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RESEARCH

# Multi-Indicator analysis of the impact of preoperative inflammatory states on complications following pancreatoduodenectomy

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## Abstract

**Purpose** Pancreatoduodenectomy (PD) is a complex surgery with a high rate of postoperative complications, for which effective preoperative indicators are currently lacking. Inflammatory indices such as the pan-immune-inflammation value (PIV), platelet-neutrophil product (PPN), and platelet-albumin ratio (PAR) have shown potential as biomarkers for postoperative prognosis in various cancers. However, their predictive value for complications in open-PD (OPD) patients remains underexplored. This study aims to investigate the relationship between these inflammatory indices and postoperative complications, identify new preoperative biomarkers, and provide a theoretical basis for improving perioperative management in OPD patients.

**Methods** We analyzed data from 309 patients who underwent open-PD (OPD). Six preoperative inflammatory indices—platelet-to-lymphocyte ratio (PLR), PIV, PPN, PAR, neutrophil-to-HDL ratio (NHR), and neutrophil-albumin ratio (NAR)—were assessed for their association with postoperative complications using logistic regression and restricted cubic spline analysis. Predictive performance was evaluated with ROC curves and decision curve analysis.

**Results** PLR, PIV, and PPN were significantly linked to most outcomes and had good predictive performance. NHR was associated with severe complications. PAR effectively predicted hemorrhage (AUC = 0.684) and delayed gastric emptying (DGE) (AUC = 0.701). Combining indices enhanced predictive accuracy.

**Conclusions** PLR, PIV, and PPN are key preoperative indicators for OPD patients, with PAR also useful for predicting complications like hemorrhage and DGE.

**Keywords** Pancreatoduodenectomy · Inflammatory indices · Complications · Restricted cubic splines

## Introduction

Pancreatoduodenectomy (PD) is a highly complex abdominal surgery primarily used to treat pancreatic head cancer, bile duct cancer, and periampullary tumors [1]. Despite its crucial role in treating these conditions, the high rate of postoperative complications and mortality significantly hinders patient recovery, increases treatment costs, and elevates the risk of death. Current studies indicate that the incidence of complications following PD can reach 20-40% [2]. Therefore, early identification and proactive prevention of postoperative complications are vital for improving patient quality of life and prognosis.

In recent years, researchers have increasingly focused on the relationship between preoperative inflammatory status and postoperative complications in cancer patients. Neutrophils play a critical role in cancer development by releasing extracellular matrix components and inflammatory factors in the tumor microenvironment, thereby promoting cancer progression [3]. In contrast, changes in lymphocytes significantly affect tumor immune responses, inhibiting cancer cell proliferation [4]. Additionally, platelets, aside from their role in hemostasis, can trigger and exacerbate inflammation through interactions with immune cells and the secretion of pro-inflammatory cytokines [5]. Existing research has demonstrated that inflammatory markers composed of neutrophils, lymphocytes, and platelets can serve as predictors of

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postoperative complications in cancer patients [6], such as the pan-immune-inflammation value (PIV), product of platelet count and neutrophil count (PPN), platelet to albumin ratio (PAR), and neutrophil-albumin ratio (NAR). Although these indicators are considered reliable biomarkers in various cancer types [7], their relationship with postoperative complications following PD remains largely underexplored, particularly for PIV, PPN, and PAR.

Consequently, this study aims to leverage the logistic regression approach across three models, sensitivity analysis, and restricted cubic spline analysis to explore the relationship between the aforementioned inflammatory indices and postoperative complications in open-PD (OPD) patients from multiple perspectives, uncovering their predictive potential. This is aimed at identifying new preoperative biomarkers specific to different complications, providing a theoretical basis for improving perioperative management in OPD patients.

## Materials and methods

### Study population

The process of this study is illustrated in Fig. 1. Based on inclusion and exclusion criteria, we retrospectively reviewed the medical records of 464 consecutive patients who underwent OPD surgery at the General Hospital of Western Theater Command from January 2013 to January 2024. Specifically, the study subjects included OPD patients without a history of neoadjuvant therapy, distant metastasis, or other organ surgeries, while excluding those with incomplete data or postoperative pathology confirming non-periampullary primary tumors. Ultimately, 309 patients were included in this study for analysis.

### Surgical procedures and perioperative management

To avoid potential influences on postoperative complications from different surgical teams and techniques (open surgery and minimally invasive surgery), this study exclusively included patients who underwent OPD. All surgeries

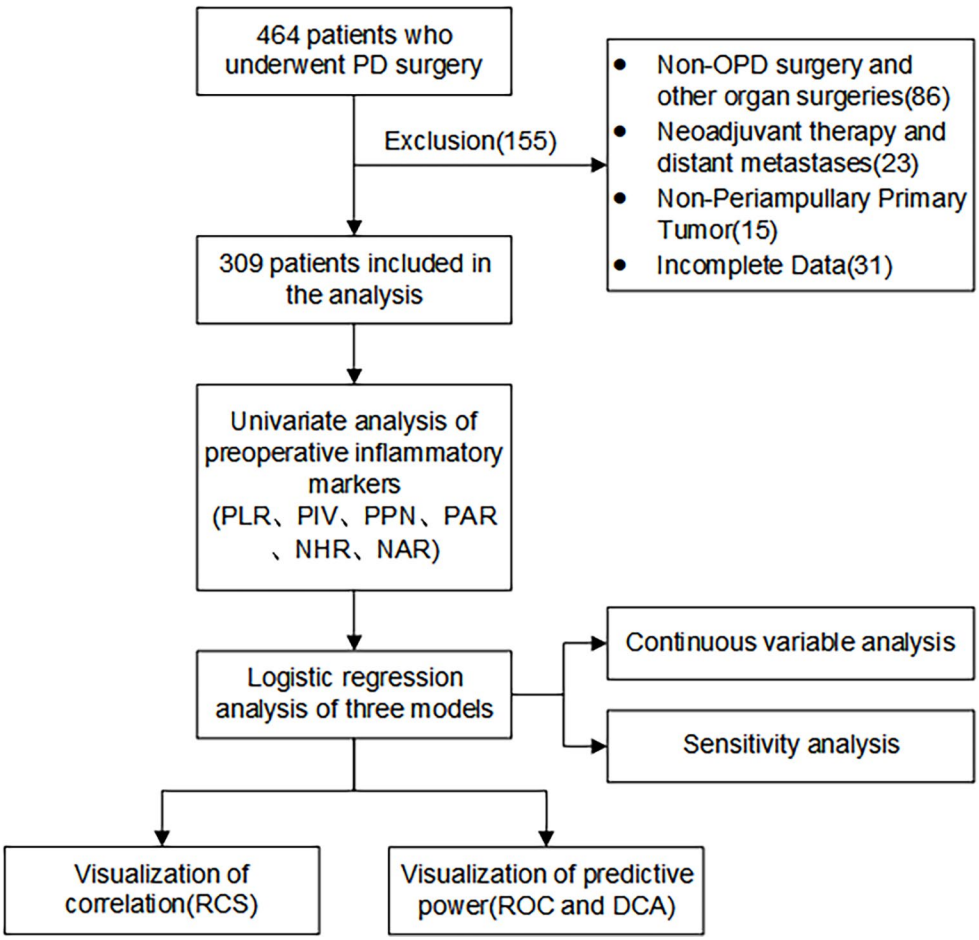


**Fig. 1** Flowchart of enrollment and analysis of patients undergoing OPD. PD, pancreaticoduodenectomy; OPD, open-PD; PLR, platelet to lymphocyte ratio; PIV, pan-immune-inflammation value; PPN, product of platelet count and neutrophil count; PAR, platelet to albumin ratio; NHR, neutrophil to high density lipoprotein cholesterol ratio; NAR, neutrophil-albumin ratio; RCS, restricted cubic spline; ROC, receiver operating characteristic curves; DCA, decision curve analysis

were performed by an experienced surgical team at our hospital, following standardized procedures.

### Data collection and parameter definition

Preoperative clinical data were collected, including age, gender, height, weight, body mass index (BMI), ASA classification, and laboratory indicators (complete blood count, liver function, and blood lipids). Intraoperative data included surgical method, operative time, intraoperative blood loss, and whether a blood transfusion was performed. Clinicians, blinded to preoperative indicators, recorded postoperative outcomes according to the International Study Group of Pancreatic Surgery's systematic definitions, including postoperative pancreatic fistula (B/C POPF), surgical site infection (SSI: superficial, deep, and organ/space), hemorrhage, DGE, CD≥3 complications, and 90-day readmission and postoperative pathology results.

In this study, the preoperative inflammatory status of patients was reflected by collecting the last preoperative measurements of lymphocyte, neutrophil, and platelet-related indices, defined as follows: (1) PLR = PLT/L; (2) PIV = (PLT + N + M)/L; (3) PPN = PLT * N; (4) PAR = PLT/Alb; (5) NHR = N/HDL-c; (6) NAR = N/Alb. (PLT: platelet 10^9/L; N: neutrophil 10^9/L; Alb: albumin g/L; L: lymphocyte 10^9/L; M: monocyte 10^9/L; HDL-c: high-density lipoprotein cholesterol mmol/L). All measurements and calculations were performed by two trained clinicians, with any disputes reviewed by a third clinician, all of whom were blinded to postoperative outcomes during data analysis.

### Statistical analysis

All statistical analyses were performed using SPSS version 28.0 and R programming language version 4.2.3. The normality of all continuous variables was tested using the Shapiro-Wilk (SW) test (Table S1). Variables following a normal distribution were expressed as mean ± standard deviation (SD), while non-normally distributed variables were presented as median and interquartile range (IQR). Categorical variables were described as frequencies and percentages (%). Continuous variables were compared using the t-test or the rank-sum test, and categorical variables were compared using the Chi-square ($X^2$) test or Fisher's exact test. All P-values were two-sided, with $P < 0.05$ considered statistically significant.

Logistic regression was performed to evaluate the odds ratios (ORs) and 95% confidence intervals (CIs) of different indices, elucidating the association between preoperative inflammatory status and various outcomes. To facilitate comparison of ORs across different indices, some inflammation-related indices were standardized. Three regression models were constructed and analyzed, with varying levels of adjustment. Model 1 included no covariate adjustments; Model 2 adjusted for general patient characteristics, including age, gender, BMI, comorbidities (hypertension and diabetes), and ASA classification; Model 3 further adjusted for OPD surgery-related characteristics, including PBD, operative time, estimated blood loss, and intraoperative blood transfusion. Additionally, to explore the sensitivity of the analysis, the indices were converted from continuous to categorical variables based on quartiles and medians, and logistic regression was re-conducted.

Restricted cubic spline (RCS) analysis based on the three logistic regression models was performed to visually display the linear or nonlinear relationship between preoperative inflammatory indices and different postoperative complications in OPD patients [8]. Three knots were chosen to construct the models, and the included covariates were consistent with the aforementioned logistic regression models. Receiver operating characteristic (ROC) curve analysis was also conducted to evaluate the predictive power of different indices or combinations of indices for postoperative outcomes. Moreover, decision curve analysis (DCA) was performed to assess the clinical utility of the different indices.

## Results

### Baseline characteristics and outcomes

A total of 464 patients who underwent PD from 2013 to 2024 were included. Based on the inclusion and exclusion criteria, 155 patients were excluded, leaving 309 patients for final analysis. Their demographic and clinical characteristics are summarized in Table 1. The cohort included 178 male patients (57.61%) and 131 female patients (42.39%), with a median age of 61 years (IQR 53–67). The median operation time was 395 min (IQR 335–460). The most frequent postoperative complications were B/C POPF (24.27%, $n = 75$), SSI (17.80%, $n = 55$), hemorrhage (9.39%, $n = 29$), and DGE (6.80%, $n = 21$). Additionally, 59 patients experienced CD≥3 complications (19.09%), and 46 were readmitted within 90 days (14.89%).

### Association between preoperative inflammatory markers and different outcomes

#### Univariate analysis for different outcomes

Table 2 shows the univariate analysis results with B/C POPF as the outcome. Significant differences were observed in inflammatory markers such as PLR, PIV, PPN, and PAR

**Table 1** Demographic characteristics and clinical information of patients undergoing OPD (2013–2024)

| Characterstics | Total($n$=309) | Characterstics | Total($n$=309) |
|---|---|---|---|
| Age(years) | 61(53,67) | Monocytes(10^9/l) | 0.4(0.3,0.53) |
| Sex | | Total Cholesterol(mmol/l) | 4.98(4.06,6.12) |
| Male | 178(57.61%) | HDL-c(mmol/l) | 1.24(0.96,1.63) |
| Female | 131(42.39%) | Preoperative biliary drainage | 102(33.01%) |
| Hypertension | 59(19.10%) | Malignant histology | |
| Diabetes | 44(14.24%) | Bile duct cancer | 99(32.04%) |
| BMI(kg/m²) | 22.22(20.18,23.88) | Duodenal/Ampullary cancer | 92(29.77%) |
| ASA class | | Pancreatic cancer | 88(28.48%) |
| I | 100(32.36%) | IPMN | 14(4.53%) |
| II | 170(55.02%) | NET | 8(2.59%) |
| III | 34(11.00%) | Other | 8(2.59%) |
| IV | 5(1.62%) | Operative time(min) | 395(335,460) |
| Preoperative laboratory evaluation | | Intraoperative blood loss(ml) | 400(300,600) |
| Albumin(g/l) | 38.7(35.9,41.9) | Postoperative outcomes | |
| Alanine aminotransferase(u/l) | 84(35.8,159.1) | B/C POPF | 75(24.27%) |
| Aspartate aminotransferase(u/l) | 57.5(32.2,100.05) | SSI | 55(17.80%) |
| White blood cells(10^9/l) | 5.72(4.62,7) | Hemorrhage | 29(9.39%) |
| Platelets(10^9/l) | 209(160.5,263) | DGE | 21(6.80%) |
| Neutrophils(10^9/l) | 3.86(2.96,4.92) | CD≥3 complication | 59(19.09%) |
| Lymphocytes(10^9/l) | 1.17(0.88,1.5) | Readmission | 46(14.89%) |

OPD, open pancreaticoduodenectomy; BMI, body mass index; ASA class, american society of anesthesiologists physical status classification system; HDL-c: High-Density Lipoprotein Cholesterol; IPMN, intraductal papillary mucinous neoplasms; NET, neuroendocrine tumor; POPF, postoperative pancreatic fistula; SSI, surgical site infection; DGE, delayed gastric emptying; CD≥3, clavien-dindo grade III, IV, and V.

**Table 2** Univariate analysis of preoperative inflammatory markers(B/C POPF)

| Characterstics | Non-B/C POPF(234) | B/C POPF(75) | t/z/$\chi$2 | $P$ |
|---|---|---|---|---|
| Age(years) | 61(52,67) | 61(53,68) | -0.523 | 0.601 |
| Sex | | | 0.003 | 0.956 |
| Male | 135(57.69%) | 43(57.33%) | | |
| Female | 99(42.31%) | 32(42.67%) | | |
| Hypertension | 42(17.95%) | 17(22.67%) | 0.818 | 0.366 |
| Diabetes | 31(13.25%) | 13(17.33%) | 0.776 | 0.378 |
| BMI(kg/m²) | 21.91(19.84,23.53) | 23.31(20.76,24.84) | -2.984 | 0.003 |
| ASA class | | | 21.459 | <0.001 |
| I | 86(36.75%) | 14(18.67%) | | |
| II | 129(55.13%) | 41(54.67%) | | |
| III | 17(7.26%) | 17(22.67%) | | |
| IV | 2(0.85%) | 3(4%) | | |
| Preoperative laboratory evaluation | | | | |
| PLR | 168.72(116.16,224.77) | 210.56(150,287.06) | -3.116 | 0.002 |
| PIV | 171.21(118.5,229.45) | 213.05(153.96,291) | -3.135 | 0.002 |
| PPN | 51.44(35.46,68.36) | 62.01(45.38,78.25) | -2.901 | 0.004 |
| PAR | 5.13(4.04,6.53) | 5.85(4.92,7.33) | -3.366 | 0.001 |
| NHR | 3.14(2.18,4.54) | 3.14(2.25,5.34) | -0.001 | 0.999 |
| NAR | 0.1(0.08,0.13) | 0.1(0.07,0.13) | -0.193 | 0.847 |
| Preoperative biliary drainage | 76(32.48%) | 26(34.67%) | 0.123 | 0.726 |
| Operative time(min) | 390(335,450) | 420(355,480) | -1.789 | 0.074 |
| Intraoperative blood loss(ml) | 400(300,600) | 400(200,600) | -0.271 | 0.787 |
| Intraoperative blood transfusion | 96(41.03%) | 31(41.33%) | 0.002 | 0.962 |

POPF, postoperative pancreatic fistula; ASA class, american society of anesthesiologists physical status classification system; PLR, platelet to lymphocyte ratio; PIV, pan-immune-inflammation value; PPN, product of platelet count and neutrophil count; PAR, platelet to albumin ratio; NHR, neutrophil to high density lipoprotein cholesterol ratio; NAR, neutrophil-albumin ratio.

between groups ($P<0.05$). PLR, PIV, and PPN showed significant associations with most postoperative complications (Table 2, Tables S2-S6). Additionally, PAR, NHR, and NAR were closely related to specific postoperative outcomes (Tables S2-S6). As expected, the occurrence of postoperative complications was also strongly associated with general patient characteristics (age, sex, comorbidities, BMI, ASA classification) and surgery-related features (Table 2, Tables S2-S6). Therefore, the association between these inflammatory markers and postoperative outcomes in OPD patients needs to be considered with potential confounders in mind.

### B/C POPF

Table 3 presents the logistic regression analysis results with B/C POPF as the outcome. PLR, PIV, and PPN consistently showed significant associations with B/C POPF across different regression models (P-overall < 0.05). Sensitivity analysis indicated that higher PLR, PIV, and PPN as categorical variables were significantly associated with increased risk of B/C POPF (Table S7, OR-overall > 1, P-overall < 0.05). RCS visualized a significant positive linear relationship between these markers and B/C POPF (Fig. 2, P-overall < 0.05), confirmed in multivariate models (Fig. S1, S3, P-overall < 0.05). Significant thresholds for each marker were as follows: PLR 177.545, PIV 182.874, PPN 55.149. Although PAR as a continuous variable was not significant, higher PAR as a categorical variable was associated with increased B/C POPF risk across three models (Table S7, OR-overall > 1, P-overall < 0.05), supported by RCS curves indicating a significant positive non-linear relationship (Fig. 3, S2, S4, P-overall < 0.05, PAR threshold = 5.251). NHR and NAR did not show significant associations in logistic regression analyses across different models.

### SSI

Logistic regression models adjusting for various confounders indicated that lower PLR, PIV, and PPN were associated with increased SSI risk (Table 3, OR-overall < 1, P-overall < 0.05). This was consistent with RCS results showing a significant negative linear relationship between PLR, PIV, and SSI (P-overall < 0.05), while PPN exhibited a significant non-linear relationship (Fig. 2, S1, S3, P-overall < 0.05). Sensitivity analysis further supported the close association of these three markers with SSI when assessed as categorical variables (Table S7, OR-overall < 1, P-overall < 0.05). Although PAR, NHR, and NAR showed some associations with SSI in a few regression models, these associations were not significant after considering various confounders and sensitivity analysis results (Table 3, Table S7).

### Hemorrhage

Multiple logistic regression models indicated that PLR, PIV, and PPN, along with PAR, were significantly negatively associated with hemorrhage, both as continuous and categorical variables (Table 3, Table S8, OR-overall < 1, P-overall < 0.05). This consistency was also reflected in RCS results (Figs. 2 and 3, S1-S4). No significant associations

**Table 3** Logistic regression analysis of three models(B/C POPF、SSI、Hemorrhage)

| Characterstics | Model 1 | | Model 2 | | Model 3 | |
|---|---|---|---|---|---|---|
| | OR(95% CI) | *P* | OR(95% CI) | *P* | OR(95% CI) | *P* |
| B/C POPF | | | | | | |
| PLR | 1.002(1,1.004) | 0.015 | 1.003(1.001,1.005) | 0.012 | 1.003(1.001,1.005) | 0.01 |
| PIV | 1.002(1,1.004) | 0.017 | 1.003(1.001,1.005) | 0.015 | 1.003(1.001,1.005) | 0.013 |
| PPN | 1.015(1.006,1.025) | 0.002 | 1.017(1.007,1.028) | 0.001 | 1.017(1.006,1.028) | 0.002 |
| PAR | 1.013(0.973,1.055) | 0.522 | 1.003(0.963,1.046) | 0.869 | 1.002(0.961,1.045) | 0.923 |
| NHR | 0.985(0.943,1.029) | 0.492 | 0.976(0.928,1.026) | 0.338 | 0.974(0.929,1.022) | 0.284 |
| NAR* | 0.988(0.966,1.011) | 0.317 | 0.982(0.954,1.01) | 0.211 | 0.981(0.954,1.009) | 0.184 |
| SSI | | | | | | |
| PLR | 0.996(0.992,0.999) | 0.015 | 0.996(0.992,0.999) | 0.018 | 0.995(0.991,0.999) | 0.013 |
| PIV | 0.996(0.993,0.999) | 0.017 | 0.996(0.992,0.999) | 0.02 | 0.995(0.992,0.999) | 0.015 |
| PPN | 0.984(0.972,0.997) | 0.012 | 0.982(0.969,0.995) | 0.006 | 0.982(0.969,0.995) | 0.007 |
| PAR | 0.892(0.771,1.031) | 0.122 | 0.83(0.7,0.984) | 0.032 | 0.824(0.693,0.981) | 0.029 |
| NHR | 1.026(0.998,1.056) | 0.074 | 1.021(0.991,1.053) | 0.17 | 1.023(0.993,1.054) | 0.141 |
| NAR* | 1.008(0.998,1.018) | 0.101 | 1.007(0.997,1.017) | 0.191 | 1.007(0.996,1.017) | 0.205 |
| Hemorrhage | | | | | | |
| PLR | 0.994(0.99,0.999) | 0.03 | 0.995(0.99,1) | 0.036 | 0.995(0.99,1) | 0.036 |
| PIV | 0.995(0.99,1) | 0.034 | 0.995(0.99,1) | 0.039 | 0.995(0.99,1) | 0.039 |
| PPN | 0.971(0.953,0.989) | 0.002 | 0.971(0.952,0.989) | 0.002 | 0.972(0.953,0.991) | 0.003 |
| PAR | 0.704(0.559,0.887) | 0.003 | 0.678(0.53,0.868) | 0.002 | 0.651(0.501,0.844) | 0.001 |
| NHR | 1.012(0.979,1.046) | 0.468 | 1.01(0.976,1.046) | 0.561 | 1.008(0.973,1.045) | 0.643 |
| NAR* | 1.007(0.996,1.018) | 0.213 | 1.007(0.996,1.018) | 0.236 | 1.006(0.994,1.017) | 0.339 |

*, multiply the original value by 100; POPF, postoperative pancreatic fistula; SSI, surgical site infection; PLR, platelet to lymphocyte ratio; PIV, pan-immune-inflammation value; PPN, product of platelet count and neutrophil count; PAR, platelet to albumin ratio; NHR, neutrophil to high density lipoprotein cholesterol ratio; NAR, neutrophil-albumin ratio.

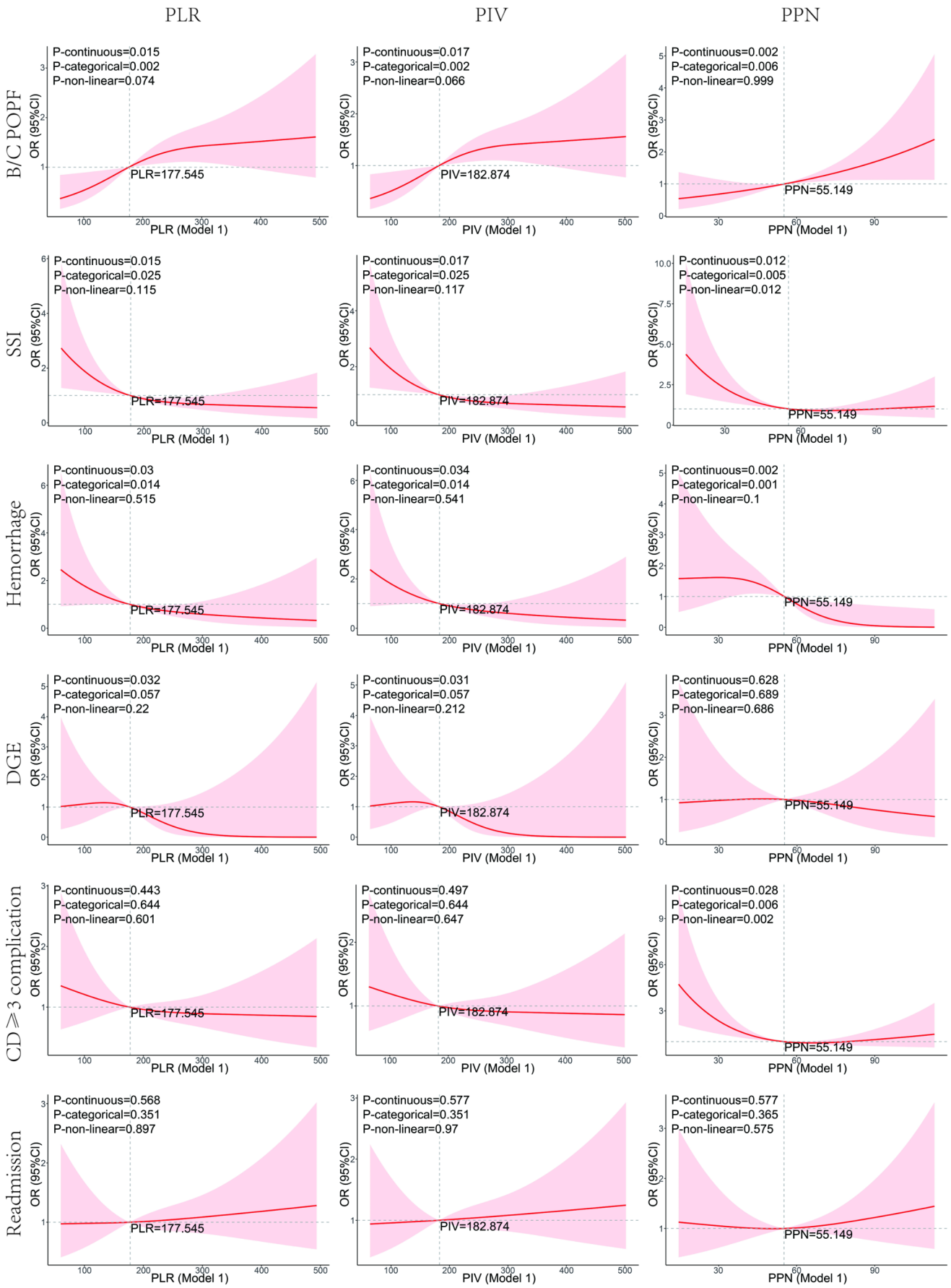
PLR
PIV
PPN
B/C POPF
SSI
Hemorrhage
DGE
CD⩾3 complication
Readmission
OR (95%CI)
P-continuous=0.015
P-categorical=0.002
P-non-linear=0.074
PLR=177.545
PLR (Model 1)
P-continuous=0.017
P-categorical=0.002
P-non-linear=0.066
PIV=182.874
PIV (Model 1)
P-continuous=0.002
P-categorical=0.006
P-non-linear=0.999
PPN=55.149
PPN (Model 1)
P-continuous=0.015
P-categorical=0.025
P-non-linear=0.115
P-continuous=0.017
P-categorical=0.025
P-non-linear=0.117
P-continuous=0.012
P-categorical=0.005
P-non-linear=0.012
P-continuous=0.03
P-categorical=0.014
P-non-linear=0.515
P-continuous=0.034
P-categorical=0.014
P-non-linear=0.541
P-continuous=0.002
P-categorical=0.001
P-non-linear=0.1
P-continuous=0.032
P-categorical=0.057
P-non-linear=0.22
P-continuous=0.031
P-categorical=0.057
P-non-linear=0.212
P-continuous=0.628
P-categorical=0.689
P-non-linear=0.686
P-continuous=0.443
P-categorical=0.644
P-non-linear=0.601
P-continuous=0.497
P-categorical=0.644
P-non-linear=0.647
P-continuous=0.028
P-categorical=0.006
P-non-linear=0.002
P-continuous=0.568
P-categorical=0.351
P-non-linear=0.897
P-continuous=0.577
P-categorical=0.351
P-non-linear=0.97
P-continuous=0.577
P-categorical=0.365
P-non-linear=0.575

**Fig. 2** Restricted cubic spline plots of PLR, PIV, and PPN (Model 1). Continuous variables overall significance threshold is P-continuous; categorical variables overall significance threshold is P-categorical (selecting the smallest P value for display); significance threshold for non-linear relationships between variables and outcomes is P-non-linear. Model node selection is 3; red lines represent odds ratios (OR), shading represents 95% CI, grey horizontal lines indicate OR = 1, grey vertical lines denote variable values at OR = 1, and significant thresholds for each variable are marked simultaneously. POPF, postoperative pancreatic fistula; SSI, surgical site infection; DGE, delayed gastric emptying; CD ≥ 3, clavien-dindo grade III, IV, and V. PLR, platelet to lymphocyte ratio; PIV, pan-immune-inflammation value; PPN, product of platelet count and neutrophil count

were found between other markers and hemorrhage in different models.

### DGE

Unlike other complications, only PLR and PIV as continuous variables, but not as categorical variables, showed significant associations with DGE (Table 4, Table S8). This inconsistency was also reflected in RCS results (Fig. 2, S1, S3). Interestingly, PAR was significantly associated with DGE across all logistic regression models, with lower PAR indicating higher DGE risk (Table 4, OR-overall < 1, P-overall < 0.05), confirmed by sensitivity analysis and RCS curves (Table S8, Fig. 3, S2, S4). No other markers showed significant associations with DGE.

### CD ≥ 3 complication

Similarly, only PPN and NHR were associated with CD ≥ 3 complications, but with different effects. Lower PPN was associated with higher risk of CD ≥ 3 complications, while NHR had the opposite effect (Table 4, Table S9, OR-overall > 1, P-overall < 0.05). RCS results were consistent, indicating non-linear relationships (Figs. 2 and 3, S1-S4). Although NAR was not significant as a categorical variable, as a continuous variable, higher NAR indicated increased risk of CD ≥ 3 complications (Table 4, Table S9, OR-overall > 1, P-overall < 0.05).

### Readmission

In regression analysis, NHR as a continuous variable was associated with increased readmission risk in model 2 (Table 4, OR = 1.033, $P = 0.045$). However, this association was not confirmed in sensitivity and RCS analyses (Table S9, Fig. 3, S2, S4).

### Predictive value of different preoperative inflammatory markers and their combinations

To evaluate the predictive value of different inflammatory markers and their combinations for postoperative outcomes, we performed ROC curve analysis (Fig. 4). PLR, PIV, and PPN had predictive value for most complications. For predicting hemorrhage, AUC values and thresholds were: PLR (AUC 0.654, threshold 160.526), PPN (AUC 0.695, threshold 50.336). For predicting SSI: PPN (AUC 0.644, threshold 46.589). For predicting DGE: PIV (AUC 0.643, threshold 190.544). However, the predictive ability of these markers for B/C POPF was weak: PLR (AUC 0.62, threshold 206.804), PIV (AUC 0.62, threshold 209.933). Consistent with logistic regression results, PAR showed good predictive ability for hemorrhage (AUC 0.684, threshold 5.038) and DGE (AUC 0.701, threshold 5.421). For CD ≥ 3 complications, NHR had good predictive performance (AUC 0.666, threshold 4.424), and PPN (AUC 0.618, threshold 47.707) could also predict CD ≥ 3 complications to some extent. However, these markers had poor predictive ability for readmission (AUC-overall < 0.6).

To further explore the predictive value of combined preoperative inflammatory markers for different postoperative outcomes, we performed combination analysis based on the above results. We found that the combined predictive ability for different postoperative outcomes was significantly higher than single markers (Fig. 4). The main combination models and their predictive abilities were: hemorrhage (PLR + PIV + PPN + PAR, AUC 0.735), DGE (PLR + PIV + PAR, AUC 0.724), CD ≥ 3 complications (PPN + NHR + NAR, AUC 0.667). Additionally, the model composed of PLR, PIV, and PPN also predicted the risk of B/C POPF (AUC 0.639) and SSI (AUC 0.651) to some extent. DCA curves indicated that these markers and models provided clinical benefit across a wide range of threshold probabilities for predicting postoperative complications in OPD (Fig. 5).

## Discussion

The high complication rate following PD is a significant barrier to the prognosis of patients with periampullary malignant tumors. Severe complications, including but not limited to B/C POPF, SSI, hemorrhage, and DGE, often require additional interventions and can even lead to patient mortality if not managed promptly. Clinically, these complications increase the complexity of postoperative management, reducing patient quality of life. Therefore, early detection and intervention are crucial for lowering treatment costs and enhancing survival outcomes. Studies have revealed

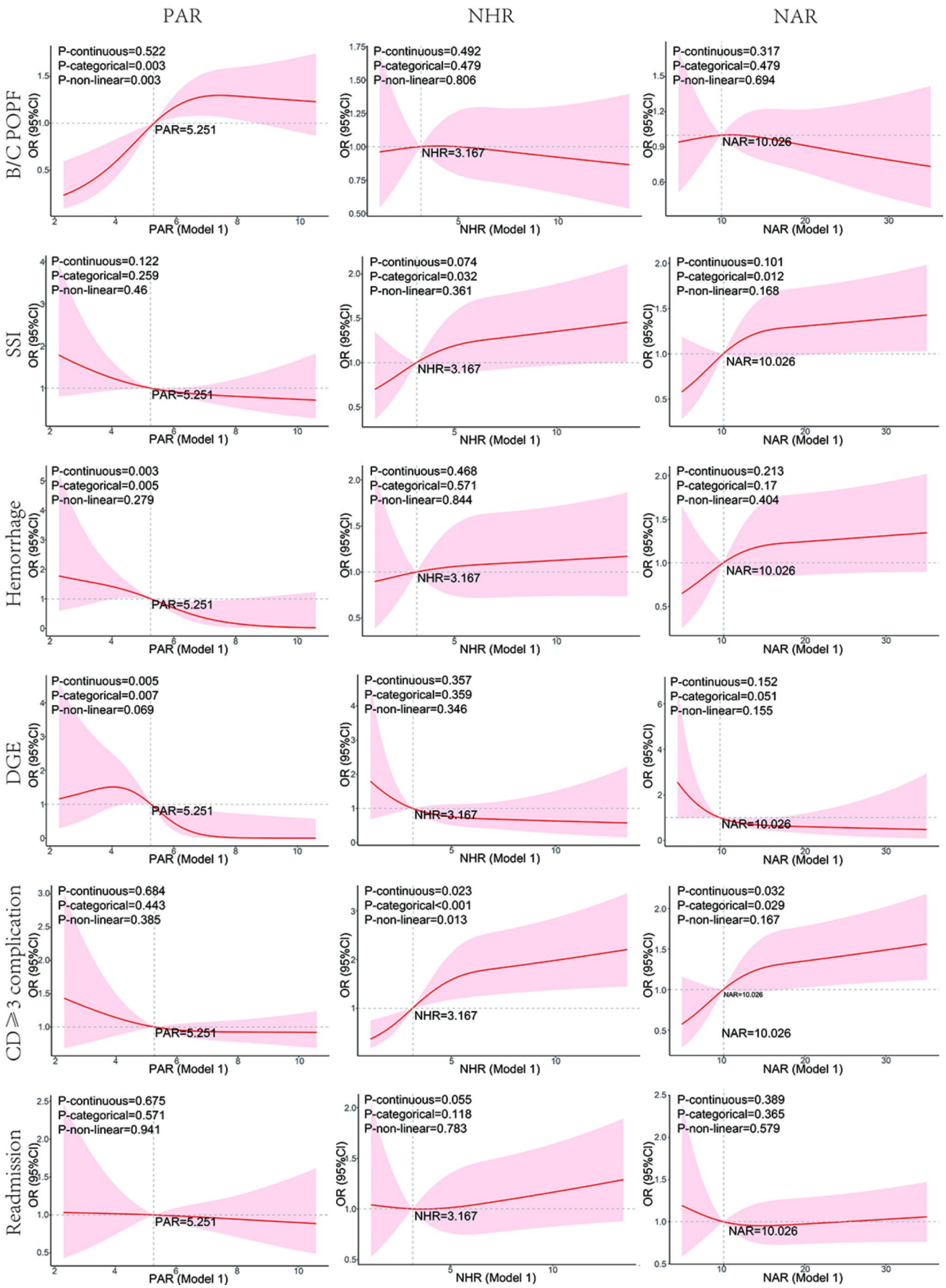
PAR
NHR
NAR
B/C POPF
P-continuous=0.522
P-categorical=0.003
P-non-linear=0.003
PAR=5.251
PAR (Model 1)
P-continuous=0.492
P-categorical=0.479
P-non-linear=0.806
NHR=3.167
NHR (Model 1)
P-continuous=0.317
P-categorical=0.479
P-non-linear=0.694
NAR=10.026
NAR (Model 1)
SSI
P-continuous=0.122
P-categorical=0.259
P-non-linear=0.46
PAR=5.251
PAR (Model 1)
P-continuous=0.074
P-categorical=0.032
P-non-linear=0.361
NHR=3.167
NHR (Model 1)
P-continuous=0.101
P-categorical=0.012
P-non-linear=0.168
NAR=10.026
NAR (Model 1)
Hemorrhage
P-continuous=0.003
P-categorical=0.005
P-non-linear=0.279
PAR=5.251
PAR (Model 1)
P-continuous=0.468
P-categorical=0.571
P-non-linear=0.844
NHR=3.167
NHR (Model 1)
P-continuous=0.213
P-categorical=0.17
P-non-linear=0.404
NAR=10.026
NAR (Model 1)
DGE
P-continuous=0.005
P-categorical=0.007
P-non-linear=0.069
PAR=5.251
PAR (Model 1)
P-continuous=0.357
P-categorical=0.359
P-non-linear=0.346
NHR=3.167
NHR (Model 1)
P-continuous=0.152
P-categorical=0.051
P-non-linear=0.155
NAR=10.026
NAR (Model 1)
CD⩾3 complication
P-continuous=0.684
P-categorical=0.443
P-non-linear=0.385
PAR=5.251
PAR (Model 1)
P-continuous=0.023
P-categorical<0.001
P-non-linear=0.013
NHR=3.167
NHR (Model 1)
P-continuous=0.032
P-categorical=0.029
P-non-linear=0.167
NAR=10.026
NAR=10.026
NAR (Model 1)
Readmission
P-continuous=0.675
P-categorical=0.571
P-non-linear=0.941
PAR=5.251
PAR (Model 1)
P-continuous=0.055
P-categorical=0.118
P-non-linear=0.783
NHR=3.167
NHR (Model 1)
P-continuous=0.389
P-categorical=0.365
P-non-linear=0.579
NAR=10.026
NAR (Model 1)
OR (95%CI)

**Fig. 3** Restricted cubic spline plots of PAR, NHR, and NAR (Model 1). POPF, postoperative pancreatic fistula; SSI, surgical site infection; DGE, delayed gastric emptying; CD≥3, clavien-dindo grade III, IV, and V. PAR, platelet to albumin ratio; NHR, neutrophil to high density lipoprotein cholesterol ratio; NAR, neutrophil-albumin ratio

that early postoperative complications after PD are often closely related to the patient's preoperative inflammatory state, suggesting that preoperative inflammatory markers are important indicators of complication risk [9, 10]. These markers include neutrophils, lymphocytes, platelets, and their combinations. Despite being derived from common preoperative blood tests, there has been limited systematic exploration of the association between preoperative inflammatory indices and postoperative complications following PD. This study aims to determine the relationship between PLR, PIV, PPN, PAR, NHR, and NAR with postoperative complications in PD patients, identifying specific preoperative biomarkers for different postoperative complications in OPD patients, thereby providing support for clinicians to improve perioperative management.

In this study, PLR, PIV, and PPN emerged as key indicators associated with most outcomes, including clinical B/C POPF, SSI, hemorrhage, DGE, and CD≥3 complications. PIV, a novel prognostic biomarker combining PLT, N, M, and L, was first proposed by Fuca et al. in 2020 as a systemic inflammation-related prognostic biomarker for metastatic colorectal cancer [11]. Since then, it has been widely regarded as a convenient and reliable indicator for assessing the prognosis of various cancers. Although its correlation with PD prognosis had not been previously reported, studies have shown that PIV is associated with prognosis in esophageal squamous cell carcinoma treated with radical resection, suggesting its utility in improving preoperative assessment [7]. Additionally, PIV has shown relevance to the prognosis of rectal, breast, and prostate cancers, with elevated early PIV indicating poor survival outcomes [11, 12]. In our study, PIV was also associated with several PD-related complications, including B/C POPF, SSI, and hemorrhage, and potentially DGE, despite some inconsistencies in results when PIV was treated as a categorical variable. For another preoperative marker, PPN, limited research indicates its potential to reflect immune-inflammatory status [13], with some reports suggesting that increased PPN is an independent risk factor for renal cancer [14]. A recent study on postoperative inflammatory markers in PD patients found that PPN on postoperative day three was significantly positively correlated with the risk of postoperative pancreatic fistula and speculated a negative correlation with postoperative hemorrhage [15]. Our findings are consistent with this, showing that preoperative PPN was significantly positively correlated with B/C POPF and that lower PPN was associated with increased hemorrhage risk. We also confirmed that decreased PPN increases the risk of SSI and CD≥3 complications. Therefore, despite the lack of robust evidence, PIV and PPN may emerge as new prognostic indicators for PD outcomes in the future.

Furthermore, numerous studies have regarded PLR as a reliable indicator of preoperative immune-inflammatory

**Table 4** Logistic regression analysis of three models(DGE、CD≥3 complication、Readmission)

| Characterstics | Model 1 | | Model 2 | | Model 3 | |
|---|---|---|---|---|---|---|
| | OR(95% CI) | *P* | OR(95% CI) | *P* | OR(95% CI) | *P* |
| DGE | | | | | | |
| PLR | 0.993(0.987,0.999) | 0.032 | 0.993(0.987,1) | 0.047 | 0.993(0.986,0.999) | 0.032 |
| PIV | 0.993(0.987,0.999) | 0.031 | 0.993(0.987,1) | 0.044 | 0.993(0.986,0.999) | 0.031 |
| PPN | 0.996(0.979,1.013) | 0.628 | 0.994(0.977,1.011) | 0.502 | 0.995(0.977,1.013) | 0.561 |
| PAR | 0.678(0.516,0.89) | 0.005 | 0.645(0.476,0.873) | 0.005 | 0.593(0.424,0.828) | 0.002 |
| NHR | 0.909(0.742,1.114) | 0.357 | 0.939(0.781,1.129) | 0.506 | 0.93(0.766,1.13) | 0.467 |
| NAR* | 0.922(0.825,1.03) | 0.152 | 0.925(0.824,1.038) | 0.186 | 0.899(0.789,1.024) | 0.109 |
| CD≥3 complication | | | | | | |
| PLR | 0.999(0.997,1.002) | 0.443 | 0.998(0.995,1.001) | 0.264 | 0.998(0.995,1.001) | 0.27 |
| PIV | 0.999(0.997,1.002) | 0.497 | 0.999(0.996,1.001) | 0.306 | 0.999(0.996,1.001) | 0.313 |
| PPN | 0.987(0.975,0.999) | 0.028 | 0.982(0.97,0.995) | 0.007 | 0.981(0.969,0.995) | 0.006 |
| PAR | 0.984(0.911,1.063) | 0.684 | 0.934(0.805,1.084) | 0.369 | 0.932(0.802,1.083) | 0.358 |
| NHR | 1.055(1.007,1.105) | 0.023 | 1.06(1.009,1.114) | 0.022 | 1.059(1.008,1.113) | 0.023 |
| NAR* | 1.012(1.001,1.024) | 0.032 | 1.012(1.001,1.023) | 0.03 | 1.012(1.001,1.023) | 0.035 |
| Readmission | | | | | | |
| PLR | 1.001(0.998,1.003) | 0.568 | 1.001(0.998,1.003) | 0.6 | 1.001(0.998,1.003) | 0.624 |
| PIV | 1.001(0.998,1.003) | 0.577 | 1.001(0.998,1.003) | 0.605 | 1.001(0.998,1.003) | 0.624 |
| PPN | 1.003(0.992,1.015) | 0.577 | 1.003(0.991,1.015) | 0.651 | 1(0.988,1.013) | 0.943 |
| PAR | 0.979(0.887,1.081) | 0.675 | 0.95(0.816,1.107) | 0.514 | 0.942(0.806,1.102) | 0.457 |
| NHR | 1.028(0.999,1.058) | 0.055 | 1.033(1.001,1.067) | 0.045 | 1.034(1,1.069) | 0.052 |
| NAR* | 1.005(0.994,1.015) | 0.389 | 1.007(0.995,1.018) | 0.247 | 1.007(0.995,1.018) | 0.246 |

*, multiply the original value by 100; DGE: delayed gastric emptying; CD≥3, clavien-dindo grade III, IV, and V; PLR, platelet to lymphocyte ratio; PIV, pan-immune-inflammation value; PPN, product of platelet count and neutrophil count; PAR, platelet to albumin ratio; NHR, neutrophil to high density lipoprotein cholesterol ratio; NAR, neutrophil-albumin ratio.

status, closely related to the prognosis of various malignancies. Previous studies have also found that preoperative PLR is associated with poor prognosis in patients with periampullary malignant tumor [16], distal bile duct cancer [6, 17], and pancreatic head cancer undergoing PD [18]. Our study demonstrated significant associations between PLR and outcomes such as B/C POPF, SSI, and hemorrhage, contrary to some studies that found no such correlations [15, 19]. Our analysis suggests that elevated PLR increases the risk of B/C POPF, while lower PLR indicates higher risks of SSI and hemorrhage. Although these conclusions were supported by further RCS and sensitivity analyses, more detailed research is needed for confirmation.

Interestingly, our study also found that for hemorrhage and DGE, decreased preoperative PAR was more indicative of higher postoperative complication rates than the above three markers. This may be because PAR, composed mainly of PLT and Alb, reflects preoperative inflammatory and nutritional status, both closely related to the occurrence of hemorrhage and DGE. Some studies have reported PAR as an indicator of comprehensive inflammatory-nutritional status, with Jiaxing et al. finding a significant correlation between PAR and CRP ($P<0.001$) [20]. Moreover, as a composite marker, PAR may be more stable and accurate, less likely affected by dynamic physiological conditions compared to other platelet parameters and/or inflammatory markers [21]. Current studies also indicate PAR's association with poor prognosis in tumor patients, mainly focusing on long-term survival outcomes, with less exploration of its role in short-term postoperative complications [22, 23]. Additionally, we found that NHR plays a significant role in CD≥3 complications. NHR, composed of NC and HDL-c, is a new indicator reflecting inflammation and dyslipidemia, commonly associated with cardiovascular and metabolic diseases, and is considered a predictor of all-cause mortality in cardiovascular diseases [24, 25]. Given its close relationship with inflammatory responses, NHR has gradually been recognized as a biomarker for predicting different tumor prognoses, with studies reporting a significant correlation between high NHR levels and poor prognosis in HCC [26].

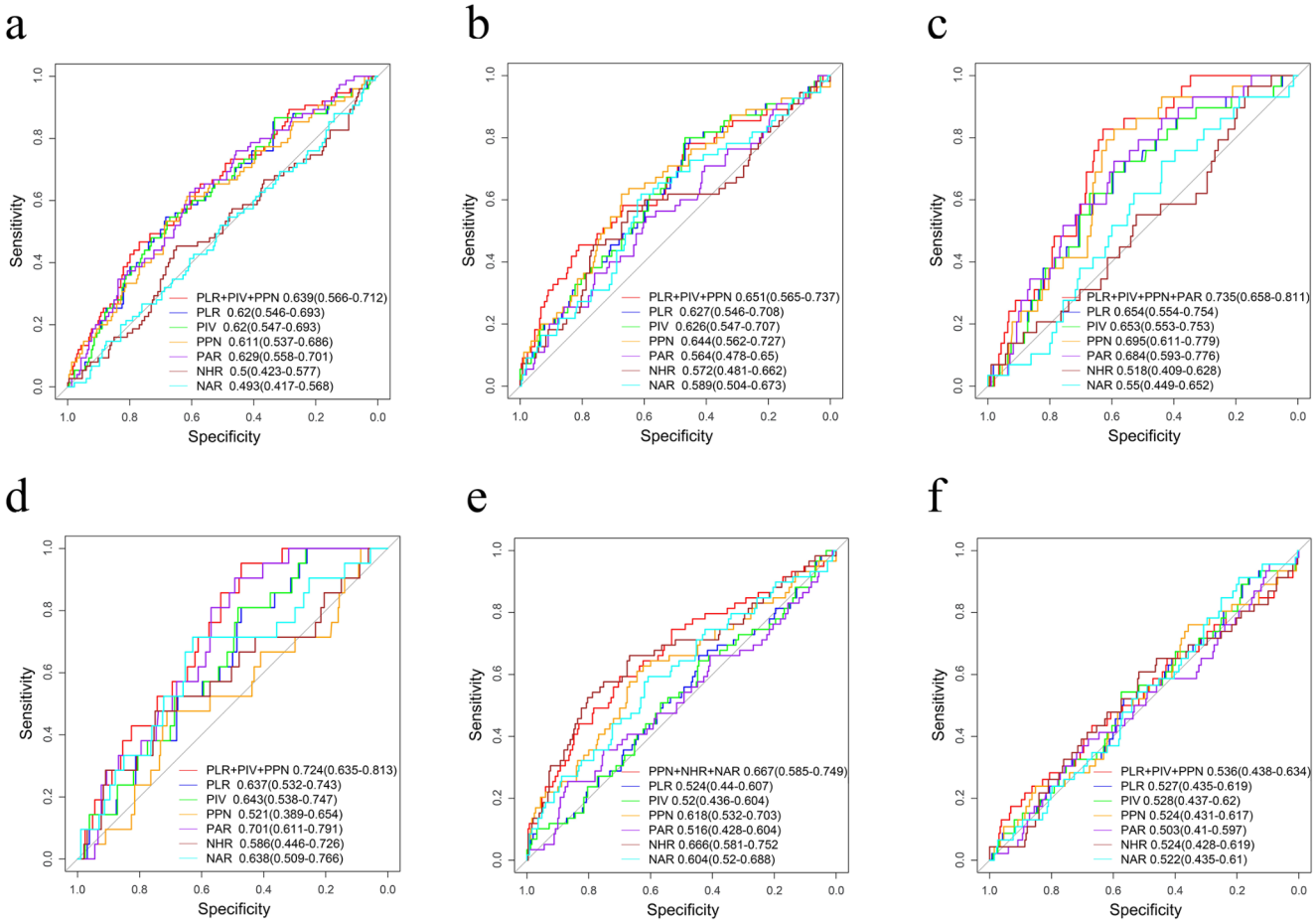


**Fig. 4** ROC curves of various inflammation markers (single and combined) with postoperative outcomes. a-f represent six postoperative outcomes: POPF, SSI, hemorrhage, DGE, CD≥3 complications, and reoperation. ROC, receiver operating characteristic curve; PLR, platelet to lymphocyte ratio; PIV, pan-immune-inflammation value; PPN, product of platelet count and neutrophil count; PAR, platelet to albumin ratio; NHR, neutrophil to high density lipoprotein cholesterol ratio; NAR, neutrophil-albumin ratio

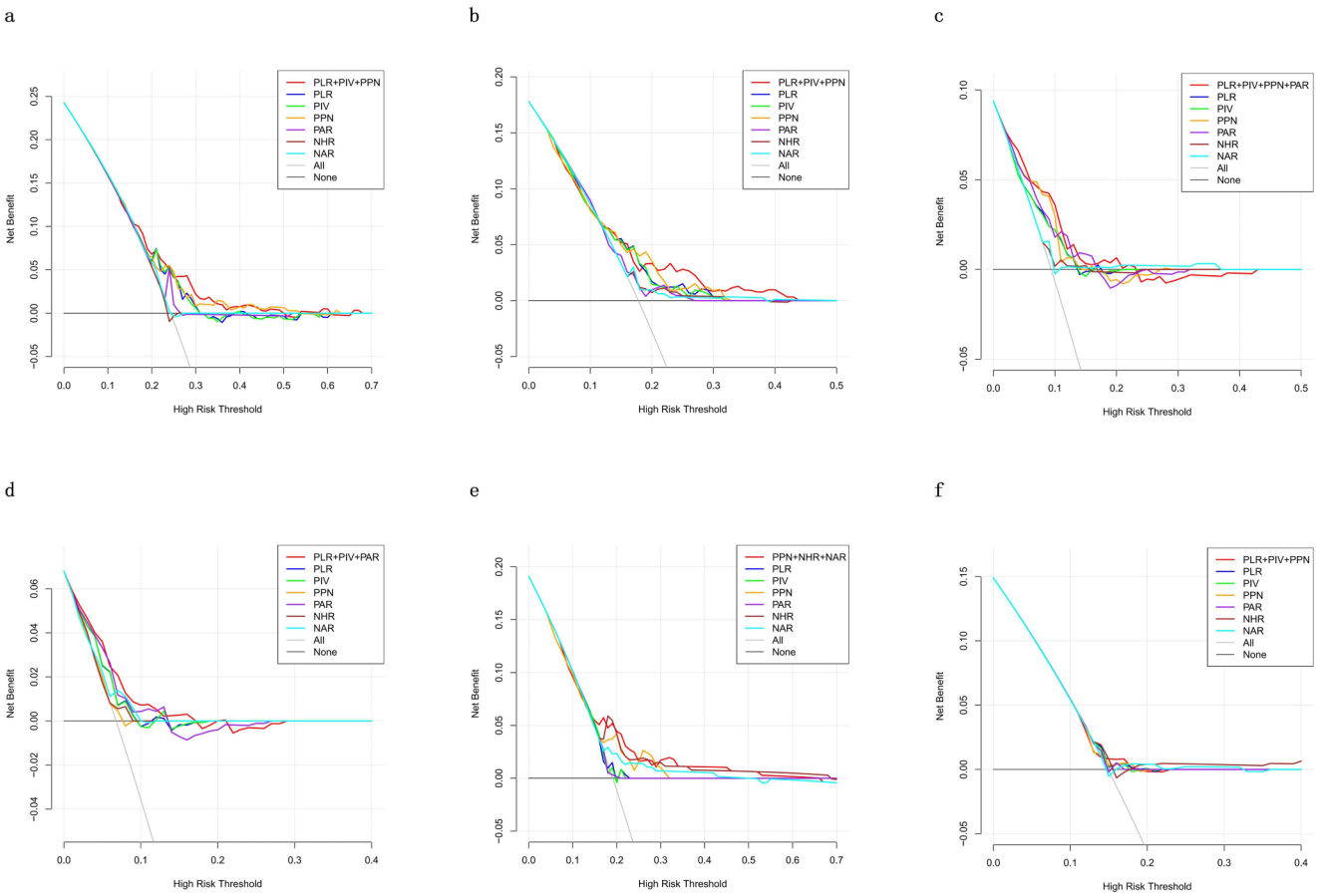


**Fig. 5** DCA curves of various inflammation markers (single and combined) with postoperative outcomes. **a-f** represent six postoperative outcomes: POPF, SSI, hemorrhage, DGE, CD≥3 complications, and reoperation. DCA, decision curve analysis

In our study, high NHR levels were also associated with high-risk CD≥3 complications. Although NAR has been found to correlate closely with survival rates after palliative treatment in pancreatic cancer patients and as a predictor of pathologic complete response to neoadjuvant chemoradiotherapy in locally advanced rectal cancer [27], in this study, it was only observed to be associated with increased risk of CD≥3 complications as a continuous variable.

After exploring the relationships between the identified markers and different outcomes, we performed ROC curve and DCA to evaluate the predictive value of individual inflammation markers and their combinations for postoperative complications. The results showed that individual markers such as PLR, PIV, and PPN have a certain predictive value for most postoperative outcomes (including POPF, SSI, hemorrhage, and DGE), particularly for postoperative hemorrhage, but their predictive power for POPF is weaker. Although the AUC values of these markers are relatively low, indicating that they may not have high precision when used individually to predict all types of postoperative complications, we still consider these markers to be valuable for identifying risk factors to inform clinical decision-making. To further improve the predictive performance, we analyzed the effects of marker combinations and found that the combination model showed significant improvement in predicting postoperative complications, but the performance remains moderate to low (AUC below 0.7 in some cases). This may be because these markers belong to the same category, making it difficult to comprehensively reflect the overall patient condition. Therefore, despite the statistical significance of individual markers and the combination model, their clinical utility should be carefully evaluated. Future studies can incorporate more markers or other clinical variables (such as pancreatic duct diameter and tumor size [28]) to further enhance the predictive ability of the model.

We must acknowledge certain limitations in our study. Firstly, being a retrospective single-center study, there may be some inevitable biases. Secondly, we focused primarily on the relationship between preoperative inflammatory markers and short-term outcomes, with limited knowledge of the dynamic changes of these markers during subsequent complication treatment and their impact on long-term outcomes. Thirdly, we did not perform external validation, which limits the generalizability of the model, especially

for other medical institutions and different regions. Lastly, we did not include other detection indices, such as imaging and pathological markers, in our analysis. Therefore, future high-quality studies incorporating these factors are needed to enhance the predictive accuracy and clinical utility of the model.

## Conclusion

In summary, this study focused on analyzing six inflammatory markers (PLR, PIV, PPN, PAR, NHR, and NAR) that are closely related to the preoperative inflammatory status of OPD patients. We explored the relationship between these markers and various postoperative complications from multiple perspectives. The findings revealed that PLR, PIV, and PPN are associated with most postoperative outcomes and should be considered key indicators for preoperative assessment in PD patients. Additionally, PAR should be taken into account when evaluating the risk of hemorrhage and DGE, as lower preoperative PAR may indicate an increased risk of postoperative complications. Finally, compared to the other markers, PPN and NHR may be more significant in assessing the risk of CD≥3 complications.

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**Author contributions** All authors above appropriately contributed to the development of this manuscript. The conceptualization of the aims of the article was made by J.F. and R.D. The formal acquisition and analysis of the data were carried out by J.F., Y.Z., and H.L. J.F., Y.Z., H.L., Y.Z., K.J., and R.D. were involved in interpreting the data, drafting, revising, and approving the final version for submission. R.D. was responsible for funding acquisition and supervision.

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**Data availability** The datasets analysed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate** This study received approval from the Ethics Committee of the General Hospital of Western Theater Command and was conducted in accordance with the principles of the Declaration of Helsinki. The ethical approval number is 2024EC4-ky017. Due to the retrospective design of the study and the analysis of anonymized data, the Ethics Committee granted a waiver for informed consent.

**Competing interests** The authors declare no competing interests.



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