


The Potential Value of Mean Platelet Volume and Platelet Distribution Width as Inflammatory Indicators in Surgical Necrotizing Enterocolitis

Yunhan Zhang^{1,*}, Yuyun Chen^{2,*}, Jilin Lv¹, Xiao Xiang¹, Peiyao Wang¹, Wei Feng¹, Zhenhua Guo¹ 

¹Department of Neonatal Surgery, Children's Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development, Chongqing Key Laboratory of Structural Birth Defect and Reconstruction, Chongqing, People's Republic of China; ²Fujian Children's Hospital, Fujian Branch of Shanghai Children's Medical Center, College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, Fuzhou, People's Republic of China

*These authors have contributed equally to this work

Correspondence: Zhenhua Guo, Department of neonatal surgery, Children's Hospital of Chongqing Medical University, 20 Jinyu Road, Yubei District, Chongqing, 400025, People's Republic of China, Tel +86-23-68370286, Email zhguo@cqmu.edu.cn

Background: This study aims to investigate the potential significance of mean platelet volume (MPV) and platelet distribution width (PDW) in predicting surgical neonatal necrotizing enterocolitis (NEC) and establish the correlation between MPV/PDW levels and the severity/prognosis of NEC.

Methods: A retrospective study was conducted on a cohort of 372 patients diagnosed with NEC. The patients were categorized into two groups based on whether they underwent surgical therapy. Univariate /multivariate analysis were employed to compare the MPV and PDW between the two groups. Moreover, patients in surgical group were categorized into multiple subgroups based on intraoperative findings and postoperative prognosis, and the levels of MPV and PDW were compared among these subgroups.

Results: Of the 372 patients, the operative group exhibited significantly higher levels of MPV and PDW than the nonoperative group ($P < 0.05$). Logistic regression analysis revealed that MPV (OR = 4.895, $P < 0.001$) and PDW (OR = 1.476, $P < 0.001$) independently associated with surgical NEC. The analysis of the receiver operating characteristic (ROC) curve revealed that the area under the curve (AUC) was 0.706 for MPV alone, with a cut-off value of 11.8 fL. Similarly, the AUC was 0.728 for PDW alone, with a cut-off value of 16%. However, when MPV and PDW were combined, the AUC increased to 0.906 for predicting surgical NEC. In accordance with the intraoperative findings, the levels of MPV and PDW were found to be higher in the large area necrosis group than in the partial or mild necrosis group ($P < 0.01$). Furthermore, the MPV and PDW values in the death group were significantly greater than those in the survival group ($P = 0.040$, $P = 0.008$).

Conclusion: MPV and PDW may serve as potentially valuable indicators for determining the need for surgical intervention and predicting the prognosis of patients with NEC.

Keywords: mean platelet volume, platelet distribution width, necrotizing enterocolitis, neonatal

Introduction

Neonatal necrotizing enterocolitis (NEC) is a grave and potentially fatal ailment, representing the most prevalent gastrointestinal emergency in neonatal intensive care units (NICUs), with over 90% of cases affecting premature infants.¹ Surgical intervention becomes necessary in severe instances, and prompt surgical intervention has been shown to enhance patient prognosis in NEC cases. Intestinal perforation serves as an absolute indication for surgical intervention in NEC cases; however, when abdominal X-ray reveals such perforation, the resulting abdominal cavity infection tends to be severe, often leading to septic shock and its associated consequences.² Consequently, accurate prediction of the timing of surgery is important to improve the prognosis of patients with NEC.

In recent years, certain scholars have suggested enhancing the prognosis of necrotizing enterocolitis (NEC) through the utilization of seven clinical metrics of metabolic derangement (MD7) as a means to support the necessity of timely surgical intervention.³ Several studies have demonstrated the significance of various biomarkers, including serum amyloid A,⁴ intestinal fatty acid binding protein,⁵ C5a,⁶ serum interleukin-1 receptor antagonist,⁷ ischaemia-modified albumin,⁸ and interleukin 8,⁹ in diagnosing NEC and reflecting intestinal injury. However, the sensitivity and specificity of these factors in predicting the optimal timing for NEC surgery are deemed inadequate. Furthermore, the clinical advancement of these methods continues to face numerous challenges due to the inherent complexities associated with blood collection in premature infants.

The establishment of uncomplicated and widely accepted biological markers for prompt detection and precise assessment of surgical necrotizing enterocolitis holds significant advantages. Platelets, minute cytoplasmic fragments discharged through the disintegration of mature megakaryocytes in the bone marrow, have the potential to activate and release various bioactive substances that are interconnected with the progression and prognosis of diseases. Studies indicate that thrombocytopenia may be correlated with the intensity of NEC,¹⁰ and children who succumb to NEC exhibit considerably diminished platelet counts.¹¹ Mean platelet volume (MPV) and platelet distribution width (PDW) are two platelet volume indices that have been employed in clinical settings to assess platelet activity.¹² MPV exhibits an inverse correlation with platelet count, as evidenced by its elevation in individuals with low platelet counts.¹³ A previous investigation indicated that the occurrence of a heightened MPV during the initial hours of life may potentially indicate an augmented susceptibility to the development of NEC.¹⁴ Furthermore, there is a correlation between an elevated MPV level and the severity of NEC.¹⁵ PDW, a metric that characterizes changes in platelet volume, primarily signifies megakaryocyte hyperplasia, metabolism, and platelet generation within the bone marrow.¹⁶ PDW serves as a more precise indicator of platelet activation and offers additional insights compared to MPV.^{17,18}

The present study aims to explore the association of MPV and PDW with surgical NEC, which has been scarcely investigated. To achieve this objective, a retrospective analysis was conducted on a cohort of 372 patients diagnosed with NEC. The primary goal of this research is to assess the potential of MPV and PDW as indicators for evaluating the severity and prognosis of surgical NEC, with the ultimate aim of enhancing the clinical assessment of disease severity and surgical timing.

Patients and Methods

Study Protocol

This study was approved by the Institutional Research Ethics Board of Children's Hospital affiliated Chongqing Medical University (Date: 2021/No: 391) and complies with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Study Population

The study enrolled neonates diagnosed with NEC who were admitted to the Neonatal Department of Children's Hospital of Chongqing Medical University from January 2018 to December 2022 based on the Bell staging criteria.¹⁹ The inclusion criteria were (1) Bell's stage \geq II and (2) NEC confirmed by surgery and pathology. The exclusion criteria were (1) incomplete clinical data; (2) asphyxia and spontaneous intestinal perforation in patients; and (3) patients with metabolic disease, severe infection caused by other diseases, cardiovascular diseases or congenital gastrointestinal dysplasia.

Clinical Variables

According to relevant literature and clinical practice, the variables for inclusion were carefully selected to make sure the parsimony of the final models. Data were collected from the electronic medical records of all participants in the study, encompassing various factors such as comorbidities during pregnancy, sex, gestational age, birth weight, age of onset, blood cell count analysis, C-reactive protein (CRP), procalcitonin (PCT), serum amyloid A protein (SAA), hepatic function index (albumin, alkaline phosphatase), and coagulation function parameters (fibrinogen, D-dimer). For the operative group, blood samples were obtained during the most recent preoperative period, while for the nonoperative

group, samples were taken on the day of diagnosis. This study classified the operative group as individuals exhibiting intestinal wall necrosis necessitating surgical intervention, while the nonoperative group was comprised of individuals who achieved resolution through conservative treatment.

Statistical Analysis

Data entry was performed using Excel software, and statistical analyses were conducted using SPSS version 22.0 (IBM Corporation, Armonk, NY, United States). Statistical significance was defined as $P < 0.05$. The Shapiro–Wilk test was utilized to assess the normal distribution of the data. For normally distributed data, the mean and standard deviation (mean \pm SD) were reported, while for nonnormally distributed data, the median and interquartile range (M (Q1, Q3)) were used. Group comparisons were made using the Mann–Whitney *U*-test. Categorical variables are represented using numbers and percentages. Receiver operating characteristic (ROC) curve analysis was employed to determine the area under the curve (AUC) and the cut-off value for the optimal predictor. Student's *t* test was utilized to compare the mean and 95% confidence interval (95% CI) of continuous variables. Chi-square or Fisher exact tests were employed to compare categorical variables between groups. Univariate and multivariate logistic regressions were also conducted to calculate odds ratios (ORs), 95% confidence intervals (CIs), and *P* values.

Results

Baseline Characteristics

This study included a total of 372 patients with NEC (Bell's stage \geq II) involvement, as shown in Figure 1. Among them, 244 patients belonged to the nonoperation group, while 128 patients were in the operation group, with the patients exhibiting varying degrees of intestinal necrosis. The general characteristics of the study subjects at baseline are summarized in Table 1. In the nonoperative group, there were 134 boys (54.92%) and 110 girls (45.08%), whereas the operative group consisted of 74 boys (57.81%) and 54 girls (42.18%).

Gestational age, birth weight, age of onset, and weight at onset had no statistically significant between-group differences ($P > 0.05$). For clinical manifestations, there were no statistically significant differences between the two

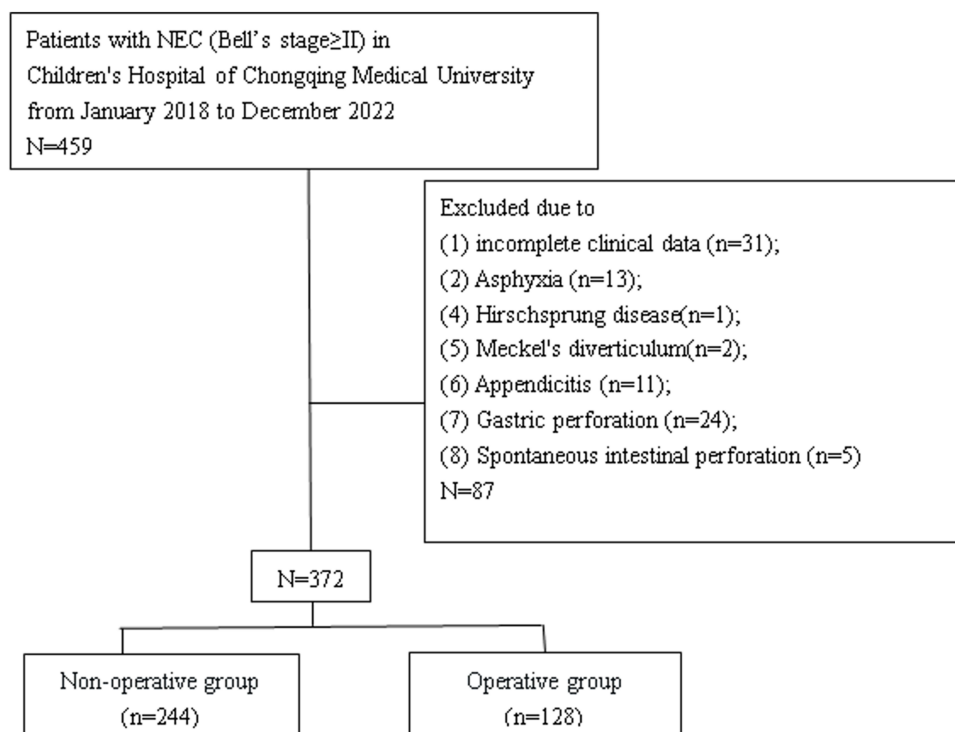


Figure 1 Population flowchart for the research project.

Table 1 General Baseline Characters of the Study Patients Between Non-Operative Group and Operative Group in This Study

	Non-Operative Group (n=244)	Operative Group (n=128)	χ^2/t	P value
Gender, n (%)				
Male	134 (54.92%)	74 (57.81%)		
Female	110 (45.08%)	54 (42.18%)		
Gestational age, (w)	34.4±3.1	33.9±3.4	1.64 ^b	0.1019
Birth weight, (g)	2245.6±562.2	2153.8±399.9	1.87 ^b	0.0632
Age of onset, (d)	11.4±3.2	10.5±3.3	1.89 ^b	0.0593
Weight of onset, (g)	2394.6±856.3	2257.9±695.7	0.75 ^b	0.4637
Clinical manifestation				
Emesis, n (%)	78 (31.97%)	52 (40.63%)	1.38 ^a	0.2394
Bloody stools, n (%)	84 (34.43%)	70 (54.69%)	7.10 ^a	0.0077
Abdominal distension, n (%)	134 (54.92%)	86 (67.19%)	2.62 ^a	0.1059
Abdominal tenderness, n (%)	30 (12.29%)	78 (60.94%)	48.21 ^a	<0.0001
Abdominal wall discolouration, n (%)	2 (0.82%)	26 (20.31%)	20.20 ^a	<0.0001
Abdominal X-ray				
Gas in the intestinal wall, n (%)	164 (67.21%)	90 (70.31%)	0.19 ^a	0.6661
Portal venous gas, n (%)	58 (23.77%)	34 (26.56%)	0.18 ^a	0.6750
Positive blood culture, n (%)	10 (4.09%)	12 (9.38%)	1.26 ^a	0.2618
LOS, (d)^{&}	32.6±22.4	44.5±34.7	6.86 ^b	<0.0001
Mortality, n (%)	2(0.82%)	18 (14.06%)	11.98 ^a	0.0005

Notes: [&]LOS: length of hospital stay; ^aChi-square test; ^bt-test. The presence of bold values indicates that the difference between the two groups for this variable was statistically significant (P<0.05).

groups in emesis, abdominal distension, or abdominal X-ray (P>0.05). However, there were statistically significant differences between the groups in bloody stools (P=0.0077), abdominal tenderness (P<0.0001), and abdominal wall discolouration (P=0.0005).

In the nonoperation group, two patients succumbed to respiratory failure resulting from bronchopulmonary dysplasia. Conversely, in the operation group, 84 patients (65.63%) underwent enteronecrotic enterostomy and enterostomy, and there were 40 patients (31.25%) who received simple enterostomy and four patients who underwent primary resection and anastomosis. The mortality rate in the operation group was 14.06%. Notably, there were statistically significant differences observed between the two groups in terms of length of hospital stay (LOS) (P< 0.0001) and mortality (P = 0.0356).

Comparison of Serum Infection markers Between the Two Groups

The MPV and PDW values of the operative group were found to be significantly higher than those of the nonoperative group in the analysis of blood cell count (12.47±1.01 vs 11.05±1.24, P<0.0001 and 17.84±3.86 vs 13.96±3.16, P<0.0001). Additionally, there were significant differences between the two groups in terms of red blood cell distribution width (RDW) and platelet count. However, no significant differences were observed between the two groups in white blood cell count, neutrophil count, haemoglobin, or immature neutrophils/total neutrophils (P>0.05). Furthermore, there were no significant differences between the two groups in CRP, PCT, SAA, albumin, or ALP (P>0.05) (Table 2).

The coagulation function tests revealed notable disparities between the two groups in terms of D-dimer (P = 0.0003) and Fib levels (P = 0.0134), as demonstrated in Table 2.

Logistic Regression Analysis of Potential Risk Factors for SNE

The logistic regression equation was employed to examine the association between five factors with P<0.05 in the univariate analysis and the risk of surgical necrotizing enterocolitis. Stepwise multiple regression analysis was conducted to investigate the risk factors for surgical necrotizing enterocolitis. The findings revealed that MPV (OR = 4.895, 95% CI = 2.694–10.37,

Table 2 Clinical Data Between Non-Operative Group and Operative Group in This Study

	Non-Operative Group (n=244)	Operative Group (n=128)	$\chi^2/t/U$	P value
White blood cell count ($\times 10^9/L$), mean\pmSD	14.69 \pm 6.43	15.11 \pm 4.77	0.45 ^a	0.6506
Neutrophil count ($\times 10^9/L$), mean\pmSD	7.32 \pm 2.89	6.69 \pm 2.38	1.46 ^a	0.1454
Hemoglobin (g/L), mean\pmSD	119.9 \pm 22.04	118.2 \pm 22.70	0.48 ^a	0.6321
RDW (%), mean\pmSD	17.43 \pm 3.47	18.97 \pm 2.69	3.01 ^a	0.0025
Platelet count, n (%)			8.05 ^b	0.0046
< 100 $\times 10^9/L$	64 (26.23%)	60 (46.88%)		
\geq 100 $\times 10^9/L$	180 (73.77%)	68 (53.12%)		
MPV (fL), mean\pmSD	11.05 \pm 1.24	12.47 \pm 1.01	5.07 ^a	<0.0001
PDW (%), mean\pmSD	13.96 \pm 3.16	17.84 \pm 3.86	5.85 ^a	<0.0001
CRP (mg/L), M (Q1, Q3)	19 (13,31)	24 (12,43)	1.89 ^c	0.0608
PCT (ng/mL), M (Q1, Q3)	3.38 (2.11,5.51)	6.05 (2.67,12.05)	1.73 ^c	0.0862
I/T, mean\pmSD	0.079 \pm 0.034	0.084 \pm 0.017	1.31 ^a	0.1926
SAA, n (%)			0.09 ^b	0.7609
< 10mg/L	86 (35.25%)	48 (37.50%)		
\geq 10mg/L	158 (64.75%)	80 (62.50%)		
Albumin, n (%)			0.29 ^b	
< 30g/L	82 (33.61%)	38 (29.69%)		
\geq 30g/L	162 (66.39%)	90 (70.31%)		
ALP (U/L), mean\pmSD	305.0 \pm 150.91	268.5 \pm 143.29	1.58 ^a	0.1143
Fib (g/L), mean\pmSD	1.02 \pm 0.45	0.86 \pm 0.30	2.49 ^a	0.0134
D-dimer (mg/L), mean\pmSD	2.11 \pm 1.65	3.09 \pm 1.79	3.72 ^a	0.0003

Notes: ^at-test. ^bChi-square test. ^cU-test. The presence of bold values indicates that the difference between the two groups for this variable was statistically significant (P<0.05).

Abbreviations: RDW, Red blood cell distribution width; MPV, Mean platelet volume; PDW, Platelet distribution width; CRP, C-reaction protein; PCT, Procalcitonin; I/T, Immature neutrophils/total neutrophils; SAA, Serum Amyloid A Protein; ALP, Alkaline phosphatase.

P<0.001), PDW (OR = 1.476, 95% CI = 1.244–1.811, P<0.001), and Fib (OR = 0.181, 95% CI = 0.033–0.832, P = 0.035) were independent risk factors for surgical necrotizing enterocolitis (Table 3).

Diagnostic Utility of MPV and PDW for Surgical Necrotizing Enterocolitis

The analysis of the receiver operating characteristic (ROC) curve indicated that an MPV value cut-off greater than 11.8 fL was optimal for predicting surgical necrotizing enterocolitis, with a sensitivity of 79.69% and specificity of 77.87% (AUC=0.706). Similarly, a PDW value cut-off greater than 16% was optimal for predicting surgical necrotizing enterocolitis, with a sensitivity of 68.75% and specificity of 77.05% (AUC=0.728). When MPV and PDW were combined, the AUC was 0.906, with a sensitivity of 85.94% and specificity of 78.69% (Figure 2a).

Table 3 Independent Influencing Factors for Surgical Necrotizing Enterocolitis

Characteristics	B	SE	OR	95% CI	Z	P
MPV	1.588	0.33967	4.895	2.694–10.37	4.676	<0.001
PDW	0.389	0.09447	1.476	1.244–1.811	4.122	<0.001
PLT	1.27	0.68253	3.561	0.955–14.38	1.861	0.063
D-dimer	0.158	0.18236	1.171	0.818–1.678	0.868	0.386
Fib	-1.711	0.81129	0.181	0.033–0.832	-2.109	0.035
RDW	0.158	0.10228	1.171	0.962–1.444	1.543	0.123

Notes: In multivariate Logistic regression analysis, the presence of bold values indicates that the difference between the two groups for this variable was statistically significant (P<0.05).

Abbreviations: β , regression coefficient; SE, standard error; OR, odds ratio; 95% CI, 95% confidence interval.

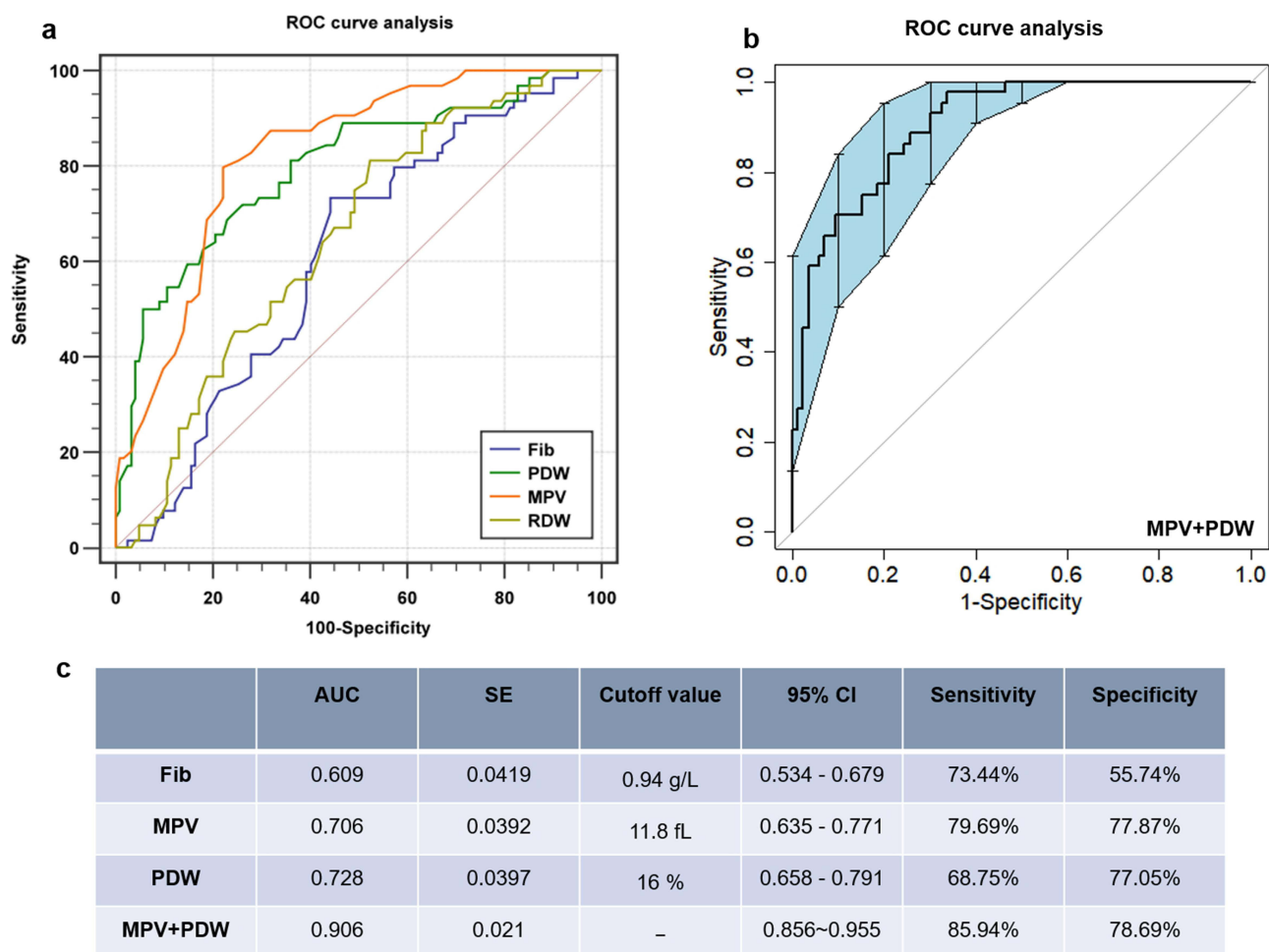


Figure 2 ROC curve analysis. (a–c) The AUC of MPV combined with PDW was 0.906, with an 85.94% sensitivity and a 78.69% specificity.

The receiver operating characteristic (ROC) analysis demonstrated that a serum Fib cut-off level of 0.94 g/L offers predictive value for surgical necrotizing enterocolitis within this cohort, exhibiting a sensitivity of 73.44% and a specificity of 55.74% (AUC = 0.609) (Figure 2b).

MPV and PDW Comparison in Various Groups of Intestinal Necrosis

During the surgical intervention, a laparotomy was performed to assess and categorize the intestinal lesions according to their extent. The classification was as follows: A) Punctate necrosis denotes the presence of lesions confined to a specific segment of the intestine (Figure 3a, n=22). B) In instances where the intestinal tract displayed focal necrosis or perforation, a solitary necrotic or perforated lesion was observed (Figure 3b, n=52). C) In instances of multifocal necrosis or perforation of the intestinal tube, more than 50% of the intestine remained healthy, with multiple necrotic or perforated lesions present (Figure 3c, n=40). D) The bowel exhibited complete intestinal disease, or the remaining healthy intestine accounted for less than 25% of the total (Figure 3d, n=14).

The findings of our study indicate that the MPV in the multifocal necrosis and extensive necrosis groups was significantly elevated compared to that in the other groups (Figure 4a). Additionally, the PDW in the multifocal necrosis and extensive necrosis groups was significantly higher than that observed in the other groups (Figure 4b).

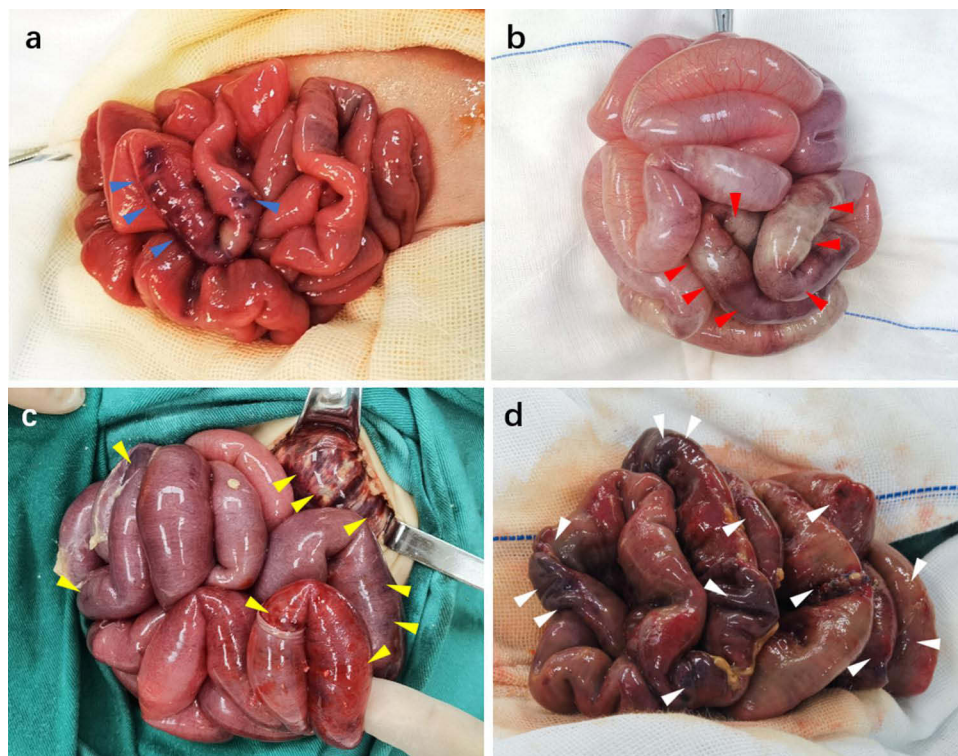


Figure 3 External examination of the intestinal canal in individuals presenting varying degrees of illness. (a) A distinct demarcation was observed between the healthy and necrotic sections of the intestinal canal, with punctate necrosis indicated by blue arrowheads. (b) The presence of necrosis was observed in a solitary intestine, with the necrotic section indicated by red arrowheads. (c) The occurrence of multifocal necrosis or perforation in the intestinal tube was noted, with the necrotic section indicated by yellow arrowheads. (d) Extensive necrosis of the intestinal tract was observed, with the necrotic section indicated by white arrowheads.

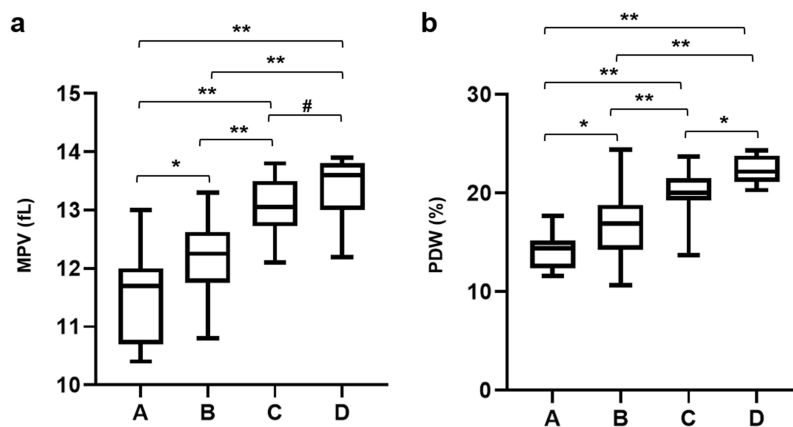


Figure 4 The comparison between MPV and PDW was conducted across multiple groups exhibiting intestinal necrosis. (a) MPV exhibited a statistically significant increase in the group with extensive necrosis. (b) PDW demonstrated a statistically significant increase in the group with extensive necrosis. Values are given as the mean \pm SE. t test, * $P < 0.01$, ** $P < 0.001$, # $P > 0.05$. A. The group characterized by punctate necrosis. B. The group consisting of a solitary necrotic or perforated lesion. C. The group exhibiting multifocal necrosis or perforation of the intestinal tube. D. The group displaying extensive intestinal necrosis.

Comparison of MPV and PDW Among Prognostic Groups

Based on the ultimate outcome upon discharge, a total of 128 patients who underwent surgery were categorized into two groups: the death group ($n=18$) and the survival group ($n=110$). The application of a *t*-test revealed that the MPV and PDW in the death group were significantly greater than those in the survival group ($t=2.099$, $P=0.0399$ & $t=2.763$, $P=0.0075$) (Figure 5).

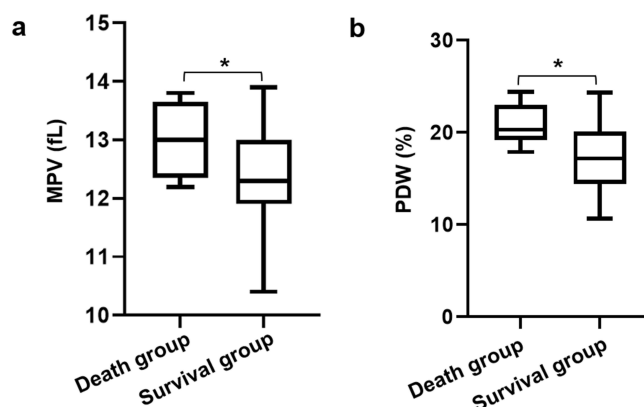


Figure 5 MPV and PDW were compared between the death group and the survival group. (a) The MPV exhibited a significant increase in the death group. (b) The PDW exhibited a significant increase in the death group. Values are given as the mean \pm SE. t-test, compared with the survival group, * $P < 0.01$.

Discussion

Surgical intervention is necessary in a substantial proportion, approximately one-third to one-half, of NEC cases.²⁰ The study found that the postoperative mortality rate for patients who underwent surgery ranged from 30.1% to 39.2%, whereas children with an ultralow birth weight had a mortality rate exceeding 50%.²¹ This investigation included 34.41% (128 out of 372) of the surgical patients, aligning with previous research.²⁰ Due to our medical institution's status as the premier neonatal treatment centre in southwest China, the implementation of timely and effective perioperative comprehensive management has resulted in a significant reduction in postoperative mortality rates. Specifically, the mortality rate among children who underwent surgery was found to be 14.06% (18/128), which is considerably lower than previously documented rates.²¹

In recent years, several medical institutions have conducted research on inflammation markers associated with NEC.^{3–9} The objective of these studies is to identify and classify NEC at an early stage by utilizing peripheral blood inflammation markers, thereby facilitating appropriate surgical interventions. Nevertheless, the limited availability of blood samples in preterm infants, due to the potential risk of anaemia, has hindered the widespread implementation of these diagnostic tests across the majority of health care facilities. Clinicians have hitherto encountered a dearth of reliable indicators to forecast the severity of NEC, consequently impeding physicians' ability to promptly render accurate assessments and potentially resulting in treatment delays that could be linked to unfavourable prognoses. Hence, our research endeavours to identify valid indicators capable of predicting the severity of NEC from among the prevailing clinical indicators.

Analysis of complete blood counts is extensively conducted in hospitals of various levels due to its benefits of minimal blood usage, cost-effectiveness, and prompt outcomes. Our research revealed that MPV and PDW were significantly elevated in the operation group compared to the nonoperation group. These notable distinctions between the two groups indicate that elevated MPV and PDW levels might serve as potential risk factors for surgical intervention in NEC. Subsequent logistic regression analysis revealed that both MPV and PDW were found to be independent predictors of surgical treatment for NEC. Consequently, it is postulated that MPV and PDW can serve as pertinent indicators of the severity of surgical NEC. To date, no investigations have examined the combined significance of MPV and PDW in forecasting the severity of NEC. Hence, our present study is distinctive in its focus on techniques for predicting the timing and severity of surgical intervention in NEC, potentially leading to a revision of the current framework for assessing surgical predictors. The findings of our study provide empirical evidence in favour of utilizing these easily accessible parameters as predictive indicators for determining the optimal timing of surgical intervention in cases of NEC.

MPV has been found to be correlated with a range of neonatal ailments, including bronchopulmonary dysplasia, intraventricular haemorrhage, and NEC, and its association with inflammation-related oxidation processes has been suggested.¹⁴ Mesenteric artery ischaemia and necrosis occur as a consequence of the activation of numerous platelet activating factors, including preterm birth, infection, hypoxia and ischaemia, and feeding intolerance. This activation

leads to the aggregation and formation of microthrombi by platelets. Concurrently, there is a reduction in the quantity of platelets in the circulating blood, prompting the promotion of megakaryocyte feedback activation to generate larger platelets. Large platelets have been found to contain higher levels of active substances, produce increased amounts of thromboxins, release dense particles and inflammatory factors and have a higher likelihood of forming thrombosis, promoting inflammation, exacerbating intestinal damage, and contributing to the formation of a vicious cycle.²² In a study conducted by Shaaban et al²³, it was demonstrated that a significant rise in MPV in premature infants with sepsis can serve as an indicator for predicting early sepsis and mortality. Currently, there is a limited body of research exploring the association between MPV and the clinical prognosis of NEC. In the neonatal mouse model of NEC investigated by Namachivayam et al²⁴, mice with moderate to severe intestinal injury exhibited an elevation in MPV. Miner et al²⁵ discovered that patients with NEC stage III displayed significantly increased MPV and higher mortality rates than those with NEC stage II. Our findings demonstrate a positive correlation between elevated MPV levels and the presence of intestinal lesions and necrotic intestinal tubes, which aligns with Namachivayam's observations. Furthermore, elevated preoperative MPV levels are indicative of a poor prognosis.

PDW serves as a consistent metric that reflects platelet volume. It represents the coefficient of variation within the distribution of platelet volumes, typically exhibiting a positive correlation with MPV. An elevation in PDW values signifies an increased heterogeneity in platelet sizes. PDW serves as an indicator of infection severity and an autonomous prognostic factor for mortality rates during the infected phase.²⁶ The relationship between PDW and the severity of NEC has not been previously documented. Our study findings indicate that PDW can serve as a reliable predictor for surgical NEC, with higher PDW levels being associated with increased intestinal necrosis and a poorer prognosis in NEC patients. Additionally, when comparing the receiver operating characteristic (ROC) curves of MPV and PDW, our results demonstrate that the area under the curve (AUC) was 0.706 for MPV alone, 0.728 for PDW alone, and 0.906 for the combination of MPV and PDW. These findings suggest that the combined use of MPV (cut-off value: 11.8 fL) and PDW (cut-off value: 16%) is superior in predicting surgical necrotizing enterocolitis.

Limitations

This study had multiple limitations. First, the retrospective study design is an inherent weakness, non-standardization of data collection may have resulted in other statistically significant factors not being shown in this analysis. Second, the determination of intraoperative bowel necrosis and the overall extent of surgical NEC relied on standardized descriptions within surgical records. However, given that the emergency procedures were conducted by various physicians, discrepancies in the depiction of the affected bowel may introduce bias. Consequently, a more comprehensive and precise investigation is warranted to thoroughly examine the association of MPV and PDW with surgical NEC.

Conclusion

To our knowledge, this is the first study analyzing the relationship between MPV/PDW and surgical intervention, prognosis. We identified that MPV, PDW, and Fib were independently associated with surgical NEC, and the combination of MPV and PDW demonstrates significant predictive value in surgical NEC. Furthermore, elevated levels of MPV and PDW are indicative of the extent of intestinal necrosis and a negative prognosis in surgical NEC patients. This finding may be utilized to triage neonates for transfer to specialist neonatal surgical centers, which would optimize surgical cot utilization, and provided reference to guide parental counselling.

Abbreviations

MPV, Mean platelet volume; PDW, Platelet distribution width; NEC, Necrotizing enterocolitis.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The ethical assessment of the information acquired in the institutions had the approval of the Children's Hospital of Chongqing Medical University (2022-No.484). All procedures in the study were carried out in accordance with national ethical guidelines for medical and health research involving human subjects, as well as the 1964 Helsinki Declaration and its subsequent amendments. All guardians of the participants signed an informed consent form prior to the study and were debriefed after the assessment. All guardians of the participants were informed that participation was voluntary and that they had the right to refuse or stop participating in the study at any time.

Acknowledgments

We gratefully acknowledge the support of the Laboratory of Child Development and Disorders of Chongqing Medical University. We sincerely appreciate the patient's parents' close cooperation.

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Funding

This work was supported by grants from the Natural Science Foundation of Chongqing (cstc2020jcyj-msxmX0249).

Disclosure

All authors declare that they have no competing interests in this work.

References

1. Rich BS, Dolgin SE. Necrotizing Enterocolitis. *Pediatr Rev.* 2017;38(12):552–559. doi:10.1542/pir.2017-0002
2. Klerk DH, van Varsseveld OC, Offringa M, et al. Core Outcome Set for Necrotizing Enterocolitis Treatment Trials. *Pediatrics.* 2024;153:e2023065619. doi:10.1542/peds.2023-065619
3. Salas AA, Gunn E, Carlo WA, et al. Timing of red blood cell transfusions and occurrence of necrotizing enterocolitis: a secondary analysis of a randomized clinical trial. *JAMA Network Open.* 2024;7(5):e249643. doi:10.1001/jamanetworkopen.2024.9643
4. Tepas JJ 3rd, Leaphart CL, Plumley D et al, et al. Trajectory of metabolic derangement in infants with necrotizing enterocolitis should drive timing and technique of surgical intervention. *J Am Coll Surg.* 2010;210(5):847-52, 852–4. doi:10.1016/j.jamcollsurg.2010.01.008
5. Cetinkaya M, Ozkan H, Koksall N, et al. The efficacy of serial serum amyloid A measurements for diagnosis and follow-up of necrotizing enterocolitis in premature infants. *Pediatr Surg Int.* 2010;26:8 835–841. doi:10.1007/s00383-010-2635-0
6. Tayman C, Tonbul A, Kahveci H, et al. C5a, a complement activation product, is a useful marker in predicting the severity of necrotizing enterocolitis. *Tohoku J Exp Med.* 2011 224 2 143 150. doi:10.1620/tjem.224.143
7. Murgas Torrazza R, Li N, Young C, et al. Pilot study using proteomics to identify predictive biomarkers of necrotizing enterocolitis from buccal swabs in very low birth weight infants. *Neonatology.* 2013;104:3 234–242. doi:10.1159/000353721
8. Yakut I, Tayman C, Oztekin O, et al. Ischemia-modified albumin may be a novel marker for the diagnosis and follow-up of necrotizing enterocolitis. *J Clin Lab Anal.* 2014;28:3 170–177. doi:10.1002/jcla.21661
9. Seo YM, Lin YK, Im SA, et al. Interleukin 8 may predict surgical necrotizing enterocolitis in infants born less than 1500 g. *Cytokine.* 2021;137():155343. doi:10.1016/j.cyto.2020.155343
10. Ververidis M, Kiely EM, Spitz L, et al. The clinical significance of thrombocytopenia in neonates with necrotizing enterocolitis. *J Pediatr Surg.* 2001;36(5):799–803. doi:10.1053/jpsu.2001.22964
11. Bracho-Blanchet E, Torrecilla-Navarrete ME, Zalles-Vidal C, et al. Prognostic factors related to mortality in newborns with necrotizing enterocolitis. *Cir Cir.* 2015;83(4):286–291. doi:10.1016/j.circir.2015.02.002
12. Kaito K, Otsubo H, Usui N et al. Platelet size deviation width, platelet large cell ratio, and mean platelet volume have sufficient sensitivity and specificity in the diagnosis of immune thrombocytopenia. *Br J Haematol.* 2005;128(5):698–702. doi:10.1111/j.1365-2141.2004.05357.x
13. Vasse M, Masure A, Lenormand B, et al. Mean platelet volume is highly correlated to platelet count *Thromb Res.* 2012;130(3):559–560 doi:10.1016/j.thromres.2012.04.014.
14. Cekmez F, Tanju IA, Canpolat FE, et al. Mean platelet volume in very preterm infants: a predictor of morbidities?. *Eur Rev Med Pharmacol Sci.* 2013;17:1 134–137. doi:
15. Cai N, Liao W, Chen Z, et al. MThe Mean Platelet Volume Combined with Procalcitonin as an Early Accessible Marker Helps to Predict the Severity of Necrotizing Enterocolitis in Preterm Infants. *Int J Gen Med.* 2022;15:3789–3795. doi:10.2147/IJGM.S346665
16. Korniluk A, Koper-Lenkiewicz OM, Kamińska J, et al. Mean Platelet Volume (MPV): New Perspectives for an Old Marker in the Course and Prognosis of Inflammatory Conditions. *Mediators Inflamm.* 2019;2019():9213074 doi:10.1155/2019/9213074.
17. Vagdatli E, Gounari E, Lazaridou E, et al.; Platelet distribution width: a simple, practical and specific marker of activation of coagulation. *Hippokratia.* 2010;14(1):28–32. doi:
18. Thakkar HS, Lakhoo K. The surgical management of necrotising enterocolitis (NEC). *Early Hum Dev.* 2016;97:25–28. doi:10.1016/j.earlhumdev.2016.03.002

19. Zani A, Pierro A. Necrotizing enterocolitis: controversies and challenges. *F1000Res*. 2015;4:F1000 Faculty Rev-1373. doi:10.12688/f1000research.6888.1
20. De Luca G, Venegoni L, Iorio S, et al. Novara Atherosclerosis Study Group. Platelet distribution width and the extent of coronary artery disease: results from a large prospective study. *Platelets*. 2010;21(7):508–514. doi:10.3109/09537104.2010.494743
21. Jones IH, Hall NJ, et al. Contemporary Outcomes for Infants with Necrotizing Enterocolitis-A Systematic Review. *J Pediatr*. 2020;220():86–92. e 3. doi:10.1016/j.jpeds.2019.11.011
22. Meinzen-Derr J, Poindexter B, Wrage L, et al. TRole of human milk in extremely low birth weight infants' risk of necrotizing enterocolitis or death. *J Perinatol*. 2009;29(1):57–62. doi:10.1038/jp.2008.117
23. Shaaban HA, Safwat N. Mean platelet volume in preterm: a predictor of early onset neonatal sepsis. *J Matern Fetal Neonatal Med*. 2020;33(2):206–211. doi:10.1080/14767058.2018.1488161
24. Namachivayam K, MohanKumar K, Garg L, et al. Neonatal mice with necrotizing enterocolitis-like injury develop thrombocytopenia despite increased megakaryopoiesis. *Pediatr Res*. 2017;81(5):817–824. doi:10.1038/pr.2017.7
25. Miner CA, Fullmer S, Eggett DL, et al. Factors affecting the severity of necrotizing enterocolitis. *J Matern Fetal Neonatal Med*. 2013;26(17):1715–1719. doi:10.3109/14767058.2013
26. Fogagnolo A, Campo GC, Mari M, et al. The Underestimated Role of Platelets in Severe Infection a Narrative Review. *Cells*. 2022;11(3):424–1719. doi:10.3390/cells11030424

Journal of Inflammation Research

Dovepress

Publish your work in this journal

The Journal of Inflammation Research is an international, peer-reviewed open-access journal that welcomes laboratory and clinical findings on the molecular basis, cell biology and pharmacology of inflammation including original research, reviews, symposium reports, hypothesis formation and commentaries on: acute/chronic inflammation; mediators of inflammation; cellular processes; molecular mechanisms; pharmacology and novel anti-inflammatory drugs; clinical conditions involving inflammation. The manuscript management system is completely online and includes a very quick and fair peer-review system. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/journal-of-inflammation-research-journal>