Original Article

Presepsin, procalcitonin, interleukin-6, and high-sensitivity C-reactive protein for predicting bacterial DNAaemia among patients with sepsis

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Background: Anti-infective therapy against pathogens is the key to treatment of sepsis. Metagenomic next-generation sequencing (mNGS) has higher sensitivity than blood culture. The aim of this study was to use mNGS to identify DNAaemia of pathogens and to assess the diagnostic accuracy of presepsin (PSEP), procalcitonin (PCT), interleukin-6 (IL-6), and high-sensitivity C-reactive protein (hsCRP) in differentiating between bacterial and nonbacterial infections in patients with sepsis.

Methods: This retrospective study included patients with sepsis from November 2020 to September 2022 in the Shenzhen Second People's Hospital. Blood samples were sent for blood culture and mNGS when the patients were diagnosed with sepsis. Plasma PSEP, PCT, and IL-6 levels were measured using whole blood specimens that were collected and analyzed after a diagnosis of sepsis. Area under the receiver operating characteristic curve (AUC) was used to evaluate the accuracy of PSEP, PCT, IL-6, and hsCRP for prediction of bacterial DNAaemia detected by mNGS in patients with sepsis.

Results: This study included 230 patients with sepsis. The bacterial DNAaemia rate was 53.0% [Gram-positive DNAaemia (GPD), Gram-negative DNAaemia (GND), and fungi DNAaemia rate was 18.2%, 37.8%, and 10.9%, respectively]. Among GND, *Klebsiella* was the most common, followed by *Escherichia coli*; meanwhile, the GPD were mainly *Enterococcus*, and *Aspergillus* was identified in 5 patients with sepsis. The PSEP median values were significantly higher in GND than in non-GND [GND: 1,291 pg/mL, interquartile range (IQR) 456–3,502 pg/mL; non-GND: 707 pg/mL, IQR 332–2,417 pg/mL; P=0.035]. There was no significant difference in PSEP values between GPD and non-GPD groups, or between fungi DNAaemia and non-fungi DNAaemia groups. Receiver operating characteristics analysis indicated that the best cutoff values for PSEP, PCT, IL-6, and hsCRP were 869 pg/mL, 1.14 ng/mL, 85.5 pg/mL, and hsCRP 96.2 mg/L, respectively. Logistic regression indicated that PSEP, PCT, IL-6, and hsCRP had significant predictive value for GND in patients with sepsis. The levels of PCT and IL-6 were different between patients with GPD and those with non-GPD. Only PCT levels differed significantly between fungal DNAaemia and nonfungal DNAaemia.

Conclusions: Bacterial-DNAaemia was detected in half of the patients with sepsis. PSEP, PCT, IL-6, and hsCRP demonstrated significant predictive value for GND, PCT and IL-6 levels demonstrated significant

predictive value for GPD. Meanwhile, only PCT demonstrated significant predictive value for fungal DNAaemia.

Keywords: Metagenomic next-generation sequencing (mNGS); presepsin (PSEP); procalcitonin (PCT); interleukin-6 (IL-6); high-sensitivity C-reactive protein (hsCRP)

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Introduction

Sepsis is a life-threatening condition caused by infection and is characterized by a dysregulated host inflammatory response and multiple organ dysfunction (1). According to the Global Burden of Disease, the global incidence of sepsis is 437 cases per 100,000 people, and 11 million sepsis-related deaths in 2017 (2). In China, the high incidence and mortality of sepsis increased due to its aging population (3). Sepsis is difficult to cure due to its complex etiology and unclear pathophysiological mechanisms. Even for patients who achieve cure, they perhaps have comorbidity organ dysfunction and cognitive impairment (4). Therefore, sepsis remains a serious threat to human life and health, with the high cost of related treatment leveraging a considerable social and economic burden (5).

Timely and accurate diagnosis of sepsis is crucial for initiating appropriate management and improving patient outcomes. Biomarkers play a key role in identifying early sepsis, and widely used markers of infection include procalcitonin (PCT), interleukin 6 (IL-6), and high-sensitivity C-reactive protein (hsCRP) (6). However, the biomarkers' levels may be elevated from both infectious and non-infectious causes (7,8). Due to the progress made in molecular biological detection, a large number of novel biomarkers have recently been identified (9) that may compensate for the shortcomings of classic biomarkers (10). Presepsin (PSEP) is produced by macrophages, monocytes, and granulocytes and appears in the circulation as early as two hours after infection and thus earlier than hsCRP and PCT (11). PSEP has excellent performance in the early diagnosis, efficacy monitoring, and prognosis of sepsis (12-15) and thus may be capable of providing more reliable evidence supporting early antibiotic use (16,17). However, few studies have been conducted that have examined the diagnostic efficacy of PSEP for pathogens in patients with sepsis. Arai *et al.* (18) reported that PSEP secretion by human monocytes is triggered by bacterial phagocytosis rather than by inflammatory stimuli. Therefore, we speculated that PSEP levels could help identify DNAaemia in patients with sepsis.

Blood culture (BC) analysis is the gold standard method for diagnosing bacteremia. Several studies (19,20) have demonstrated that the PSEP, PCT, hsCRP, and IL-6 levels is capable of predicting bacteremia according to BC in septic patients. However, the BC process is lengthy and has low sensitivity, especially after antibiotic exposure (21), and approximately 40% to 50% of sepsis are BC negative (22). With the development for molecular biology, metagenomics next-generation sequencing (mNGS) has emerged as a rapid and accurate method for pathogen diagnosis. mNGS results may be obtained within 24 hours of samples acceptance (23), which significantly improves the detection efficiency. The

Highlight box

Key findings

- According to metagenomic next-generation sequencing (mNGS), bacterial-DNAaemia was detected in half of the patients with sepsis.
- Levels of presepsin (PSEP), procalcitonin (PCT), interleukin-6 (IL-6), and high-sensitivity C-reactive protein (hsCRP) were predictive of Gram-negative bacterial DNAaemia.

What is known and what is new?

- mNGS has higher sensitivity and specificity than do traditional methods of nonviral pathogen detection. Plasma PSEP, PCT, IL-6, and hsCRP levels have been shown to be higher in patients with bacteraemic sepsis.
- PSEP, PCT, IL-6, and hsCRP demonstrated an ability to predict Gram-negative bacterial DNAaemia (mNGS test) in patients with sepsis. PCT and IL-6 levels could predict Gram-positive DNAaemia. In fungal DNAaemia, only PCT demonstrated predictive value.

What is the implication, and what should change now?

- Our findings can provide a basis for guiding initial antibiotics administration in patients with suspected sepsis.

sensitivity and specificity of mNGS are higher compared to BC (24), thereby providing strong evidence for triggering early antibiotic administration.

Therefore, we conducted a study that aimed to identify the pathogens in DNAaemia using mNGS and to assess the diagnostic accuracy of four biomarkers (PSEP, PCT, IL-6, and hsCRP) for differentiating between bacterial and nonbacterial infections in patients with sepsis. We present this article in accordance with the STARD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1714/rc).

Methods

Patients

This was a subset of a single-center, retrospective observational cohort study conducted from November 2020 to September 2022 at the Shenzhen Second People's Hospital in Futian, Shenzhen, China. Briefly, this study enrolled consecutive patients with sepsis as diagnosed by two professional physicians. Diagnostic criteria for sepsis were those from the relevant international guidelines [infection + either sequential organ failure assessment (SOFA) score ≥2 or quick SOFA (qSOFA) score ≥2] (1); Septic shock was defined as sepsis requiring vasopressors to maintain mean arterial pressure ≥65 mmHg and plasma lactate ≥2 mmol/L despite adequate fluid resuscitation (1). The criteria for participant inclusion were as follows: age ≥18 years, diagnosis of sepsis less than 24 hours, and written informed consent. Pregnant patients or those lacking mNGS data were excluded. Patient data including demographic characteristics, medical history, biochemical and inflammatory markers from patients with sepsis were collected. Follow-up was performed on day 3, 7, 14, and 30. If patients were cured and had been discharged from hospital, telephone follow-up was completed to assess and record the survival conditions. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study design and protocol were approved by the Ethics Committee of the Shenzhen Second People's Hospital (No. 20200718001). Written informed consent was obtained for all patients or their next of kin.

BC and blood mNGS

At least 10 mL of whole blood was collected from various locations and inoculated in BACTEC aerobic and anaerobic bottles (BD Biosciences, Franklin Lakes, NJ, USA) before antibiotic administration when the patients were diagnosed with sepsis. Following this, aliquots were incubated in the BACTEC FX automated BC system (BD Biosciences). All bottles flagged as positive were subjected to Gram staining and culture medium, and traditional methods were used for microbial identification. In addition, 5 mL of whole blood was sent to the Clinical Laboratory of the Shenzhen Second People's Hospital (Genskey Medical Technology Co., Ltd. Tianjin, China) for mNGS. Briefly, mNGS consisted of the following steps: nucleic acid extraction, library construction, high-throughput sequencing, bioinformatics analysis, and pathogen data interpretation (24,25).

Definitions of pathogens

If the same pathogen was detected by BC and mNGS, it was considered as pathogenic bacteria. If the pathogen findings differed between BC and mNGS, two or more intensive care unit (ICU) specialists determined whether the bacteria were pathogenic according to clinical characteristics.

Biomarker measurements

Plasma PSEP, PCT, hsCRP, and IL-6 levels were tested using whole-blood specimens that were collected in endotoxin-free tubes containing ethylenediaminetetraacetate (EDTA) when the patients were diagnosed with sepsis. The intraassay detection range of serum levels of PSEP were 5,720,000 pg/mL, the intra-assay coefficient of variation (CV, the ratio of the standard deviation to the mean) % was <5%, and the inter-assay CV% was <10%. The detection range of PCT was 0.02–100 ng/mL, the intra-assay CV% was <5%, and the inter-assay CV% was <10%. The detection range of IL-6 was 2.5–5,000 mg/L, the intra-assay CV% was <5%, and the inter-assay CV% was <8%. These levels were determined with the CL6000i chemiluminescent immunoassay (CLIA) autoanalyzer (Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China). hsCRP levels were analyzed after laboratory collection at the Shenzhen Second People's Hospital. The hsCRP detection range was 0.2–320 mg/L, the intra-assay CV% was <4.04%, and the inter-assay CV% was <3.02%. The testers were blinded to the measured levels of PSEP, PCT, and IL-6. The clinicians were aware of PCT, IL-6, or hsCRP levels but not those of PSEP.

Statistical analysis

Nonnormal variables (e.g., age) were expressed as

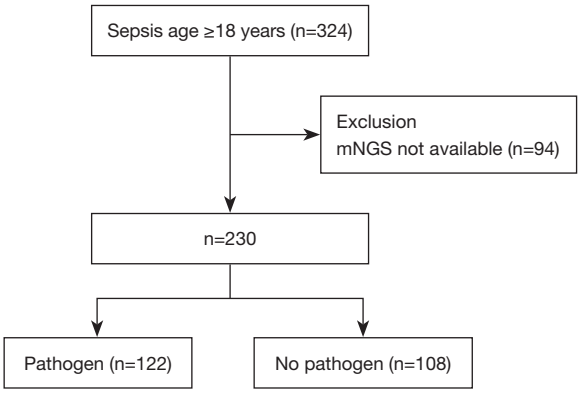

Figure 1 The flowchart of participant inclusion. mNGS, metagenomic next-generation sequencing.

median and interquartile range (IQR). Group differences were evaluated with the Kruskal-Wallis rank-sum test. Categorical data were expressed as counts and percentages, and the Fisher exact test was used to evaluate differences. The optimal cutoff points for change in inflammatory biomarkers were calculated via the area under the receiver operating characteristic curve (AUC), and the Youden index was calculated to determine the optimal discriminatory cutoff (Youden index = sensitive + specificity – 1). Kaplan-Meier survival curves were used to analyze the association between Gram-positive DNAaemia (GPD), Gram-negative DNAaemia (GND), fungi DNAaemia and survival. R and RStudio (version 4.3.1; The R Foundation for Statistical Computing, Vienna, Austria) software was used for analysis.

Results

Patient characteristics

A total of 324 patients were enrolled in this study, 94 were excluded as mNGS data was not available, and 230 patients were included in the analysis. The blood bacterial DNAaemia rate was 53.0% (122 cases). The detection rates for GPD, GND, and fungi DNAaemia rate was 18.2% (42 cases), 37.8% (87 cases), and 10.9% (25 cases), respectively (*Figure 1*). The baseline characteristics of the patients are provided in *Table 1*. The median age was 61 (IQR, 46.3–75.0) years, 129 (56.1%) patients with sepsis were admitted to ICU, and 81 (35.2%) experienced septic shock at the study entry. The primary site of infection was pneumonia (155, 67.4%), followed by urinary tract infection (30, 13.0%). The median levels of PSEP, PCT, IL-6, and hsCRP were 913 (IQR, 360–2,759) pg/mL, 1.32 (IQR, 0.23–11.69) ng/mL, 113 (IQR, 44–344) pg/mL, and 97 (IQR, 36–183) mg/L, respectively. There were significant differences in the prevalence of septic shock, monocyte count, and albumin between patients with and without pathogens. The levels of PCT, IL-6, and hsCRP were significantly elevated in those with pathogens. However, there was no significant difference in the other variables.

The distribution of pathogens in patients with sepsis

Among the bacteria detected in the blood of 122 patients with sepsis, 44.3% were GND only, 12.3% were GPD only, and 7.4% were fungi only. Of note, mixed infection (at least two types of bacteria) accounted for 31.1% of these patents, with the combination of GND and GPD accounting for 15.6% (*Figure 2*). The distribution of bacterial detection is shown in *Figure 3*. The GND detected in blood samples of patients with sepsis included *Klebsiella* (n=38), *Escherichia coli* (n=21), and *Pseudomonas aeruginosa* (n=8) (*Figure 3*); meanwhile, the GPD were mainly *Enterococcus faecalis* and *Streptococcus*. Notability, *Aspergillus* was detected in 5 patients. In general, more pathogens were detected in septic patients in the ICU than in the general wards (*Figure 3*).

The accuracy of PSEP, PCT, hsCRP, and IL-6 levels in detecting pathogens

The median PSEP values of GND were significantly higher than those of non-GND (GND: 1,291 pg/mL, IQR 456–3,502 pg/mL; non-GND: 707 pg/mL, IQR 332–2,417 pg/mL; P=0.035) (*Table 2*). There was no significant difference in PSEP values between GPD and non-GPD groups, or between fungi DNAaemia and non-fungi DNAaemia groups (Tables S1,S2). Receiver operating characteristics analysis indicated that the optimal cutoff values of PSEP, PCT, IL-6, and hsCRP were 869 pg/mL, 1.14 ng/mL, 85.5 pg/mL, and 96.2 mg/L, respectively (*Figure 4A-4D*). According to best cutoff, the sensitivities of PSEP, PCT, IL-6, and hsCRP were 0.545, 0.587, 0.559, and 0.594. The specificities were 0.621, 0.701, 0.782, and 0.667. According to logistic regression, PSEP, PCT, IL-6, and hsCRP levels had predictive values for GND in patients with sepsis (*Table 3*). The AUC of PSEP, PCT, IL-6, and hsCRP levels to predict the GND were 0.583, 0.658, 0.684, and 0.628 respectively. The AUC of combining four biomarkers for predicting GND was 0.716 (*Figure 4E*). The correlations between PSEP, PCT, IL-6, and hsCRP are shown in Figure S1, while the Kaplan-Meier survival curves for the association between mortality and different pathogens are

Table 1 Baseline characteristics of the patients with sepsis

Variable	Total (n=230)	No pathogen (n=108)	Pathogen (n=122)	P value
Age (years)	61 [46.3, 75.0]	64 [47.0, 75.3]	58 [46.0, 72.0]	0.24
Male sex	138 (60.0)	66 (61.1)	72 (59.0)	0.78
ICU	129 (56.1)	55 (50.9)	74 (60.7)	0.15
Septic shock	81 (35.2)	28 (25.9)	53 (43.4)	0.006
HTN	84 (36.5)	39 (36.1)	45 (36.9)	>0.99
DM	60 (26.1)	30 (27.8)	30 (24.6)	0.65
CAD	69 (30.0)	31 (28.7)	38 (31.1)	0.77
Tumor	46 (20.0)	22 (20.4)	24 (19.7)	>0.99
Cerebrovascular disease	109 (47.4)	54 (50.0)	55 (45.1)	0.51
Hematological malignancy	56 (24.3)	27 (25.0)	29 (23.8)	0.88
Pneumonia	155 (67.4)	73 (67.6)	82 (67.2)	>0.99
Urinary tract infection	30 (13.0)	12 (11.1)	18 (14.8)	0.44
PSEP (pg/mL)	913 [360, 2,759]	797 [332, 2,468]	1,107 [404, 3,332]	0.18
PCT (ng/mL)	1.32 [0.23, 11.69]	0.52 [0.16, 3.90]	3.66 [0.54, 22.59]	<0.001
IL-6 (pg/mL)	113 [44, 344]	66 [30, 243]	151 [73, 553]	<0.001
hsCRP (mg/L)	97 [36, 183]	69 [28, 151]	135 [61, 200]	<0.001
WBC ($\times 10^9$/L)	8.73 [2.46, 16.16]	9.12 [3.84, 16.26]	8.50 [1.79, 16.00]	0.57
LYM ($\times 10^9$/L)	0.61 [0.27, 1.08]	0.72 [0.33, 1.16]	0.53 [0.23, 0.97]	0.050
MON ($\times 10^9$/L)	0.40 [0.13, 0.72]	0.50 [0.18, 0.85]	0.28 [0.11, 0.64]	0.006
Cr (μmol/L)	79 [51.1, 159.6]	73 [52.2, 139.8]	88 [49.5, 170.7]	0.70
ALB (g/L)	31 [27.1, 35.5]	32 [27.7, 36.0]	30 [26.8, 34.4]	0.01
AST (U/L)	40 [21.3, 80.0]	39 [19.0, 72.3]	41 [22.8, 80.8]	0.43
NT-proBNP (pg/mL)	1,715 [364, 8,462]	1,568 [162, 6,310]	2,322 [568, 9,940]	0.10
Follow-up time (days)	20 [9.0, 30.0]	20 [8.0, 30.0]	21 [9.3, 30.0]	0.18
Death	33 (14.3)	10 (9.3)	23 (18.9)	0.04

Data are presented as median [interquartile range] or n (%). ICU, intensive care unit; HTN, hypertension; DM, diabetes mellitus; CAD, coronary artery disease; PSEP, presepsin; PCT, procalcitonin; IL-6, interleukin-6; hsCRP, high-sensitivity C-reactive protein; WBC, white blood cell count; LYM, lymphocyte count; MON, monocyte count; ALB, albumin; AST, aspartate aminotransferase; NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

shown in *Figure 5*. The survival probability of patients with GND was not significantly different from non-GND.

Discussion

In this study, the blood bacterial DNAaemia rate was 53.0% while the rate of mixed bacterial infection was 31.2%. According to the mNGS, in patients with sepsis, the most common GND was *Klebsiella*, followed by *Escherichia coli*, while the most common GPD was *Enterococcus faecalis*; notably, *Aspergillus* was identified in 5 patients. According to logistic regression, PSEP, PCT, IL-6, and hsCRP levels demonstrated significant predictive value for GND in patients with sepsis. PCT and IL-6 levels were different between GPD-positive and GPD-negative patients. Only PCT levels were significantly different between fungal

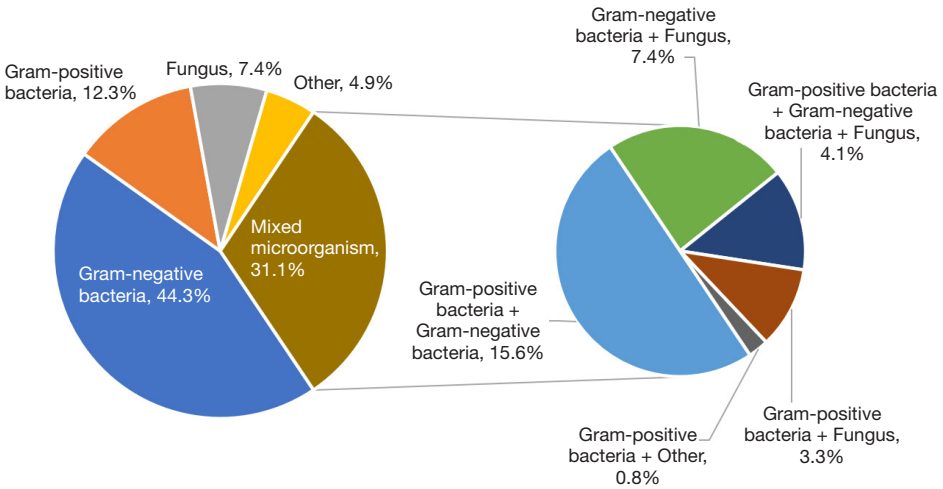

Figure 2 Pie charts illustrating the distribution of pathogens in 122 patients with sepsis.

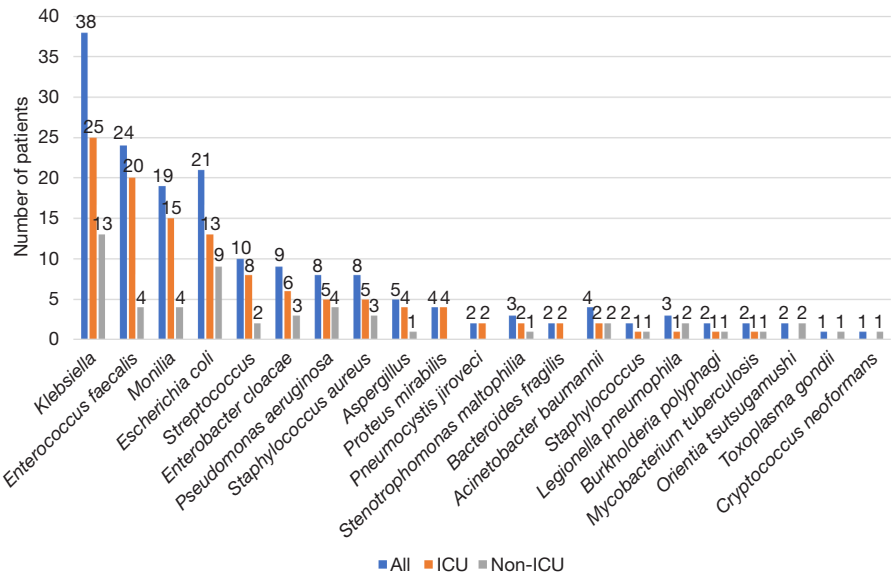

Figure 3 The distribution of pathogens in septic patients in the intensive care unit and general wards. ICU, intensive care unit.

Table 2 Levels of four biomarkers in GND and non-GND

Variable	Non-GND (n=145)	GND (n=87)	P value
PSEP (pg/mL)	707 [332, 2,417]	1,291 [456, 3,502]	0.035
PCT (pg/mL)	0.65 [0.18, 5.35]	4.16 [0.72, 24.23]	<0.001
IL-6 (pg/mL)	73 [30.1, 162.8]	137 [65.0, 211.6]	0.001
hsCRP (mg/L)	72 [32.0, 252.5]	194 [88.5, 627.0]	<0.001

Data are presented as median [interquartile range]. GND, Gram-negative DNAaemia; PSEP, presepsin; PCT, procalcitonin; IL-6, interleukin-6; hsCRP, high-sensitivity C-reactive protein.

DNAaemia and nonfungal DNAaemia.

In a study from Korea (26), *Escherichia coli* accounted for the majority (32.3%) of patients and was followed by *Klebsiella* (15.5%), *Staphylococcus aureus* (10.4%), and *Enterococcus faecium* (7.4%). Another study reported that the main type of GND was mainly *Klebsiella* (12.7%) (27), which is consistent with our findings. In our study, the most common GND were *Klebsiella* and *Escherichia coli*. Any discrepancies in findings with previous research may be attributed to region and the use of antibiotics.

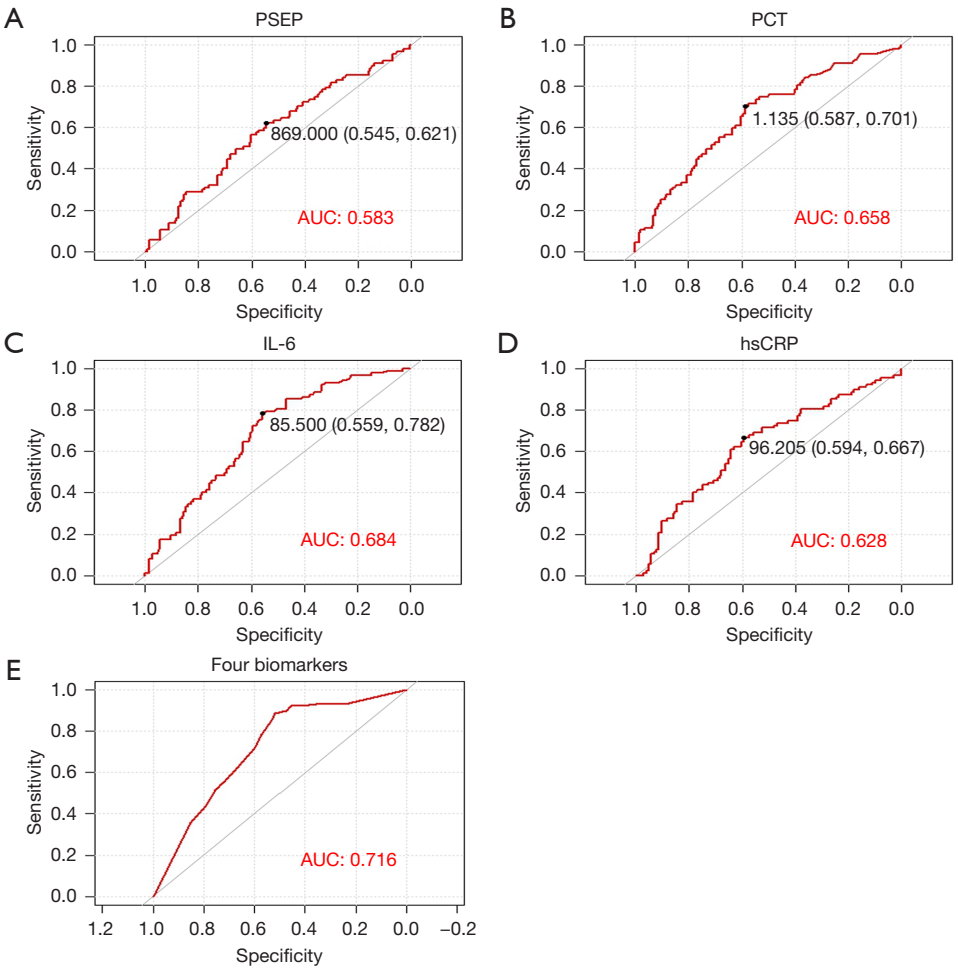

Figure 4 The AUC of four biomarkers in predicting Gram-negative bacteria. Parentheses contain the confidence interval of the AUC. (A) The AUC of PSEP in predicting Gram-negative bacteria, with an optimal cutoff of 869 pg/mL and an AUC 0.583. (B) The AUC of PCT for predicting Gram-negative bacteria, with an optimal cutoff of 1.135 pg/mL and an AUC of 0.658. (C) The AUC of IL-6 in predicting Gram-negative bacteria, with an optimal cutoff of 85.5 pg/mL and an AUC of 0.684. (D) The AUC of hsCRP in predicting Gram-negative bacteria, with an optimal cutoff of 96.205 pg/mL and an AUC of 0.628. (E) The AUC of four biomarkers predicts Gram-negative bacteria and an AUC of 0.716. AUC, area under the receiver operating characteristic curve; PSEP, presepsin; PCT, procalcitonin; IL-6, interleukin-6; hsCRP, high-sensitivity C-reactive protein.

Table 3 The predictive value of PSEP, PCT, IL-6 and hsCRP in GND

Variable	β	OR (95% CI)	P value
PSEP >869 pg/mL	0.67	1.96 (1.145–3.405)	0.015
PCT >1.14 ng/mL	1.15	3.16 (1.817–5.618)	<0.001
IL-6 >85.5 pg/mL	1.08	4.54 (2.517–8.504)	<0.001
hsCRP >96.2 mg/L	1.51	2.93 (1.692–5.165)	<0.001

PSEP, presepsin; PCT, procalcitonin; IL-6, interleukin-6; hsCRP, high-sensitivity C-reactive protein; GND, Gram-negative DNAaemia; OR, odds ratio; CI, confidence interval.

PSEP has been proven to be a biomarker for the early diagnosis of sepsis. Several studies (12,14) have demonstrated the potential of PSEP in differentiating sepsis from noninfectious systemic inflammatory response syndrome and in predicting sepsis. Similarly, PCT has shown promise in aiding the diagnosis of bacterial infections and guiding antibiotic therapy. IL-6 has also been implicated in the pathogenesis of sepsis and has been proposed as a prognostic marker for sepsis severity. Elevated levels of PCT and IL-6 have been associated with bacterial sepsis, while low levels are suggestive of viral or

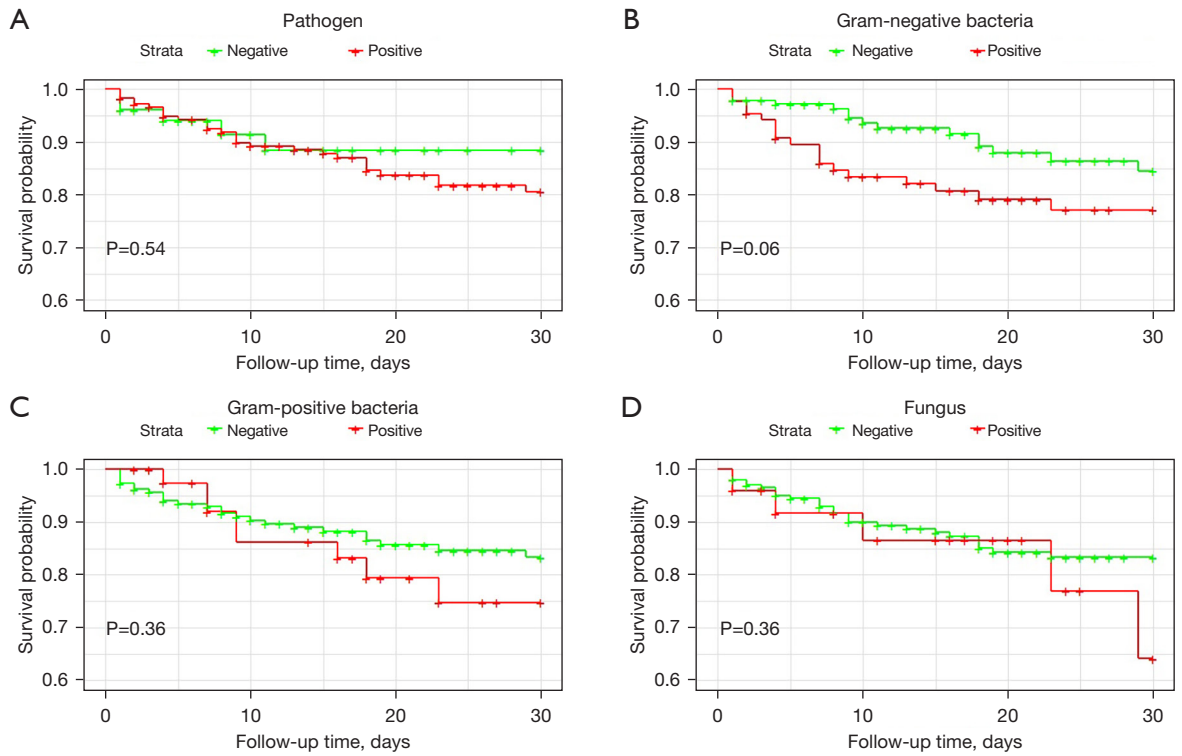

Figure 5 The Kaplan-Meier curves of different pathogens in predicting mortality in sepsis. (A) Kaplan-Meier curve for pathogens. (B) Kaplan-Meier curve for Gram-negative bacteria. (C) Kaplan-Meier curve for Gram-positive bacteria. (D) Kaplan-Meier curve for fungus.

noninfectious causes of inflammation (28).

Sepsis is a serious consequence of infectious disease and bacteremia increases the risk of hospital mortality (29). The incidence of sepsis was 4.7% (929/19,961) Gram-positive bacteria (30). In a multicenter, prospective study of ICU patients with sepsis, GND accounted for 67.1%, GPD for 21.5%, and fungi 11.2% of the pathogens (31). Serum PCT level may potentially be a diagnostic marker for *Escherichia coli* (32) infection. In one study (33), PCT exhibited the best ability to detect bacteremia (AUC 0.80; 95% CI: 0.72–0.88), followed by PSEP (AUC 0.69; 95% CI: 0.60–0.79), and CRP (AUC 0.60; 95% CI: 0.49–0.70). Bamba *et al.* (34) found that levels of PSEP were higher in fungal blood infection than nonfungal infection. In a BC study, the serum levels of the CRP, PSEP, and PCT were associated with levels of culture-confirmed candidemia and bacteremia (35). Another study (36) reported that PSEP, PCT, and CRP levels were higher in septic patients with bacteremia than in patients without. A diagnostic study (37) from a clinical laboratory in Italy included 92 patients and examined their PSEP, PCT, and CRP levels. PSEP and PCT showed a better ability to predict DNAaemia (AUC: 0.777 *vs.* 0.880). In our study, PSEP, PCT, IL-6, and hsCRP demonstrated good diagnostic accuracy for predicting GND. Finally, in a mouse model of sepsis, while PSEP was diagnostically specific for bacteremia and was elevated early in an equal puncture model. PCT was less specific as it was elevated in both bacterial and also lipopolysaccharide injection models of sepsis (38).

This study has several limitations. First is its single center design and limited size. The prognostic assessment of biomarkers should be investigated in larger studies. A multicenter study could be designed to further validate our findings in the future. Second, the patients involved in this study were living in the south of China, and the generalizability of our findings to other populations needs to be confirmed.

Conclusions

In our study, half of the patients with sepsis were found to have bacterial DNAaemia, and one-third had mixed bacteremia. PSEP, PCT, IL-6, and hsCRP demonstrated good predictive value for GND, while PCT and IL-6 levels

demonstrated good predictive value for GPD. For fungi, only PCT exhibited predictive value. Further research may elucidate the optimal use of these biomarkers to guide antibiotic use in clinical practice. The integration of biomarkers into sepsis management algorithms holds promise for improving patient care and outcomes.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1714/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1714/dss

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