screening organ dysfunction and has recently been used to assess disease severity in patients with other diseases such as pneumonia and liver cirrhosis (9, 10).

In approximately 20%–30% of patients, sepsis resulted from urinary tract infection (UTI) (11). Due to the anatomical, clinical, and pathophysiological differences of infectious causes, effectiveness of scoring systems in predicting disease severity may differ depending on the disease. Previous studies on this subject have primarily focused on patients suspected with infection (12, 13).

In this study, we investigated the performance of CRB, CRB-65, and qSOFA to predict intensive care unit (ICU) admission and in-hospital mortality in UTI patients and determined the appropriate cut-off values. We also compared them with the system inflammatory response syndrome (SIRS), which has been used previously.

## Materials and methods

### Study design

This was a single-centre retrospective study performed using the electronic medical records (EMRs) of patients who visited the ED. The study design was approved by the Institutional Review Board, and the requirement for written informed consent was waived.

### Study setting and population

This study included patients who visited an urban, tertiary, academic hospital with 65,000 annual emergency visits between February 2018 and March 2020. The inclusion criteria were (1) an age of 18 years or more, (2) ED diagnosis of urinary tract infection, based on international classification of diseases (ICD)-10. Patients who visited for non-medical purposes and who had missing data, including vital sign and laboratory test results, were excluded.

### Data collection and outcome measurement

Two board-certified emergency physicians selected all ED patients with ED diagnosis of urinary tract infection based on ICD-10. We collected data from each patient's EMR. The collected data were (1) patient demographics, including sex and age; (2) initial vital signs in the ED, including systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate, body temperature, and mental status; (3) clinical details, including laboratory findings, such as white blood cell (WBC) count, neutrophil count, lymphocyte count, platelet count, levels of c-reactive protein (CRP), serum blood urea nitrogen (BUN), and serum creatinine; (4) The ED treatment results, which could be hospital discharge, general ward (GW) admission, or ICU admission. CRB was defined by confusion, respiratory rate  $\geq 30$ /minute, and low systolic [ $<90$  mmHg] or diastolic [ $\leq 60$  mmHg] blood pressure. CRB-65 was defined by confusion, respiratory rate  $\geq 30$ /minute, low systolic [ $<90$  mmHg] or diastolic [ $\leq 60$  mmHg] blood pressure, and age  $\geq 65$  years. The qSOFA criteria

were defined by SBP  $\leq 100$  mmHg, respiratory rate  $\geq 22$  breaths/min and Glasgow Coma Score (GCS)  $\leq 13$ . SIRS was defined by body temperature  $>38$  °C or  $<36$  °C, heart rate  $>90$  beat/min, respiratory rate  $>20$  breath/min and white blood cell count  $>12,000/\text{mm}^3$  or  $<4000/\text{mm}^3$ . The primary outcome was ICU admission. The secondary outcome was in-hospital mortality. Due to all patients included in the study were patients whose inpatient treatment was terminated, in-hospital mortality was defined as patients who died during the entire admission period.

### Statistical analyses

In this study, the ICU positive group (ICU [+]) group consisted of patients who were admitted to the ICU and the ICU negative group (ICU [-]) group consisted of those who were discharged or transferred to the GW. The mortality positive group (mortality [+]) group comprised patients who died in the hospital, and the mortality negative group (mortality [-]) group comprised those who survived and were discharged. Differences in the baseline characteristics were summarized using the independent t-test performed for continuous variables and Pearson's chi-squared test or Fisher's exact test performed for categorical variables. Continuous variables are presented as means with standard deviations (SD) and ranges, while categorical variables are presented as count (percent).

The predictive accuracy of CRB, CRB-65, qSOFA, and SIRS for ICU admission and in-hospital mortality was evaluated using the area under the receiver operating characteristic (AUROC) curve. AUROC curve between 0.8–0.9 is described as “good”, between 0.7–0.8 is described as “adequate”, and between 0.6–0.7 is described as “poor” performance (14). The optimal cut-off values of each scoring system were determined by the Youden index of ROC curves (15). Additionally, the sensitivity, specificity, and positive and negative predictive value with 95% CI were used to estimate the prognostic accuracy of each criteria for the proposed cut-off values. The significance level was considered as  $p$  value  $<0.05$ . Statistical analyses were performed using SPSS for Windows Version 26.0 (Armonk, NY: IBM Corp). The standard error of the area under the curve (AUC) and of the difference between two AUCs were calculated using the same method as DeLong et al. (16). The ROC curve analysis was performed using the MedCalc Statistical Software version 19 (MedCalc Software bvba, Ostend, Belgium).

## Results

### Patient characteristics of study population

A total of 1151 patients were enrolled for the study. The baseline characteristics are presented in Table 1. The mean age of all the patients was 63.2 years (SD: 19.6), and 24.3% were male. Of all the patients, 132 (11.5%) were admitted to the ICU and 30 (2.6%) succumbed to in-hospital mortality. The ICU [+] group had significantly lower systolic and diastolic blood pressures (SBP and DBP), higher pulse rate (PR), and respiratory rate (RR) than the ICU [-] group. The ICU [+] group had significantly higher WBC count, neutrophil count, BUN, creatinine, CRP, lower lymphocyte count, and platelet count than the ICU [-] group.

**Table 1.** General characteristics of patients in the study cohort

Variable	Total (n=1,151)	ICU admission		p-value	In-hospital mortality		p-value
		Negative (n=1019)	Positive (n=132)		Negative (n=1121)	Positive (n=30)	
Age (years)	63.2±19.6	61.7±20.0	74.5±11.4	<0.001	62.8±19.6	80.3±11.0	<0.001
Sex				0.981			0.989
Male	280 (24.3)	248 (24.3)	32 (24.8)		273 (24.4)	7 (23.3)	
Female	868 (75.7)	771 (75.7)	100 (75.8)		848 (75.6)	23 (76.7)	
Vital sign							
Systolic blood pressure (mmHg)	126.2±24.5	129.0±22.4	104.1±28.4	<0.001	126.6±24.0	110.9±34.1	0.018
Diastolic blood pressure (mmHg)	69.3±15.3	70.7±14.3	58.4±17.7	<0.001	69.6±15.2	58.7±15.5	<0.001
Heart rate(/min)	98.7±18.8	98.0±18.1	103.4±23.1	0.011	98.5±18.7	106.2±19.7	0.025
Respiratory rate(/min)	20.2±1.9	20.1±1.7	21.0±2.9	0.002	20.2±1.8	22.0±3.6	0.009
Body temperature (°C)	37.9±1.1	38.0±1.1	37.8±1.2	0.119	38.0±1.1	37.2±1.0	0.001
Mental status				<0,001			<0.001
Alert	1,084 (94.2)	982 (96.4)	102 (77.3)		1,062 (94.7)	22(73.3)	
Verbal response	41 (3.6)	22 (2.2)	19 (14.4)		37 (3.3)	4 (13.3)	
Painful response	26 (2.3)	15 (1.5)	11 (8.3%)		22 (2.0)	4 (13.3)	
Unresponsive	0	0	0		0	0	
Laboratory finding							
WBC (x10 <sup>3</sup> /μl)	12.1±6.1	11.7±5.2	15.1±10.1	<0.001	12.0±5.8	17.3±11.9	0.020
Neutrophil (x10 <sup>3</sup> /μl)	10.0±5.7	9.6±4.8	13.3±9.7	<0.001	9.9±5.5	14.2±9.4	0.019
Lymphocyte (x10 <sup>3</sup> /μl)	1.2±0.7	1.2±0.7	1.0±0.7	<0.001	1.2±0.7	1.0±0.7	0.177
Platelet (x10 <sup>3</sup> /μl)	221.6±92.9	227.2±91.5	177.6±92.6	<0.001	222.8±91.9	176.7±120.2	0.046
BUN (mg/dL)	21.8±17.5	19.6±14.7	38.0±26.2	<0.001	21.2±16.8	42.2±28.4	<0.001
Creatinine (mg/dL)	1.2±1.0	1.1±0.8	2.0±1.6	<0.001	1.2±0.9	2.0±1.9	0.018
C-reactive protein (mg/dL)	10.0±8.9	9.2±8.5	16.3±9.8	<0.001	9.9±8.9	15.7±8.8	<0.001

Quantitative data are expressed as mean ± standard deviation, categorical data are presented as number of subjects (percentages). Independent t-test was used for continuous variable analysis, while chi-squared test or Fisher's exact test were used for categorical variable analysis as appropriate. ICU: Intensive Care Unit, WBC: White Blood Cell, BUN: Blood Urea Nitrogen

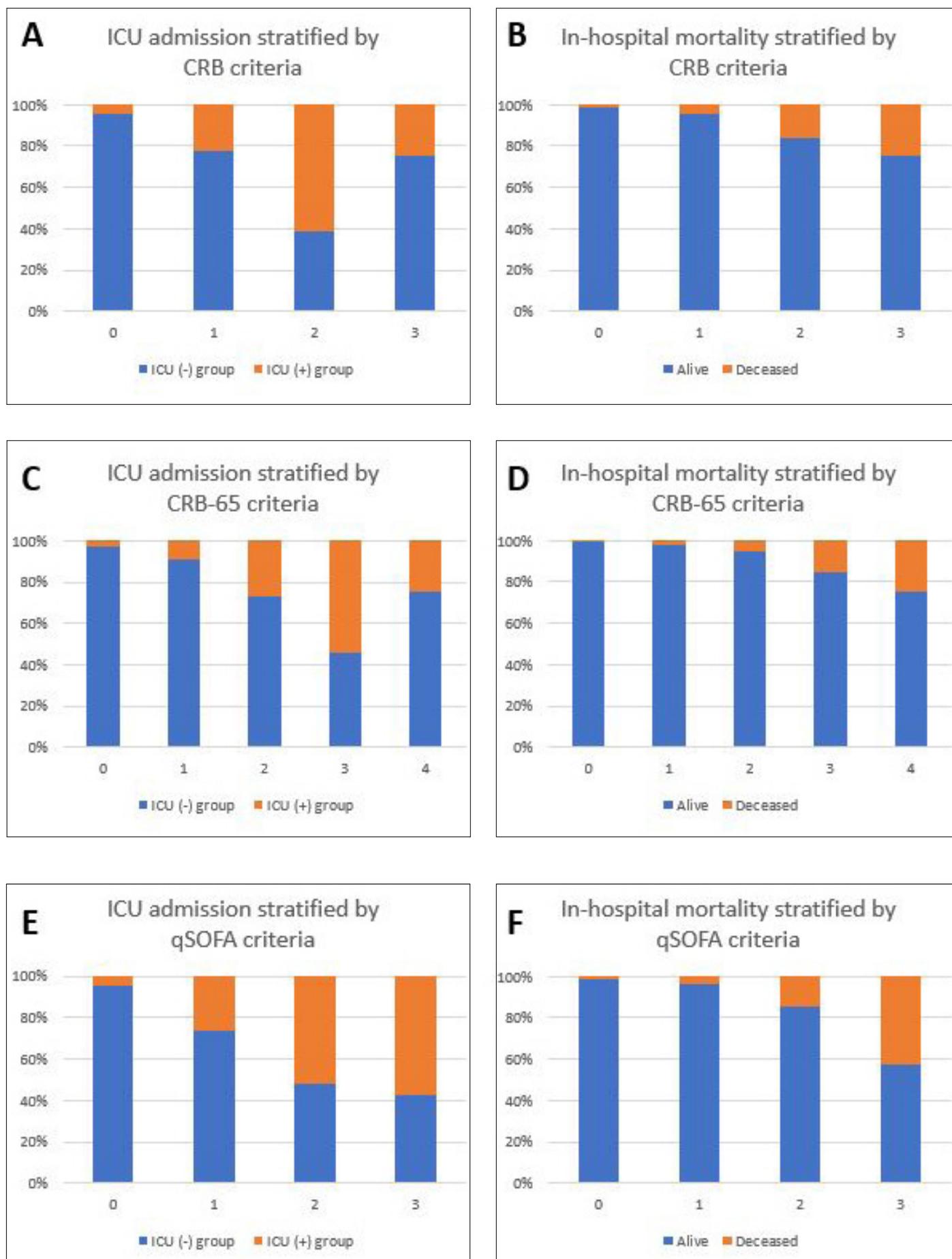
The mortality [+ ] group had lower SBP, DBP, body temperature, and higher PR and RR than the mortality [- ] group. The mortality [+ ] group had higher WBC count, neutrophil count, BUN, creatinine, CRP, and lower platelet count than the mortality [- ] group.

### Score distribution of CRB, CRB-65, and qSOFA according to ICU admission and in-hospital mortality

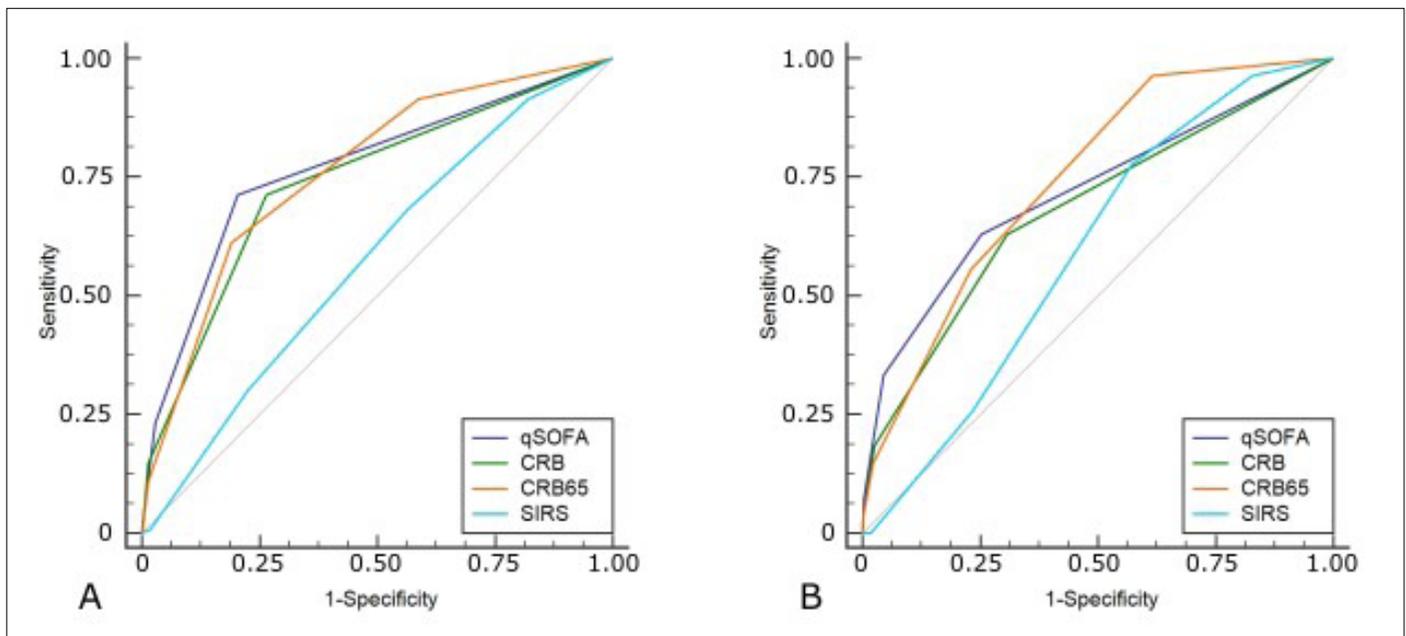
Among the criteria, only CRB, CRB-65, and qSOFA, not SIRS, showed significant differences in the score distribution with respect to ICU admission and in-hospital mortality. The number of patients with ICU admission and in-hospital mortality, according to the CRB, CRB-65, and qSOFA scores, are shown in Figure 1. In case of CRB and qSOFA, the ratio of 0 points in the ICU [- ] group and the ratio of 1,2,3 points in the ICU [+ ] group were relatively high. In the case of CRB-65, the ratio of 0,1 point in ICU [- ] and 2,3,4 point in ICU [+ ] group were relatively high. For mortality, CRB, CRB-65, and qSOFA score distributions were significantly different, and their results were the same as those for ICU admission. In the case of SIRS, there was no significant difference in score distribution (p=0.126).

### Validation of CRB, CRB-65, qSOFA, and SIRS for ICU admission and in-hospital mortality

The ROC curves of CRB, CRB-65, qSOFA, and SIRS are depicted in Figure 2. For predicting ICU admission, the AUROCs of CRB, CRB-65, qSOFA, and SIRS were 0.742 (95% CI 0.716–0.767), 0.765 (95% CI 0.740–0.790), 0.772 (95% CI 0.747–0.796), and 0.580 (95% CI 0.551–0.609), respectively (Figure 2A). AUROCs in each criterion were statistically significant, but when compared between the two criteria, CRB vs SIRS, CRB-65 vs SIRS, and qSOFA vs SIRS were significantly different (p < 0.001). The differences between each AUROC were 0.162 (95% CI, 0.097–0.226), 0.185 (95% CI, 0.125–0.245), and 0.192 (95% CI, 0.133–0.251), respectively. For in-hospital mortality, the AUROCs of CRB, CRB-65, qSOFA and SIRS were 0.702 (95% CI 0.674–0.728), 0.761 (95% CI 0.735–0.785), 0.740 (95% CI 0.714–0.765), and 0.617 (95% CI 0.588–0.645), respectively (Figure 2B). All of these were also statistically significant (p < 0.001). When comparison was made between the two criteria for in-hospital mortality, CRB vs CRB-65, CRB-65 vs SIRS, and qSOFA vs SIRS were significantly different (p values were 0.04, 0.02 and <0.01, respectively). The differences between each AUROC were 0.059 (95% CI, 0.009–0.110), 0.147 (95% CI, 0.037–0.257), and 0.126 (95% CI, 0.05–0.248), respectively.



**Figure 1.** Score distribution of CRB, CRB-65, qSOFA and SIRD according to ICU admission and in-hospital mortality



**Figure 2.** ICU admission (A) and In-hospital mortality (B) receiver operating characteristic curve for qSOFA, CRB, CRB-65, and SIRS

**Table 2.** AUROC, cut-off value, sensitivity and specificity for ICU admission and in-hospital mortality

	Cut-off value	AUROC (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	+PV (95%CI)	-PV (95%CI)
<b>ICU admission</b>						
CRB	1	0.742 (0.716–0.767)	71.3 (62.7–78.9)	73.5 (70.7–76.2)	26.0 (23.3–29.0)	95.3 (93.9–96.4)
CRB-65	2	0.765 (0.740–0.790)	61.2 (52.3–69.7)	80.9 (78.3–83.2)	29.6 (25.9–33.6)	94.3 (93.0–95.4)
qSOFA	1	0.772 (0.747–0.796)	71.3 (62.7–78.9)	79.6 (77.0–82.0)	31.4 (28.0–34.9)	95.6 (94.3–96.7)
SIRS	1	0.580 (0.551–0.609)	68.2 (59.4–76.1)	43.6 (40.5–46.7)	13.7 (12.2–15.2)	91.5 (89.3–93.4)
<b>In-hospital mortality</b>						
CRB	1	0.702 (0.674–0.728)	66.7 (47.2–82.7)	69.2 (66.4–71.9)	5.5 (4.2–7.0)	98.7 (97.9–99.2)
CRB-65	2	0.761 (0.735–0.785)	60.0 (40.6–77.3)	76.9 (74.3–79.3)	6.5 (4.8–8.7)	98.6 (97.9–99.1)
qSOFA	1	0.740 (0.714–0.765)	66.7 (47.2–82.7)	74.8 (72.1–77.3)	6.6 (5.1–8.5)	98.8 (98.1–99.3)
SIRS	1	0.617 (0.588–0.645)	80.0 (61.4–92.3)	42.7 (39.8–45.7)	3.6 (3.0–4.3)	98.8 (97.5–99.4)

CRB: Confusion, Respiratory rate, Blood pressure; CRB - 65: Confusion, Respiratory rate, Blood pressure, age >65; qSOFA: quick Sequential Organ Failure Assessment; SIRS: Systemic Inflammatory Response Syndrome; ICU: Intensive Care Unit; AUROC: Area Under the Receiver Operating Characteristic; CI: Confidence Interval; +PV: Positive Predictive Value; - PV: Negative Predictive Value

The cut-off values and the sensitivity and specificity of each criterion are shown in Table 2.

## Discussion

The Sepsis-3 task force emphasized that sepsis was the primary cause of death from infection, especially if not recognized and treated early. Thus, its identification requires urgent attention (5). Continuous monitoring, according to the degree of priority assigned during triage, allows for the rapid identification of sepsis (17). Nonetheless, attempts to identify patients with sepsis at the triage stage have continued (18). Hayden et al. evaluated the efficacy of a sepsis work-up and treatment (SWAT) protocol for rapid identification of sepsis during triage (19). Although the qSOFA score was recommended by the Sepsis-3 task, its usefulness has remained debatable. Previously, several studies compared the accuracy of different scoring systems, such as qSOFA, SIRS, and SOFA. Raith et al. reported that an increase in SOFA score of 2 or more points indicated greater prognostic

accuracy for in-hospital mortality than SIRS or qSOFA (20). On the other hand, Park et al. found that qSOFA is more effective than SIRS in predicting the occurrence of organ failure in patients with suspected infection (21).

In the investigation of pneumonia, CRB and CRB-65 scoring systems are easy to use, especially in those cases where laboratory result of blood, urea, and nitrogen is unavailable (22, 23). These systems were proven highly effective in predicting the prognosis and were used widely for several years (24). In previous studies for pneumonia, CRB and CRB-65 were similar and did not provide additional predictive performance compared with qSOFA (9, 25). Both CRB and qSOFA had three identical vital signs as criteria: respiratory rate, mental status, and blood pressure. Although CRB and qSOFA used the same vital signs as mentioned above, the thresholds for respiratory rate and blood pressure were stricter for CRB than for qSOFA (CRB: respiratory rate >30, systolic blood pressure <90 or diastolic blood pressure ≤60; qSOFA: respiratory rate ≥22, systolic

blood pressure  $\leq 100$ ). Therefore, CRB was expected to be more effective in predicting outcomes (ICU admission and in-hospital mortality) than qSOFA. CRB-65 used an added parameter of age  $\geq 65$  years, so it was expected to provide additional predictive performance. However, in this study, the AUROCs of CRB, CRB-65, and qSOFA revealed similar effectiveness in the prediction of outcomes. In addition, these differences were not statistically significant, but when compared with SIRS, CRB and CRB-65 were significantly more effective in predicting ICU admission. The AUROC value of SIRS for predicting ICU admission was  $< 0.6$ , which indicated its poor effectiveness. On the other hand, AUROC values of CRB and CRB-65 were between 0.7 and 0.8, which is described as “adequate”. For predicting in-hospital mortality, only CRB-65 provided better predictive performance than SIRS. AUROC values of CRB-65 were between 0.7 and 0.8, which was quite accurate. In the comparison between CRB and CRB-65, despite the addition of age as a parameter, CRB-65 was statistically superior only in predicting in-hospital mortality ( $p = 0.02$ ). In previous studies that compared the effectiveness of prediction by qSOFA and SIRS in UTI patients, qSOFA had a higher predictive accuracy for in-hospital mortality and ICU admissions than SIRS (26, 27). Likewise, in our study, the ability of qSOFA to identify the requirement of ICU admission and in-hospital mortality in patients with UTI was better than that of SIRS.

There are several limitations to this study. Firstly, this was a single-centre, retrospective study. Thus, selection bias may exist because of the limited sample size available from a single institute. Therefore, caution should be used in generalizing our results, and further studies are required with multi-centre, prospective designs for generalization. Secondly, patients with UTI, especially the elderly, tended to have co-morbidities. Thus, multiple organ dysfunction syndrome may have affected the prognosis. Lastly, being a large tertiary academic hospital, our institution receives patients transferred from smaller hospitals and primary healthcare institutions who are already in a poor condition. Thus, their mortality is generally higher than normal, which may result in inaccurate study results.

In conclusion; CRB, CRB-65, and qSOFA have better predictive performance than SIRS with regard to the initial assessment of patients with UTI. CRB-65, and qSOFA have superior performance compared to CRB and SIRS in predicting mortality, however the prediction performance of the risk for intensive care unit admission was not significantly different between CRB, CRB-65 and qSOFA.

#### AUTHOR CONTRIBUTIONS:

**Concept:** YHC; **Design:** YHC; **Supervision:** YHC; **Materials:** SJB; **Data Collection and/or Processing:** SJB, JHL; **Analysis and/or Interpretation:** SJB, JHL; **Literature Search:** SJB; **Writing Manuscript:** SJB, JHL; **Critical Review:** YHC

**Ethics Committee Approval:** This study was approved by the institutional review board of Ewha Womans University Mokdong Hospital, and the requirement for written informed consent was waived. (IRB No. 2020-06-044)

**Informed Consent:** The requirement for written informed consent was waived.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** Authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

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