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Combining PCT with CRP is better than separate testing for patients with bacteriuria in the intensive care unit: a retrospective study

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Abstract

Background Previous studies on PCT for urinary tract infections (UTI) have focused primarily on minors. This study investigated the predictive value of the neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP) level and procalcitonin (PCT) level in adult patients with bacteriuria in IUC.

Methods This case–control study included 85 patients with bacteriuria (PB) in the ICU from March 2021 to Jan 2024 based on positive urine culture results and a control group ($n = 136$) from Jan 2024 to March 2024. Patient data were collected using a hospital information management system. ROC curves of the NLR, CRP and PCT were use to predict the PB.

Results The AUCs of the NLR, CRP and PCT for the prediction of PB in ICU were 0.711 (95% CI 0.644–0.772), 0.855 (95% CI 0.800–0.900), and 0.884 (95% CI 0.832–0.924), respectively; the optimal thresholds were 8.02, 18.52 mg/L, and 0.215 ng/mL, respectively; the sensitivities were 69.0 (95% CI 56.9–79.5), 90.1 (95% CI 80.7–95.9), and 83.1 (95% CI 72.3–91.0), respectively; and the specificities were 67.6 (95% CI 59.1–75.4), 68.4 (95% CI 59.9–76.1), and 80.9 (95% CI 73.3–87.1), respectively. The negative predictive value (NPV) of CRP is greater than that of PCT. In bacteriuria caused by Candida infections, CRP and PCT have higher sensitivity and NPV.

Conclusions Combined CRP and PCT testing is more helpful for diagnosing bacteriuria. CRP and PCT have higher sensitivity and NPV in diagnosing bacteriuria caused by Candida infection.

Keywords Procalcitonin, C-reactive protein, Neutrophil-to-lymphocyte ratio, Urinary tract infection

Introduction

In the intensive care unit (ICU), accurate and timely diagnosis of bacterial infections is critical for patient outcomes [1]. Bacteriuria, a common condition in which bacteria are present in the urine, can lead to serious infections if not promptly identified and treated. The neutrophil-to-lymphocyte ratio (NLR) [2], C-reactive protein (CRP) [1, 3, 4] level, and procalcitonin (PCT) [1, 4, 5] level are blood markers of inflammation that have been shown to help support the diagnosis and monitoring of bacterial respiratory tract infections and urinary tract infections (UTI) [6, 7].

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While these markers are individually useful, their role in the diagnosis and treatment of bacterial infections, particularly in the ICU setting, cannot be overlooked. However, studies have often used subjective cutoff values for PCT rather than optimal thresholds based on the maximum Youden index [8–10], a common measure of overall diagnostic effectiveness. Some studies have even suggested that PCT may not be suitable for diagnosing UTI [11, 12].

UTI is the most common bacterial infection and one of the most common reasons for hospitalization due to infection in elderly people [6]. The clinical signs of UTI are often non-characteristic or asymptomatic, and urine cultures can be time-consuming, delaying the initiation of appropriate treatment [6, 7]. Therefore, it is necessary to detect inflammatory markers such as the NLR, CRP, and PCT in patients with suspected bacteriuria. Early detection of bacteriuria in ICU patients is vital, as it can reveal underlying infections that may be asymptomatic or masked by critical illness. Bacteriuria is often a precursor to more severe infections, such as urinary sepsis, which can have a significant impact on patient mortality and the length of stay (LOS) in the ICU. Timely identification and treatment of bacteriuria can improve patient outcomes and reduce the burden on healthcare resources.

This study aimed to determine the diagnostic value of the NLR, CRP, and PCT for positive urine cultures in the ICU, thereby providing real-world clinical research and a theoretical basis for the clinical diagnosis and treatment of bacteriuria. By combining these markers, we may achieve more accurate and timely detection of bacterial infections, leading to improved patient outcomes and more efficient use of healthcare resources.

Materials and methods

Study cohort and data extraction

Eighty-five patients with suspected bacteriuria in the ICU (from March 2021 to Jan 2024) and a control group ($n=136$) (from Jan 2024 to March 2024, hospitalized patients with no relevant bacterial culture records, etc.) were included. We obtained data from the hospital information management system (HIS) of the *Affiliated Shuyang Hospital of Xuzhou Medical University* for retrospective analysis by retrieving complete blood count (CBC) (e.g., WBC, neutrophil count, and lymphocyte count), serum CRP and PCT, and mid-section urine culture data from March 2021 to Jan 2024. The specimens were subjected to urine culture (submission for inspection was completed within 6 h). The specimens of CBC, serum CRP and PCT were obtained at the same time point due to suspected bacteriuria, and the corresponding sampling equipment was used.

The inclusion criteria for bacteriuria patients included positive urine culture results, CBC test results, admission to the ICU, and serum CRP and PCT test results. The inclusion criteria for the control group included CBC test results and serum CRP and PCT test results. Blood specimens were drawn at the same time point. The urine culture specimens were collected from mid-section urine. All positive urine cultures were confirmed by a clinician. The basic characteristics of the bacteriuria patients and controls are shown in Table 1. The exclusion criteria were the use of antibacterial drugs before urine culture sampling, the presence of contaminating bacteria, or age < 18 years. According to the literature, positive sputum culture results are not related to PCT levels, so patients with positive sputum culture results were not excluded [13].

Laboratory methods and instruments

A Cobas e411 analyser (the reagents used are original supporting reagents from F. Hoffmann-La Roche, Basel, Switzerland) was used to measure the serum CRP and PCT levels. A Sysmex XN-10 analyser (the reagents used are original supporting reagents from Sysmex, Kobe, Japan) was used for CBC counts. Annual calibration and verification of the instruments were completed as planned, which also included truthiness, reportable range, and precision of CBC, CRP and PCT (from the reagent instructions). Internal quality control according to the SOP and external quality assessment evaluation were performed throughout the study period. A DL96A system (Zhuhai Deere Bioengineering Co., Ltd., China) was used for bacterial identification and antimicrobial susceptibility testing (AST). The urine culture time was up to 5 days to ensure the interpretability of the results and the identification of inert bacteria according to CLSI standards (ISBN 978-1-68440-067-6).

Statistical analysis

For the NLR calculations, refer to Document 2 [14]. The data for all studies were preentered or imported into Excel Version 2021 (Armonk, NY, USA). We performed statistical analyses using MedCalc Version 22.018-64-bit (MedCalc Software, Ostend, Belgium) [15] to use ROC curves to predict bacteriuria. A P value no greater than 0.01 was considered to indicate statistical significance. The greater the Youden index of an indicator is, the closer it is to the gold standard. The Youden index is equal to the sum of the sensitivity and specificity minus 1 [9, 16]. The point at which the optimal cutoff value is reached is the value corresponding to the maximum Youden index [16, 17] in the ROC curve according to the area under the curve (AUC). The optimal threshold, Youden index, and sensitivity (a 95% confidence interval) are also given.

Table 1 Characteristics of the participants

Parameter	Bacteriuria ($n=85$)	Control ($n=136$)	*P* value*
Female			
n	45	61	
Age (years)	71 (64–81)	59 (37–71)	
Male			
n	40	75	
Age (years)	70 (64–83)	60 (50–70)	
Etiology group			
Nervous system disease	$n=16$		
Respiratory diseases	$n=17$		
Shock or organ failure	$n=26$		
Digestive system inflammation	$n=8$		
DM	$n=2$		
Bacteremia	$n=13$		
Positive sputum culture	$n=16$		
Pathogen group			
Enterobacteriaceae	$n=56$		
E. coli	$n=30$		
Candida	$n=23$		
NLR	11.9 (6.2–20.3)	5.6 (3.1–10.8)	< 0.001
CRP (mg/L)	108.7 (35.1–173.6)	7.5 (1.9–35.7)	< 0.001
PCT (ng/mL)	1.390 (0.265–14.175)	0.068 (0.033–0.166)	< 0.001

All data are presented as the median and interquartile range

CRP C-reactive protein, *PCT* procalcitonin, *NLR* neutrophil-to-lymphocyte ratio

*Kruskal–Wallis test

Specificity (a 95% confidence interval is also given), positive predictive value (PPV), and negative predictive value (NPV) were calculated based on this optimal threshold point. Comparison of ROC curves was performed using the method of DeLong et al. [18].

Results

There were 85 PBs (13 samples had positive blood cultures, and 16 had positive sputum cultures, among the 13 cases with positive blood culture, 6 cases (46.2%) had the same pathogen as the urine culture; among the 16 cases with positive sputum cultures, 4 cases (25%) had the same pathogen as the urine culture). The number of samples with both positive blood culture and sputum cultures was 3, and 136 controls met the inclusion criteria. Among the PBs in the ICU, 56 (65.9%), 30 (35.3%), and 23 (27.1%) were Enterobacteriaceae, *Escherichia coli*, and Candida bacteria, respectively. The 25th percentile of PCT in the PB group was greater than the 75th percentile of PCT in the control group (Table 1). The NLR, CRP and PCT in the control group were significantly lower than those in the bacteriuria group (Fig. 1).

Figure 2 shows the ROC curves of the NLR, CRP and PCT for predicting bacteriuria. In terms of predicting bacteriuria, the diagnostic performance of the NLR, CRP and PCT gradually decreased. The performance of the unexpanded and easily available NLR in predicting bacteriuria was relatively greater (Table 2). Table 2 shows the optimal threshold, Youden index, AUC, sensitivity, and specificity of different pathogenic bacteria. The Youden indices of the NLR, CRP and PCT gradually decreased, indicating that the performance of the three indicators decreased from worst to best. There was no significant difference between CRP and PCT according to the methods of DeLong et al. [18]. A PCT concentration exceeding 0.5 was abnormal, and the cutoffs for NLR and CRP for the prediction of PCT abnormalities were 9.19 and 33.3 mg/L, respectively.

Regardless of grouping, the sensitivity of CRP was not lower than that of PCT, and the NPV of CRP was greater than that of PCT. Although the specificity of PCT is greater than that of CPR, the PPVs of both CRP and PCT do not exceed 80%. In bacteriuria caused by Candida infections, CRP and PCT have higher sensitivity and NPV.

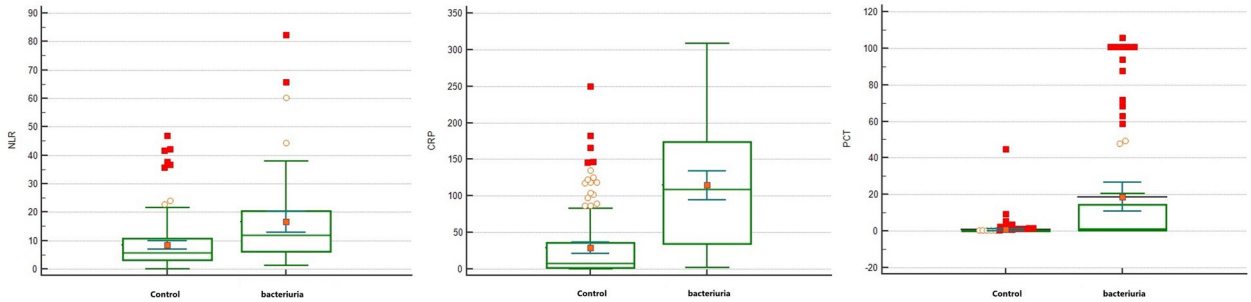

Fig. 1 Comparison of the NLR and CRP and PCT levels between the bacteriuria group and the control group. *NLR* neutrophil-to-lymphocyte ratio, *CRP* C-reactive protein (mg/L), *PCT* procalcitonin (ng/mL)

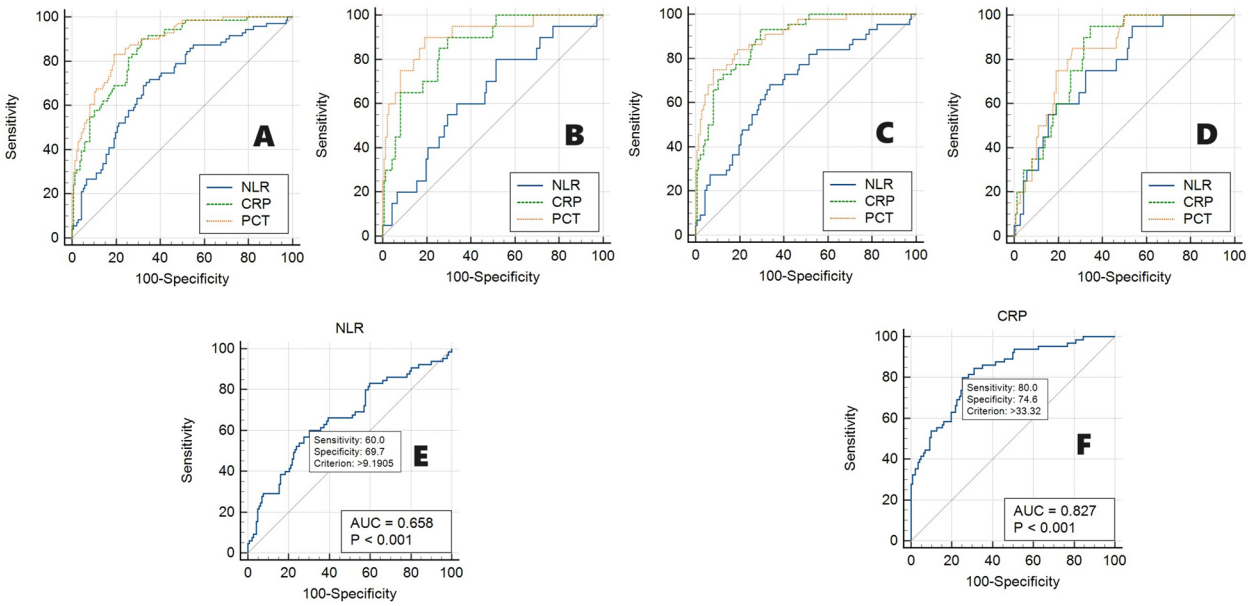

Fig. 2 ROC curves of the neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP, mg/L), and procalcitonin (PCT, ng/mL) for predicting bacteriuria (**A** ALL; **B** *E. coli*; **C** Enterobacteriaceae; **D** Candida) and ROC curves of NLR (**E**) and CRP (**F**) for predicting abnormal PCT (more than 0.5 ng/mL)

Discussion

This retrospective study of bacteriuria patients with positive urine cultures demonstrated that both CRP and PCT have high clinical value. This positive result is in sharp contrast to those of previous studies [11, 12]. Previous studies [7, 19] on the use of PCT in the diagnosis and treatment of UTI focused mostly on minors. The results of this study may supplement the use of PCT in the diagnosis of UTI in adults.

A single-center retrospective study by Levine et al. [20] revealed that a PCT cutoff of < 0.25 ng/mL had an NPV of 91% for excluding UTI and the NPV for using a PCT cutoff of < 0.25 ng/mL in a retrospective study was 89% according to Rothe et al. [17] (very similar to our findings), a more stringent empirical cutoff of < 0.215 ng/mL resulted in sensitivity (83.1%) and specificity (80.9%) with an NPV of 90.2%. In Levine et al.'s study [20], the sensitivity and specificity of PCT were 67% and 63%, respectively. According to the Youden index calculation formula, the Youden index is only 0.3, which is significantly lower than the Youden index (0.64) in this study and previous studies [21, 22]. In this study, the sensitivity of PCT for diagnosing bacteriuria was greater than the specificity, which is consistent with the findings of previous studies [21, 22]. However, not all UTI increase PCT [7], so a combination with CRP may be needed to diagnose UTI. This study revealed that the sensitivity and NPV of CRP for diagnosing bacteriuria are greater than those of PCT. These findings suggest that PCT combined with CRP

Table 2 Performance of NLR, CRP, and PCT in predicting patients with bacteriuria in the ICU

Group	Index	NLR	CRP	PCT	Comparison between PCT and CRP of ROC curves
All (the number of bacteria = 71, excludes 13 bacteremias. The number of control = 136)	Optimal threshold	8.02	18.52	0.215	
	Youden index	0.366	0.5852	0.6398	
	AUC	0.711 (95% CI 0.644–0.772)	0.855 (95% CI 0.800–0.900)	0.884 (95% CI 0.832–0.924)	$Z = 1.091$ $P = 0.2754$
	Sensitivity	69.0 (95% CI 56.9–79.5)	90.1 (95% CI 80.7–95.9)	83.1 (95% CI 72.3–91.0)	
	Specificity	67.6 (95% CI 59.1–75.4)	68.4 (95% CI 59.9–76.1)	80.9 (95% CI 73.3–87.1)	
	PPV	52.7 (95% CI 45.5–59.8)	59.8 (95% CI 53.5–65.8)	69.4 (95% CI 61.3–76.5)	
	NPV	80.7 (95% CI 74.4–85.8)	93 (95% CI 86.7–96.4)	90.2 (95% CI 84.5–93.9)	
E. coli ($n = 30$, includes 10 bacteremias)	Optimal threshold	7.39	27.7	0.215	
	Youden index	0.3284	0.6426	0.7088	
	AUC	0.695 (95% CI 0.619–0.764)	0.885 (95% CI 0.827–0.929)	0.927 (95% CI 0.876–0.961)	$Z = 1.611$ $P = 0.1073$
	Sensitivity	66.7 (95% CI 47.2–82.7)	90.0 (95% CI 73.5–97.9)	90.0 (95% CI 73.5–97.9)	
	Specificity	66.2 (95% CI 57.6–74.1)	74.3 (95% CI 66.1–71.4)	80.9 (95% CI 73.3–87.1)	
	PPV	30.3 (95% CI 23.5–38.0)	43.5 (95% CI 36.1–51.2)	50.9 (95% CI 41.9–60)	
	NPV	90.0 (95% CI 84.3–93.8)	97.1 (95% CI 92.0–99.0)	97.3 (95% CI 92.6–99.1)	
Enterobacteriaceae ($n = 56$, includes 12 bacteremias)	Optimal threshold	7.39	22.3	0.791	
	Youden index	0.3582	0.6523	0.6901	
	AUC	0.706 (95% CI 0.636–0.770)	0.896 (95% CI 0.844–0.935)	0.917 (95% CI 0.868–0.952)	$Z = 0.916$ $P = 0.3598$
	Sensitivity	69.6 (95% CI 55.9–81.2)	94.6 (95% CI 85.1–98.9)	78.6 (95% CI 65.6–88.4)	
	Specificity	66.2 (95% CI 57.6–74.1)	70.6 (95% CI 62.2–78.1)	90.4 (95% CI 84.2–94.8)	
	PPV	45.9 (95% CI 38.8–53.2)	57.0 (95% CI 50.3–63.4)	77.2 (95% CI 66.5–85.2)	
	NPV	84.1 (95% CI 77.8–88.9)	97.0 (95% CI 91.4–99.0)	91.1 (95% CI 86.1–94.4)	
E. coli ($n = 20$)	Optimal threshold	5.34	22.3	0.215	
	Youden index	0.2853	0.6059	0.7088	
	AUC	0.640 (95% CI 0.559–0.715)	0.861 (95% CI 0.797–0.911)	0.908 (95% CI 0.851–0.948)	$Z = 1.351$ $P = 0.1766$
	Sensitivity	80.0 (95% CI 56.3–94.3)	90.0 (95% CI 68.3–98.8)	90.0 (95% CI 68.3–98.8)	
	Specificity	48.5 (95% CI 39.9–57.2)	70.6 (95% CI 62.2–78.1)	80.9 (95% CI 73.3–87.1)	
	PPV	18.6 (95% CI 14.8–23.1)	31.0 (95% CI 25.0–37.8)	40.9 (95% CI − 32.2–50.2)	
	NPV	94.3 (95% CI 87.1–97.6)	98.0 (95% CI 92.8–99.4)	97.3 (95% CI 93.6–99.5)	
Enterobacteriaceae ($n = 44$)	Optimal threshold	7.39	22.3	0.947	
	Youden index	0.3436	0.6377	0.6691	
	AUC	0.688 (95% CI 0.614–0.755)	0.887 (95% CI 0.832–0.930)	0.905 (95% CI 0.852–0.943)	$Z = 0.698$ $P = 0.4854$
	Sensitivity	68.2 (95% CI 52.4–81.4)	93.2 (95% CI 81.3–98.6)	75.0 (95% CI 59.7–86.8)	
	Specificity	66.2 (95% CI 57.6–74.1)	70.6 (95% CI 62.2–78.1)	91.9 (95% CI 86.0–95.9)	
	PPV	39.5 (95% CI 32.4–47.1)	50.6 (95% CI 43.8–57.4)	75.0 (95% CI 62.4–84.4)	
	NPV	86.5 (95% CI 80.4–91.0)	97.0 (95% CI 91.4–99.0)	91.9 (95% CI 87.2–95.0)	
Candida ($n = 23$, includes 1 bacteremias)	Optimal threshold	13.13	15.5	0.158	
	Youden index	0.4582	0.6474	0.6514	$Z = 0.166$ $P = 0.8679$
	AUC	0.779 (95% CI 0.712–0.836)	0.852 (95% CI 0.793–0.899)	0.869 (95% CI 0.812–0.914)	
	Sensitivity	65.2 (95% CI 42.7–83.6)	95.7 (95% CI 78.1–99.9)	87.0 (95% CI 66.4–97.2)	
	Specificity	80.6 (95% CI 73.7–86.3)	69.1 (95% CI 61.4–76.0)	78.2 (95% CI 71.1–84.2)	
	PPV	31.9 (95% CI 23.3–41.9)	30.1 (95% CI 25.3–35.5)	35.7 (95% CI 28.6–43.6)	
	NPV	94.3 (95% CI 90.4–96.7)	98.3 (95% CI 94.4–99.9)	97.7 (95% CI 93.7–99.2)	

ROC curves were compared using the method of DeLong et al.[18]

NLR neutrophil-to-lymphocyte ratio, *CRP* C-reactive protein, *PCT* procalcitonin, *PPV* positive predictive value, *NPV* negative predictive value

for diagnosing UTI will improve the diagnostic performance. In this study, the Youden index of PCT was greater than the Youden index of CRP, which showed that PCT was superior for diagnosing UTI, which is consistent with previous studies [23].

NLR, CRP and PCT levels in the bacteriuria group were significantly greater than those in the control group in this study, suggesting that NLR, CRP and PCT can be used to predict positive urine cultures (Table 1). The detailed data in Table 2 also support this point. According to the Youden index of the NLR, CRP and PCT, the ability of the NLR, CRP and PCT to predict urine culture positivity increases. The results of this study revealed that although the performance of PCT in predicting bacteriuria was better than that of CRP, there was no significant difference between the AUC of PCT and the AUC of CRP, indicating that the diagnostic ability of bacteriuria in the population is basically equivalent. This does not mean that the sensitivity and specificity of PCT are better than those of CRP. The differences in sensitivity, specificity, and optimal thresholds are related not only to the detection systems used for detecting CRP and PCT but also to the population included in the study and the representativeness of the population. In particular, the selection of control groups is particularly important [24].

The sensitivity and NPV of the CRP for predicting infections caused by Candida infections in the ICU are greater than those for predicting infections caused by bacterial infections. PCT has high sensitivity for predicting bacteriuria caused by *E. coli*. PCT has a high NPV for predicting bacteriuria caused by fungi. The NLR is easy to obtain and inexpensive, but its diagnostic efficiency is only moderate. Therefore, to evaluate the diagnostic value of the NLR, CRP and PCT for bacteriuria and their significance for patient prognosis, it is recommended that the above inflammatory indicators be detected simultaneously to improve the sensitivity and NPV.

This study has several limitations. First, a urine culture is performed only when a UTI is suspected. The rate of UTI positivity may be artificially high. Since the sample size of this study was small and it was a single-center study, bias was inevitable. Second, the proper collection of urine samples is essential for the accurate diagnosis of urinary tract infections (UTIs). Midstream clean-catch urine samples are favor over catheterized specimens due to their lower risk of urethral contamination. Moreover, the volume of urine obtained and the timing of sample collection can significantly influence the reliability of the results. The timing of urine collection is critically influenced by the use of antibiotics, as well as the interval since their administration, which consequently determines the positivity of urine culture results. Third, because there are too many real controls and not all pairs are used and are selected over a period of time, this may lead to a certain deviation of the data from the real world. In future studies, we will be able to draw more valuable conclusions by expanding the sample size and conducting prospective and multicenter studies.

In conclusion, the main pathogenic bacteria of bacteriuria are Enterobacteriaceae. Our study revealed that CRP and PCT are good diagnostic markers for diagnosing bacteriuria. When bacteriuria is suspected, PCT should be tested together with CRP and complete blood count to improve the sensitivity and NPV of diagnosis.

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Author contributions
Conception and design: GM Z. Acquisition of data: GM Z, XX G. Analysis and interpretation of data: GM Z XX G. Manuscript writing: all authors. Revision of the manuscript draft: GM Z, XX G. Administrative support and study supervision or coordination: both authors. Final approval of manuscript: both authors.

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Availability of data and materials
All the data reported in this study are included in this published article. Further details are available from the corresponding author upon request. No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The ethics committee of Shuyang Hospital approved this study (SYYYLL202352).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Formenti P, Gotti M, Palmieri F, Pastori S, Roccaforte V, Menozzi A, Galimberti A, Umbrello M, Sabbatini G, Pezzi A. Presepsin in critical illness: current knowledge and future perspectives. Diagnostics. 2024;14(12):1311.
2. Ma S, Zhang F, Zhou F, Li H, Ge W, Gan R, Nie H, Li B, Wang Y, Wu M, et al. Metagenomic analysis reveals oropharyngeal microbiota alterations in patients with COVID-19. Signal Transduct Target Ther. 2021;6(1):191.
3. Zhou W, Sailani MR, Contrepois K, Zhou Y, Ahadi S, Leopold SR, Zhang MJ, Rao V, Avina M, Mishra T, et al. Longitudinal multi-omics of host-microbe dynamics in prediabetes. Nature. 2019;569(7758):663–71.
4. Formenti P, Isidori L, Pastori S, Roccaforte V, Mantovani EA, Iezzi M, Menozzi A, Panella R, Galimberti A, Brenna G, et al. A secondary retrospective analysis of the predictive value of neutrophil-reactive intensity (NEUT-RI) in septic and non-septic patients in intensive care. Diagnostics. 2024;14(8):821.
5. Schlapbach LJ, Graf R, Woerner A, Fontana M, Zimmermann-Baer U, Glauser D, Giannoni E, Roger T, Muller C, Nelle M, et al. Pancreatic stone protein as a novel marker for neonatal sepsis. Intensive Care Med. 2013;39(4):754–63.

6. Chu CM, Lowder JL. Diagnosis and treatment of urinary tract infections across age groups. Am J Obstet Gynecol. 2018;219(1):40–51.
7. Mattoo TK, Spencer JD. Biomarkers for urinary tract infection: present and future perspectives. Pediatr Nephrol. 2024. https://doi.org/10.1007/s00467-024-06321-9.
8. Masajtis-Zagajewska A, Nowicki M. New markers of urinary tract infection. Clin Chim Acta. 2017;471:286–91.
9. Pencina MJ, Steyerberg EW, D'Agostino RB Sr. Net reclassification index at event rate: properties and relationships. Stat Med. 2017;36(28):4455–67.
10. Zhang GM, Liu J, Guo XX, Yang FM. A novel LDLC equation is superior to the NIH LDLC equation and the Friedewald equation. Int J Gen Med. 2024;17:559–66.
11. Choi JJ, McCarthy MW, Meltzer KK, Cornelius-Schecter A, Jabri A, Reshetnyak E, Banerjee S, Westblade LF, Mehta S, Simon MS, et al. The diagnostic accuracy of procalcitonin for urinary tract infection in hospitalized older adults: a prospective study. J Gen Intern Med. 2022;37(14):3663–9.
12. Kuil SD, Hidad S, Fischer JC, Harting J, Hertogh C, Prins JM, de Jong MD, van Leth F, Schneeberger C. Sensitivity of C-reactive protein and procalcitonin measured by point-of-care tests to diagnose urinary tract infections in nursing home residents: a cross-sectional study. Clin Infect Dis. 2021;73(11):e3867–75.
13. Soler N, Esperatti M, Ewig S, Huerta A, Agusti C, Torres A. Sputum purulence-guided antibiotic use in hospitalised patients with exacerbations of COPD. Eur Respir J. 2012;40(6):1344–53.
14. Luo H, He L, Zhang G, Yu J, Chen Y, Yin H, Goyal H, Zhang GM, Xiao Y, Gu C, et al. Normal reference intervals of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, and systemic immune inflammation index in healthy adults: a large multi-center study from western China. Clin Lab. 2019;65(3):255–65.
15. Zhang GM, Zhuang ZH. The maximum amplitude of thromboelastography can be used for predicting recurrent spontaneous abortion. Am J Reprod Immunol. 2022;87(5): e13538.
16. Yin J, Samawi H, Linder D. Improved nonparametric estimation of the optimal diagnostic cut-off point associated with the Youden index under different sampling schemes. Biom J. 2016;58(4):915–34.
17. Bantis LE, Nakas CT, Reiser B. Construction of confidence regions in the ROC space after the estimation of the optimal Youden index-based cut-off point. Biometrics. 2014;70(1):212–23.
18. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988;44(3):837–45.
19. Fleischhack G, Cipic D, Juettner J, Hasan C, Bode U. Procalcitonin—a sensitive inflammation marker of febrile episodes in neutropenic children with cancer. Intensive Care Med. 2000;26(Suppl 2):S202-211.
20. Iwamoto S, Kimoto M, Mure T, Onuma E, Yamamoto Y, Iki K, Yoshida K, Tadaoka Y, Majima T, Kawasaki S, et al. Sequential chemotherapy with methotrexate and 5-fluorouracil for advanced gastric cancer. Gan To Kagaku Ryoho. 1998;25(4):541–6.
21. Zhang H, Yang J, Lin L, Huo B, Dai H, He Y. Diagnostic value of serum procalcitonin for acute pyelonephritis in infants and children with urinary tract infections: an updated meta-analysis. World J Urol. 2016;34(3):431–41.
22. Shaikh KJ, Osio VA, Leeflang MM, Shaikh N. Procalcitonin, C-reactive protein, and erythrocyte sedimentation rate for the diagnosis of acute pyelonephritis in children. Cochrane Database Syst Rev. 2020;9(9):CD009185.
23. Cui N, Zhang YY, Sun T, Lv XW, Dong XM, Chen N. Utilizing procalcitonin, C-reactive protein, and serum amyloid A in combination for diagnosing sepsis due to urinary tract infection. Int Urol Nephrol. 2024;56:2141–6.
24. Zhang GM, Zhang GM, Gu B. Serum transforming growth factor beta1 level for knee osteoarthritis diagnosis. Clin Chim Acta. 2017;474:136.

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