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The impact of preoperative immunonutritional status on postoperative complications in ovarian cancer

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Abstract

Background Preoperative immunonutritional status can influence postoperative complications. Malnutrition in ovarian cancer patients diminishes the body's resilience to abdominal surgery, resulting in inferior surgical outcomes and increased postoperative complications. We aim to investigate the effect of preoperative immunonutritional status, including NLR, PLR, LMR, TCLR, FAR, FLR, SII, PNI and CONUT on postoperative complications in epithelial ovarian cancer (EOC) in a large population.

Methods A multicenter real-world study included 922 patients with histologically confirmed EOC who received comprehensive staged surgery or debulking surgery at seven tertiary hospitals in China between 2012 and 2023. Logistic regression and Lasso regression analyses were employed to identify variables associated with postoperative complications. A predictive nomogram model was developed based on multivariate modeling.

Results The study included a total of 922 patients diagnosed with epithelial ovarian cancer across seven medical centers with 565 (61.3%) patients experiencing postoperative complications. Significant differences were found in the distribution of inflammatory and nutritional risk indicators, including NLR, PLR, LMR, TCLR, FAR, FLR, SII, PNI and CONUT between the two groups (all $P < 0.01$). A multivariable model identified several predictive factors for postoperative complications: PNI > 46.73 (odds ratio [OR] = 0.49, $P < 0.001$), FAR > 10.77 (OR = 1.60, $P = 0.019$), LMR > 3.70 (OR = 0.68, $P = 0.044$), hydrothorax (OR = 2.60, $P = 0.005$), laparoscopy (OR = 0.59, $P = 0.010$ vs. laparotomy), enterectomy (OR = 2.50, $P = 0.001$).

Conclusion Poor immunonutritional status can increase the risk of postoperative complications. These findings suggest that prompt nutritional interventions may reduce the incidence of postoperative complications and improve

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surgical outcomes. The risk prediction model, including PNI, FAR, LMR, hydrothorax, laparoscopy vs. laparotomy, and enterectomy, might facilitate patient-centered decision-making and risk stratification.

Clinical trial registration The study was registered in the Clinical trial registry: NCT06483399. (https://clinicaltrials.gov/study/NCT06483399)

Keywords Ovarian cancer, Preoperative immunonutritional status, Postoperative complications

Introduction

Ovarian cancer is a fatal gynecological malignancy, ranking eighth among the most prevalent malignancies in women, with approximately 313,959 new cases and 207,252 fatalities worldwide in 2020 [1]. In the management of ovarian cancer, surgery stands out as the primary treatment modality, with comprehensive staging or effective tumor cytoreduction significantly enhancing the survival outcomes for patients [2]. The size and quantity of remaining lesions after surgery are crucial factors affecting the prognosis of ovarian cancer [3]. A meta-analysis revealed that each 10% increase in tumor cytoreduction in patients with advanced ovarian cancer was associated with a 5.5% rise in their median survival time [4].

However, the physiological strain induced by extensive abdominal surgery and significant surgical resection promotes the occurrence of surgical complications in patients with ovarian cancer, which leads to detrimental impacts on subsequent treatment and prognosis [5, 6]. Currently, several studies have reported numerous factors affecting the development of postoperative complications in ovarian cancer patients, predominantly focusing on surgery-associated indicators such as surgical complexity, surgical extent, and resection site. Preoperative assessment of patients' surgical risk and identification of high-risk patients confront significant challenges, underscoring the critical need to identify preoperative markers for predicting postoperative complications in ovarian cancer patients [7–11].

Preoperative immunonutritional status can significantly influence postoperative complications. Malnutrition in ovarian cancer patients diminishes the body's resilience to abdominal surgery, resulting in inferior surgical outcomes and increased postoperative complications [6, 12, 13]. As a significant indicator for nutritional risk assessment and prediction of perioperative complications in a wide range of surgical conditions, low prognostic nutritional index (PNI) and high controlling nutritional status (CONUT) are associated with a higher risk and increased severity of postoperative complications [14, 15]. Furthermore, inflammatory markers such as high preoperative neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and low preoperative lymphocyte-to-monocyte ratio (LMR) represent compromised perioperative recovery and increased mortality in patients [16, 17]. The impact of immunonutrition interventions on cancer treatment outcomes has the potential to be groundbreaking [18]. Optimizing the efficacy of immunonutrition leads to improved cancer outcomes [18]. A significant proportion of multidisciplinary healthcare professionals (41.8%) have limitations in their level of knowledge and practice of immunonutrition [19]. Greater emphasis on nutritional education and multidisciplinary collaboration will help improve the immunonutritional status of patients. However, few studies have examined the impact and predictive value of these indicators on postoperative complications in patients with epithelial ovarian cancer (EOC). It is not clear which indicators should be prioritized for monitoring complications, and a better understanding of these indicators would greatly benefit the prevention and management of postoperative complications in EOC patients.

The present study retrieved data on EOC patients from the China Real World Gynecological Oncology Platform (NUWA) to analyze the associations between nutritional risk indicators and inflammation indicators with postoperative complications. Additionally, it aimed to explore the independent factors affecting the occurrence of postoperative complications in the EOC cohort. By building an EOC postoperative complication risk prediction model, this study aims to establish a practical framework for identifying high-risk groups for postoperative complications and offering tailored interventions and perioperative care guidance.

Methods and materials

Patients

Patients diagnosed with epithelial ovarian cancer between January 2012 and February 2023 were recruited from seven tertiary medical centers (see Supplementary Table S1) in the China Real World Gynecological Oncology Platform. The inclusion criteria were as follows: (1) histologically confirmed primary epithelial ovarian, peritoneal, and fallopian tube cancers; (2) patients who received comprehensive staged surgery or debulking surgery; (3) available data of laboratory examination within 7 days before surgery. The exclusion criteria encompassed: (1) borderline ovarian tumor; (2) receipt of neoadjuvant chemotherapy; (3) presence of other conditions influencing laboratory data, such as hepatitis, kidney disease, autoimmune diseases, infectious diseases, blood disease,

etc.; (4) concurrent cancer in other organs; (5) absence of surgery or biopsy only; (6) multiple staged surgeries.

Data collection

We extracted data from the patients' laboratory tests, including complete blood count, serum albumin, total cholesterol, and fibrinogen, conducted within 7 days before surgery. Moreover, clinical features, initial treatment, and prognostic details were retrieved from patients' medical records and follow-up information. The inflammatory indicators and nutritional risk indexes were calculated as follows:

Neutrophil to Lymphocyte ratio (NLR) = neutrophil count (10^9/L) / lymphocyte count (10^9/L);

Platelet to Lymphocyte ratio (PLR) = platelet count (10^9/L) / lymphocyte count (10^9/L);

Lymphocyte to Monocyte ratio (LMR) = lymphocyte count (10^9/L) / monocyte count (10^9/L);

Total cholesterol to Lymphocyte ratio (TCLR) = total cholesterol (mmol/L) / lymphocyte count (10^9/L);

Fibrinogen to Lymphocyte ratio (FLR) = fibrinogen (g/L) / lymphocyte count (10^9/L);

Fibrinogen to Albumin ratio (FAR) = fibrinogen (g/L) / serum albumin (g/L);

Systemic immune-inflammation index (SII) = neutrophil count (10^9/L) × platelet count (10^9/L) / lymphocyte count (10^9/L);

Prognostic nutritional index (PNI) = serum albumin (g/L) + 5 × total lymphocyte count (10^9/L);

Controlling nutritional status score (CONUT) is a scoring system based on serum albumin, total lymphocyte count, and total cholesterol, with detailed scoring criteria shown in Supplementary Table S2.

Postoperative complications are defined as any deviation from the normal postoperative course, including new and progressive complications. According to the Clavien-Dindo classification, grade 0 indicates no postoperative complications, and grades I-V indicate postoperative complications requiring different degrees of treatment [20, 21]. All postoperative complications occurring within 30 days for each patient were recorded, and the highest complication grade was used as the patient's complication grade. The family history of cancer was recorded according to the presence of malignant tumor in first-degree relatives of patients [22]. Comorbidities included chronic medical diseases such as hypertension, chronic respiratory disease, and thyroid disorders. Surgical outcomes were recorded depending on the size of the residual disease [23]. No residual disease is defined as complete tumor resection with no visible residual disease. Optimal cytoreduction means the maximum diameter of single residual disease ≤ 1 cm, and suboptimal cytoreduction means the maximum diameter of single residual disease lesion > 1 cm. In our study, "laparoscopically treated patients" refers specifically to those who have undergone surgery through laparoscopy, not just those diagnosed using this technique.

This study was approved by the Medical Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (TJ-IRB202401053). A waiver of informed consent has been applied for this study, and the results are intended for scientific research only.

Table 1 The cut-off value of inflammatory indicators and nutritional risk indexes

Indexes	Cut-off value
NLR	2.46
PLR	227.52
LMR	3.70
TCLR	3.39
FLR	2.64
FAR	10.77
SII	818.23
PNI	46.73
CONUT	4

CONUT, Controlling nutritional status score; FAR, Fibrinogen to albumin ratio; FLR, Fibrinogen to lymphocyte ratio; LMR, Lymphocyte to monocyte ratio; NLR, Neutrophil to lymphocyte ratio; PLR, Platelet to lymphocyte ratio; PNI, Prognostic nutritional index; SII, Systemic immune-inflammation index; TCLR, Total cholesterol to lymphocyte ratio

Statistical analysis

Continuous variables were displayed as the median and interquartile range (IQR), and were compared using the Mann-Whitney U test. Categorical variables were shown as frequency number and percentage and were compared by Chi-square test or Fisher's exact test. The optimal cut-off values for inflammatory and nutritional risk indicators to predict postoperative complications were determined using receiver operating characteristic (ROC) curves and Youden's index (Table 1). The median values of progression-free survival (PFS) and overall survival (OS) were calculated by the Kaplan-Meier survival curve.

The entire study population was divided into a training set and an internal validation set at a ratio of 7:3 using the R software package "caret". Logistic regression and Lasso regression analyses were employed to identify variables associated with postoperative complications in the training set. A predictive nomogram model was developed based on these significant factors. The accuracy, discrimination, and clinical utility of the nomogram were assessed using ROC curves, the area under the curve (AUC), calibration curves, the Hosmer-Lemeshow goodness-of-fit test, and decision curve analysis (DCA). A P value < 0.05 was considered statistically significant, and all tests were two-sided. All statistical analyses and graphical representations were performed using R version 4.2.1.

Results

Patient characteristics

The study included a total of 922 patients diagnosed with epithelial ovarian cancer across seven medical centers (Fig. 1). Of these, 565 (61.3%) patients encountered postoperative complications. Specifically, 109 (11.8%) patients experienced grade I complications, 400 (43.4%) patients had grade II complications, and 59 (6.4%) patients faced grade III-V complications. Although a considerable proportion of EOC patients encountered postoperative complications, the incidence of severe complications (grades III-V) was relatively low. Furthermore, 315 patients (34.2%) experienced two or more types of postoperative complications.

Table 2 shows the clinical characteristics of subgroups with or without postoperative complications. There were significant differences in the distribution of inflammatory and nutritional risk indicators including NLR, PLR, LMR, TCLR, FAR, FLR, SII, PNI and CONUT between the two groups (all $P<0.01$). In the group with postoperative complications, the proportion of patients with preoperative ascites (79.1% vs. 61.9%, $P<0.001$) or hydrothorax (17.0% vs. 5.3%, $P<0.001$) was higher. The postoperative complications group also had a higher proportion of patients undergoing laparotomy (83.5% vs. 69.7%, $P<0.001$), upper abdominal surgery (5.0% vs. 2.0%, $P<0.001$) and enterectomy (18.8% vs. 7.8%, $P<0.001$) but a lower proportion of patients achieving no residual disease (47.4% vs. 58.8%, $P=0.003$). In addition, the postoperative hospitalization was shorter, while both PFS and OS were significantly longer in the group without postoperative complications (all $P<0.01$). Differences in other characteristics were not statistically significant.

Factors associated with postoperative complications and prediction model

The overall patients were partitioned into a training set and an internal validation set, with 649 patients in the training set and 279 patients in the internal validation set (Fig. 1). The comparison between the two sets showed good consistency (see Supplementary Table S3).

Through logistic regression and Lasso regression analysis, we identified the factors influencing the risk of postoperative complications in the training set. In the univariate analysis, several variables were associated with complications (all $P<0.05$) (Table 3), including age, NLR, PLR, LMR, TCLR, FLR, FAR, SII, PNI, CONUT, RBC, Hb, FIGO stage, ascites, hydrothorax, surgery methods,

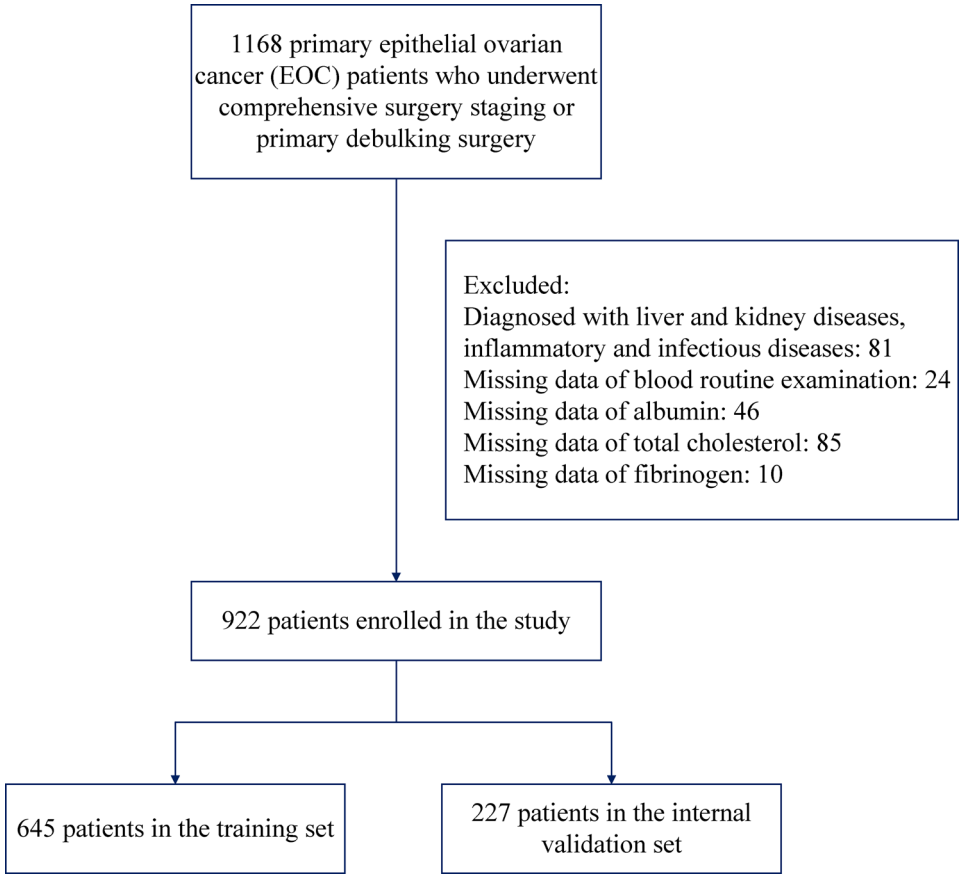

Fig. 1 Flow chart of patient inclusion and exclusion

Table 2 Comparison of clinical characteristics between patients with and without postoperative complications

	No postoperative complications (*N* = 357)	Postoperative complications (*N* = 565)	*P* value
Age at diagnosis (years), median (IQR)	52 (46, 58)	53 (47, 60)	0.060
NLR			< 0.001
≤ 2.46	177 (49.6)	187 (33.1)	
> 2.46	180 (50.4)	378 (66.9)	
PLR			< 0.001
≤ 227.52	268 (75.1)	320 (56.6)	
> 227.52	89 (24.9)	245 (43.4)	
LMR			< 0.001
≤ 3.70	170 (47.6)	387 (68.5)	
> 3.70	187 (52.4)	178 (31.5)	
TCLR			0.001
≤ 3.39	250 (70.0)	338 (59.8)	
> 3.39	107 (30.0)	227 (40.2)	
FLR			< 0.001
≤ 2.64	208 (58.3)	217 (38.4)	
> 2.64	149 (41.7)	348 (61.6)	
FAR			< 0.001
≤ 10.77	258 (72.3)	278 (49.2)	
> 10.77	99 (27.7)	287 (50.8)	
SII			< 0.001
≤ 818.23	228 (63.9)	260 (46.0)	
> 818.23	129 (36.1)	305 (54.0)	
PNI			< 0.001
≤ 46.73	112 (31.4)	348 (61.6)	
> 46.73	245 (68.6)	217 (38.4)	
CONUT			< 0.001
≤ 4	308 (86.3)	384 (68.0)	
> 4	49 (13.7)	181 (32.0)	
RBC (10^12/L)			< 0.001
< 3.5	11 (3.1)	64 (11.3)	
≥ 3.5	346 (96.9)	501 (88.7)	
Hemoglobin (g/L)			< 0.001
< 120	136 (38.1)	310 (54.9)	
≥ 120	221 (61.9)	255 (45.1)	
CA125 (U/mL)	357.8 (116.7, 1000.0)	680.0 (240.4, 1703.6)	< 0.001
BMI (kg/m2)	22.3 (20.6, 24.3)	21.9 (20.0, 23.8)	0.438
Histology			0.096
High-grade serous carcinoma	214 (59.9)	383 (67.8)	
Low-grade serous carcinoma	9 (2.5)	19 (3.4)	
Endometrioid carcinoma	36 (10.1)	37 (6.5)	
Mucinous carcinoma	36 (10.1)	45 (8.0)	
Ovarian clear cell carcinoma	32 (9.0)	48 (8.5)	
Others	30 (8.4)	33 (5.8)	
FIGO stage			< 0.001
I	99 (27.7)	92 (16.3)	
II	61 (17.1)	71 (12.6)	
III	177 (49.6)	341 (60.4)	
IV	20 (5.6)	61 (10.8)	
Tumor laterality			0.073
Unilateral	168 (47.1)	237 (41.9)	
Bilateral	189 (52.9)	328 (58.1)	
Ascites			< 0.001

Table 2 (continued)

	No postoperative complications (*N* = 357)	Postoperative complications (*N* = 565)	*P* value
No	136 (38.1)	118 (20.9)	
Yes	221 (61.9)	447 (79.1)	
Hydrothorax			< 0.001
No	338 (94.7)	469 (83.0)	
Yes	19 (5.3)	96 (17.0)	
Menopause			0.395
No	155 (43.4)	239 (42.3)	
Yes	202 (56.6)	326 (57.7)	
Comorbidities			0.316
No	297 (83.2)	478 (84.6)	
Yes	60 (16.8)	87 (15.4)	
Family history of cancer			0.329
No	303 (84.9)	472 (83.5)	
Yes	54 (15.1)	93 (16.5)	
Surgery methods			< 0.001
Laparotomy	249 (69.7)	472 (83.5)	
Laparoscopy	108 (30.3)	93 (16.5)	
Surgery procedure			
Upper abdominal surgery	7 (2.0)	28 (5.0)	0.014
Enterectomy	28 (7.8)	106 (18.8)	< 0.001
Lymphadenectomy	270 (75.6)	416 (73.6)	0.275
Lymph node metastasis			0.004
Negative	194 (71.9)	249 (59.9)	
Positive	76 (28.1)	167 (40.1)	
Residue disease			0.003
No residual disease	210 (58.8)	268 (47.4)	
≤ 1 cm	91 (25.5)	181 (32.0)	
> 1 cm	56 (15.7)	116 (20.5)	
Postoperative hospitalization (days), median (IQR)	14 (8,14)	13 (10,17)	< 0.001
Postoperative chemotherapy			0.298
No	29 (8.1)	53 (9.4)	
Yes	328 (91.9)	512 (90.6)	
Chemotherapy cycle			0.395
< 6	155 (43.4)	239 (42.3)	
≥ 6	202 (56.6)	326 (57.7)	
PARP inhibitors			0.718
No	353 (98.9)	561 (99.3)	
Yes	4 (1.1)	4 (0.7)	
Bevacizumab			1.000
No	356 (99.6)	563 (99.7)	
Yes	1 (0.4)	2 (0.3)	
Recurrence status			< 0.001
No	202 (56.6)	250 (44.2)	
Yes	155 (43.4)	315 (55.8)	
PFS (months, 95% CI)[a]	69.8 (45.8, 93.8)	37.6 (31.6, 43.6)	< 0.001
Survival status			< 0.001
Alive	249 (69.7)	330 (58.4)	
Death	108 (30.3)	235 (41.6)	
OS (months, 95% CI)[a]	85.7 (79.6, 91.8)	69.7 (60.9, 78.6)	0.001

a. The median PFS or OS and 95% CI were calculated by the K-M survival curve BMI, Body mass index; CA125, Carbohydrate antigen 125; CONUT, Controlling nutritional status score; FAR, Fibrinogen to albumin ratio; FIGO, International Federation of Gynecology and Obstetrics; FLR, Fibrinogen to lymphocyte ratio; IQR, Interquartile range; LMR, Lymphocyte to monocyte ratio; NLR, Neutrophil to lymphocyte ratio; OS, Overall survival; PFS, Progression-free survival; PLR, Platelet to lymphocyte ratio; PNI, Prognostic nutritional index; RBC, Red blood cell count; SII, Systemic immune-inflammation index; TCLR, Total cholesterol to lymphocyte ratio

Table 3 Univariate logistic regression analysis for postoperative complications

Variables	OR (95% CI)	*P* value
Age (years)		
≤ 53	Ref.	
> 53	1.38 (1.00, 1.92)	0.049
NLR		
≤ 2.46	Ref.	
> 2.46	1.76 (1.27, 2.44)	< 0.001
PLR		
≤ 227.52	Ref.	
> 227.52	2.18 (1.53, 3.12)	< 0.001
LMR		
≤ 3.70	Ref.	
> 3.70	0.38 (0.27, 0.53)	< 0.001
TCLR		
≤ 3.39	Ref.	
> 3.39	1.59 (1.13, 2.23)	0.008
FLR		
≤ 2.64	Ref.	
> 2.64	2.04 (1.47, 2.83)	< 0.001
FAR		
≤ 10.77	Ref.	
> 10.77	2.81 (1.98, 3.99)	< 0.001
SII		
≤ 818.23	Ref.	
> 818.23	1.96 (1.41, 2.74)	< 0.001
PNI		
≤ 46.73	Ref.	
> 46.73	0.29 (0.21, 0.41)	< 0.001
CONUT		
≤ 4	Ref.	
> 4	2.50 (1.65, 3.78)	< 0.001
RBC (10^12/L)		
< 3.5	Ref.	
≥ 3.5	0.31 (0.14, 0.67)	0.003
Hb (g/L)		
< 120	Ref.	
≥ 120	0.54 (0.39, 0.75)	< 0.001
FIGO stage		
I	Ref.	
II	1.04 (0.60, 1.80)	0.899
III	1.98 (1.30, 3.02)	0.001
IV	3.18 (1.58, 6.38)	0.001
Ascites		
No	Ref.	
Yes	2.12 (1.48, 3.03)	< 0.001
Hydrothorax		
No	Ref.	
Yes	3.76 (1.99, 7.12)	< 0.001
Surgery methods		
Laparotomy	Ref.	
Laparoscopy	0.49 (0.33, 0.72)	< 0.001
Upper abdominal surgery		
No	Ref.	
Yes	3.71 (1.27, 10.82)	0.016
Enterectomy		
No	Ref.	
Yes	2.94 (1.71, 5.05)	< 0.001
Lymphadenectomy		
No	Ref.	
Yes	0.90 (0.66, 1.22)	0.498
Lymph node metastasis		
Negative	Ref.	
Positive	2.01 (1.34, 3.01)	< 0.001
Residue		
No residual disease	Ref.	
≤ 1 cm	1.85 (1.26, 2.71)	0.002
> 1 cm	1.47 (0.95, 2.26)	0.081

BMI, Body mass index; CA125, Carbohydrate antigen 125; CONUT, Controlling nutritional status score; FAR, Fibrinogen to albumin ratio; FIGO, International Federation of Gynecology and Obstetrics; FLR, Fibrinogen to lymphocyte ratio; IQR, Interquartile range; LMR, Lymphocyte to monocyte ratio; NLR, Neutrophil to lymphocyte ratio; PLR, Platelet to lymphocyte ratio; PNI, Prognostic nutritional index; RBC, Red blood cell count; SII, Systemic immune-inflammation index; TCLR, Total cholesterol to lymphocyte ratio

upper abdominal surgery, enterectomy, and lymph node metastasis and residual disease. Then we included these factors in Lasso regression (Fig. 2) and selected the model variables corresponding to lambda 1se in the multivariate analysis (Table 4). The multivariate analysis results showed that the following were independent factors influencing postoperative complications: PNI > 46.73 (odds ratio [OR] = 0.49, $P < 0.001$), FAR > 10.77 (OR = 1.60, $P = 0.019$), LMR > 3.70 (OR = 0.68, $P = 0.044$), hydrothorax (OR = 2.60, $P = 0.005$), laparoscopy (OR = 0.59, $P = 0.010$ vs. laparotomy), and enterectomy (OR = 2.50, $P = 0.001$). To visualize the extent of the influence of each variable and to predict the risk of postoperative complications in patients, we constructed a prediction model and designed a nomogram based on the results of the multivariate analysis (Fig. 3).

As shown in Fig. 4, the predictive performance and clinical practicability of the prediction model were evaluated using the ROC curve and AUC, calibration curve and DCA. The AUC of the postoperative complication risk prediction model was 0.723 (95% CI: 0.684–0.763) in the training set and 0.709 (95% CI: 0.648–0.771) in the internal validation set, which were higher than the AUC of PNI, LMR, and FAR. The calibration curves and Hosmer-Lemeshow goodness-of-fit test showed that there was an absence of significant difference between the predicted probability and the actual probability in the two datasets ($P = 0.987$, $P = 0.310$). Decision curve analysis showed that in the training set, the net benefit curve of the prediction model was above the extreme reference lines in the threshold probability range of 0.35–0.86. In the validation set, the net benefit curve of the prediction

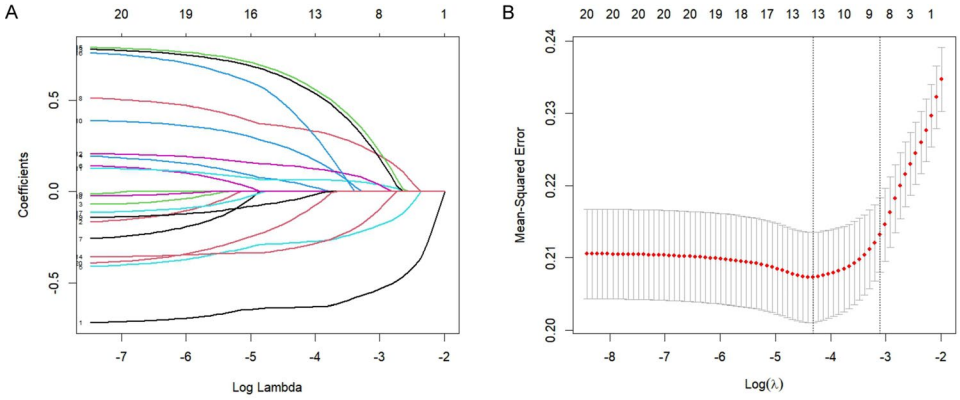

Fig. 2 Lasso regression analysis of variables associated with postoperative complications. (**A**) Dynamic variation of Lasso regression coefficients, (**B**) Tenfold cross-validation for LASSO model parameter adjustment using Lambda.1se criteria. Lasso, Least absolute shrinkage and seletion operator; MSE, Mean-squared error

Table 4 Multivariate Logistic regression analysis for postoperative complications

Variables	OR (95% CI)	*P* value
PNI		
≤ 46.73	Ref.	
> 46.73	0.49 (0.33–0.73)	< 0.001
FAR		
≤ 10.77	Ref.	
> 10.77	1.60 (1.08–2.38)	0.019
LMR		
≤ 3.70	Ref.	
> 3.70	0.68 (0.47–0.99)	0.044
Hydrothorax		
No	Ref.	
Yes	2.60 (1.33–5.06)	0.005
Surgery methods		
Laparotomy	Ref.	
Laparoscopy	0.59 (0.39–0.88)	0.010
Enterectomy		
No	Ref.	
Yes	2.5 (1.42–4.40)	0.001

FAR, Fibrinogen to albumin ratio; LMR, Lymphocyte to monocyte ratio; PNI, Prognostic nutritional index

model was above the extreme reference lines in the threshold probability range of 0.25–0.93. These findings demonstrated that the nomogram had a greater clinical net benefit compared to "None" or "All" in a wide range of threshold probabilities.

Discussion

Based on the factors associated with postoperative complications, including preoperative nutritional and inflammatory indicators, this study constructed a prediction model for postoperative complications in EOC patients, which performed well on both the training set and the internal validation set. The independent factors of postoperative complications identified were: PNI > 46.73, FAR > 10.77, LMR > 3.70, hydrothorax, laparoscopy, and enterectomy. By preoperatively evaluating the patient's PNI, FAR, and LMR, the patient's immunonutritional status can be adjusted to minimize the occurrence of postoperative complications. This predictive model facilitates the early identification of those at high risk for postoperative complications and their focused monitoring and preventive interventions, thereby guiding the surgical treatment and postoperative care of patients.

Surgery combined with platinum-containing chemotherapy is an important therapeutic strategy for EOC and significantly prolongs the survival of patients. However, due to extensive surgery and poor nutritional status of patients, the incidence of postoperative complications in ovarian cancer patients is comparatively high. Previous studies have reported that the incidence of postoperative complications in patients with ovarian cancer could be as high as 70-80%, with the incidence of serious complications (grades III-V) ranging from 7 to 38% and the mortality rate ranging from 1.8-8.2% [24–26]. In our study, the incidence of postoperative complications among the 922 EOC patients included was 61.3%, with a grade III-V complication rate of 6.4%. In the group of patients with postoperative complications, more than half (55.8%) had two or more complications. Compared with previous studies, the incidence of severe postoperative complications of EOC patients in this study was relatively low. This might be attributed to the fact that the patients included in this study were from tertiary hospitals in China, where the quality of surgical care and postoperative management might be better.

Postoperative complications not only prolong hospitalization, increase medical costs, and reduce patients' quality of life, but even affect patients' subsequent chemotherapy and prognosis [27]. Angeles et al.. revealed that disease-free survival (DFS) decreased significantly with the occurrence of severe postoperative

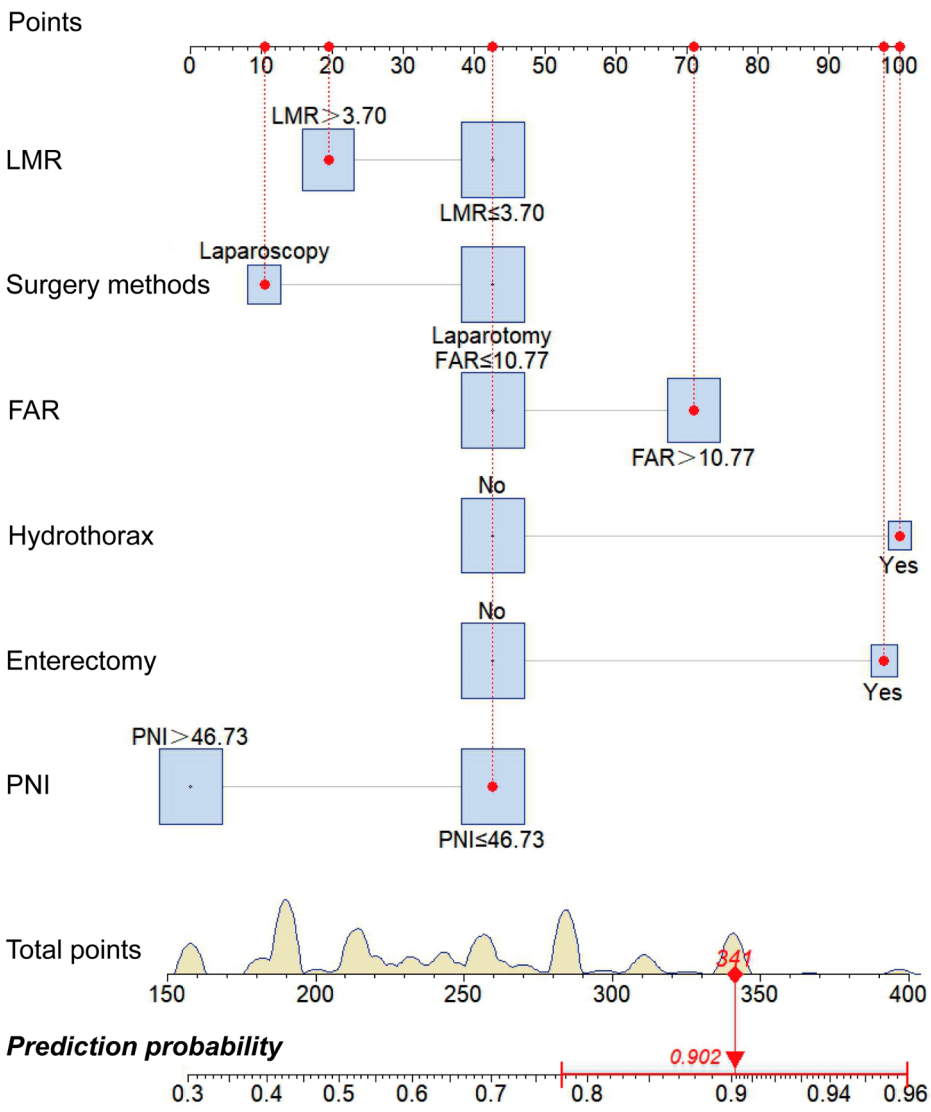

Fig. 3 The nomogram for predicting the risk of postoperative complications. FAR, Fibrinogen to albumin ratio; LMR, Lymphocyte to monocyte ratio; PNI, Prognostic nutritional index

complications, especially in patients who underwent initial tumor cytoreduction [26]. Similarly, findings from a study conducted by Wright et al.. involving nearly 4,000 women diagnosed with advanced ovarian cancer who underwent tumor cytoreduction, showed that postoperative complications resulted in delays in chemotherapy and significantly decreased PFS [28]. Moreover, Wright et al.. indicated that experiencing two or more significant perioperative complications raised the mortality risk in ovarian cancer patients [28]. Another study that included 5,223 patients with advanced EOC ovaries indicated that the 1-year overall and cancer-specific survival rates were significantly lower in the group with postoperative complications compared to the group without postoperative complications [5]. The results of our study also showed that EOC patients with postoperative complications had a significantly longer postoperative hospitalization and significantly shorter PFS and OS compared with EOC patients without postoperative complications. Therefore, minimizing postoperative complications is crucial for improving both short-term and long-term survival outcomes of ovarian cancer patients.

Previous studies have investigated factors affecting postoperative complications in ovarian cancer patients, such as age, the timing of surgery, and surgical procedure, but have placed limited focus on the impact of immunonutritional status. Although few studies have specifically addressed the effect of immunonutritional status on postoperative complications in ovarian cancer, immunonutritional status has been found to predict postoperative complications in patients with other types of cancer. For instance, in esophageal cancer, PNI was an independent

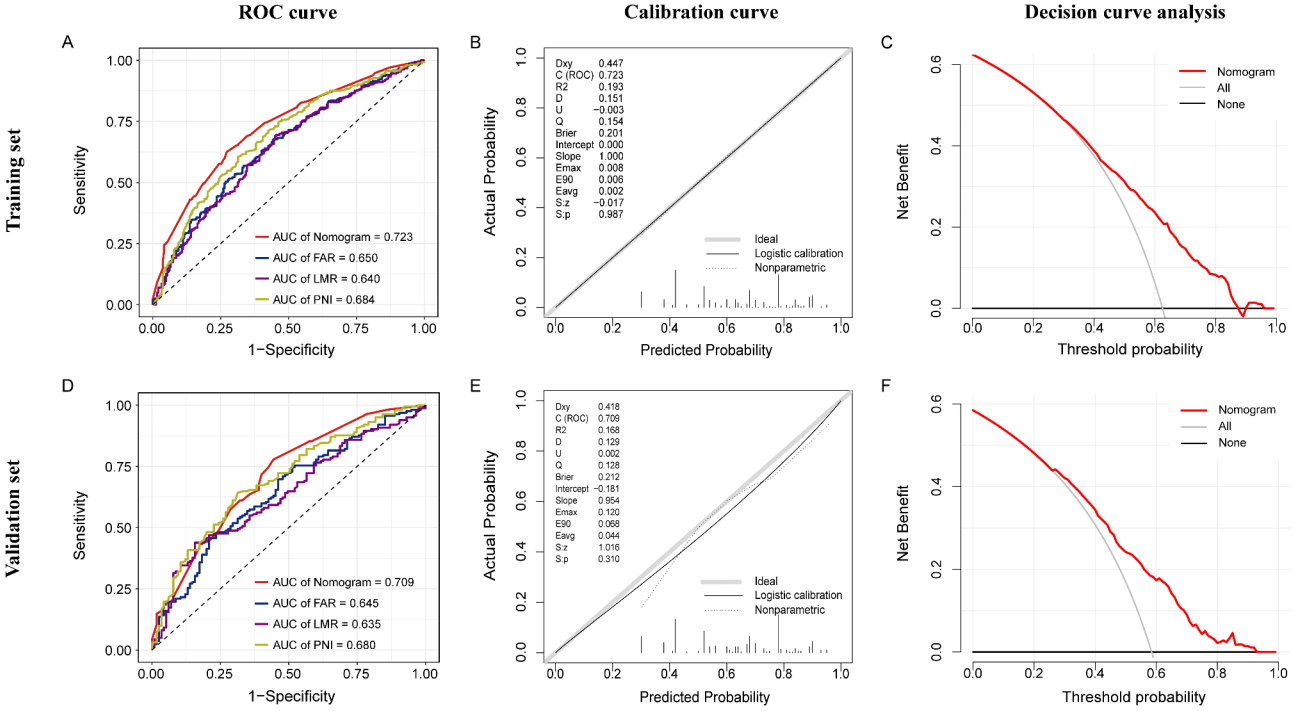

Fig. 4 Evaluation of the prediction model in the training and validation sets. (**A**) Receiver operating characteristic (ROC) curve for the training set, (**B**) Calibration curve for the training set, (**C**) Decision curve analysis (DCA) for the training set, (**D**) ROC curve for the internal validation set, (**E**) Calibration curve for the internal validation set, (**F**) DCA for the internal validation set

predictor of postoperative complications after adjusting for other clinicopathologic factors ($P = 0.008$), with a higher rate of grade II-IV complications in the lower PNI group [29]. Similarly, the PNI score was a crucial independent predictor of postoperative complications in patients with head and neck cancer undergoing surgical resection [30]. In addition, PNI, CONUT, and SII were found to be independent risk factors for postoperative complications in stage II-III colorectal cancer [17, 31]. In a study including 369 lung cancer patients, SII was the inflammatory marker most strongly associated with postoperative venous thromboembolism in lung cancer patients [32]. These studies demonstrated that immunonutritional status could affect the development and progression of postoperative complications. In patients with ovarian cancer, Christine et al. found a higher rate of postoperative complications in patients with a CONUT score > 2 than in patients with a score of 0–2 (60.5% vs. 51.4%) [33]. In our study, we found that PNI, FAR, and LMR were independent risk factors for postoperative complications in ovarian cancer patients. Furthermore, we developed a risk prediction model for postoperative complications in ovarian cancer patients to predict the probability of postoperative complications based on preoperative immunonutritional status. The administration of preoperative immunonutrition to ovarian cancer patients at risk of malnutrition improved postoperative outcomes and reduced postoperative complications, with a rise in CD3 + CD8 + cytotoxic T lymphocytes following immunonutrition [6]. Nutritional interventions seemed to shorten hospitalization, and bowel recovery time, and reduce postoperative complications [34].

Age is a significant factor in postoperative complications. In our study, we found an increased risk of postoperative complications in women older than 53 years (OR = 1.38, $P = 0.049$). Aging enhances the physiological stress of surgery, resulting in longer recovery times and higher complication rates [35]. Age primarily influences physiological surgical stress through nutrition and immunity. Aging impacts dietary needs and diminishes the body's capacity to absorb and utilize nutrients effectively, making older adults more vulnerable to malnutrition and elevating the risk of postoperative complication [36]. Furthermore, frailty, immune senescence and reduced physiologic reserves associated with aging augment the risk of postoperative infections [35]. Targeted nutritional and immunonutritional interventions can enhance surgical outcomes for the elderly, reducing postoperative mortality, morbidity, length of stay, readmission rates, and healthcare costs [35]. Well-nourished patients are three times less likely to experience postoperative complications and have a fivefold lower risk of death compared to malnourished patients [37]. Therefore, personalized nutrient supplementation given at the right time is essential to improve postoperative recovery and prognosis in elderly cancer patients. In the future, we

need to explore the optimal timing, duration, and composition of immune nutrient supplementation for individualized and precise nutrient treatments. Integration of biomarkers and personalized assessments may also help assess preoperative frailty and immunonutritional status. New technologies (e.g., artificial intelligence for risk stratification, wearable devices for continuous monitoring) may provide new ways to enhance surgical care for older patients.

To the best of our knowledge, this is the largest multicenter study investigating the effect of immunonutritional status on postoperative complications in ovarian cancer patients. Moreover, we formulated a risk prediction model for postoperative complications based on preoperative immunonutritional status in EOC patients, which performed well on both the training set and the internal validation set. This study also has several limitations. While this study represents the largest multicenter investigation into the effect of immunonutritional status on postoperative complications in ovarian cancer patients, the inclusion of only 922 patients necessitates additional large-scale randomized controlled studies to comprehensively elucidate the predictive value of immunonutritional status. The risk prediction model constructed in this study was not validated in an external validation set. Further validation of its effects in other settings is necessary.

Conclusion

In conclusion, we demonstrated the effect of immunonutritional status on postoperative complications and formulated a validated risk prediction model for postoperative complications based on preoperative immunonutritional status in ovarian cancer patients. By forecasting the probability of postoperative complications using preoperative immunonutritional status, clinicians could promptly ameliorate the preoperative immunonutritional status of ovarian cancer patients, consequently lowering the incidence of postoperative complications and improving the prognosis.

Abbreviations

AUC	Area under the curve
CI	Confidence interval
CONUT	Controlling nutritional status score
DCA	Decision curve analysis
EOC	Epithelial ovarian cancer
FIGO	International Federation of Gynecology and Obstetrics
HR	Hazard ratio
NLR	Neutrophil to Lymphocyte ratio
PLR	Platelet to Lymphocyte ratio
LMR	Lymphocyte to Monocyte ratio
TCLR	Total cholesterol to Lymphocyte ratio
FLR	Fibrinogen to Lymphocyte ratio
FAR	Fibrinogen to Albumin ratio
IQR	Interquartile range
PNI	Prognostic nutritional index
PFS	Progression-free survival
SII	Systemic immune-inflammation index
OS	Overall survival
ROC	Receiver operating characteristic

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13048-025-01624-3.

Supplementary Material 1: Additional file 1. Supplementary Table S1. List of Study Sites. Supplementary Table S2. Controlling nutritional status (CONUT) Scoring system. Supplementary Table S3. Homogeneity test between the training and validation sets.

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Not applicable.

Author contributions

XY.L. and M.L. developed the study concept and performed data analysis. YJ.Z, XF.J, and Y.Y. assisted in data collection and data crosscheck. RY.L, SQ.Z, JH.C, GC.M, YB.H, ZK.P, and JH.L. assisted in literature searching and information collection. Q.Z, DL.Z, L.W, QS.L, J.W, SZ.Y, YG.C. and D.M. were responsible for project administration. XY.L. and M.L. drafted the manuscript. QL.G. and T.H. were responsible for the supervision of the study, and revised this manuscript. All authors read and approved the final manuscript.

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Data availability

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

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Commission of Tongji Medical College of Huazhong University of Science and Technology (TJ-IRB202401053) and the consent was waived.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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