

## PANCREATIC STONE PROTEIN IN CO-EVALUATION WITH QSOFA AND NEWS2 FOR EARLY SEPSIS DETECTION AT THE EMERGENCY DEPARTMENT

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**ABSTRACT—Background:** Early sepsis identification at the emergency department (ED) triage is essential for timely treatment and improved outcomes. This study evaluated the diagnostic performance of pancreatic stone protein (PSP) in combination with the quick Sequential Organ Failure Assessment (qSOFA) and the National Early Warning Score (NEWS2) for early sepsis detection. **Methods:** As part of the PROMPT study—a noninterventive, multicenter trial across six Greek hospitals—blood samples were collected within the first hour of admission in the emergency department. PSP levels were retrospectively assessed using a nanofluidic near-patient immunoassay device (abioSCOPE, Abionic SA, Switzerland) in 362 adult patients with suspected infections and evaluated their qSOFA and NEWS2 scores. Objectives included evaluating qSOFA's performance, assessing the performance of PSP to identify high-risk patients with qSOFA  $\leq 1$ , and determining the added value of combining PSP with qSOFA or NEWS2 (cutoff  $\geq 7$ ), using standard performance metrics. **Results:** Among 156 sepsis cases, 128 (82.1%) had qSOFA scores  $\leq 1$ . A qSOFA score  $\geq 2$  demonstrated sensitivity 17.9% and specificity 97.1% for sepsis diagnosis. In comparison, a qSOFA score of 1 showed a sensitivity of 44.2% and a specificity of 63.6%, while a score of 0 yielded a sensitivity of 37.8% and a specificity of 39.3%. The addition of PSP (cutoff: 300 ng/mL) to qSOFA  $\leq 1$  improved specificity to 94.0%, with a sensitivity of 14.8%—closely mirroring the performance of qSOFA  $\geq 2$ . Similarly, combining PSP with NEWS2  $< 7$  increased true positive cases from 34 to 52, enhancing sensitivity while maintaining high specificity. **Conclusions:** This study highlights the utility of combining PSP levels in the patient's blood with existing scoring systems to enhance early sepsis detection in high-risk ED patients. Future research will explore near-patient PSP measurements at ED triage to further refine and expedite sepsis management.

**KEYWORDS—**Pancreatic stone protein; PSP assay; point-of-care; diagnostic; sepsis; biomarker; ED triage

### INTRODUCTION

Sepsis is a life-threatening condition characterized by organ dysfunction resulting from a dysregulated host response to infection, posing a significant public healthcare challenge (1). According to data published in 2020, there were 48.9 million

cases of sepsis and 11 million sepsis-related deaths globally, accounting for 19.7% of all deaths worldwide (2). Early detection of high-risk patients to guide timely treatment is crucial for preventing unfavorable outcomes in sepsis, emphasizing the need for diagnostic tools that enable early identification. Administering antimicrobial treatment within the first hour yields a 79.9% survival rate, with each additional hour of delay increasing mortality by approximately 8% (3).

Pancreatic stone protein (PSP) is an early sepsis biomarker used in clinical practice, with evidence supporting its use for screening nosocomial sepsis in high-risk patients and aiding in sepsis diagnosis within hospital settings (4). Since 2020, PSP levels can be rapidly and reliably measured within 10 minutes using a CE-marked and FDA-cleared near-patient immunoassay (abioSCOPE, Abionic SA, Epalinges, Switzerland). This PSP assay has been evaluated across various clinical settings, including intensive care units, emergency departments (EDs), and pediatric high dependency care units, demonstrating diagnostic accuracy for identifying sepsis comparable to that of traditional biomarkers such as C-reactive protein, procalcitonin, and white blood cell count (5–7).

The Sepsis-3 definitions introduced the quick Sequential Organ Failure Assessment (qSOFA) as a bedside clinical tool to aid in early sepsis detection, though it has been associated with low sensitivity and is not recommended as a standalone screening tool according to the 2021 Surviving Sepsis Campaign guidelines (1,8–10). The qSOFA is a simple tool that combines mental

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confusion, increased respiratory rate, and hypotension. Patients with suspected infection and at least two of these signs face a nearly 3-fold higher risk of 28-day mortality (1). Early resuscitation is advised for those with 2–3 qSOFA points, but there is uncertainty regarding the management of patients with 0–1 qSOFA points (9–12). Combining biomarkers with the Sepsis-3 criteria has been proposed as a strategy to improve the performance of the current criteria for more accurate diagnoses (13).

The National Early Warning Score (NEWS) was introduced in 2012 and revised in 2017 as NEWS2. Developed and implemented by the National Health Service in the United Kingdom, NEWS2 supports clinicians in assessing illness severity, detecting clinical deterioration, and facilitating timely interventions (14). Current evidence suggests that NEWS2 may be a superior screening tool for identifying sepsis and predicting mortality in the ED (15,16).

In this retrospective study, we utilized blood samples collected during the PROMPT study—a prospective, noninterventional, multicenter clinical study aiming to assess the clinical validity of heparin-binding protein for the diagnosis of sepsis and the prediction of outcome over the first 72 hours after ED admission (17)—to evaluate PSP as a predictor of sepsis. As a next step, we asked if in the study population with a qSOFA score of 0 or 1, PSP can detect at the ED those who suffer from sepsis. Finally, we assessed the performance of NEWS2 (using a predefined cutoff of  $\geq 7$ , corresponding to the high-risk category for clinical deterioration) and its combination with PSP.

## PATIENTS AND METHODS

The PROMPT study was conducted between September 2017 and September 2018, in the EDs of six hospitals in Greece within the Hellenic Sepsis Study Group network (ClinicalTrials.gov registration NCT03295825). The study protocol was approved by the Ethics Committees of the participating hospitals. Patients were enrolled after written informed consent was provided by themselves or by first-degree relatives for those unable to consent.

Enrolled patients were adult patients of both sexes with suspected infection who met at least one of the following criteria: core temperature  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ , heart rate  $\geq 90$  beats per minute, respiratory rate  $>20$  breaths per minute, or self-reported fever or chills. There were no exclusion criteria. Patients were classified as no-sepsis or sepsis based on the Sepsis-3 criteria within the first 72 hours (1,9). More precisely, sepsis was classified as the presence of acute infection aggravated by at least a 2-point increase in baseline total SOFA; patients with unknown baseline SOFA score were classified into sepsis when acute infection was accompanied by a total SOFA score  $\geq 2$ . For full details of the methodology of the PROMPT study, refer to previously published papers (17,18).

Clinical criteria that constitute the qSOFA include a respiratory rate of 22/min or greater, altered mentation, or systolic blood pressure of 100 mmHg or less (1). Each criterion is assigned 1 point, resulting in a total score ranging from 0 to 3. NEWS2 incorporates seven physiological parameters, including respiratory rate, oxygen saturation, requirement for supplemental oxygen, heart rate, blood pressure, level of consciousness

or new confusion, and temperature (14,19). NEWS2 stratifies patients into risk categories based on total score: low risk (0–4), medium risk (5–6), and high risk ( $\geq 7$ ).

Blood was drawn after venipuncture of one forearm vein under aseptic conditions. Five milliliters of whole blood were collected in the ED within the first hour of admission into a tube containing ethylenediaminetetraacetic acid. The blood was centrifuged at 5,000 rpm for 10 minutes to separate the plasma, which was then stored at  $-80^{\circ}\text{C}$  until further analysis. For the PSP analyses, we were able to utilize the blood samples collected during the PROMPT study. PSP levels were determined from 50 mL of  $\text{K}_2$ -ethylenediaminetetraacetic acid anticoagulated venous plasma samples using the *in vitro* diagnostic IVD CAPSULE PSP capsule, which is a single-use, rapid immunofluorescence assay used together with the near-patient abioSCOPE reading platform. The PSP cutoff of 300 ng/mL specified in the manufacturer's instructions for use was used.

## ANALYSIS

Parameters were summarized using descriptive statistics. For each diagnostic criterion analyzed (i.e., qSOFA  $\geq 2$ , NEWS2  $\geq 7$ , PSP, or combinations with PSP) and each cutoff (i.e., qSOFA = 0, qSOFA = 1, qSOFA  $\leq 1$ , and qSOFA  $\geq 2$ , 300 ng/mL for PSP, NEWS2  $\geq 7$ ), the number of patients diagnosed as either positive or negative for sepsis was counted. Patients with a result within the specific score/threshold range were classified as “true positive” (TP) if they were actually sepsis positive by meeting the Sepsis-3 definitions, or as “false positive” (FP) if they were sepsis negative. If the result was outside of the specific score/threshold range, they were classified as “true negative” (TN) if they were actually sepsis negative or as “false negative” (FN) if they were sepsis positive. The following metrics and their 95% confidence intervals were then derived: sensitivity or TP rate calculated as TP/(TP + FN); specificity or TN rate calculated as TN/(TN + FP); positive and negative predictive values, calculated as positives/(TP + FP) and negatives/(TN + FN), respectively; and positive and negative likelihood ratios (LR+ and LR–) calculated as (Sensitivity)/(1 – Specificity) and (1 – Sensitivity)/(Specificity). The accuracy was calculated as (TP + TN)/(TP + TN + FP + FN). A cutoff of 300 ng/mL was chosen based on a previous study by Pugin et al., (7) which identified an optimal PSP threshold of 292 ng/mL in intensive care unit patients. This cutoff aligns with the established intended use of the PSP test, and the available clinical performance data of the assay where PSP levels  $\geq 300$  ng/mL indicate a high-risk of sepsis and ensure a specificity of  $\geq 95\%$ , comparable to qSOFA scores  $\geq 2$  and NEWS2  $\geq 7$ . This diagnostic test is used in conjunction with other clinical assessments and laboratory findings to aid in the early detection of sepsis. Comparisons of PSP across different types of infections were done by the Kruskal–Wallis test with Bonferroni corrections for multiple comparisons.

## RESULTS

For detailed demographics of the PROMPT study participants, please refer to the previously published paper of

TABLE 1. Diagnostic performance of PSP positivity ( $\geq 300$  ng/mL) versus positive clinical scores (qSOFA  $\geq 2$  or NEWS2  $\geq 7$ )

Parameter	PSP $\geq 300$ ng/mL	qSOFA $\geq 2$	NEWS2 $\geq 7$
Accuracy	60.8% (56.6%–65.0%)	63.0% (58.8%–67.2%)	64.9% (60.8%–69.0%)
NPV	59.9% (55.4%–64.4%)	61.0% (56.5%–65.4%)	62.2% (57.8%–66.7%)
PPV	68.4% (56.0%–80.8%)	82.4% (71.6%–93.1%)	87.2% (78.4%–96.0%)
Sensitivity	16.7% (11.8%–21.6%)	17.9% (12.9%–23.0%)	21.8% (16.4%–27.2%)
Specificity	94.2% (91.5%–96.9%)	97.1% (95.2%–99.0%)	97.6% (95.8%–99.3%)
LR+	2.86 (1.66–4.94)	6.16 (3.00–12.65)	8.98 (4.16–19.36)
LR–	0.88 (0.83–0.94)	0.85 (0.79–0.90)	0.80 (0.75–0.86)
TP	26	28	34
FP	12	6	5
FN	130	128	122
TN	194	200	201
Total number	362	362	362

FN, false negative; FP, false positive; NEWS2, National Early Warning Score; NPV, negative predictive value; PPV, positive predictive value; PSP, pancreatic stone protein; qSOFA, quick Sequential Organ Failure Assessment; TN, true negative; TP, true positive.

Katsaros et al. (17). The analysis in this study included 362 (out of 371) patients for whom PSP, qSOFA, and NEWS2 outcomes were available. Of 156 sepsis cases in this study, 128 (82.1%) were represented by qSOFA scores of 0 and 1 (Table 1). The qSOFA and NEWS2 results in the PROMPT study for specificity (qSOFA  $\geq 2$ : 97.1%, NEWS2  $\geq 7$ : 91.3%) and sensitivity (qSOFA  $\geq 2$ : 17.9%, NEWS2  $\geq 7$ : 30.1%) confirm its established performance for ruling-in patients at high-risk of sepsis at qSOFA score  $\geq 2$  and NEWS2 score  $\geq 7$  (Table 1). At a PSP threshold of 300 ng/mL, the accuracy for diagnosing sepsis was 60.8%, the sensitivity was 16.7%, the specificity was 94.2%, the positive predictive value was 68.4%, the negative predictive value was 59.9%, and the LR+ and LR– ratios were 2.86 and 0.88, respectively (Table 1). In the patients' subpopulation with qSOFA scores 0 and 1, PSP  $\geq 300$  ng/mL showed specificity 94.0% and sensitivity 14.8% for sepsis diagnosis (Table 2).

This generates the question of what the diagnostic performance for sepsis would be if clinicians use both PSP and qSOFA to early track sepsis patients. Indeed, in that case, the diagnosis sensitivity would increase to 30.1% (nearly double the sensitivity observed with qSOFA  $\geq 2$  alone); specificity remains high at 92.2% (Table 3).

Following a similar rationale, the diagnostic performance of both NEWS2 and PSP is summarized in Table 3. Using the combined criterion (NEWS2  $\geq 7$  or PSP  $\geq 300$  ng/mL), 52 septic patients were correctly identified, compared to 34 with NEWS2 alone, representing an increase of 18 additional TP cases.

The diagnostic performance of PSP, qSOFA, NEWS2, and their combinations was also evaluated using area under the receiver operator curve (AUROC) analysis (Fig. 1, A and B). All measures performed significantly better than random chance (AUROC = 50%;  $P < 0.0001$ , tested with 10,000 permutations). The AUROC values were as follows: PSP alone (69.2%), qSOFA alone (63.7%), and PSP or qSOFA combined (71.7%). NEWS2 alone showed an AUROC of 66.6%, while PSP or NEWS2 combined achieved 77.3%.

The distribution of values of PSP per type of infection is shown in Figure 2. Following corrections by Bonferroni for multiple comparisons, the only differences found were for intra-abdominal infections having PSP higher than both upper respiratory tract infections ( $P = 0.026$ ), and lower urinary tract infections ( $P = 0.049$ ).

TABLE 3. Diagnostic performance of combined qSOFA-PSP and NEWS2-PSP algorithms

Parameter	qSOFA + PSP	NEWS2 + PSP
Cutoff	qSOFA $\geq 2$ or PSP $\geq 300$ ng/mL	NEWS2 $\geq 7$ or PSP $\geq 300$ ng/mL
Accuracy	64.9% (60.8%–69.0%)	66.6% (62.5%–70.7%)
NPV	63.3% (58.7%–67.9%)	64.5% (59.9%–69.1%)
PPV	72.3% (63.2%–81.4%)	75.4% (66.8%–83.9%)
Sensitivity	30.1% (24.1%–36.2%)	33.3% (27.1%–39.5%)
Specificity	91.3% (88.0%–94.5%)	91.7% (88.6%–94.9%)
LR+	3.45 (2.26–5.25)	4.04 (2.64–6.18)
LR–	0.77 (0.70–0.84)	0.73 (0.66–0.80)
TP	47	52
FP	18	17
FN	109	104
TN	188	189
Total number	362	362

TABLE 2. Diagnostic performance of positive PSP ( $\geq 300$  ng/mL) in patients with negative clinical scores (qSOFA  $< 2$  and NEWS2  $< 7$ )

Parameter	qSOFA $\leq 1$	NEWS2 $< 7$
Cutoff	PSP $\geq 300$ ng/mL	PSP $\geq 300$ ng/mL
Accuracy	63.1% (58.7%–67.5%)	64.1% (58.7%–69.1%)
NPV	63.3% (58.7%–67.9%)	64.5% (58.9%–69.8%)
PPV	61.3% (46.9%–75.7%)	60.0% (43.2%–74.6%)
Sensitivity	14.8% (9.7%–20.0%)	14.8% (9.2%–22.3%)
Specificity	94.0% (91.2%–96.8%)	94.0% (89.9%–96.7%)
LR+	2.47 (1.39–4.41)	2.47 (1.32–4.63)
LR–	0.91 (0.85–0.97)	0.91 (0.83–0.99)
TP	19	18
FP	12	12
FN	109	104
TN	188	189
Total number	328	323

FN, false negative; FP, false positive; LR, likelihood ratio; NEWS2, National Early Warning Score; NPV, negative predictive value; PPV, positive predictive value; PSP, pancreatic stone protein; qSOFA, quick Sequential Organ Failure Assessment; TN, true negative; TP, true positive.

FN, false negative; FP, false positive; LR, likelihood ratio; NEWS2, National Early Warning Score; NPV, negative predictive value; PPV, positive predictive value; PSP, pancreatic stone protein; qSOFA, quick Sequential Organ Failure Assessment; TN, true negative; TP, true positive.

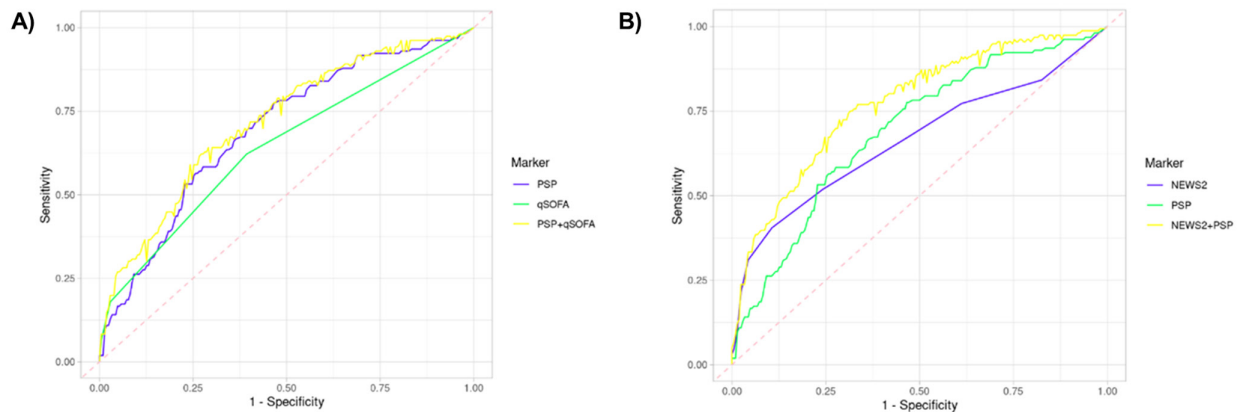


FIG. 1. **Diagnostic performance of PSP, qSOFA, NEWS2, and their combinations by receiver operating characteristic (ROC) analysis.** A, Displays ROC curves comparing PSP, qSOFA, and their combined use. B, Illustrates the comparative performance of PSP, NEWS2, and their respective combinations. NEWS2, New Early Warning Score 2; PSP, pancreatic stone protein; qSOFA, quick sequential organ failure assessment.

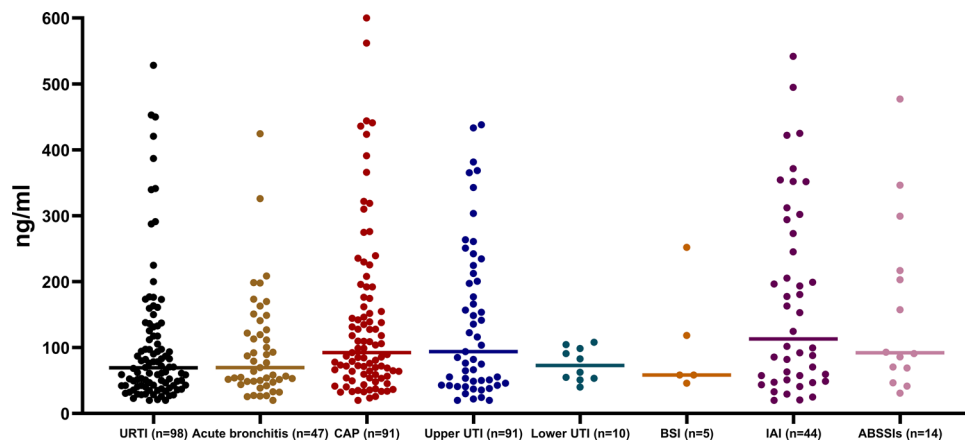


FIG. 2. **Concentrations of PSP across types of infection.** Lines represent medians. ABSSI, acute bacterial skin and skin structure infection; BSI, primary bacteremia; CAP, community-acquired pneumonia; IAI, intra-abdominal infection; PSP, pancreatic stone protein; URTI, upper respiratory tract infection; UTI, urinary tract infection.

## DISCUSSION

In this retrospective analysis, we analyzed plasma blood samples from the prospective PROMPT study to evaluate the diagnostic performance of the PSP assay for sepsis detection in ED patients, alongside an assessment of qSOFA and NEWS2  $\geq 7$  scores. When patients present at the ED, triage serves as the initial step to prioritize care based on the urgency of their medical needs, as determined by scales like the Emergency Severity Index (20). Patients with seemingly less severe conditions may face extended waiting times, often several hours, which poses a significant concern for sepsis patients, who may initially show minimal clinical symptoms.

In our study, a considerable proportion of sepsis patients presented limited initial clinical signs, with 82.1% of cases scoring 0 or 1 on the qSOFA scale. This lack of observable symptoms often leads to misclassification of patients as nonurgent, delaying diagnosis and treatment. The qSOFA score in this study reaffirmed its high specificity (97.1% at qSOFA  $\geq 2$ ) but low sensitivity (17.9% at qSOFA  $\geq 2$ ), aligning with previous findings that also reported low sensitivities for qSOFA scores in early risk assessments in emergency settings (9,10). This underscores the need for complementary tools to enhance sepsis detection in the

ED. In our analysis, the PSP assay proved advantageous in identifying high-risk sepsis patients even with qSOFA scores of 0 or 1. For instance, at PSP thresholds of 300 ng/mL for qSOFA  $\leq 1$ , the specificity was 94.0%, making it a suitable tool for “ruling in,” similar to the qSOFA. Combining PSP and qSOFA further improved diagnostic performance, resulting in a sensitivity of 30.1% (almost doubled compared with qSOFA  $\geq 2$  alone) and a specificity of 92.2%. This specificity was comparable to that observed for qSOFA score  $\geq 2$  (97.1%).

In addition, we assessed the performance of NEWS2 using a predefined cutoff of  $\geq 7$ , corresponding to the high-risk category for clinical deterioration. When used alone, NEWS2  $\geq 7$  correctly identified 34 septic patients. However, combining NEWS2 with PSP (NEWS2  $\geq 7$  or PSP  $\geq 300$  ng/mL) increased the number of TPs to 52, identifying 18 additional sepsis cases. This combined approach improved sensitivity (from 21.5% to 33.3%), while maintaining high specificity (91.7% instead of 97.6%). These findings demonstrate the value of using PSP to enhance the diagnostic accuracy of existing scoring systems for early sepsis detection, paralleling findings from other studies that have shown improvements in sepsis detection in emergency settings through the incorporation of newer biomarkers (11,17,21).

The performance of PSP, qSOFA, NEWS2, and their combinations was evaluated using AUROC curves. The AUROC analysis confirms that integrating PSP with clinical scores (qSOFA or NEWS2) enhances diagnostic accuracy for sepsis detection. While qSOFA and NEWS2 alone showed moderate discrimination (AUROC 63.7%–66.6%), their combination with PSP significantly improved performance (71.7%–77.3%). This aligns with prior studies demonstrating that biomarkers complement clinical scores by mitigating their sensitivity limitations, particularly in early sepsis, where clinical signs may be subtle. The superior AUROC of the PSP-NEWS2 combination (77.3%) suggests utility in ED settings, where rapid risk stratification is critical. However, we note that AUROC values <80% indicate room for further optimization, possibly through multimarker panels or dynamic monitoring.

Current triage practices typically involve simple measurements, like vital signs or finger-prick, with minimal time allotted per patient. A PSP-based point-of-care solution could address these constraints by providing rapid and reliable biomarker measurements to complement traditional triage assessments. Findings suggest that patient evaluation should first rely on qSOFA and NEWS2, which are purely clinical scores. In case these scores do not aid in sepsis diagnosis, further evaluation using PSP should be considered.

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### REFERENCES

- Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801–810.
- Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the global burden of disease study. *Lancet*. 2020;395(10219):200–211.
- Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*. 2006;34(6):1589–1596.
- Ventura F, Eggimman P, Daix T, Francois B, Pugin J. Pancreatic stone protein measurement to screen and diagnose sepsis in the context of the Surviving Sepsis Campaign recommendations. *Med Res Arch*. 2024;11:1–19.
- Bottari G, Paionni E, Fegatelli DA, et al. Pancreatic Stone protein in the diagnosis of sepsis in children admitted to high-dependency care: a single-center prospective cohort study. *Pediatr Crit Care Med*. 2024;25(10):937–946.
- de Hond TAP, Oosterheert JJ, van Hemert-Glaubitx SJM, Musson REA, Kaasjager KAH. Pancreatic stone protein as a biomarker for sepsis at the emergency department of a large tertiary hospital. *Pathogens*. 2022;11(5):559.
- Pugin J, Daix T, Pagani JL, et al. Serial measurement of pancreatic stone protein for the early detection of sepsis in intensive care unit patients: a prospective multicentric study. *Crit Care*. 2021;25(1):151.
- Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Crit Care Med*. 2021;49(11):e1063–e1143.
- Giamarellos-Bourboulis EJ, Tsaganos T, Tsangaris I, et al; Hellenic Sepsis Study Group. Validation of the new Sepsis-3 definitions: proposal for improvement in early risk identification. *Clin Microbiol Infect*. 2017;23(2):104–109.
- Tusgul S, Carron PN, Yersin B, Calandra T, Dami F. Low sensitivity of qSOFA, SIRS criteria and sepsis definition to identify infected patients at risk of complication in the prehospital setting and at the emergency department triage. *Scand J Trauma Resusc Emerg Med*. 2017;25(1):108.
- Adami ME, Kotsaki A, Antonakos N, et al. qSOFA combined with suPAR for early risk detection and guidance of antibiotic treatment in the emergency department: a randomized controlled trial. *Crit Care*. 2024;28(1):42.
- Cho YS, Chun BJ, Moon JM. The qSOFA Score: a simple and accurate predictor of outcome in patients with glyphosate herbicide poisoning. *Basic Clin Pharmacol Toxicol*. 2018;123(5):615–621.
- Giamarellos-Bourboulis EJ, Aschenbrenner AC, Bauer M, et al. The pathophysiology of sepsis and precision-medicine-based immunotherapy. *Nat Immunol*. 2024;25(1):19–28.
- Royal College of Physicians. *National Early Warning Score (NEWS) 2: Standardising the Assessment of Acute-Illness Severity in the NHS. Updated Report of a Working Party*. London: Royal College of Physicians; 2017. Available at: [https://www.rcp.ac.uk/media/a4ibkbbf/news2-final-report\\_0\\_0.pdf](https://www.rcp.ac.uk/media/a4ibkbbf/news2-final-report_0_0.pdf).
- Mellhammar L, Linder A, Tverring J, et al. NEWS2 is superior to qSOFA in detecting sepsis with organ dysfunction in the emergency department. *J Clin Med*. 2019;8(8):1128.
- Sabir L, Ramlakhan S, Goodacre S. Comparison of qSOFA and hospital early warning scores for prognosis in suspected sepsis in emergency department patients: a systematic review. *Emerg Med J*. 2022;39(4):284–294.
- Katsaros K, Renieris G, Safarika A, et al. Heparin binding protein for the early diagnosis and prognosis of sepsis in the emergency department: the PROMPT multicenter study. *Shock*. 2022;57(4):518–525.
- Safarika A, Wacker JW, Katsaros K, et al. A 29-mRNA host response test from blood accurately distinguishes bacterial and viral infections among emergency department patients. *Intensive Care Med Exp*. 2021;9(1):31.
- Welch J, Dean J, Hartin J. Using NEWS2: an essential component of reliable clinical assessment. *Clin Med (Lond)*. 2022;22(6):509–513.
- Wolf L, Ceci K, McCallum D, Brecher D. *Emergency Severity Index Handbook (5th ed.)*. Zahn C, ed. Emergency Nurses Association; 2023.
- Rasmussen LJH, Ladelund S, Haupt TH, Ellekilde GE, Eugen-Olsen J, Andersen O. Combining national early warning score with Soluble Urokinase Plasminogen Activator Receptor (SUPAR) improves risk prediction in acute medical patients: a registry-based cohort study. *Crit Care Med*. 2018;46(12):1961–1968.

