

## Original Article

# Diagnostic value of NLR, PLR and SIRI in peritoneal dialysis-associated peritonitis

Ye Liu, Ling Zhang, Tian Tian, Zhihui Guo, Yi Shao, Xiaoying Ma, Yuping Sheng, Fuyun Sun

Department of Nephrology, Cangzhou Central Hospital, Cangzhou 061000, Hebei, China

Received August 21, 2024; Accepted December 6, 2024; Epub March 15, 2025; Published March 30, 2025

**Abstract:** Objective: To evaluate the diagnostic value of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SIRI) in peritoneal dialysis-associated peritonitis (PDAP). Methods: In this retrospective study, the clinical data from 130 patients who underwent peritoneal dialysis (PD) for the first time at the Cangzhou Central Hospital from January 2019 to January 2022 were rigorously reviewed and analyzed. Based on the occurrence of PDAP during treatment, patients were classified into the peritonitis group (n=31) and the non-peritonitis group (n=99). The expression levels and diagnostic value of NLR, PLR, and SIRI were analyzed in the context of PDAP. Pearson correlation analysis was performed to examine the correlations between NLR, PLR and SIRI in PDAP patients, and the joint diagnostic value of NLR, PLR, and SIRI was evaluated. Additionally, risk factors associated with PDAP were identified. Results: Patients in the peritonitis group were older than those in the non-peritonitis group, and experienced longer duration of dialysis ( $P<0.05$ ). The peritonitis group exhibited significantly higher NLR, PLR and SIRI levels than the non-peritonitis group ( $P<0.001$ ). Pearson correlation analysis revealed significant positive correlations between NLR, PLR and SIRI in PDAP patients. Logistic regression analysis identified NLR, PLR, and SIRI as independent influencing factors for the occurrence of PDAP. ROC curve analysis revealed that the combined use of NLR, PLR, and SIRI for diagnosing PDAP yielded an AUC of 0.935, significantly higher than their individual predictions, along with superior diagnostic accuracy. Conclusion: NLR, PLR, and SIRI are independent risk factors for the occurrence of PDA. These indices hold significant diagnostic value for PDAP, and their combined utilization can enhance diagnostic accuracy.

**Keywords:** NLR, PLR, SIRI, peritoneal dialysis-associated peritonitis

## Introduction

Chronic kidney disease (CKD) is a kidney disorder caused by various factors, characterized by changes in the estimated glomerular filtration rate and abnormalities in blood or urine [1]. The global prevalence of CKD is approximately 13.4%, with an estimated 120 million adults affected in China [2]. End-stage CKD necessitates renal replacement therapy, which includes dialysis and kidney transplantation. Given the escalating prevalence of type 2 diabetes and an aging population, CKD is evolving into a significant global health and economic concern.

In peritoneal dialysis (PD), the peritoneum acts as a natural semi-permeable membrane, using its selective permeability to remove waste and excess fluid from the blood [3]. Peritoneal dialysis-associated peritonitis (PDAP) is a critical complication of PD treatment that can trigger

peritoneal fibrosis or sclerosis [4]. The International Society for Peritoneal Dialysis (ISPD) guidelines state that the incidence of peritonitis in each dialysis regimen should not exceed 0.5 episodes per patient per year. Although most cases of peritonitis can be managed without removing the catheter, PDAP remains a major cause of hospitalization and death in PD patients, with up to 25% requiring catheter removal or conversion to hemodialysis, and a mortality rate of 8.6% [5]. The medical community generally believes that the pathogenesis of PDAP is related to immune dysfunction of the peritoneum, increased risk of exogenous infections, and dysbiosis of the intestinal microbiota in patients [6]. The systemic inflammation and immune deficiency specific to end-stage renal disease can lead to atherosclerosis, cardiovascular disease, cachexia, and anemia [7]. In addition, immune system defects can also lead

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to dysregulation of the immune response, increasing the risk and severity of microbial infections [8].

The neutrophil/lymphocyte ratio (NLR) reflects the balance between neutrophils and lymphocytes, providing insight into a patient's infection and immune status [9]. The platelet/lymphocyte ratio (PLR) reflects platelet and lymphocyte counts, providing a reflection of a patient's thrombotic and coagulation status [10]. The systemic inflammation response index (SIRI) is a comprehensive index calculated from peripheral blood parameters, including neutrophils, lymphocytes, monocytes, and platelets [11]. As a comprehensive indicator reflecting systemic inflammation and immune status, SIRI is less influenced by individual factors such as age, sex, and comorbidities compared to other single routine blood parameters, demonstrating greater stability [12].

The novelty of this study lies in the systematic evaluation of the clinical value of NLR, PLR, and SIRI in PDAP being evaluated together for the first time. Through the analysis of these comprehensive blood indices, this study aims to gain a deeper understanding of the pathological and physiological mechanisms of PDAP and explore the potential applications of these indices in predicting and monitoring the progression of PDAP.

### Methods and data

#### *Clinical data*

A retrospective analysis was conducted on 130 patients who received PD for the first time at Cangzhou Central Hospital from January 2019 to January 2022. The study was conducted with the approval of the Medical Ethics Committee of Cangzhou Central Hospital.

#### *Inclusion and exclusion criteria*

Inclusion criteria: (1) Patients aged 18 years or older; (2) Patients requiring dialysis treatment who had undergone at least 4 weeks of PD; (3) Patients with complete microbiological investigation results; (4) Patients with available, complete clinical and follow-up data.

Exclusion criteria: (1) Patients who have undergone hemodialysis before treatment or had switched dialysis modalities during the treat-

ment course; (2) Patients with a history of abdominal surgery before initiating dialysis or with other sources of infection, such as skin infections; (3) Patients with malignant tumors or severe impairment of cardiac, pulmonary, or hepatic function; (4) Patients with peritonitis caused by environmental or operational factors.

#### *Diagnostic criteria*

According to the diagnostic criteria established by the ISPD in 2016, the diagnosis of peritonitis includes the following [13]: cloudy dialysis fluid, abdominal pain, fever, nausea, vomiting; presence of pathogens in the dialysis fluid; white blood cell count in the dialysis fluid exceeding  $100 \times 10^6/L$ , with neutrophils accounting for more than 50%. Peritonitis can be confirmed if any two of these criteria are met.

#### *Patient grouping*

Based on the occurrence of PDAP during the treatment, the patients were divided into the peritonitis group (n=31) and the non-peritonitis group (n=99).

#### *Data gathering*

Patient data were collected from medical records, follow-up information, and laboratory records. The collected data included age, sex, duration of dialysis, primary kidney disease, history of diabetes, history of hypertension, history of smoking, NLR, PLR and SIRI. NLR = neutrophil count/lymphocyte count; PLR = platelet/lymphocyte count; SIRI = (neutrophil count  $\times$  monocyte count)/lymphocyte count.

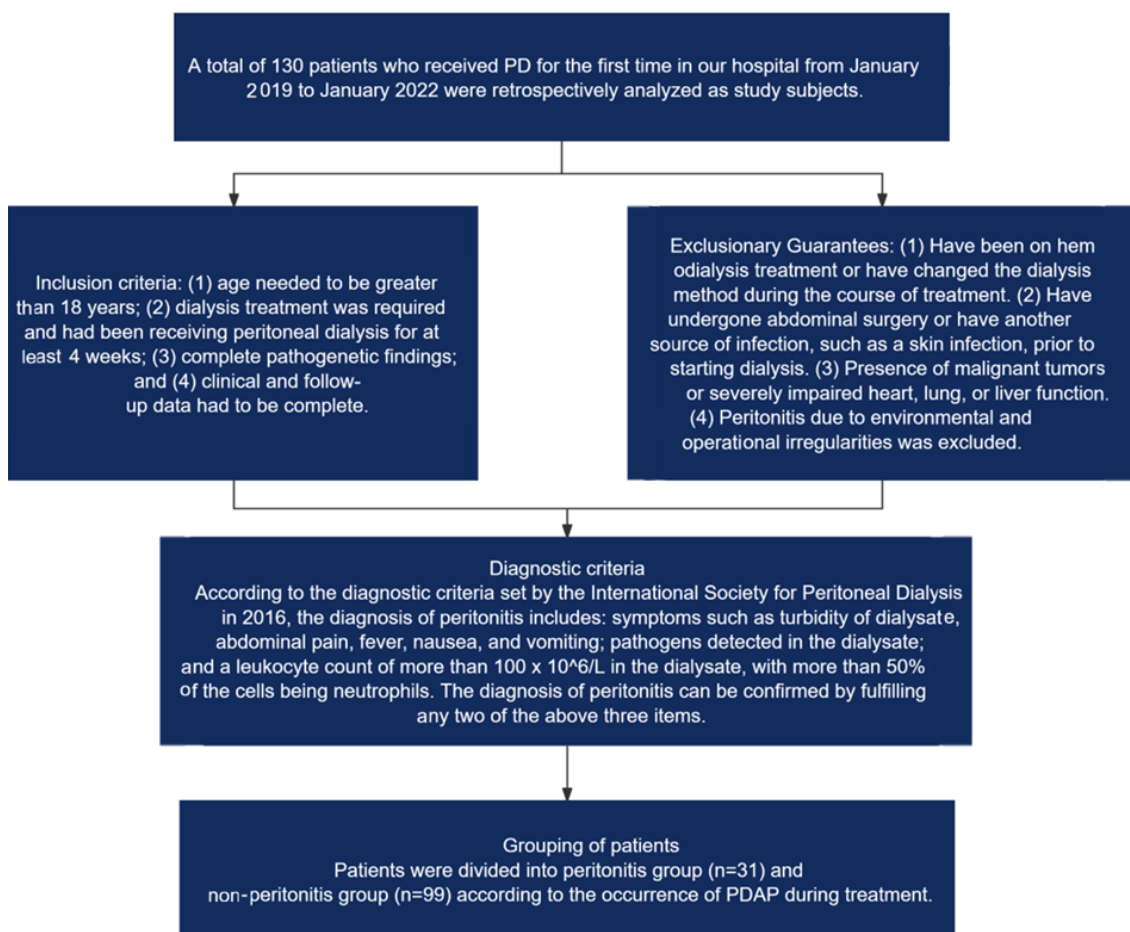
#### *Outcome measures*

1. Baseline characteristics of the two groups were compared. 2. The expression and diagnostic value of NLR, PLR, and SIRI in PDAP patients were analyzed. 3. The correlations between NLR, PLR and SIRI in PDAP patients were analyzed with Pearson correlation analysis. 4. Risk factors contributing to PDAP were identified. 5. The diagnostic value of NLR, PLR, and SIRI and their combination was evaluated (**Figure 1**).

#### *Statistical analyses*

SPSS 26.0 software package was used for statistical analyses. Measurement variables were

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**Figure 1.** Flow chart of this study. Notes: NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SIRI: systemic immune-inflammation index; PDAP: peritoneal dialysis-associated peritonitis.

normally distributed and expressed as mean  $\pm$  standard deviation; the independent samples t-test was used for inter-group comparisons. Counting variables were presented as n (%) and compared using the chi-square test. Pearson correlation analysis was used to explore the correlations of NLR and PLR with SIRI in PDAP patients. Logistic regression analysis was conducted to identify risk factors associated with the occurrence of PDAP. The diagnostic value of NLR, PLR, SIRI and their combination for PDAP was assessed using receiver operating characteristic (ROC) curves.  $P < 0.05$  was considered statistically significant.

### Results

#### *Comparison of baseline data between the peritonitis group and non-peritonitis group*

Inter-group comparison of baseline characteristics revealed significantly higher age and longer

duration of dialysis in the peritonitis group compared to the non-peritonitis group ( $P < 0.05$ , **Table 1**). However, there were no significant differences between the two groups in sex, primary renal disease, history of diabetes, history of hypertension, and history of smoking ( $P > 0.05$ , **Table 1**).

#### *Comparison of NLR, PLR and SIRI between the peritonitis group and non-peritonitis group*

Inter-group comparison revealed significantly higher NLR, PLR, and SIRI in the peritonitis group compared to the non-peritonitis group (all  $P < 0.001$ , **Figure 2**).

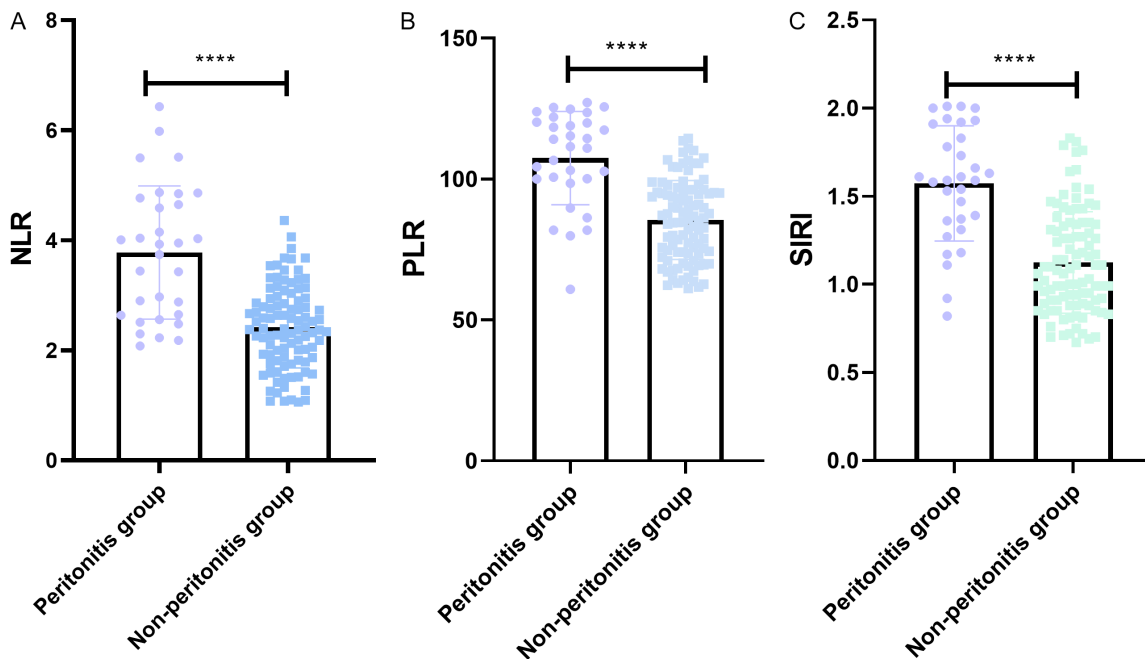
#### *Correlations between NLR, PLR and SIRI in PDAP patients*

Pearson correlation analysis revealed significant positive correlation between NLR and SIRI

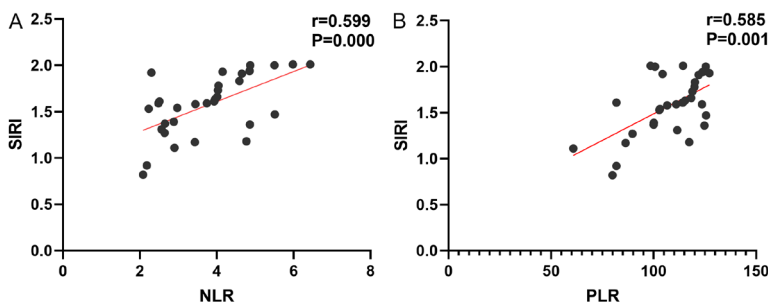
## The value of NLR, PLR and SIRI in diagnosing PDAP

**Table 1.** Comparison of baseline data between the peritonitis and non-peritonitis groups

Factors		Peritonitis group (n=31)	Non-peritonitis group (n=99)	$\chi^2/t$	P value
Age (years)		59.84±4.68	57.18±6.03	2.562	0.013
Sex	Male/Female	19/12	57/42	0.134	0.714
Duration of dialysis (month)		12.61±2.09	10.25±3.35	4.677	<0.001
Primary renal disease	Nephrotic syndrome/Diabetic nephropathy	17/14	48/51	0.381	0.537
History of diabetes	Yes/No	6/25	18/81	0.022	0.883
History of hypertension	Yes/No	6/25	25/74	0.452	0.501
History of smoking	Yes/No	20/11	69/30	0.293	0.588



**Figure 2.** Comparison of NLR (A), PLR (B), and SIRI (C) between peritonitis and non-peritonitis groups. \*\*\*\*,  $P<0.0001$ . Notes: NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SIRI: systemic immune-inflammation index; PDAP: peritoneal dialysis-associated peritonitis.



**Figure 3.** Correlations between NLR, PLR and SIRI in PDAP patients. A: Correlation of NLR with SIRI in PDAP patients; B: Correlation of PLR with SIRI in PDAP patients. Notes: NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SIRI: systemic immune-inflammation index; PDAP: peritoneal dialysis-associated peritonitis.

in PDAP patients ( $P<0.05$ ), as well as a positive correction between PLR and SIRI ( $P<0.05$ , **Figure 3**).

### Identification of factors contributing to the occurrence of PDAP

Based on the above findings, notable distinctions in age, duration of dialysis, NLR, PLR, and SIRI were observed between the two groups ( $P<0.05$ ). The indicators were assigned values (**Table 2**) and subjected to multifactorial analysis. Logistic regression analysis identified NLR, PLR, and SIRI as independent factors influencing the occurrence of PDAP, as shown in **Table 3**.

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**Table 2.** Assignment table

Factors	Assignment	
	0	1
Age	<57.3 years old	≥57.3 years old
Duration of dialysis	<11.19 months	≥11.19 months
NLR	<2.75	≥2.75
PLR	<90.72	≥90.72
SIRI	<1.23	≥1.23
PDAP	No	Yes

Notes: NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SIRI: systemic immune-inflammation index; PDAP: peritoneal dialysis-associated peritonitis.

### *Diagnostic value of NLR, PLR, SIRI and their combination in PDAP patients*

The diagnostic performance of NLR, PLR, and SIRI, both individually and in combination, was evaluated. ROC curve analysis revealed that the combined use of NLR, PLR, and SIRI for diagnosing PDAP yielded an AUC of 0.935, significantly higher than the AUCs of the individual indices. This combination also demonstrated greater accuracy compared to the individual predictions (**Figure 4** and **Table 4**).

### **Discussion**

Peritoneal dialysis-associated peritonitis (PDAP) is a major complication of PD [14]. The annual incidence of peritonitis in the United States, Japan, and Canada is approximately 0.26 to 0.29 episodes, while in Australia, New Zealand, the United Kingdom, and Thailand, it ranges from 0.35 to 0.40 episodes [15]. Advancements in PD technology have reduced complications and improved the survival rate of PD patients, making it comparable to that of hemodialysis patients [16]. Early diagnosis of PDAP typically relies on clinical symptoms, laboratory testing, and microbiological examination [17]. However, in primary care hospitals and outpatient settings, screening for PDAP is often limited due to high equipment costs and complex operations [18]. Therefore, it becomes particularly important to develop low-cost and simple methods to assess the prognosis of PDAP patients.

Inflammation is known to be a significant factor influencing the mortality rate in PD patients and is associated with various physiological changes [19]. While markers such as C-reactive

protein and interleukin-6 can predict the risk in PD and hemodialysis patients, their application in primary health-care is limited due to cost and operational constraints [20]. In this study, we focused on evaluating NLR, PLR, and SIRI levels in patients with PD. PLR, the ratio of platelets to lymphocytes, reflects the primary cellular components in the blood [21]. NLR, the ratio of neutrophils to lymphocytes, serves as an indicator of infection

defense and immune response [12]. SIRI comprehensively evaluates the immune and inflammatory status of the body according to the count of neutrophils, monocytes and lymphocytes [22]. Our findings revealed notably higher NLR, PLR, and SIRI in the peritonitis group compared to the non-peritonitis group, suggesting that these indices reflect the intensity of the inflammatory response, activation status of the immune system, and severity of the pathological process in PDAP. Moreover, we observed significant positive correlations between NLR, PLR and SIRI in PDAP patients, primarily reflecting the inflammatory processes associated with PDAP. The inflammatory response trigger by PDAP leads to an increase in neutrophils and a decrease in lymphocytes, which is reflected in the elevated NLR [12]. Additionally, platelets play a crucial role in inflammation and disease progression, with increased platelet count in peritoneal dialysis patients possibly associated with elevated PLR [21], indicating a potential link between platelet activation, inflammation, and disease development. Additionally, SIRI integrates neutrophils, lymphocytes, and monocytes, providing a comprehensive reflection of both systemic inflammation and nutritional status of PDAP patients [22]. The positive correlation between NLR, PLR and SIRI further suggests that these inflammatory markers collectively reflect the pathological process in PDAP patients.

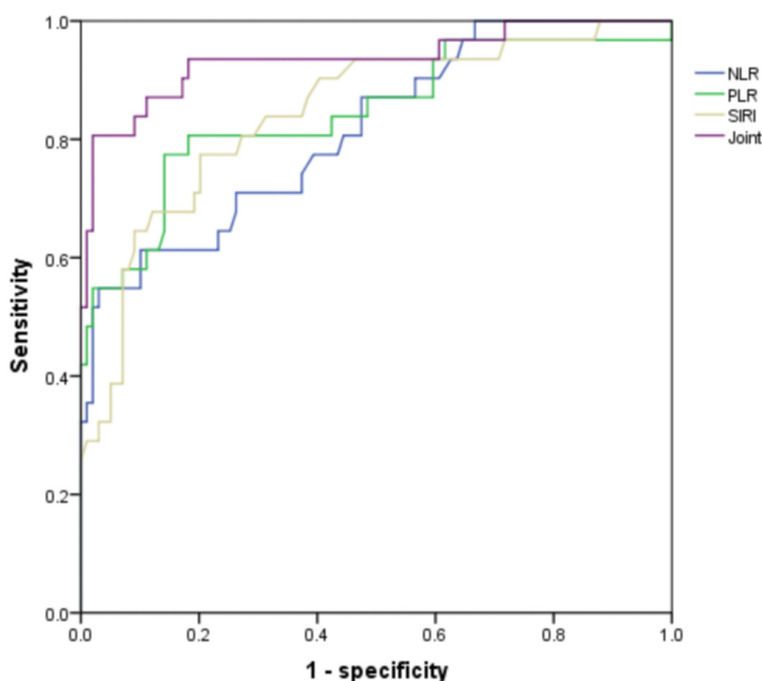
In this study, logistic regression analysis identified NLR, PLR, and SIRI as independent factors for PDAP. Neutrophils and monocytes are important components of white blood cells. Neutrophils serve as the first line of defense against acute infections, primarily responsible for eliminating pathogens, especially bacteria

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**Table 3.** Logistic regression analysis of factors influencing the occurrence of peritonitis

	$\beta$	S.E.	Wals	df	Sig.	Exp ( $\beta$ )	95% CI for EXP ( $\beta$ )	
							Lower limit	Upper limit
Age	0.915	0.621	2.171	1	0.141	2.497	0.739	8.434
Duration of dialysis	1.023	0.569	3.226	1	0.072	2.780	0.911	8.486
NLR	2.044	0.575	12.633	1	<0.001	7.722	2.501	23.839
PLR	2.428	0.616	15.521	1	<0.001	11.335	3.387	37.930
SIRI	2.001	0.630	10.104	1	0.001	7.400	2.154	25.420

Notes: NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SIRI: systemic immune-inflammation index; PDAP: peritoneal dialysis-associated peritonitis.



**Figure 4.** ROC curves of NLR, PLR, SIRI and their combination in diagnosing PDAP. Notes: NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SIRI: systemic immune-inflammation index; PDAP: peritoneal dialysis-associated peritonitis.

**Table 4.** ROC parameters of NLR, PLR, SIRI and their combination in diagnosing peritonitis

Marker	AUC	Specificity	Sensitivity	Accuracy
NLR	0.815	54.80%	97.00%	86.90%
PLR	0.844	77.40%	85.90%	83.80%
SIRI	0.845	77.40%	79.80%	79.20%

Notes: ROC: receiver operating characteristic; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SIRI: systemic immune-inflammation index.

and fungi [23]. Monocytes circulate in the blood and, upon migration to tissues, differentiate into macrophages or dendritic cells. These cells play an essential role in pathogen engulfment, production of inflammatory mediators, and

antigen presentation, contributing significantly to chronic inflammatory responses and tissue repair [24]. Platelets are also essential in sterile inflammatory processes, responding to tissue damage and cell death, especially in pathological conditions such as ischemia, atherosclerosis, and gout [25]. Inflammatory conditions can lead to alterations in protein metabolism, promoting protein breakdown while inhibiting protein synthesis. This imbalance affects the patient's nutritional status, stimulates the intestinal microbiota, and facilitates the transfer of bacteria and toxins from the intestines into the bloodstream, resulting in an inflammatory state and creating a vicious cycle [26]. This inflammatory state can further lead to the activation of the immune system, releasing more inflammatory mediators such as cytokines and chemokines, thereby exacerbating the inflammatory response. Moreover, when coupled with a bacterial infection, this heightened inflammatory state makes the body more susceptible to infections, particularly in the peritoneal cavity.

The heightened inflammatory response alters body's internal environment, impairing immune system functionality, causing tissue damage, and influencing the release of inflammatory mediators. These factors collectively

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create a more conducive environment for bacterial growth and reproduction, thereby increasing the risk of infection [27]. Bacterial infections are more prone to spreading and triggering inflammation-related complications, such as peritonitis, in an environment where the inflammatory response is intensified [28]. Therefore, a bacterial infection, combined with an exacerbated inflammatory state, can trigger an inflammatory reaction in the peritoneal region, ultimately culminating in the development of peritonitis.

Finally, our study revealed that a comprehensive assessment incorporating NLR, PLR, and SIRI provides a more robust diagnostic approach for PDAP. This outcome implies that while individual indicators offer valuable diagnostic insights for PDAP, their collective integration leads to a more precise and nuanced diagnostic profile. These results underscore the importance of integrating diverse inflammation and immune markers in PDAP diagnosis, highlighting the potential for enhanced diagnostic accuracy and personalized treatment strategies.

This study still has a few limitations. The small sample size, retrospective design, and single-center setting may restrict the generalizability and validity of our findings. To overcome these constraints, future research should focus on increasing the sample size, adopting a prospective design, and conducting multi-center studies. These steps would enhance the external validity and provide a more accurate representation of the diagnostic value of NLR, PLR, and SIRI in broader clinical settings.

### Conclusion

NLR, PLR, and SIRI are independent factors influencing the occurrence of PDAP. These indices hold significant diagnostic value, and their combined use can improve diagnostic accuracy. Future studies, incorporating larger and more diverse patient populations, will be essential to further validate these findings and refine diagnostic strategies for PDAP.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Ye Liu, Department of Nephrology, Cangzhou Central Hospital, No. 16

Xinhua West Road, Cangzhou 061000, Hebei, China. E-mail: liuye230626@163.com

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