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A prospective validation of Sepsis-3 guidelines in acute hepatobiliary sepsis: qSOFA lacks sensitivity and SIRS criteria lacks specificity (Cohort Study)

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ABSTRACT

Background: Since its introduction in 2016, the Sepsis-3 guidelines, with emphasis on the quick Sequential Organ Failure Assessment (qSOFA) score, have generated much debate and controversy. It is recognised that the new definitions require validation in specific clinical settings and have yet to be universally adopted. We aim to validate new Sepsis-3 guidelines in acute hepatobiliary infection.

Material and methods: A prospective cohort of patients admitted with acute hepatobiliary infection from the emergency department from July 2016 to June 2017 was studied. The Systemic Inflammatory Response Syndrome (SIRS) criteria, SOFA and qSOFA scores were calculated and predictive performance evaluated with area under the receiver operating characteristic (AUROC) curves for predictive ability of these indices for critical care unit admission and morbidity.

Results: 124 patients with a median age of 64.5 years and majority males (n = 75, 60.5%) were admitted with acute hepatobiliary infection during the study period. Acute cholecystitis was the most common admission diagnosis (n = 83, 66.9%) and most patients were managed in general ward (n = 91, 73.3%) with median length of stay of 6 days (range 1–40). On multivariate analysis, diabetes mellitus (p = 0.003) predicted high dependency unit (HDU) admission, while age (p = 0.001), positive blood culture (p = 0.012), positive fluid culture (p = 0.015) and SOFA score (p = 0.002) predicted length of hospital stay. The sensitivity of SIRS in predicting HDU admission (60% vs. 4%), intensive care unit (ICU) admission (62.5% vs. 0%) and morbidity (66.7% vs. 0%) was higher than qSOFA score. The specificity of qSOFA in predicting HDU admission (100% vs. 49.5%), ICU admission (99.1% vs. 53.3%) and morbidity (99.2% vs. 47.9%) was higher than SIRS criteria.

Conclusion: The SIRS criteria has high sensitivity and the qSOFA score has high specificity in predicting outcomes of patients with acute hepatobiliary infection.

1. Introduction

Sepsis is a global public health concern with increasing incidence and is the leading cause of mortality [1]. Patients who survive sepsis often have long-term functional impairment and cognitive disabilities, with significant health care and social implications [2]. Biliary tract infections are a common cause of sepsis and are associated with high morbidity and mortality [3]. Outcomes are determined by timely treatment with antibiotics and biliary decompression [4]. Therapeutic interventions are determined by risk stratification and this necessitates standardized severity assessment criteria. In 2016, the definition and terminology of sepsis have been revised and now designated as the Sepsis-3 (SEP-3) guidelines [5]. This updated the previous recommendations (Sepsis-1 in 1991, and Sepsis-2 in 2001), removing the need for the systemic inflammatory response syndrome (SIRS) criteria.

Sepsis is now clinically determined by the Sequential Organ Failure Assessment (SOFA) score [5]. Additionally, a bedside score for risk stratification with the quick SOFA (qSOFA) score has been proposed [5]. Since its introduction, the SEP-3 guidelines have attracted much debate and controversy from the international community [6,7], and the authors of the SEP-3 guidelines recognise that the new definitions require validation in specific clinical settings. Studies have been published validating the new Sepsis-3 criteria in the Emergency Department [8], Intensive Care Unit [9], as well as in specific conditions such as community acquired pneumonia [10], cirrhosis [11], and cancer patients [12]. There are conflicting views with regards to validation of qSOFA scores as compared to SIRS and some societies have refused to endorse the SEP-3 definitions [6,13,14]. In a retrospective audit

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including 30,677 patients admitted with suspicion of infection at emergency department in America over a span of seven years, Churpek et al. reported that commonly used early warning scores are more accurate than the qSOFA score for predicting death and intensive care unit (ICU) transfer in non-ICU patients [15]. In their study, most patients who experienced the composite outcome of death and ICU transfer met ≥2 SIRS criteria more than 17 h before the composite outcome compared with only 5 h for ≥2 qSOFA. In addition, some authors have expressed concerns that qSOFA may identify patients too late in the course of illness and the increased specificity is at the cost or unacceptably reduced sensitivity [15–17]. In a prospective European study including 879 patients, Freund et al. has shown that qSOFA has high specificity at the cost of reduced sensitivity and it more accurately predicts in hospital mortality compared with SIRS (AUROC 0.77 versus 0.65) [8]. The higher sensitivity of SIRS criteria is welcome as a clinician would prefer not to miss any patient with suspected sepsis who may remain under treated and potentially suffer adverse outcomes. This is particularly relevant in hepatobiliary sepsis as prompt treatment has been shown to restore physiology and improve outcomes [18,19]. There are no studies validating the new SEP-3 criteria for biliary tract infections and comparing it with traditional SIRS criteria. We aim to prospectively validate new SEP-3 criteria in patients with hepatobiliary infection and compare it with old Sepsis-2 criteria which are determined by SIRS.

2. Materials and methods

We prospectively collected data of 125 patients admitted to department of General Surgery for hepatobiliary infection over a period of 11 months from July 2016 to June 2017. The inclusion criteria were: (a) age ≥ 18 years, (b) clinical diagnosis of hepatobiliary infection, including cholecystitis, cholangitis, and pyogenic liver abscess. The diagnosis of hepatobiliary infection was made based on combination of clinical assessment, laboratory markers and imaging. The local management algorithms of acute cholecystitis, acute pyogenic cholangitis and pyogenic liver abscess have been previously published [19–21]. Written informed consent was obtained from patients who fulfilled the inclusion criteria and patients who declined to participate in the study were excluded. One patient withdrew from the study leaving 124 patients for analyses. This study was approved by our institution domain specific review board (Approval number 2017/00266). Patient records and relevant information were anonymized and de-classified prior to analysis. This study has been reported in line with the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) criteria [22].

We collected demographic data including age, gender, comorbidities, and American Society of Anaesthesiologists (ASA) score. Admission parameters, including blood pressure, heart rate, temperature, Glasgow Coma Scale (GCS) score, and laboratory markers including total white blood cell count, C-reactive protein, arterial blood gas (ABG), serum electrolytes and liver function tests were collated. These allowed for calculation of the SIRS, SOFA, and qSOFA scores.

Our primary outcome studied was all-cause inpatient mortality and morbidity. Mortality was defined as death before hospital discharge. Morbidity included hospital acquired pneumonia, cardiac arrhythmias, myocardial infarction, stroke and urinary tract infections. Our secondary outcome was admission to the surgical intensive care unit (SICU), high dependency unit (HDU), duration of inpatient hospital stays, and the use of inotropes or vasopressors.

All patients with clinical diagnosis of hepatobiliary infection had SIRS, SOFA and qSOFA scores calculated. The definition of sepsis as per SEP-3 guidelines was defined by an increase of SOFA score ≥2 points, with the baseline SOFA score assumed to be zero in patients not known to have pre-existing organ disfunction [5].The qSOFA score was considered positive when at least two of the following were met: altered mental state, respiratory rate ≥ 22/min, and systolic blood pressure ≤ 100 mm Hg [5]. SIRS was defined as fulfilling at least two out of four criteria: (a) Body temperature < 36 °C or > 38 °C, heart rate > 90 beats per minute, respiratory rate > 20 per min, and white blood cell count (WBC) < 4000/μL or > 12,000 μL, or immature bands > 10% [23]. Hospital stay was calculated based on admission and discharge dates. The decision for admission to the HDU or SICU was made based on clinical judgement by the primary team consultant. Indications for HDU admission include support for single-organ failure and closer monitoring and indications for SICU admission include support for multi-organ failure and patients requiring intubation for ventilatory support.

Statistical tests were performed using IBM SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) and MedCalc Statistical Software version 18.5 (MedCalc Software, Ostend, Belgium; http://www.medcalc.org; 2018). Univariate analyses were performed using chi-square tests. Multivariate analyses were performed with binary logistic regression model. The predictive performance of SIRS, SOFA, and qSOFA scores for the primary and secondary outcomes were assessed with area under the receiver operating characteristic (AUC) curves and compared with Delong et al. method. AUC measures diagnostic accuracy of a test with graphical display between the 'sensitivity' and the '1–specificity' relationship. It can range from 0.5 to 1.0. An AUC value of < 0.60 means poor discrimination, 0.60–0.80 means moderate discrimination, 0.8–0.9 means good discrimination and a value of > 0.9 mean an excellent discriminator between different prediction models [24]. A p-value of less than 0.05 was used to indicate statistical significance for all tests.

3. Results

124 patients with median age of 64.5 years (range 24–91) were included in the analysis. There were 75 (60.5%) males. Admission diagnosis was acute cholecystitis (n = 83, 66.9%), acute cholangitis (n = 36, 29.0%) and pyogenic liver abscess (n = 8, 6.5%). Two (1.6%) patients had concomitant cholecystitis and cholangitis, two (1.6%) patients had concomitant cholecystitis and liver abscess, and one (0.8%) patient had concomitant cholangitis and liver abscess. Patient demographic and clinical profile are summarised in Table 1.

All patients had GCS score of 15 at admission. Most patients (n = 91, 73.3%) were treated in the general ward setting, 25 (20.2%) were treated in the HDU and eight (6.5%) were treated in the surgical ICU. Three (2.4%) patients developed morbidity during hospital stay, including two (1.6%) hospital acquired pneumonia and one (0.8%) cardiac arrhythmia. There was one (0.8%) mortality due to metastatic cancer.

Table 2 shows the associations between patient characteristics and factors predictive of study outcomes. On univariate analysis, mortality was associated with metastatic cancer ($p < 0.001$) and morbidity was associated with chronic liver disease ($p < 0.001$) and malignancy ($p = 0.001$). One patient passed away due to sepsis from metastatic cholangiocarcinoma. This patient was initially admitted for suspected acute cholecystitis due to fever and right hypochondrial pain. Subsequent investigations revealed metastatic cholangiocarcinoma and the patient passed away from multi organ failure despite antibiotics and biliary decompression. No factors were significant on multivariate analysis. Due to only one mortality in our series, analysis and comparison of ROC curves for mortality was not done.

On univariate analysis, diabetes mellitus ($p = 0.042$) and qSOFA score ($p = 0.046$) were associated with admission to the HDU. On multivariate analysis, existing DM remains an independent prognostic factor for admission to the HDU ($p = 0.003$, OR 16.23, CI 2.54–103.79). Fig. 1(a) below shows the ROC curve performance for the SIRS (AUROC = 0.547, sensitivity 60.0%, specificity 49.5%), SOFA (AUROC = 0.513, sensitivity 44.0%, specificity 58.6%), and qSOFA (AUROC = 0.520, sensitivity 4.0%, specificity 100.0%) criteria for HDU admission. There was no statistical significance between the comparison of ROC curves.

Table 1
Demographic and clinical profile of patients with hepatobiliary infection.

	n = 124 (%)
Age (years)	24-91 [Median = 64.5]
Gender	
Male	75 (60.5)
Female	49 (39.5)
Admission diagnosis	
Acute cholecystitis	83 (66.9)
Acute cholangitis	36 (29)
Pyogenic liver abscess	8 (6.5)
Comorbidities	
Hypertension	69 (55.6)
Diabetes mellitus	43 (34.7)
Hyperlipidaemia	58 (46.8)
Previous myocardial infarction	17 (13.7)
Congestive cardiac failure	3 (2.4)
Stroke	12 (9.7)
Chronic renal failure	9 (7.3)
Chronic liver disease	7 (5.6)
Malignancy	13 (10.5)
Peptic ulcer disease	9 (7.3)
Chronic obstructive pulmonary disease	3 (2.4)
Metastatic cancer	2 (1.6)
American Society of Anaesthesiologists score	
1	7 (5.6)
2	69 (55.6)
3	28 (22.6)
4	20 (16.1)
Blood culture positive [n = 100]	17 (17.0)
Fluid culture positive [n = 41]	24 (58.5)
Type of bacteria	
Klebsiella pneumoniae	18 (14.5)
Escherichia coli	13 (10.5)
Others	2 (1.6)
SIRS[a]	
0	23 (18.5)
1	42 (33.9)
2	38 (30.6)
3	16 (12.9)
4	4 (4.0)
qSOFA[b] score	
0	117 (96.4)
1	6 (4.8)
2	1 (0.8)
3	nil
SOFA[c] score	
0	47 (37.9)
1	25 (20.2)
2	27 (21.8)
3	12 (9.7)
4	8 (6.5)
5	3 (2.4)
6	1 (0.8)
8	1 (0.8)
Admission	
General ward	91 (73.3)
Surgical Intensive Care Unit	8 (6.5)
High Dependency Unit	25 (20.2)
Length of hospital Stay in days (median) (range)	6 (1–40)
Use of inotropes/vasopressors	2 (1.8)
Morbidity	
Hospital acquired pneumonia	2 (1.6)
Cardiac arrythmia	1 (0.8)
Acute myocardial infarction	nil
Stroke	nil
Urinary tract infection	nil
Mortality	1 (0.8)

[a] Systemic Inflammatory Response Syndrome.
[b] Quick Sequential Organ Failure Assessment.
[c] Sequential Organ Failure Assessment.

On univariate analysis, age ≥ 65 ($p = 0.028$), male gender ($p = 0.018$), previous myocardial infarction ($p = 0.043$), positive blood ($p = 0.043$) and fluid ($p = 0.023$) culture were associated with SICU admission. No factors were independently associated with admission to the SICU. Fig. 1(b) below shows the ROC curve performance for the SIRS (AUROC = 0.580, sensitivity 62.5%, specificity 53.4%), SOFA (AUROC = 0.610, sensitivity 62.5%, specificity 59.5%), and qSOFA (AUROC = 0.504, sensitivity 0.0%, specificity 99.1%) criteria for SICU admission. There was no statistical significance between the comparison of ROC curves.

On univariate analysis, age ≥ 65 ($p = 0.001$), hypertension ($p = 0.006$) and hyperlipidaemia ($p = 0.012$), blood culture ($p < 0.001$), fluid culture ($p < 0.004$), and positive SOFA criteria ($p = 0.013$) were associated with increased length of hospital stay. On multivariate analysis, age > 65 ($p = 0.001$, OR 6.57 [2.07–20.91]), blood culture ($p = 0.012$, OR 17.59[1.86–166.04]), fluid culture ($p = 0.015$, OR 6.441 [1.43–29.01]) and SOFA score ($p = 0.002$, OR 6.16 [1.99–19.04]) were independently associated with length of hospital stay. Fig. 1(c) shows the ROC curve for the SIRS (AUROC = 0.573, sensitivity 66.7%, specificity 47.9%), SOFA (AUROC = 0.627, sensitivity 66.7%, specificity 58.7%), and qSOFA (AUROC = 0.504, sensitivity 0.0%, specificity 99.2%) criteria for inpatient morbidity. This difference was not significant.

4. Discussion

Our results show that in patients with hepatobiliary infection, SIRS, qSOFA and SOFA score were all poor and comparable in predicting morbidity and admission to critical care unit. On multivariate analysis, diabetes mellitus predicted HDU stay, while age, blood culture, fluid culture and SOFA score predicted length of stay. The bedside qSOFA score lacked sensitivity in prediction for all outcomes.

Acute hepatobiliary infection is a diverse clinical entity with varied pathology. Clinical outcomes are determined based on the organ focus of infection [18,25,26]. In our cohort comprising predominantly of acute cholecystitis patients, the mortality was low (0.8%). The small numbers of mortality and morbidity could be explained due to the high compliance with the sepsis treatment bundle and implementation of liver abscess care bundle at our institution [27]. Due to the low mortality rate, we assessed the predictive value of the new SEP-3 guidelines for morbidity and admission to critical care units such as the ICU and HDU. The new guidelines promote the SOFA score and its simpler version (quick) qSOFA score as a bedside tool to guide management of patients with sepsis. A good bedside tool should be both sensitive and specific for this purpose. The qSOFA score lacked sensitivity in our experience, and this is similar to other reports in the literature [28–32]. In a single centre prospective observational study conducted in medical wards and excluding patients with systemic illness, Akinosoglou et al. showed that qSOFA lacks sensitivity for the diagnosis of sepsis and they advocate prompt management of critically ill patients in presence of SIRS criteria regardless of qSOFA score [28]. In a meta-analysis of 229,480 patients from ten studies comparing SIRS and qSOFA criteria, sensitivity for diagnosis of sepsis was higher for SIRS, while specificity for diagnosis of sepsis was higher for qSOFA (97.3% vs. 84.4%) and qSOFA was better predictor of in-hospital mortality [32]. The low sensitivity of qSOFA could be due to the exclusion of organ failure criteria related to coagulopathy, hyperbilirubinemia or acute kidney injury. Additionally, an altered mental state, a component of the qSOFA score, is often a late sign of hepatobiliary sepsis. In our cohort, all patients had a GCS score of 15 at admission, which may explain the limited sensitivity of the qSOFA score in hepatobiliary sepsis.

The role of SIRS and qSOFA both need clarity with regards to diagnostic ability, outcome prediction and in guiding clinical management. Vincent et al. has reported in the editorial that qSOFA is (1) not a replacement for SIRS and (2) not a part of definition of sepsis but meant to be used to raise suspicion of sepsis and prompt further action [33]. Our experience and many reports suggest that SIRS is superior to detect patients with ‘suspected sepsis’ so that ‘prompt further action’ can be performed in a timely manner. The oversensitivity of SIRS criteria is advantageous in routine clinical practice and clinical judgment made

Table 2
Univariate and multivariate analysis of associations between patient characteristics and factors predictive of study outcomes.

Characteristic	Study outcome, p-value					
	Use of vasopressors	HDU[a] admission	SICU[b] admission	Length of Hospital Stay	Morbidity	Mortality
Univariate Analysis						
Age ≥ 65	1.000	0.502	**0.028**	**0.001**	0.559	0.315
Male gender	0.249	0.956	**0.018**	0.319	0.156	0.214
Diagnosis						
Cholecystitis	**0.043**	0.076	0.067	**0.049**	0.992	0.480
Cholangitis	**0.026**	0.390	0.177	0.156	0.868	0.521
Liver Abscess	0.708	0.206	0.443	0.119	0.645	0.792
Comorbidities	N.S[c]	DM[d], **p = 0.042**	Previous MI[e], **p = 0.043**	Hypertension, **p = 0.006** Hyperlipidaemia, **p = 0.012**	CLD[f], **p < 0.001** Malignancy, **p = 0.001**	Metastatic cancer, **p < 0.001**
ASA[g] score	0.382	0.204	0.073	0.159	0.075	0.067
Blood Culture	0.132	0.306	**0.043**	**< 0.001**	0.485	0.689
Fluid Culture	0.485	0.511	**0.023**	**< 0.004**	0.390	0.623
SIRS[h] criteria	0.135	0.396	0.382	0.577	0.617	0.339
qSOFA[i] score	0.898	0.046	0.792	0.300	0.874	0.928
SOFA[j] score	0.093	0.815	0.223	**0.013**	0.380	0.394
Multivariate Analysis						
Age ≥ 65	N.S.	N.S.	N.S.	**0.001**, (OR[k] 6.57, CI[l] 2.07–20.91)	N.S.	N.S.
Male gender	N.S.					
Diagnosis	N.S.					
Comorbidities	N.S.	DM, **p = 0.003**, (OR 16.23, CI 2.54–103.79)	N.S.	N.S.	N.S.	N.S.
ASA[g] score	N.S.					
Blood Culture	N.S.	N.S.	N.S.	**0.012**, (OR 17.59, CI 1.86–166.04)	N.S.	N.S.
Fluid Culture	N.S.	N.S.	N.S.	**0.015**, (OR 6.44, CI 1.43–29.01)	N.S.	N.S.
SIRS[h] criteria	N.S.					
qSOFA[i] score	N.S.					
SOFA[j] score	N.S.	N.S.	N.S.	**0.002**, (OR 6.16, CI 1.99–19.04)	N.S.	N.S.

[a] High dependency unit.
[b] Surgical intensive care unit.
[c] Not significant.
[d] Diabetes mellitus.
[e] Myocardial infarction.
[f] Chronic liver disease.
[g] American Society of Anesthesiology score.
[h] Systemic Inflammatory Response Syndrome.
[i] Sequential Organ Failure Assessment.
[j] Quick Sequential Organ Failure Assessment.
[k] Odds ratio.
[l] Confidence interval.

with regards to care burden, rather than relying on qSOFA score to guide prompt action in patients with heightened suspicion as qSOFA lacks sensitivity. qSOFA is instead shown to be more specific for in-hospital mortality [9,34] and we advocate that SIRS be used as a screening tool along with clinical judgment, while qSOFA should be used as a clinical outcome prediction tool until its role in detecting and diagnosing patients with infection is redefined.

The new SEP-3 guideline does not include SIRS in the definition of sepsis and given the limitations of the qSOFA score, we agree with Vincent et al. that qSOFA should not replace SIRS in the definition of sepsis [33]. While the qSOFA score may be more specific for sepsis-related mortality, using the qSOFA criteria alone may de-emphasize and delay treatment and intervention at the earlier stages of sepsis when it is at its most treatable, especially in the case of hepatobiliary sepsis where early intervention is vital to obtaining source control of sepsis. Hence, the clinical utility of qSOFA is questionable as compared with SIRS for early detection or screening for patients with suspected sepsis. In 103 patients with acute cholecystitis managed with percutaneous cholecystostomy, Yeo et al. reported that prompt source control reverses organ dysfunction and improves clinical outcomes with co-morbidity being the main determinant of mortality [18].

The SOFA criteria has been shown to have greater prognostic accuracy for in-hospital mortality than SIRS criteria or the qSOFA score in ICU patients [9]. In our cohort, we found the SOFA criteria comparable with the SIRS criteria, with the SOFA criteria being more specific. In contrast with SIRS and qSOFA, the SOFA criteria may capture more patients. This was evident in our cohort, with 50% of patients who fulfilled SOFA criteria having negative SIRS criteria. However, the qSOFA can be used as a bedside point of care screening tool and clinical judgment made even before laboratory parameters (e.g. white blood cell count) which are necessary for both SIRS and SOFA criteria. Fig. 2 illustrates this, and it is possible that qSOFA and SIRS are rather complementary and not competing for their roles in prompt recognition of sick patients with underlying sepsis. The use of baseline SOFA scores also allows the clinician to account for the presence of pre-existing acute or chronic organ dysfunction before the onset of infection and also allows for serial evaluation [35]. In our study, a positive SOFA score has also been shown to be independently associated with length of hospital stay. Additional findings from our study that positive blood or fluid cultures were associated with longer length of hospital stay is

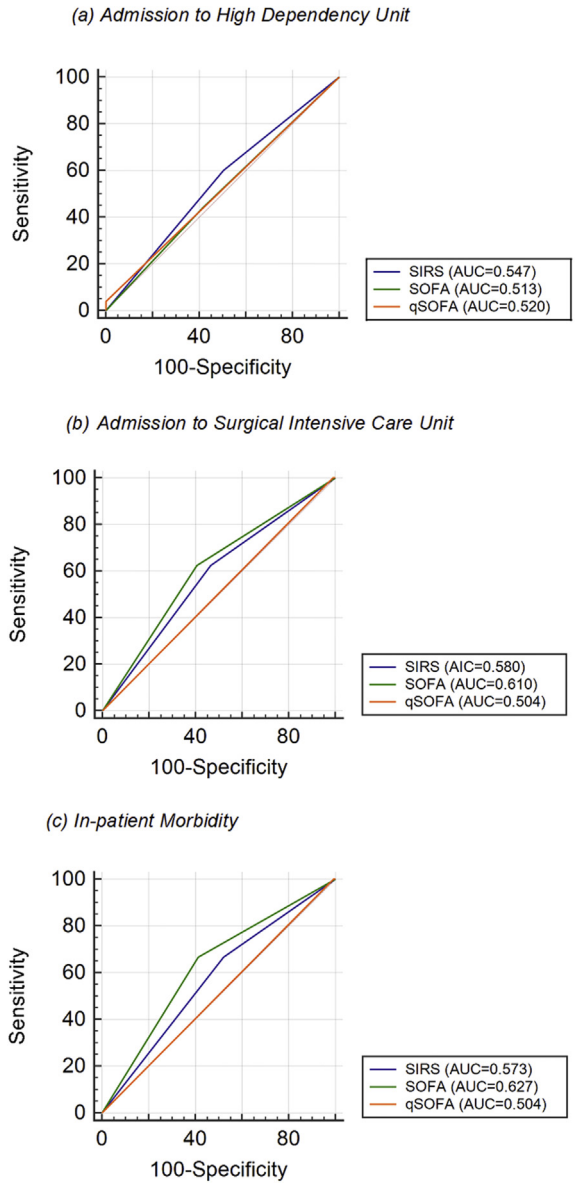

Fig. 1. (a), (b) and (c): Receiver operating characteristic curves for (a) admission to high dependency unit, (b) admission to surgical intensive care unit, and (c) in-patient morbidity for Systemic Inflammatory Response Syndrome (SIRS), Sequential Organ Failure Assessment (SOFA), and Quick Sequential Organ Failure Assessment (qSOFA) criteria.

likely due to our institution practice of requiring at least 1–2 weeks of intravenous antibiotics for patients with positive cultures. This however did not translate to a higher morbidity or mortality. Future studies on the prospective evaluation comparing both criteria are needed to aid clinicians in identifying patients with acute hepatobiliary sepsis who may benefit from closer monitoring and early intervention. It also remains to be determined if future hybrid or modified scores based on the SIRS criteria and qSOFA score to generate a modified prediction model may enhance the sensitivity of the present qSOFA score.

The limitation in our study was that parameters were only recorded upon admission. Analysis of serial changes could have provided more accurate information as sepsis is often an evolving process with varying systemic host response. The qSOFA score was established as a dynamic score that can be repeated as necessary by the bedside, with Dorsett et al. demonstrating that sensitivity of qSOFA increased from 27.9% to 67.4% during emergency department stay as compared to the initial signs [31]. The small sample size of our study with low mortality and morbidity rate may limit statistical significance of our results, and future design with larger, prospective clinical trials may be advocated to validate and define the role of qSOFA. As a single-centre study conducted in selected cohort of patients with acute hepatobiliary infection, the generalizability of our results is limited.

5. Conclusion

The SIRS and SOFA criteria are comparable and complementary in predicting morbidity and critical care unit admission in patients with acute hepatobiliary infection, while the qSOFA score is poorly sensitive. The use of both the SIRS and SOFA criteria could provide a better model to initiate or escalate therapy in patients with hepatobiliary infection. The SIRS criteria are more sensitive to the qSOFA score for sepsis diagnosis and prediction of outcomes of hepatobiliary infection, while the qSOFA is more specific in comparison. Considering the present results, future studies should focus on the prospective evaluation comparing both criteria as a part of the decision-making process for clinicians caring for septic patients. It also remains to be determined if combining the SIRS criteria along with qSOFA score to generate a modified prediction model may enhance the sensitivity of the qSOFA score.

Provenance and peer review

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Data statement

The authors do not have permission to share data.

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Ethical approval

This study was approved by our institution domain specific review board (Approval number 2017/00266).

Research registration Unique Identifying number (UIN)

Name of the registry: Research Registry.
Unique Identifying number or registration ID: researchregistry5053.
Hyperlink to the registration (must be publicly accessible): https://www.researchregistry.com/browse-the-registry#home/registrationdetails/5d41549b8314890011b1d564/

Author contribution

MHW Mak: Data collection, analysis and interpretation of data, drafted the initial manuscript.
JK Low: Data collection, critical review of the manuscript.
SP Junnarkar: Data collection, critical review of the manuscript.
TCW Huey: Data collection, critical review of the manuscript.
VG Shelat: Conception and design of the study, data collection, analysis and interpretation of data, critical revision of manuscript, last review of the paper prior to submission.
All authors read and approved the final manuscript.

Guarantor

MHW Mak, VG Shelat.

Declaration of competing interest

Nil.

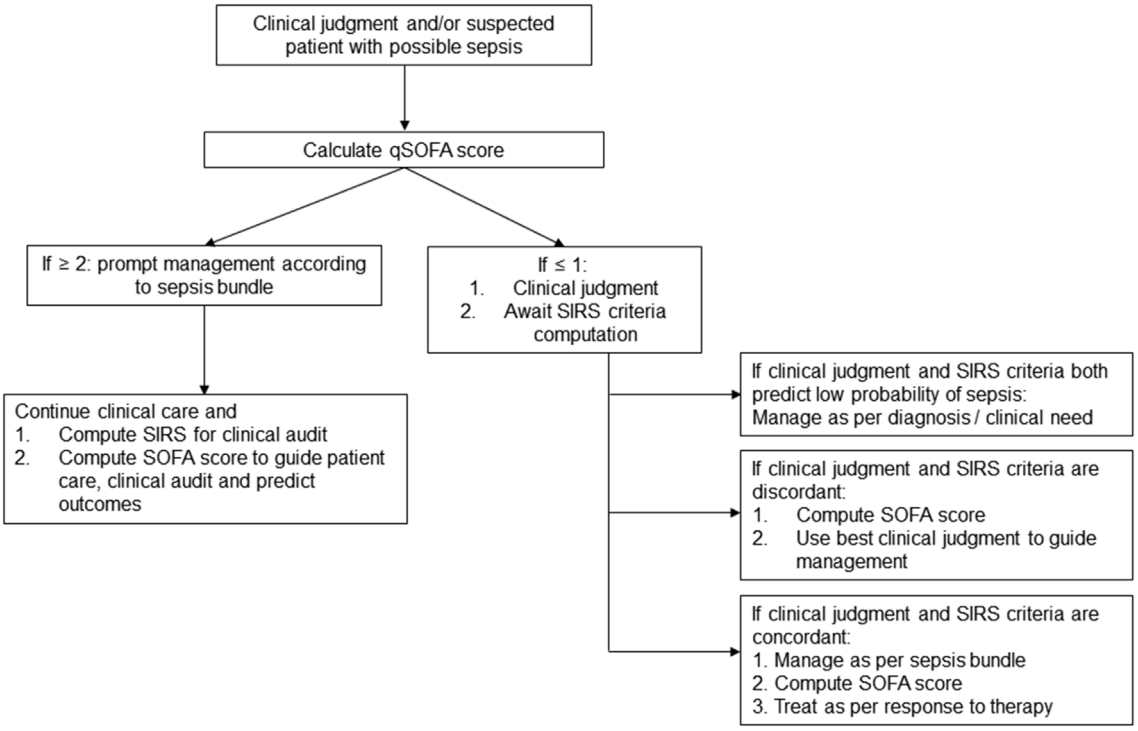

Fig. 2. Proposed flowsheet for use of SIRS, SOFA, and qSOFA scoring in sepsis.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.10.022.

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