การศึกษาประสิทธิภาพในการวินิจฉัยโดยใช้โพรแคลซิโทนิน เทียบกับเกณฑ์การวินิจฉัยภาวะพิษเหตุติดเชื้อ พ.ศ. 2544 และ พ.ศ. 2559 ในแผนกเวชศาสตร์ฉุกเฉิน

ชายวุฒิ สววิบูลย์[1], จิราภรณ์ ศรีอ่อน[1], พิมล บูรณะอมร[1,2], พวงรัตน์ ตั้งธิติกุล[1], ไปรยาภัค สกุลวทัญญู[3], ธนานันต์ ตัณฑ์ไพบูลย์[4], อนุชา คำส้อม[5], อนุแสง จิตสมเกษม[4]

[1] ภาควิชาเวชศาสตร์ฉุกเฉิน คณะแพทยศาสตร์ มหาวิทยาลัยนวมินทราธิราช
[2] กลุ่มงานผู้ป่วยนอก รพ.ตำรวจ
[3] ภาควิชาพยาธิวิทยาคลินิก คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช
[4] ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช
[5] ศูนย์ส่งเสริมการวิจัย คณะแพทยศาสตร์วชิรพยาบาล

*ผู้ประพันธ์บรรณกิจ
พิมล บูรณะอมร
กลุ่มงานผู้ป่วยนอก โรงพยาบาลตำรวจ
492/1 ถนนพระราม 1 ปทุมวัน กรุงเทพฯ 10330
อีเมล: emergeny.pimol@gmail.com
โทรศัพท์ที่ทำงาน: 094-552-5146

บทคัดย่อ

บทนำ

โพรแคลซิโทนิน (procalcitonin; PCT) เป็นตัวชี้วัดทางกายภาพซึ่งนิยมใช้แพร่หลายเพราะสามารถบ่งชี้ภาวะติดเชื้อในกระแสโลหิตได้อย่างรวดเร็ว เนื่องจากระดับ PCT ยังมีความสัมพันธ์กับระดับของ SOFA ในหอผู้ป่วยเวชบาบัดวิกฤต ผู้วิจัยจึงตั้งสมมุติฐานว่า PCT อาจจะสามารถใช้แทน SOFA ในการประเมินภาวะพิษเหตุเชื้อที่แผนกเวชศาสตร์ฉุกเฉิน

วัตถุประสงค์

ศึกษาเปรียบเทียบประสิทธิภาพของ PCT ,SIRS, qSOFA , SOFA ในการวินิจฉัยภาวะพิษเหตุติดเชื้อตามเกณฑ์ SSC พ.ศ. 2559

วิธีการศึกษา

การศึกษาเชิงพรรณนาไปข้าง ตั้งแต่ เดือนมิถุนายน พ.ศ. 2560 ถึง เดือนกันยายน พ.ศ. 2560 ณ แผนกเวชศาสตร์ฉุกเฉิน โรงพยาบาลวชิรพยาบาล จังหวัดกรุงเทพ ประเทศไทย พิจารณาเกณฑ์เข้าร่วมวิจัย ดังนี้ ผู้ที่อายุมากกว่า 18 ปี และสงสัยภาวะติดเชื้อ บันทึกสัญญาณชีพและการประเมิน

ระดับความรู้สึกตัวโดย Glasgow Coma Scale (GCS) ที่จุดคัดกรองเบื้องต้น เพื่อประเมินเกณฑ์ SIRS, qSOFA, SOFA และส่งตรวจระดับ PCT ผู้ป่วยจะได้รับการวินิจฉัยภาวะพิษเหตุเชื้อโดยการพิจารณาผลเพาะเชื้อในกระแสเลือดและภาวะอวัยวะล้มเหลว ประสิทธิภาพในการวินิจฉัยของแต่ละเครื่องมือโดยถูกวิเคราะห์โดยใช้พื้นที่ใต้กราฟอาร์โอซี

ผลการศึกษา

ผู้ป่วยที่สงสัยภาวะติดเชื้อจำนวน 207 คน ร้อยละ 49.8 ได้รับการวินิจฉัยภาวะพิษเหตุติดเชื้อ การศึกษาการประสิทธิภาพในการวินิจฉัยภาวะพิษเหตุติดเชื้อ พบว่า PCT มีประสิทธิภาพใกล้เคียงกับ qSOFA ค่าพื้นที่ใต้กราฟอาร์โอซี ดังนี้ 0.73 และ 0.71 เรียงตามลาดับ ค่านัยสำคัญ (p-value) = 0.742 PCT มีประสิทธิภาพมากกว่า SIRS อย่างมีนัยสำคัญ ค่าพื้นที่ใต้กราฟอาร์โอซี ดังนี้ 0.73 และ 0.58 เรียงตามลำดับ ค่านัยสำคัญ (p-value) = 0.001 ค่าสหสัมพันธ์บ่งชี้ความสัมพันธ์ระหว่าง SOFA และ PCT ในขณะที่การศึกษานี้ไม่พบความสัมพันธ์ระหว่าง qSOFA และ PCT

สรุปผล

PCT และ qSOFA ทั้งคู่มีความแม่นยำในการวินิจฉัยภาวะพิษเหตุติดเชื้อได้เท่ากัน แต่ทว่า จากการศึกษานี้กลับไม่พบความสัมพันธ์ระหว่าง PCT และ qSOFA ฉะนั้น การพิจารณา PCT วินิจฉัยภาวะพิษเหตุติดเชื้อจึงมีข้อกำจัดในห้องฉุกเฉิน

คำสำคัญ

ภาวะพิษเหตุติดเชื้อ โพรแคลซิโทนิน อวัยวะล้มเหลว โพรแคลซิโทนิน qSOFA SOFA แผนกเวชศาสตร์ฉุกเฉิน

Diagnostic accuracy of procalcitonin compared with sepsis-2 and sepsis-3 criteria in emergency department

Chaiwut Sawawiboon[1], Jiraporn Sri-on[1], Pimol Burana-amorn[1,2*], Poungrat Thungtitigul[1], Prirayapak Sakoonwatanyoo[3], Tananun Tanpaibule[4], Anucha Kamsom[5], Anusang Chitsomkasem[4]

[1] Department of Emergency Medicine, Vajira Hospital, Faculty of Medicine, Navamindradhiraj University, Thailand
[2] Department of Emergency Medicine, Police General Hospital, Thailand
[3] Department of Clinical Pathology, Vajira Hospital, Faculty of Medicine, Navamindradhiraj University, Thailand
[4] Department of Medicine, Vajira Hospital, Faculty of Medicine, Navamindradhiraj University, Thailand
[5] Research Facilitation Unit, Vajira Hospital, Faculty of Medicine, Navamindradhiraj University, Thailand

*coresponding author
Department of emergency medicine
Police General Hospital
92, 1 Rama I Rd, Khwaeng Pathum Wan, Khet Pathum Wan
Bangkok Thailand 10330
Email: emergeny.pimol@gmail.com
Tel. 094-552-5146

Abstract

Objective

As procalcitonin (PCT) level is significantly correlated with sequential organ failure assessment (SOFA) in ICU setting, we postulate that PCT could be substituted for SOFA in assessing sepsis in an emergency department (ED). Therefore, this study aims to compare the validity of PCT with Sepsis-2 and Sepsis-3 for diagnosing sepsis.

Methods

This prospective observational study was conducted in the ED, at one tertiary care hospital, Thailand from June 2017 to September 2017. Inclusion were consecutive adults, aged 18 years and older, with presumed infection admitted to the ED. Vital signs and the Glasgow Coma Scale (GCS) at nurse triage had been collected to access quick SOFA (qSOFA) and systemic inflammatory response syndrome (SIRS), including blood test for procalcitonin (PCT) level. Sepsis was diagnosed by positive hemoculture result or end-organ dysfunction.

The diagnostic efficiency has been analyzed in the context of the area under the receiver operating characteristic (AUROC), sensitivity and specificity. The connection between serum PCT, qSOFA and SOFA was evaluated by the correlation test.

Results

We had 207 patients enrolled to the study, 49.8% were diagnosed with sepsis. The diagnostic value of PCT was as accurate as qSOFA. (AUROC 0.73 (0.66-0.80) vs. AUROC 0.71 (0.65-0.77), p 0.742). Compared to SIRS, the diagnostic accuracy was significantly higher for PCT (AUROC 0.58 (0.50-0.65) vs 0.73 (0.66-0.80), p 0.001). There was a statistical correlation between SOFA and procalcitonin, on the contraly, no correlation was found between qSOFA and procalcitonin.

Conclusions

Diagnostic efficacy of serum PCT was equivalent to qSOFA, but there was no correlation between qSOFA and PCT, consequently serum PCT played a limitation role in an ED.

Keywords

SIRS, qSOFA, Procalcitonin, Organ dysfunction, Emergency Department

Introduction

Sepsis is a global serious illness, which causes a significant morbidity and mortality as high as 25% to 60%.[1-3] Key to improve survival rate are early recognition and early diagnosis.[4-5] American College of Chest Physician and Society of Critical Care Medicine (ACCP/SCCM) defined sepsis as systemic inflammatory response (SIRS) ≥ 2 with suspected infection.[6] Still there was limitations of SIRS for diagnosis sepsis. SIRS can be positive in other sterile inflammatory processes, for example burn, trauma and acute pancreatitis.[7] SIRS can also be neglected if patients take medications, including beta-blocker, aspirin and opioid.[8]

The European Society of Intensive Care Medicine (ESICM) and the Society of Critical Care Medicine (SCCM) endorsed a new sepsis-3 definition as severe infection that caused life threatening organ dysfunction.[9] The end organ dysfunction was identified by using sequential organ failure assessment (SOFA) score ≥ 2 or quick (q)SOFA ≥ 2 in case of situation outside intensive care unit (ICU) due to its simple usage. qSOFA consists of 3 clinical elements: altered mental status, respiratory rate (RR) ≥ 22/min and systolic blood pressure (SBP) ≤ 100 mmHg. Sepsis is a critically illness and requires high sensitivity test for early diagnosis, whereas the main concern is that qSOFA has high accuracy, but low sensitivities.[10,11] Other limitations are the interpretation problems of clinical elements, such as bed ridden patients. It is difficult to detect altered mental status. Also, qSOFA cannot predict the outcome of infected cirrhosis patient.[12]

Procalcitonin [PCT] is a novel sepsis biomarker. It has an advantage over lactate because it can differentiate non-specific poor tissue perfusion from infectious process. Serum procalcitonin rises early within 4 hours and level of serum PCT predicts severity, mortality as well as guides an antibiotic strategy.[13,14]

Sudhir U et al. 's study reported a statistically significant correlation between PCT and SOFA in ICU setting.[15] We hypothesize that in an emergency room, we can alternate between SOFA and serum PCT for diagnosing sepsis. The propose of this study is

1. to compare the diagnostic accuracy of PCT, sepsis-2 definition, and sepsis-3 definition.

2. to find out whether serum PCT has a significant correlation with qSOFA and SOFA in an emergency department.

Material and methods

Study design

This prospective observational study was conducted in the emergency department of Vajira hospital, a university and tertiary care hospital in Bangkok, Thailand. This study has been approved by the ethical committee of Vajira hospital's research center. Informed consent has been conducted in all patients.

Protocol and data collection

All patients to the ED will have their vital signs, oxygen saturation, the Glasgow Coma Score, SIRS and qSOFA score recorded at nursing triage. During 8:00 A.M.-12:00 P.M., the emergency resident or emergency staff took an exam and selected patients in both inclusion and exclusion criteria. The Inclusion criteria were patients aged 18 and up with SIRS or qSOFA score ≥ 2 (infection presumption). The exclusion criteria were

1. non-infectious conditions,
2. the presence of cardiac arrest in ED, and
3. conditions that could result in

3.1 false negative of PCT -for example, clinical suspicion of viral infections

3.2 false positive of PCT -for example, severely traumatic injury, heat stroke, burn, postsurgical condition, cardiogenic shock, thyroid cancer (medullary type), small cell lung cancer, carcinoid, acute respiratory distress syndrome [ARDS], malarial infection [plasmodium falciparum type], post organ transplantation with immunosuppressant therapy, transplantation rejection reaction and chemical pneumonitis.

Informed consent was provided by 3rd year paramedic students who were not involved with patient care. Blood test protocol in this research includes complete blood count (CBC), blood urea nitrogen (BUN), creatinine (Cr), electrolyte, liver function test, procalcitonin, 2 hemoculture bottles and arterial blood gas, only in case of impeding respiratory failure or respiratory failure. PCT concentration was measured by an electrochemiluminescence immunoassay (ECLIA) with BRAHMS PCT Elecsys assays. Serum procalcitonin level result revealed in research's hospital number, for blind the treating physician and chart reviewer.

All medical records in the ED were reviewed by 2 physicians: one was ICU physician and the other ID one. Both of them were blinded each other, the objective of the study and the result of procalcitonin.

The gold standard diagnosis of sepsis in this study was at least one of these criteria:

1. positive hemoculture resulted in both 2 bottles,

2. positive hemoculture resulted in one bottle only, identifying pathogen as gram negative organism or gram-positive cocci in chain, and

3. The presence of end organ dysfunction, in which occurred in ED (table 1).

In case of discrepancy diagnosis, both ICU and ID physicians would be appointed to have an agreement.

Primary and secondary objectives

This study aims to compare the accuarcy of various sepsis screening tool in the ED. So, the primary outcome of this study was the diagnosis of sepsis. The secondary one was the correlation between qSOFA, SOFA and procalcitonin in ED.

Statistical analysis

For baseline characteristic, continuous data were represented as mean with standard deviation or median with interquartile test. The categorial data were represented as percentage. The interrater reliability between two reviewers diagnosing all participants were calculated by Cohen's kappa coefficient in K = 0.641 (p-value < 0.001). To access the accuracy of each tool as the primary outcome, the data were analyzed by AUROC curve. The difference in AUROC curves were calculated by Chi square test. The efficacy of qSOFA, SOFA, procalcitonin and procalcitonin combining qSOFA at each cut point was studied by sensitivity, specificity, PPV, NPV and AUROC curve. For the secondary objective, the correlation tests were used. In this study, all statistical analyses were performed by STATA version 13.0 and a P value less than 0.05, considered as significance.

Table 1 Modified criteria for end organ dysfunction

Major organ	Characteristic
Cardiovascular system	- Mean arterial blood pressure (MAP) ≤ 65 mmHg - Systolic blood pressure (SBP) ≤ 90 mmHg - Decrease baseline SBP ≥ 40 mmHg
Respiratory system	- Acute respiratory failure - Impending respiratory failure, due to non-reversible cause
Renal system	- AKI (defined by KDIGO guideline) Cr raising ≥ 0.3 mg/dL within 48 hrs Cr raising ≥ 1.5 times baseline within 1 week Urine Output < 0.5 ml/kg/hr for 6 hrs
Hematologic system	- Platelet < 100,000 - INR ≥ 1.5
Gastrointestinal tract system	- Transaminitis raising more than 3 times of UNL - Total Bilirubin > 2 mg/dL - Decompensated cirrhosis
Central nervous system	- In case of non-bed ridden, GCS ≤ 13 - In case of bed ridden, by history or decrease of GCS ≥ 2 from baseline status
Metabolism system	- In case of non-diabetic, Capillary blood glucose < 50 mg/dL - In case of diabetic, Capillary blood glucose < 70 mg/dL, despite appropriate treatment ** - Lactate > 4 mmol/L - Hyperglycemia ≥ 200 mg/dL

Results

The total of 303 patients were consecutively enrolled in this study during June 2017 through September 2017. Exclusion criteria precluded 96 patients, remaining 207 patients enrolled in this study. Further, all patients were investigated for sepsis, and almost half of them (49.8%) had sepsis (figure 1).

The baseline characteristic of all participating patients was demonstrated in table 2. Median age was 69 years old, (interquartile range 54-80). The percentage of female was slightly higher than this of male (57% vs. 43%). The top three underlying diseases were hypertension (56.0%), diabetes (38.2%) and cardiovascular disease (18.4%). The median of the SIRS and qSOFA were 3 (interquatile range [IQR] 2-3) and 1 (IQR 1-2). The most common source of sepsis was pneumonia (38.2 %). The second common source was urinary tract infection (20.3%). Thirty patients out of 207 were expired during this admission (in-hospital mortality 14.5 %). According to the table 3, SIRS-negative sepsis (57.1%) was higher than qSOFA-negative sepsis (34.4%). SOFA negative sepsis had the lowest percentage (21.5%).

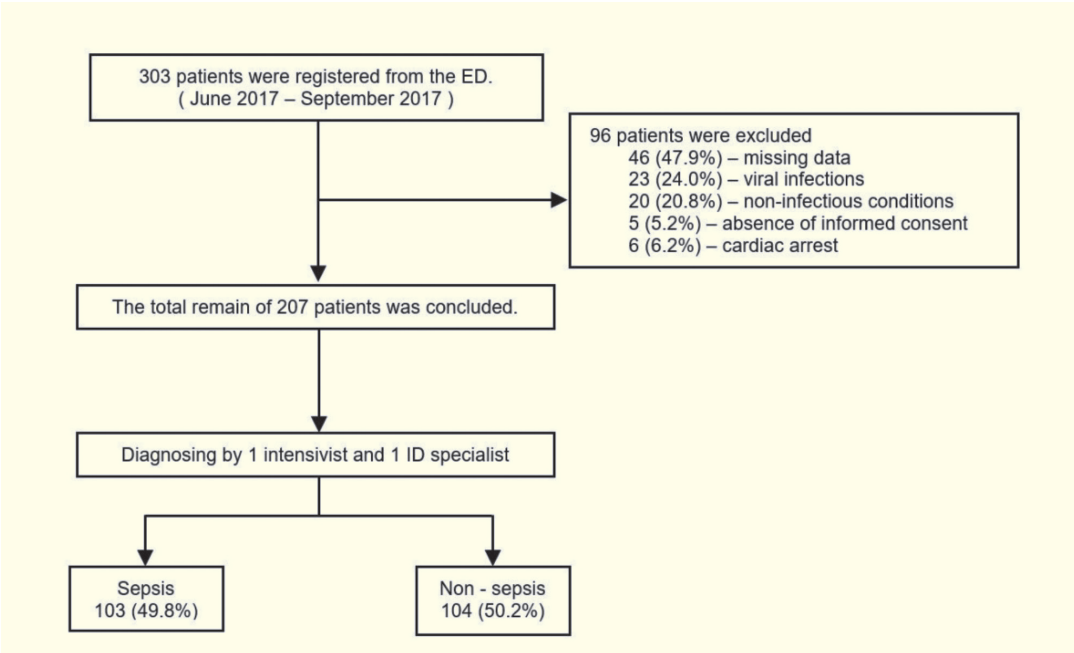

Figure 1 Flow Diagram of this study

Table 2 Baseline characteristic (n=207)

Age	69	(54-80)
Female	118	57.0%
Body mass index (kg/m^2)	22.77	±5.15
Underlying diseases		
Hypertension	116	56.0%
Diabetes	79	38.2%
Cardiovascular disease	38	18.4%
Malignancy	31	15.0%
Renal disease	26	12.6%
Respiratory disease	24	11.6%
Cerebrovascular disease	20	9.7%
Liver disease	14	6.8%
On immunosuppressant	10	4.8%
HIV infection	9	4.3%
Vital signs		
Body Temperature	37.94	±1.03
Systolic blood pressure	136.44	±31.92
Mean arterial pressure	98.67	±21.36
Respiratory rate	22	(24-32)
Pulse rate	106.91	±19.67
GCS	15	(13-15)
Laboratory result		
Hematocrit (%)	32.90	±7.58
White blood cell (WBC)	10,940	(7885-15320)
Band	1	(0-6)
Platelet (x103/µL)	221	(162-307)
Creatinine (mg/dL)	1	(0.745-1.46)
Acute kidney injury (AKI)	54	(26.1)

Age	69	(54-80)
Total Bilirubin (mg/dL)	0.72	(0.54-1.375)
pH	7.35	(7.3-7.4)
Procalcitonin (ng/ml)	0.74	(0.17-3.07)
Lactate	2.2	(1.5-3.5)
Hemoculture 1st bottle	44	21.3%
Hemoculture 2nd bottle	39	18.8%
SIRS	3	(2-3)
qSOFA	1	(1-2)
SOFA	2	(0-4)
APACHE2	16	(12-22)
Sepsis	103	49.8%
Source of infection		
Pneumonia	79	38.2%
Urinary tract infection	42	20.3%
Soft tissue infection	15	7.2%
Intraabdominal infection	32	15.5%
Central nervous system	2	1.0%
Unspecific organ	37	17.9%
Hospital admission	154	74.4%
Discharge	39	18.8%
Admitted ED observation unit	6	2.9%
Refer	8	3.9%
Outcomes	30	14.5%
In-hospital mortality	172	83.1%
Alive	5	2.4%
Unknown		

Data are presented as n (%), mean ± SD, or median (interquartile range).

Table 3 Percentage of qSOFA-negative sepsis, SIRS-negative sepsis, SOFA-negative sepsis

Variables	Sepsis (n=103)		non-Sepsis (n=104)		p-value*
	n	(%)	n	(%)	
qSOFA ≥ 2					
no	43	(34.4)	82	(65.6)	< 0.001
yes	60	(73.2)	22	(26.8)	
SOFA ≥ 2					
no	17	(21.5)	62	(78.5)	< 0.001
yes	86	(67.2)	42	(32.8)	
SIRS ≥ 2					
no	4	(57.1)	3	(42.9)	0.721
yes	99	(49.5)	101	(50.5)	

* Chi-square test for qSOFA SOFA Procalcitonin and Lactate, and Fisher's exact test for SIRS.

The primary objective of this study is the accuracy of each sepsis screening tool in the ED. Procalcitonin had AUC(0.73 (0.66-0.80) more than qSOFA AUC 0.71 (0.65-0.77), p = 0.742) but there was no statistically significant. When compared with SIRS, the diagnostic accuracy of procalcitonin outperforms SIRS (0.73 [0.66-0.80] vs 0.58 [0.50-0.65], p = 0.001). This study indicated that SIRS had the lowest AUC curve which performed inferior to qSOFA particularly (0.58[0.50-0.65] vs 0.71 [0.65-0.77], p = 0.006). To compare the ability to diagnose sepsis among sepsis biomarkers, the AUC of procalcitonin was as effective as lactate (0.73[0.66-0.80] vs 0.72[0.65-0.79], p = 0.868) (figure 2-5).

For the secondary objective, this study shows a statistical correlation between SOFA and procalcitonin (correlation coefficient = 0.297, p < 0.001), but no correlation was found between qSOFA and procalcitonin (correlation coefficient = 0.063, p = 0.366).

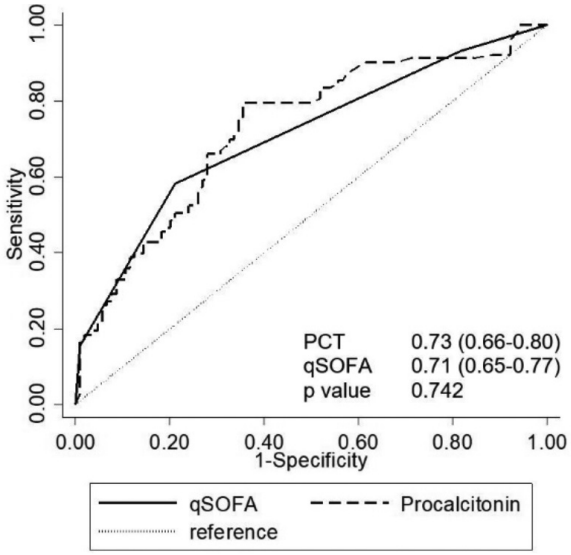

Figure 2 AUROC curve of PCT and qSOFA for diagnosing sepsis

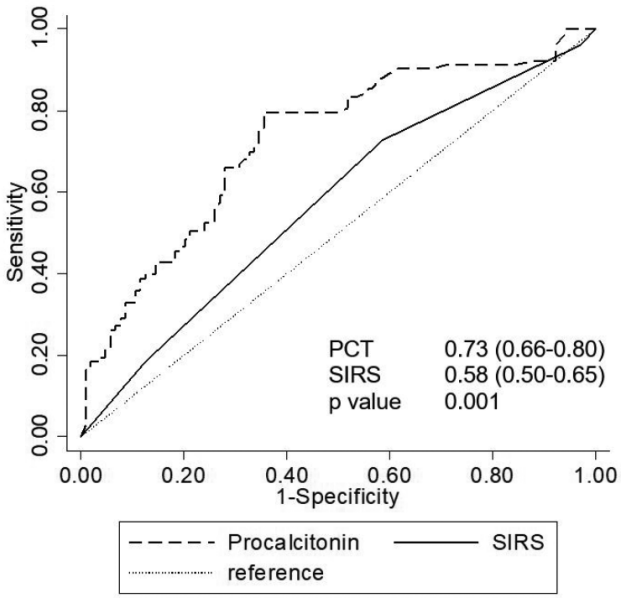

Figure 3 AUROC curve of PCT and SIRS for diagnosing sepsis

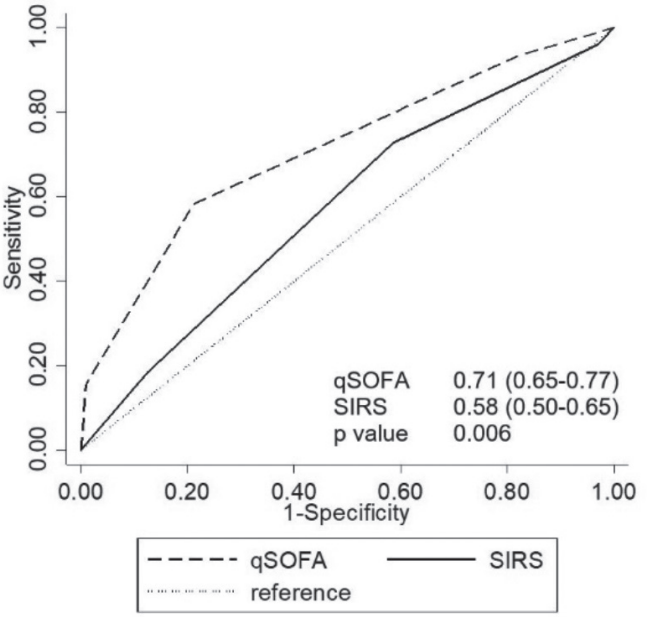

Figure 4 AUROC curve of qSOFA and SIRS for diagnosing sepsis

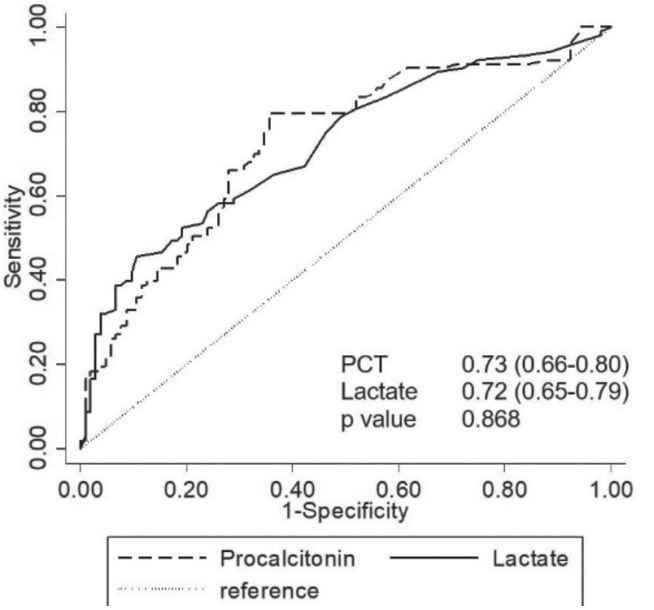

Figure 5 AUROC curve of PCT and lactate for diagnosing sepsis

To consider accuracy of qSOFA at each cut point, sensitivity of qSOFA ≥ 1 was 93.2 % (95% CI 86.5-97.2), specificity of qSOFA ≥ 1 was 18.27 (95% CI 11.4-27.1), whereas sensitivity and specificity of qSOFA ≥ 2 were 58.25 % (95% CI 48.1-67.9), 78.85 (95% CI 69.7-86.2), respectively.

The ROC curves for diagnosing sepsis of qSOFA ≥ 1, qSOFA ≥ 2, PCT ≥ 0.5 ng/mL were 0.56 (0.51-0.60), 0.69 (0.62-0.75), 0.71 (0.64-0.77) respectively. Combining qSOFA ≥ 2 with procalcitonin ≥ 0.5 ng/mL resulted in as same the AUC as qSOFA ≥ 2 (0.69 (0.64-0.75) vs 0.69(0.62-0.75)), when combining qSOFA ≥ 1 with procalcitonin ≥ 0.5 ng/mL slightly increased the AUC (0.72(0.66-0.78) vs 0.69(0.62-0.75)).

Table 5 Sensitivity, Specificity, PPV, NPV, PLR, NLR and AUROC for diagnosing sepsis

Screening tool	SIRS ≥ 2	qSOFA ≥ 1	qSOFA ≥ 2	PCT ≥ 0.5	qSOFA ≥ 1 and PCT ≥ 0.5	qSOFA ≥ 2 and PCT ≥ 0.5	SOFA ≥ 2
Sensitivity%, (95%CI)	96.1 (90.4-98.9)	93.2 (86.5-97.2)	58.3 (48.1-67.9)	75.7 (66.3-83.6)	69.9 (60.1-78.5)	42.7 (33.0-52.8)	83.5 (74.9-90.1)
Specificity%, (95%CI)	2.9 (0.6-8.2)	18.3 (11.4-27.1)	78.8 (69.7-86.2)	65.4 (55.4-74.4)	74.0 (64.5-82.1)	96.2 (90.4-98.9)	59.6 (49.5-69.1)
Predictive Value							
Positive,(95%CI)	49.5 (42.4-56.6)	53.0 (45.5-60.5)	73.2 (62.2-82.4)	68.4 (59.1-76.8)	72.7 (62.9-81.2)	91.7 (80.0-97.7)	67.2 (58.3-75.2)
Negative,(95%CI)	42.9 (9.9-81.6)	73.1 (52.2-88.4)	65.6 (56.6-73.9)	73.1 (62.9-81.8)	71.3 (61.8-79.6)	62.9 (54.9-70.4)	78.5 (67.8-86.9)
Likelihood ratio							
Positive,(95%CI)	0.99 (0.94-1.04)	1.14 (1.03-1.27)	2.75 (1.84-4.13)	2.19 (1.64-2.91)	2.69 (1.90-3.81)	11.11 (4.14-29.79)	2.07 (1.61-2.65)
Negative,(95%CI)	1.35 (0.31-5.87)	0.37 (0.16-0.85)	0.53 (0.41-0.68)	0.37 (0.26-0.54)	0.41 (0.30-0.56)	0.60 (0.50-0.71)	0.28 (0.17-0.44)
AUROC,(95%CI)	0.50 (0.47-0.52)	0.56 (0.51-0.60)	0.69 (0.62-0.75)	0.71 (0.64-0.77)	0.72 (0.66-0.78)	0.69 (0.64-0.75)	0.72 (0.66-0.78)

Discussion

Considering as sepsis screening tool in an ED, diagnostic accuracy of procalcitonin was comparable to qSOFA (AUROC 0.73 (0.66-0.80) vs 0.71 (0.65-0.77), p = 0.742), whereas sensitivity of PCT ≥ 0.5 ng/mL was much higher than qSOFA ≥ 2 (75.7(66.3-83.6) VS 58.3(48.1-67.9)). The hypothesis we suppose is that sepsis triggers the sudden release of intrinsic inflammatory cytokine, then leads to the end organ dysfunction respectively. As a result, PCT is more sensitive than the manifestation of organ failure. Study by Harbarth et al., Brunkhorst et al. and Annam et al. shows that severe sepsis patients have high level of serum PCT.[16-18]

Compared with SIRS, diagnostic accuracy of qSOFA outperformed statistically (AUROC 0.71(0.65-0.77) vs 0.58(0.50-0.65), p = 0.006). qSOFA was not shown to be the best tool because when we compared qSOFA at the cut point 2 with SIRS, qSOFA has lower sensitivity than SIRS ≥ 2 (58.3(48.1-67.9) VS 96.1(90.4-98.9)). To maximize sensitivity of qSOFA, considering at cut point 1 resulted in higher sensitivity than cut point 2 (93.2 (86.5-97.2) VS 58.3(48.1-67.9)). Our study supports the result of Park HK et al.'s study.[19]

AUROC of combining qSOFA ≥ 1 with PCT ≥ 0.5 ng/mL was equivalent to AUROC of SOFA ≥ 2 [0.72(0.66-0.78) VS 0.72 (0.66-0.78)]. We considered PCT along with clinical score qSOFA at cut-point 1 because it could raise the sensitivity, while slightly decreasing the specificity, and interestingly increasing AUROC. Ho KM, Lan NS reported that combining qSOFA with plasma lactate could have the predictive equivalent of standard SOFA score. In conclusion, our study and Ho KM study show that considering clinical scoring system with laboratory sepsis biomarker was likely to improve diagnostic accuarcy.[20]

Our study confirms the result from the study by Uchil Sudhir et al. reported that there was a significant association between serum PCT and SOFA score (P < 0.05)(15). Our study was the first study that analyzed a correlation between serum PCT and qSOFA. The result of serum PCT has no correlation with qSOFA doubting our hypothesis. qSOFA was a screening tool that considered only 3 organ dysfunctions; respiratory system, cardiovascular system, central nervous system, while SOFA considered more 6 organ dysfunctions; central nervous system, GI, Coagulation, renal system, respiratory system and cardiovascular system. SOFA has broadened

spectrums to detect abnormalities and has more chance to correlate with PCT than qSOFA.

Limitations in this study were 1. a single center study, 2. the investigation of end organ dysfunction in this study was established at emergency department only, so that patients who developed toward the end organ dysfunction later in the ward would be under-detected, 3. using qSOFA ≥ 2 and SIRS ≥ 2 as inclusion criteria causes a selective bias. So, the diagnostic value of qSOFA ≥ 2 and SIRS ≥ 2 can be overestimated.

In clinical practice, PCT might not commonly be used because the efficacy of PCT was comparable to qSOFA, more expensive, not available in small institutes. And it took take more time to get a result, which could result in delayed antibiotic administration. However, PCT could be used/considered in case that has some limitation on interpretation of qSOFA. For example, chronic cirrhosis patients have low baseline blood pressure; bed ridden ones whose GCS can't be evaluated; COPD exacerbation ones and pneumonia ones had concurrent congestive heart failure. We would suggest to use using PCT as screening tool in the institute that the laboratory could revealed quickly or point-of-care test of PCT was available.

Conclusions

Diagnostic efficacy of serum PCT was equivalent to qSOFA, but sensitivity of PCT was higher, consequently serum PCT was valuable in some specific patients that qSOFA can't be interpreted. A further study needed to be investigated.

Funding

This work was supported by the Faculty of medicine, Navamindradhiraj university [grant numbers CEU/C038/2560, 2017]

Declarations of interest

none

Acknowledgements

We would like to thank you Winai Taowalanon, Kulwadee Thanamit, Natnicha Lanak

Partimapron Boonrawd , Rittikiet Meepuangphon , Duanghathai Thaitan, Punyapron Khemnak

Tharika Mahayodsanan , Runya Panna for data collected

References

1. Engel C, Brunkhorst FM, Bone HG, Brunkhorst R, Gerlach H, Grond S, et al. Epidemiology of sepsis in Germany: results from a national prospective multicenter study. Intensive Care Med. 2007;33(4):606-18.
2. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001;29(7):1303-10.
3. Lever A, Mackenzie I. Sepsis: definition, epidemiology, and diagnosis. BMJ (Clinical research ed). 2007;335(7625):879-83.
4. Carlet J. Rapid diagnostic methods in the detection of sepsis. Infect Dis Clin North Am. 1999;13(2):483-94, xi.
5. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41(2):580-637.
6. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med 2003;31(4):1250-6.
7. Vincent JL, Opal SM, Marshall JC, Tracey KJ. Sepsis definitions: time for change. Lancet (London, England). 2013;381(9868):774-5.
8. Sawawiboon C. Pitfalls in the management of sepsis in Thailand. J Med Asso Thai 2014;97 Suppl 1:S137-41.
9. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801-10.
10. Simpson SQ. New Sepsis Criteria: A Change We Should Not Make. Chest. 2016;149(5):1117-8.
11. Cortes-Puch I, Hartog CS. Opening the Debate on the New Sepsis Definition Change Is Not Necessarily Progress: Revision of the Sepsis Definition Should Be Based on New Scientific Insights. Am J Res Crit Care Med. 2016;194(1):16-8.
12. Patidar KR, Shaw J, Acharya C, Thacker LR, White MB, Ganapathy D, et al. No Association Between Quick Sequential Organ Failure Assessment and Outcomes of Patients With Cirrhosis and Infections. Clinical gastroenterology and hepatology : the official clinical practice journal of the Am Gastro Asso. 2017;15(11):1803-4.
13. Faix JD. Biomarkers of sepsis. Critical reviews in clinical laboratory sciences. 2013;50(1):23-36.
14. Schuetz P, Albrich W, Mueller B. Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future. BMC medicine. 2011;9:107.
15. Sudhir U, Venkatachalaiah RK, Kumar TA, Rao MY, Kempegowda P. Significance of serum procalcitonin in sepsis. Indian J Crit Care Med. 2011;15(1):1-5.
16. Harbarth S, Holeckova K, Froidevaux C, Pittet D, Ricou B, Grau GE, et al. Diagnostic value of procalcitonin, interleukin-6, and interleukin-8 in critically ill patients admitted with suspected sepsis. Am J Res Crit Care Med. 2001;164(3):396-402.
17. Brunkhorst FM, Wegscheider K, Forycki ZF, Brunkhorst R. Procalcitonin for early diagnosis and differentiation of SIRS, sepsis, severe sepsis, and septic shock. Intensive Care Med. 2000;26 Suppl 2:S148-52.

18. Annam V, Maleedhu P, Bhaskar MV, Venugopal L. Evaluation of Serum Procalcitonin Levels and Sequential Organ Failure Assessment Score in Assessing the Severity and Outcome of Sepsis. Hematology. 2016;67(141):100.
19. Park HK, Kim WY, Kim MC, Jung W, Ko BS. Quick sequential organ failure assessment compared to systemic inflammatory response syndrome for predicting sepsis in emergency department. J Crit Care. 2017;42:12-7.
20. Ho KM, Lan NS. Combining quick Sequential Organ Failure Assessment with plasma lactate concentration is comparable to standard Sequential Organ Failure Assessment score in predicting mortality of patients with and without suspected infection. J Crit Care. 2017;38:1-5.