Original Article

Feasibility of the qSOFA Score Compared with the Modified Early Warning Score at ER Visit to Predict 24-Hour In-Hospital Cardiac Arrest: A Retrospective Review

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Background: The quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) is a simple test to predict in-hospital cardiac arrest (IHCA) from sepsis but its role to predict from overall causes is unknown. The modified early warning score (MEWS) is another scoring system to predict IHCA but a low MEWS cannot rule out IHCA and it is more difficult to calculate than the qSOFA.

Objective: The authors sought to determine the correlation of the qSOFA and 24-hour IHCA with the MEWS.

Materials and Methods: The present report was a retrospective case-control study that included adult patients who had IHCA within 24 hours after presenting to the emergency department (ED). The control cases were randomly selected from ESI levels 1 to 3. The scores were calculated at the initial presentation. The primary outcome was 24-hour IHCA. Predictors of the outcome were identified with binary logistic regression. ROC curves compared the predictive ability.

Results: Of the 19,522 ED visits, 35 patients were enrolled as the study cases and 140 patients as controls. High-risk qSOFA (2 or greater) was a significant predictor for 24-hour IHCA (OR 3.9, 95% CI 1.59 to 9.58) ($p<0.05$), but high-risk MEWS (5 or greater) was not (OR 1.86, 95% CI 0.83 to 4.11) ($p=1.28$). The AUC of the qSOFA score was also higher than the MEWS (0.736 versus 0.622) ($p<0.05$).

Conclusion: High-risk qSOFA is significantly correlated with 24-hour IHCA. The qSOFA scores of 2 or 3 are four times more likely to have 24-hour IHCA than scores of 0 or 1. The qSOFA tends to better predict 24-hour IHCA than the MEWS.

Keywords: qSOFA, MEWS, IHCA, In-hospital cardiac arrest

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According to the 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, searching for dangerous clinical risks has been involved in the first chain of in-hospital cardiac arrest (IHCA) chain of survival[1]. Together with developing a Rapid Response Team to respond to these deteriorating patients, it may help to reduce the mortality and morbidity from cardiac arrest. Many scoring systems have been developed to activate those teams or to select patients for close monitoring.

The quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) score is a new simple screening tool to predict in-hospital mortality from sepsis. The qSOFA includes respiratory rate (RR) of 22 or more per minute, systolic blood pressure (SBP) of 100 mmHg or less, and altered mental status[2]. The original study proved that sepsis patients with qSOFA of 2 or more were associated with a high-risk of IHCA and its predictive ability is on par with other complicated scoring systems[3].

Use of the qSOFA to predict in-hospital mortality from sepsis was validated and compared to other common scores in many studies. Chen et al[4] compared the qSOFA with the CRB-65 rule (confusion, respiratory rate of 30 or more per minute, systolic

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blood pressure of 90 mmHg or less, or diastolic blood pressure of 60 mmHg or less, and age of 65 years or older) in predicting the 28-day mortality rate in pneumonia patients. Results showed that patients with qSOFA scores of 2 or 3 had a higher prevalence of mortality compared to the CRB-65 rule and both had similar predictive ability. Another study by Wang et al[5] found the same results in predicting 28-day mortality in infectious patients compared to the sequential (sepsis-related) organ failure assessment (SOFA) and the Acute Physiology and Chronic Health Evaluation (APACHE) II.

The modified early warning score (MEWS) is another commonly used vital sign-based scoring system with five parameters. A MEWS greater than 5 is significantly associated with IHCA (OR 5.4, 95% CI 2.8 to 10.7)[6]. Furthermore, the MEWS showed good predictive ability to predict 48- and 72-hour IHCA in previous studies[6,7].

Importance

Although the qSOFA proved to be a good short term (28-day) mortality predictor for sepsis patients, its role to predict mortality from overall causes of life threatening organ dysfunction as the initial presentation is unknown[3]. In comparison, the MEWS can predict IHCA in 48 hours from overall causes, but it needs more meticulously measured vital signs and a complicated scoring system, which can result in human errors when doing the calculation in a busy emergency department (ED). In the authors' study, the authors expected that a qSOFA of 2 or more could also predict IHCA from any cause because each of the three components of the score represents problems in major organs that the body should preserve. Failure to preserve normal functions of more than one major organ shows the severity of a disease and risk for cardiac arrest in these patients.

Objective

In the present study, the authors aimed to investigate the correlation of the qSOFA score in both infectious and non-infectious ED patients with the 24-hour in-hospital mortality rate and compare its predictive performance with the MEWS and help decide which patient in the ED needs close monitoring in the first 24 hours.

Materials and Methods

Study design and setting

This was a single-center retrospective case-control study conducted in the ED of an academic, tertiary care 800-bed hospital in Songkhla Province, Thailand with an annual ED census of approximately 25,000 patients per year. The present study was approved by the Institutional Review Board of Faculty of Medicine, Prince of Songkla University (EC 59-245-20-4).

Selection of participants

The authors reviewed the medical charts of patients that visited the ED between January and December 2015. The study enrolled all patients older than 18 years old triaged as Emergency Severity Index (ESI) level 1 to 3 at the time they presented to the ED. Trauma patients, patients who needed operative treatment, patients who had out-of-hospital cardiac arrest, patients with a Do Not Resuscitate order, or patients who decided for palliative therapies were excluded. Patients who received cardiopulmonary resuscitation, received sedatives, induction agents, or vasopressors before arriving at the ED were also excluded. If the level of consciousness or the vital signs of the patients were not completely recorded in the chart, they were also excluded. The authors enrolled patients who had IHCA within 24 hours after presenting to the ED as the study cases and those patients who did not have IHCA in 24 hours as the control group.

Methods and measurements

The qSOFA and MEWS scores were calculated from the initial presentation data at the ED by the researchers. Data on the timing before IHCA, causes of IHCA, intensive care unit (ICU) admission, advanced resuscitation procedures, return of spontaneous circulation (ROSC) rate, and survival-to-discharge rate were also collected. The data were abstracted from the electronic medical record by two researchers and recorded in the study case record form. The data were cross-checked before encoding to the database by a research assistant.

Outcomes

The charts were reviewed until the patients were discharged from the hospital after the same ED visit. The primary outcome was 24-hour IHCA, defined as prevalence of cardiac arrest within 24 hours after presentation at the ED. The secondary outcomes were cause of cardiac arrest, ICU admission rate, ROSC rate, and survival-to-discharge rate.

Definition of variables

Advanced resuscitation procedures encountered

included vasopressors, central venous catheter, endotracheal tube, electrical or medical cardioversion, non-invasive positive pressure ventilation, acute hemodialysis, extracorporeal membrane oxygenation (ECMO), intercostal drainage, and percutaneous coronary intervention that the patient received before cardiac arrest. ROSC was defined as return of pulse or measurable blood pressure generated by the patient (not ECMO) for at least 30 seconds[8]. Diabetes mellitus included insulin-dependent and non-insulin-dependent types. Renal disease indicated mainly chronic renal failure (including patients undergoing dialysis). Liver disease was cirrhosis of any severity. Chronic obstructive pulmonary disease (COPD) was defined as a previous diagnosis of COPD. Cardiovascular disease was defined as coronary artery disease (angina or previous myocardial infarction) and/or congestive heart failure (any class of the system set by the New York Heart Association). Cerebrovascular diseases were defined as stroke whether ischemic or hemorrhagic. Cancer was defined as a neoplasm of any type. Immunocompromised patients were defined as immunodeficiency from any cause and/or using immunosuppressive drugs.

Statistical analysis

The correlation of predictive score and primary outcome was measured by binary logistic regression and expressed in odds ratio with 95% confidence interval (CI). The predictive scores were dichotomized into high-risk and low risk groups. The qSOFA high-risk group was defined as qSOFA of 2 or more, and MEWS high-risk group as MEWS of 5 or more[9]. Continuous variables with normal distribution were presented as mean with standard deviation and used the student t-test to determine the differences between the groups. Other skewed variable differences used the Mann-Whitney U test and were expressed in median and inter-quartiles range. The authors dichotomized the vital signs into positive score (1 or more) (temperature of 36.0 or less or more than 38.0, SBP of 100 mmHg or less, heart rate of 120 beats or more per minute, respiratory rate of 22 or more per minute, oxygen saturation of 90% or less, and altered mental status) and negative score (=0) that correlated with the qSOFA and MEWS. Causes of cardiac arrest were also grouped into infectious and non-infectious causes. Categorical data were expressed in percentage and the differences were determined using the Chi-square test. Receiver operating characteristic (ROC) curves were used to compare the qSOFA and MEWS predictive abilities. The measurements were statistically significant at p value of less than 0.05. All statistical analyses were performed with R software version 3.3.1 (R foundation for statistical computing, Vienna, Austria).

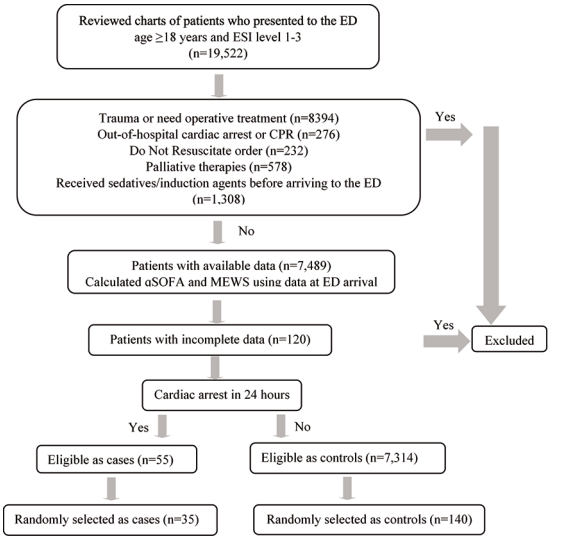

Figure 1. Patient enrollment flow chart.

The sample size was estimated with n4Studies (version 1.4.0; Prince of Songkla University, Thailand)[10]. The authors' power analysis was based on an estimate from the authors' preliminary data and the previous literature[3-5]. The sample size was calculated based on the assumption that the true odds ratio for cardiac arrest in 24 hours in the study case subjects relative to control was 3. The authors needed to study approximately 30 case-patients with four controls per case to be able to reject the null hypothesis with an 80% of power and a 2 sided-alpha of 0.05. After continuity correction, the authors included 35 patients as the study group and 140 patients in the control group.

Results

After reviewing the electronic medical records, 19,522 patients were screened for the study and 12,033 patients were excluded. The authors also excluded 120 patients for incomplete data. There were 55 patients who had cardiac arrest in 24 hours and grouped as the study cases. In an objective manner, a blinded research assistant used Microsoft Excel to randomly enrolled 35 study cases and 140 controls into the present study. The flow of patient enrollment is shown in Figure 1.

Characteristics of study subjects

The study case and the control groups were similar

Table 1. Baseline characteristics

Characteristics	Entire cohort (n = 175) n (%)	Case group (n = 35) n (%)	Control group (n = 140) n (%)	p-value
Age (years), Mean (SD)	67.42 (18.6)	69.26 (17.3)	66.96 (19.0)	0.516
Sex: male	106 (60.6)	25 (71.4)	81 (57.9)	0.142
Underlying diseases				0.263
DM	27 (15.4)	9 (25.7)	18 (12.8)	0.165
Cardiovascular disease	33 (18.9)	6 (17.1)	27 (19.3)	0.524
Renal failure	10 (5.7)	4 (11.4)	6 (4.3)	0.249
Cerebrovascular disease	12 (6.8)	6 (17.1)	6 (4.3)	0.473
Cancer	39 (22.3)	6 (17.1)	33 (23.4)	0.592
COPD	15 (8.6)	0 (0.0)	18 (10.7)	0.025
Liver failure	22 (12.6)	2 (5.7)	20 (14.3)	0.502
Immunocompromised	17 (9.7)	2 (5.7)	15 (10.7)	0.353
ESI level				
1	58 (33.1)	12 (34.3)	46 (32.9)	0.873
2	69 (39.4)	20 (57.1)	49 (35)	0.016
3	48 (27.4)	3 (8.6)	45 (32.1)	0.005
Adjusted admission vital signs				
Temp ≤36.0 or >38.0	53 (30.3)	7 (20.0)	46 (32.9)	0.139
Systolic BP ≤100 mm Hg	39 (22.3)	16 (45.7)	23 (16.4)	<0.001
Heart rate ≥120 minute	36 (20.6)	7 (20.0)	29 (20.7)	0.926
Respiratory rate ≥22 minute	139 (79.4)	31 (88.6)	108 (77.1)	0.135
Oxygen saturation ≤90%	67 (38.2)	20 (55.9)	47 (33.8)	0.018
Mental status changes	91 (52.0)	28 (80.0)	63 (45.0)	<0.001
Severity score, Median (IQR)				
ESI	2 (1 to 3)	2 (1 to 2)	2 (1 to 3)	0.102
qSOFA	2 (1 to 2)	2 (2 to 3)	1 (1 to 2)	<0.001
MEWS	4 (3 to 6)	4 (3 to 7)	3 (2 to 6)	0.024
Causes of cardiac arrest				
Infectious	70 (40.0)	12 (34.3)	58 (41.4)	0.397
ROSC rate	48 (27.4)	20 (57.1)	28 (20.0)	0.014
ICU admission	27 (15.4)	6 (17.1)	21 (15.0)	0.918
Survival to discharge	84 (48.0)	7 (20.0)	77 (55.0)	<0.001

qSOFA=quick Sequential (Sepsis-Related) Organ Failure Assessment; ESI=Emergency Severity Index; MEWS=modified early warning score; COPD=chronic obstructive pulmonary disease; DM=diabetes mellitus; ROSC=return of spontaneous circulation; ICU=intensive care unit; SD=standard deviation; IQR=interquartile range

in age, sex, and underlying disease characteristics (Table 1). The study group had fewer COPD patients than the control group (0% versus 10.6%). The percentage of patients in the study group triaged as ESI level 3 was lower than the control group (8.6% versus 32.1%), whereas, more in the study group were triaged as ESI level 2 (57.1% versus 35%). However, the percentages were similar for ESI level 1 in both groups (34.3% versus 32.9%). The study group had lower SBP than the control group in both mean and adjusted admission vital signs. There were similar percentages of infectious patients in both groups (34% versus 41%, p=0.397). Although the study group received more advanced resuscitation procedures and had higher ROSC rate, survival to discharge in the study group was lower than in the control group (20% versus 55%, p<0.05). The ICU admission rate in both groups was similar.

Main results

The medians of the qSOFA score and MEWS were significantly higher in the study group (2 versus 1 and 4 versus 3, respectively, p<0.05) (Table 1). To determine the correlation of predictive scores

Table 2. High-risk predictive score models

Predictors		OR	95% CI		p-value
			Lower	Upper	
With qSOFA High risk	qSOFA	3.907	1.593	9.578	0.003
	Age	1.002	0.978	1.026	0.885
	Sex	0.612	0.252	1.489	0.279
	DM	1.478	0.581	3.760	0.412
	Liver failure	0.499	0.097	2.581	0.407
	Renal failure	1.476	0.528	4.127	0.458
	COPD	0.000	0.000		0.998
	Cardiovascular	0.904	0.334	2.444	0.843
	Cerebrovascular	0.977	0.344	2.774	0.965
	Cancer	0.707	0.202	2.472	0.587
	Immunocompromised	0.401	0.046	3.531	0.410
	Constant	0.208			0.130
With MEWS High risk	MEWS	1.857	0.837	4.116	0.128
	Age	1.008	0.984	1.031	0.529
	Sex	0.552	0.230	1.322	0.182
	DM	1.670	0.676	4.129	0.267
	Liver failure	0.487	0.097	2.430	0.380
	Renal failure	1.305	0.487	3.498	0.597
	COPD	0.000	0.000		0.998
	Cardiovascular	0.877	0.333	2.308	0.790
	Cerebrovascular	0.887	0.311	2.530	0.822
	Cancer	0.772	0.225	2.653	0.681
	Immunocompromised	0.434	0.050	3.743	0.448
	Constant	0.290			0.219

OR=odds ratio; CI=confidence interval; qSOFA=quick Sequential (Sepsis-Related) Organ Failure Assessment; MEWS=modified early warning score; COPD=chronic obstructive pulmonary disease; DM=diabetes mellitus

with outcome, the authors conducted a baseline risk model. The baseline risk variables were age, sex, and all comorbidities. There were no differences in these variables between the groups except for COPD. After the authors analyzed the correlation of the baseline risk model to the primary outcome by binary logistic regression, all variables in the baseline risk models were not significant predictors of 24-hour IHCA. The authors then included the qSOFA score and the MEWS to the baseline risk model separately. The qSOFA model showed that the qSOFA was a statistically significant predictor for 24-hour IHCA with an odds ratio (OR) of 3.24 (95% CI 1.83 to 5.71, $p<0.05$). MEWS was also a predictor, but it did not reach the desired predictive value (OR 1.23, 95% CI 1.04 to 1.45, $p<0.05$). In addition, the high-risk score models that added the adjusted scores to the baseline risk model showed distinguished results between the qSOFA high-risk and MEWS high-risk (Table 2). A qSOFA score of 2 or more was a statistically significant predictor for 24-hour IHCA (OR 3.9, 95% CI 1.59 to 9.58) ($p<0.05$), while a MEWS of 5 or more was not (OR 1.857, 95% CI 0.83 to 4.11) ($p=0.128$).

ROC curves compared the predictive performance of high-risk qSOFA and high-risk MEWS. The results showed that the qSOFA had a higher area under the curve (AUC) than MEWS (AUC 0.74, 95% CI 0.64 to 0.83 versus 0.62 95% CI 0.52 to 0.72), and the adjusted high-risk qSOFA was also a better predictor compared to the high-risk MEWS (AUC 0.67, 95% CI 0.57 to 0.76 versus AUC 0.56, 95% CI 0.45 to 0.67, respectively, $p<0.05$) (Figure 2, 3).

Discussion

The present study confirmed that qSOFA, which is a new vital sign score with the same three components that are easier to use and comprehend, can predict the mortality rate on par with other vital sign scores as in previous studies[3-5]. The present study results revealed that a higher qSOFA score and higher MEWS were

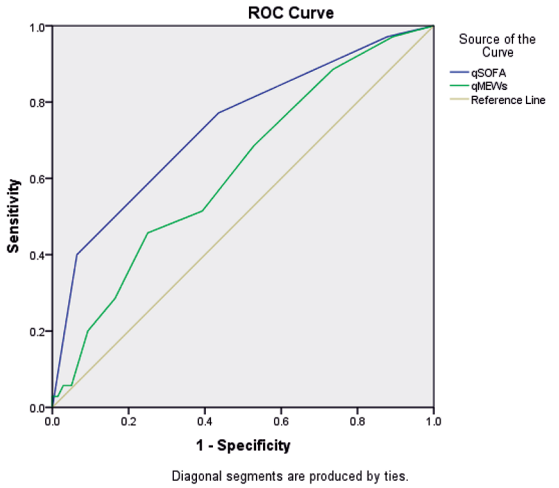

Figure 2. ROC curve of predictive scores.

qSOFA, quick Sequential (Sepsis-Related) Organ Failure Assessment; MEWS, modified early warning score

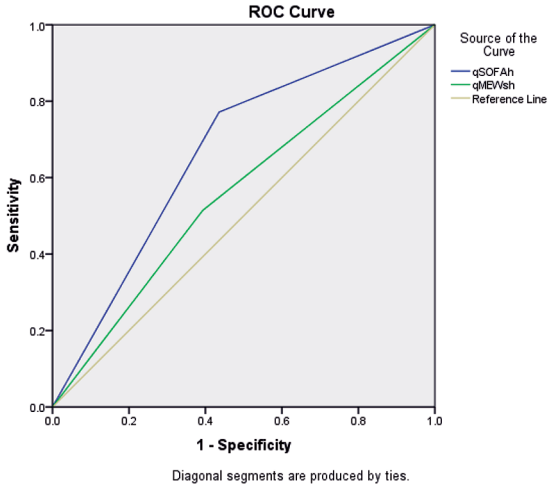

Figure 3. ROC curve of high-risk scores.

qSOFAh, high-risk quick Sequential (Sepsis-Related) Organ Failure Assessment; MEWSh, high-risk modified early warning score

significantly associated with the increased likelihood of IHCA in 24 hours after presenting to the ED. Patients with a high-risk qSOFA score were strongly correlated with 24-hour IHCA from both infectious and non-infectious causes but the high-risk MEWS did not prove its predictability regarding this outcome. A qSOFA score of 2 or 3 was almost four times more likely to have a 24-hour IHCA than scores of 0 or 1. However, regarding the ROC curve, qSOFA still had better predictive ability compared to high-risk qSOFA, which may be the effect of small sample size.

A recent retrospective validation study of the qSOFA score included 30,677 patients in the ED and ward at the University of Chicago. Those were suspected of having infection (defined as anyone who had any culture and was started on IV antibiotics)[11]. They compared the qSOFA with systemic inflammatory response syndrome (SIRS), MEWS, and the national early warning score (NEWS) to the primary outcome of in-hospital mortality and a combined outcome of mortality or ICU admission. The results of the study showed that the qSOFA had a similar test performance to SIRS (AUC 0.69, 95% CI 0.67 to 0.70 versus AUC 0.65, 95% CI 0.63 to 0.66) but was inferior to NEWS (AUC 0.77, 95% CI 0.76 to 0.79) and MEWS (AUC 0.73, 95% CI 0.71 to 0.74). Furthermore, the qSOFA in this study was also a late indicator for deterioration. The patients had a qSOFA score of 2 or more only five hours before one of the combined outcomes occurred. However, a SIRS score of 2 or more could detect the deterioration up to 17 hours. Although they concluded that the commonly used early warning sign scores (MEWS and NEWS) were more accurate than the qSOFA to predict death and ICU transfer, this result was based on the current practice influenced by the early warning sign scores to decide on activation of the rapid response team or ICU transfer. Additionally, in the present study, a qSOFA score of 2 or more still had a promising specificity of 67% that was identical to a NEWS of 8 or more (66%) and the timing for an outcome to occur was only five hours, which corresponded with the present study that a high-risk qSOFA score was a significant predictor for 24-hour IHCA. These results may warrant the need for closer monitoring and/or aggressive goal directed treatment for patients who presented to the ED with a qSOFA score of 2 or more.

The flaws of the prediction scores currently used, whether NEWS, MEWS, SIRS, or even the original SOFA score, are the user's compliance and the resources needed for their use. In order to calculate these scores, the users need to remember precisely every single digit of the variables and translate it into a wide range of score values. This can easily result in human error in a busy ED. The user will then lack any preference for a scoring system and not comply due to difficult calculations. Currently, this major problem can be solved by creating computer programs or mobile applications to do the calculation. This may result in spending more resources to develop a default calculation program for these scores after the vital signs are recorded in the electronic medical record or using mobile phones each time after examining the

patients. However, the qSOFA parameters are more user-friendly. The user can determine the severity of the patients by just one quick look. By this simple approach, patients will receive earlier treatment and more intensive investigations together with closer ED and in-patient monitoring, which can help reduce the in-hospital mortality rate[1].

Predictability of the qSOFA for IHCA could also be improved by adding another bedside test to the model. Another prospective study of 2,322 patients combined the qSOFA within the first hour of ICU admission with the serum lactate level to predict mortality in patients with and without infection[12]. The results of that prospective study were the same as the present study. The qSOFA score could predict mortality of all critically ill patients (AUROC 0.672, 95% CI 0.638 to 0.707) including the non-infectious patients (AUROC 0.685, 95% CI 0.637 to 0.732). The overall predictive ability and calibration of the qSOFA was comparable to other prognostic scores. Furthermore, after combining the qSOFA score with lactate concentrations, the predictive ability increased (AUROC 0.730, 95% CI 0.694 to 0.765) and was comparable to the standard SOFA score.

Limitation

The present study was a single center study in an academic hospital. It possibly limited the generalizability of the authors' results due to the limitations of health care in smaller hospitals and multiple co-morbid patients in the authors' center. Next, the prevalence of 24-hour IHCA in the authors' hospital was not high. This resulted in a selection bias of the overall causes of cardiac arrest that were mainly infectious diseases and myocardial infarction. Therefore, the results favored the qSOFA more than the MEWS because it was originally conducted for sepsis patients. These two limitations may be solved by conducting a multi-center prospective trial in the future.

Conclusion

In summary, an initial qSOFA of 2 or more in the ED is a significant predictor for 24-hour IHCA from overall causes despite receiving standard treatments. Its predictive performance tends to be better than the high-risk MEWS and it is also on par with other complex predictive scores such as APACHE II, SOFA, and NEWS. Moreover, due to its simplicity with only three vital sign criteria and one cut point for each, compliance in the ED would be better and could help improve the physician's awareness of disease severity. A further multi-center prospective study in a larger population is necessary to confirm its predictive ability for the short-term mortality rate in all ED patients. In addition, a mortality prediction study to add the initial lactate level in patients who present with a qSOFA score of 2 or more in the ED may provide a great aide for clinical decisions. Lastly, conducting a clinical trial using high-risk qSOFA to guide an intensive treatment protocol may help improve patient outcomes and prove its clinical benefit in the future.

What is already known on this topic

Currently, many EDs and in-patient wards used MEWS score to predict 48- and 72-hour in-hospital cardiac arrest (IHCA), stratify the risks for each patient and decide for closed monitoring or ICU admission. On the other hand, qSOFA score was used for screening sepsis patients and predict 28-day mortality only in infectious patients.

What this study adds?

The findings support that qSOFA could also be used with every patient in the ED to screen the risk of in-hospital cardiac arrest.

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Authors' contributions

Bunchit W conceived the study, designed the study and the associated data collection forms. Vattanavanit V and Limapichat T aided in the design of the study and supervised its conduct. Bunchit W conducted the chart reviews, managed the data and analyzed the data. Vattanavanit V assisted and supervised the chart reviews. Vattanavanit V and Limapichat T provided statistical advice. Bunchit W drafted the article and all authors contributed substantially to its revision. Bunchit W takes responsibility for the paper as a whole.

Disclosure

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design or conduct of the study; management, analysis or interpretation of the data; preparation, review, or approval of the article.

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Conflicts of interest

The authors declare no conflict of interest.

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