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The impact of preoperative immunonutritional status on prognosis in ovarian cancer: a multicenter real-world study

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Abstract

Background To investigate the effect of preoperative immunonutritional status on prognosis in epithelial ovarian cancer patients.

Methods A multicenter real-world study included 922 patients with histologically confirmed epithelial ovarian cancer who received comprehensive staged surgery or debulking surgery at seven tertiary hospitals in China between 2012 and 2023. Prognostic nutritional index (PNI) and systemic immune-inflammation index (SII) were used to assess the immunonutritional status for their superior predictive power to indicate the nutritional status and the inflammatory immunity. Cox regression analyses were employed to identify variables associated with progression-free survival (PFS) and overall survival (OS).

Results In the early-stage cohort of 224 epithelial ovarian cancer patients, the optimal cut-off value for PNI was 47.47 for both PFS and OS, while the optimal cut-off value for SII values were 551.37 for PFS and 771.78 for OS. In the late-stage group of 698 patients, the optimal PNI thresholds were 47.76 for PFS and 46.00 for OS, with SII values of 720.96 for PFS and 1686.11 for OS. In multivariate analysis of early-stage patients, high PNI was an independent protective factor for PFS (hazard ratio (HR), 0.39 (95% confidence interval (CI) 0.20–0.76), $P=0.006$) and OS (HR, 0.44 (95% CI 0.20–0.97), $P=0.042$), respectively. High SII was significantly associated with PFS (HR, 2.43 (95% CI 1.23–4.81), $P=0.011$) and marginally unfavorable for OS (HR, 2.05 (95% CI 0.96–4.39), $P=0.064$). In advanced population, PNI (HR, 0.77 (95% CI 0.60–0.99), $P=0.043$) and SII (HR, 1.34 (95% CI 1.01–1.78), $P=0.041$) were independent prognostic factors for OS but had no impact on PFS ($P=0.185$, $P=0.188$, respectively).

Conclusion Poor preoperative immunonutritional status has a deleterious effect on the prognosis of patients with ovarian cancer. Intervention in patients suffering from suboptimal preoperative immunonutritional status may facilitate improved survival outcomes.

Keywords Ovarian cancer, Preoperative immunonutritional status, Prognostic nutritional index, Systemic immune-inflammation index, Progression-free survival, Overall survival

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Background

As the most lethal gynecologic cancer, ovarian cancer is the eighth most common cancer among women with approximately 324,398 new cases and 206,839 deaths globally in 2022 [1]. Given the concealed position of the ovaries, coupled with early symptoms often being mild or atypical, and the absence of efficient techniques for early screening and diagnosis, approximately 70% of patients with ovarian cancer are diagnosed at advanced stages [2]. Despite significant advances in the treatment of ovarian cancer, the 5-year overall survival rate remains less than 50% due to high recurrence rates and susceptibility to chemotherapy resistance [3, 4]. Therefore, there is an urgent need to evaluate potential prognostic indicators to guide treatment strategies and to identify patients at high risk of recurrence and death.

In addition to clinicopathologic and therapeutic factors, immunonutritional status is a key host factor influencing the prognosis of patients with ovarian cancer [4]. Up to 70% of ovarian cancer patients, especially those in advanced stages, experience malnutrition attributed to factors such as the high catabolic state, malignant intestinal obstruction, and loss of appetite [5–7]. Malnutrition suppresses the immune response, increases the risk of postoperative infection, diminishes tolerance to chemotherapy, and exacerbates survival [8–10]. The prognostic nutritional index (PNI), a composite index based on serum albumin concentration and peripheral blood lymphocyte count, is significantly associated with the prognosis of ovarian cancer patients [11, 12]. Furthermore, the systemic inflammatory response, a hallmark of cancer, is instrumental in the development and progression of cancer. It promotes tumor survival, proliferation, invasion, metastasis, and angiogenesis and enhance the risk of chemotherapy resistance in cancer patients [13, 14]. High neutrophil, monocyte, and platelet counts in peripheral blood are associated with poor prognosis [15, 16], whereas low lymphocyte counts are associated with reduced antitumor response and decreased survival [17]. High values of Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte ratio, and Systemic Immune-Inflammation Index (SII) indicate the immunosuppression and correlate with higher tumor aggressiveness and poorer overall prognosis of the patients [18, 19]. Therefore, the preoperative immunonutritional status remarkably affects prognosis.

Previous studies explored the association between these indicators and the prognosis of ovarian cancer patients, with the majority being small-sample, single-center studies [11, 12, 20, 21]. Larger sample sizes and multicenter studies are warranted to demonstrate the effect of preoperative immunonutritional status on prognosis. Additionally, most studies only investigated the effect of nutritional status or inflammation on prognosis, rather than comprehensively investigating the influence of immunonutritional status on survival outcomes. In this study, we aim to investigate the effect of preoperative immunonutritional status on prognosis in ovarian cancer patients with multicenter data derived from China Real World Gynecologic Oncology Platform.

Methods and materials

Patients selection and data collection

Our study enrolled patients with ovarian cancer diagnosed at seven tertiary medical centers (as shown in Supplementary Table S1) between January 2012 and February 2023 from the China Real World Gynecologic Oncology Platform (NUWA). The inclusion criteria of patients comprised: (1) primary epithelial ovarian, peritoneal, and fallopian tube cancers diagnosed by pathologic examination; (2) underwent comprehensive surgery staging or primary debulking surgery; (3) available data of routine blood count and albumin within 7 days before surgery; (4) available prognosis data. The exclusion criteria included: (1) borderline tumor; (2) presence of diseases that interfere with laboratory examination results, such as hepatitis, nephropathy, autoimmune diseases, infectious diseases, and hematologic dysfunction; (3) multiple primary malignant neoplasms; (4) multiple cytoreductive surgeries.

The demographic information, clinicopathological characteristics, first-line treatment, and prognostic information were obtained from the medical and follow-up records. Peripheral blood cells, serum albumin, and carbohydrate antigen 125 (CA125) were extracted from patients' laboratory examinations within 7 days before the surgery. Given the superior predictive power of PNI and SII to indicate the nutritional status and the inflammatory immunity [19, 22], we opted to assess the immuno-nutritional status of patients using both PNI and SII. PNI and SII were calculated as follows:

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

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

In this study, family history of cancer was defined as malignant tumors in first-degree relatives of patients [23]. Comorbidities mainly included hypertension, chronic respiratory disease, hyperthyroidism and hypothyroidism. Postoperative residual lesions are categorized into R0, R1 and R2 in accordance with their size [24]. No visual residual lesions were classified into R0, residual lesions ≤ 1 cm were classified into R1, and residual lesions > 1 cm were classified into R2. Progression-free survival (PFS) was the time from diagnosis to recurrence, progression, death, or last follow-up, whichever comes first. Overall survival (OS) was the time from diagnosis to death from any cause or last follow-up.

An ethical approval for this study was obtained from the Medical Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (TJ-IRB202401053). As a real-world retrospective study, a waiver of informed consent was requested, and the results were used for scientific research only.

Statistical analysis

Median and interquartile range (IQR) were utilized to describe the distribution of continuous variables, while frequency counts and percentages were used to describe the distribution of categorical variables. The comparison of continuous variables was performed using the Mann–Whitney U test, whereas the comparison of categorical variables was performed by chi-square test and Fisher's exact test. Kaplan–Meier (K-M) survival curve and Cox proportional hazards model (hazard ratio (HR) and 95% confidence interval (CI)) were used for prognosis analysis.

The R package "survminer" was used to determine the optimal cut-off values of PNI and SII related to PFS or OS. The fundamental principle is based on K-M survival curve and Log-rank test to determine the point with the smallest *P* value, then the value corresponding to that point is the optimal cut-off value.

A two-tailed *P* value < 0.05 was considered statistically significant. All statistical analysis was performed using R version 4.2.1.

Results

Clinical characteristics of patients

A total of 922 patients diagnosed with epithelial ovarian cancer were ultimately enrolled in this study (Fig. 1). The median age at diagnosis was 52 (IQR, 47, 59) years of the 922 patients (Table 1). The median value was 45.9 (40.8, 49.9) for PNI, and 873.6 (559.3, 1421.3) for SII, respectively. Notably, 597 patients (64.8%) were diagnosed with high-grade serous ovarian carcinoma, while 599 patients (65.0%) presented with International Federation of Gynecology and Obstetrics (FIGO) stage III

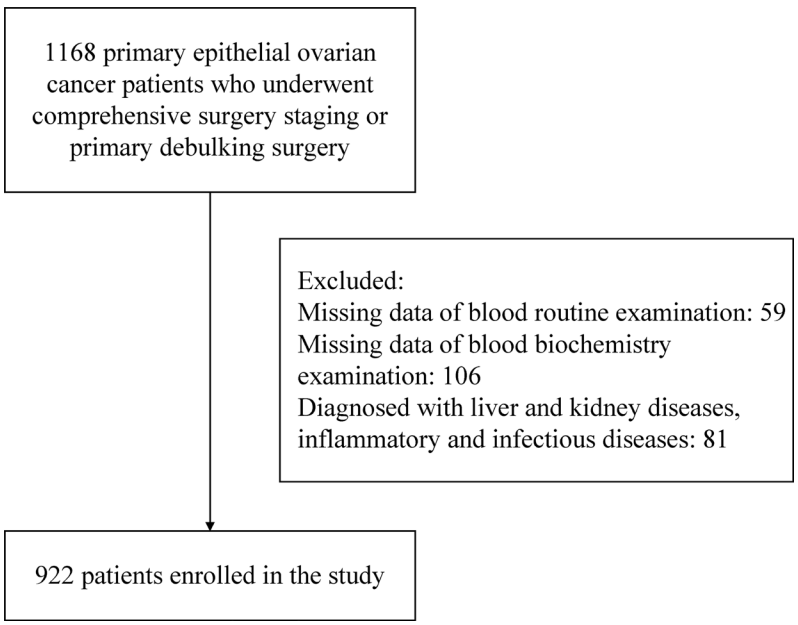

Fig. 1 Flow chart of patient inclusion and exclusion

Table 1 Clinical characteristics of patients

	Population ($N=922$)
Age at diagnosis (years), median (IQR)	52 (47, 59)
PNI, median (IQR)	45.9 (40.8, 49.9)
SII, median (IQR)	768.3 (486.2, 1260.1)
CA125 (U/mL), median (IQR)	584.2 (168.4, 1398.0)
BMI (kg/m2), median (IQR)	22.0 (20.3, 24.1)
Histology	
High-grade serous carcinoma	597 (64.8)
Low-grade serous carcinoma	28 (3.0)
Endometrioid carcinoma	73 (7.9)
Mucinous carcinoma	81 (8.8)
Ovarian clear cell carcinoma	80 (8.7)
Others	63 (6.8)
FIGO stage	
I	191 (20.7)
II	132 (14.3)
III	518 (56.2)
IV	81 (8.8)
FIGO stage	
I-IIA	224 (24.3)
IIB-IV	698 (75.7)
Tumor laterality	
Unilateral	405 (43.9)
Bilateral	517 (56.1)
Ascites	
No	254 (27.5)
Yes	668 (72.5)
Hydrothorax	
No	807 (87.5)
Yes	115 (12.5)
Menopause	
No	394 (42.7)
Yes	528 (57.3)
Comorbidities	
No	775 (84.1)
Yes	147 (15.9)
Family history of cancer	
No	775 (84.1)
Yes	147 (15.9)
Surgery methods	
Laparotomy	721 (78.2)
Laparoscopy	201 (21.8)
Lymphadenectomy	
No	236 (25.6)
Yes	686 (74.4)
Lymph node metastasis	
Negative	443 (64.6)
Positive	243 (35.4)
Residual disease	
R0	478 (51.8)
R1	272 (29.5)
R2	172 (18.7)
Postoperative chemotherapy	
No	82 (8.9)
Yes	840 (91.1)
Chemotherapy cycle	
<6	394 (42.7)
≥ 6	528 (57.3)
PARP inhibitors	
No	912 (98.9)
Yes	10 (1.1)
Bevacizumab	
No	918 (99.6)
Yes	4 (0.4)

BMI Body mass index, *FIGO* International Federation of Gynecology and Obstetrics, *IQR* Interquartile range, *PARP* Poly ADP-ribose Polymerase, *PFI* Platinum-free interval, *PNI* Prognostic nutritional index, *SII* Systemic immune-inflammation index

or IV disease. Lymphadenectomy was performed in 686 (74.4%) patients, with 243 (35.4%) patients showing lymph node metastasis. Additionally, 750 (81.3%) patients achieved optimal tumor resection. Only 10 (1.1%) patients received Poly ADP-ribose Polymerase inhibitors (PARPi), and 4 (0.4%) patients were treated with bevacizumab.

Cut-off values of PNI and SII

The optimal cut-off values of PNI and SII relative to PFS and OS were determined for the early (FIGO stage I-IIA) and advanced (FIGO stage IIB-IV) patients, respectively. As displayed in Table 2, for the early stage patients (224 individuals), the optimal cut-off values of PNI relative to PFS and OS were both 47.47, and the optimal cut-off values of SII relative to PFS and OS were 551.37 and 771.78, respectively. In the advanced stage cohort (698 individuals), the optimal cut-off value of PNI was 47.76 relative to PFS and 46.00 relative to OS. The optimal cut-off value for SII was 720.96 relative to PFS and 1686.11 relative to OS.

Prognosis analysis

The median follow-up time was 55.1 months. Patients were categorized into high and low index groups

Table 2 The cut-off value of PNI and SII

	Cut-off value for PFS		Cut-off value for OS	
	Early stage	Advanced stage	Early stage	Advanced stage
PNI	47.47	47.76	47.47	46.00
SII	551.37	720.96	771.78	1686.11

PNI Prognostic Nutritional Index, *SII* Systemic immune-inflammation index

according to the cut-off values of PNI and SII. K-M survival curves indicated that the both median PFS and OS were significantly longer in the high PNI group and low SII group (all $P<0.01$), regardless of stage (Fig. 2).

Then, we performed univariate and multivariate Cox regression analysis to identify the factors influencing the PFS and OS in both early- and advanced-stage patients. As presented in Table 3, the univariate analysis for early-stage patients revealed that both PNI and SII were significantly associated with PFS, while PNI, SII, and comorbidities were significantly associated with OS. In multivariate analysis, after controlling for confounders, high PNI was an independent protective factor for PFS (HR (95% CI) = 0.39 (0.20–0.76), $P=0.006$) and OS (HR (95% CI) = 0.44 (0.20–0.97), $P=0.042$), respectively. High SII was an independent risk factor for PFS (HR (95% CI) = 2.43 (1.23–4.81), $P=0.011$) and was a marginally unfavorable prognostic factor for OS (HR (95% CI) = 2.05 (0.96–4.39), $P=0.064$).

In advanced population, univariate analysis indicated that PNI, SII, histology, stage, lymphadenectomy, and residual disease were significantly associated with both PFS and OS (all $P<0.05$, Table 4)). However, in multivariate analysis, PNI and SII had no impact on PFS ($P=0.185$, $P=0.188$, respectively). Both PNI (HR (95% CI) = 0.77 (0.60–0.99), $P=0.043$) and SII (HR (95% CI) = 1.34 (1.01–1.78), $P=0.041$) were independent prognostic factors for OS. Besides, histology, stage, and residual disease were associated with PFS and OS (all $P<0.001$).

Discussion

In this study, we comprehensively investigate the effect of preoperative immunonutritional status on prognosis in ovarian cancer patients, including both PNI and SII. PNI and SII were both independent prognostic factors for PFS and OS in the early-stage patients (FIGO stage I-IIA). In advanced cohort (FIGO stage IIB-IV), PNI and SII were significantly associated with OS but had no impact on PFS. Overall, preoperative immunonutritional status independently affects the prognosis of patients with ovarian cancer. Intervention in patients suffering from suboptimal preoperative immunonutritional status facilitates improved survival outcomes.

Recently, there has been a growing interest in the association between preoperative nutritional indicators and the prognostic outcomes of various cancers [25–27]. Malnutrition associated with cancer is usually driven by the activation of systemic inflammation triggered by tumor advancement, which in turn compromises immune function and diminishes overall survival [28]. In addition, patients with advanced ovarian cancer often develop malnutrition associated with intestinal obstruction caused by peritoneal dissemination [29]. As a powerful nutritional indicator, PNI was observed to be significantly associated with prognosis in several ovarian cancer studies. Miao et al. found a significant association between PNI and PFS (HR 1.890, 95% CI: 1.396–2.560; $P<0.001$) as well as OS (HR 1.747, 95% CI: 1.293–2.360; $P<0.001$) in 344 epithelial ovarian cancer patients [25]. Subsequently, Zhang et al. indicated that PNI was an independent prognostic factor for PFS (HR 2.10, 95% CI: 1.38–3.19; $P=0.001$) and OS (HR 2.54, 95% CI: 1.76–3.68; $P<0.001$) in stage III ovarian cancer [22]. These findings are consistent with the results of our study. In patients with high-grade serous ovarian cancer, a continuous decrease in PNI significantly correlated with impaired OS ($P=0.021$), whereas a dichotomous decrease did not ($P=0.346$) [11]. The predictive effect of PNI on prognosis seems to differ in early and advanced ovarian cancer. Decreased PNI did not adversely impact PFS or disease-specific survival (DSS) in early-stage patients, but was significantly associated with an inferior PFS ($P<0.0001$) and DSS ($P<0.0001$) in advanced-stage patients [30]. However, Yoshikawa et al. revealed that high PNI had a significant independent favorable impact on OS ($P=0.010$) but was not correlated with PFS ($P=0.220$) in patients with early-stage ovarian clear cell carcinoma [31]. In our study, we found that increased PNI was not associated with longer PFS in early-stage patients but with longer OS, which is compatible with the findings of the previous study. Interestingly, further analyses found that the high PNI group had a significantly longer post relapse survival than in the PNI-low group [31]. These indicated that PNI was more likely to reflect susceptibility to treatment than to predict

(See figure on next page.)

Fig. 2 Kaplan–Meier (K-M) survival curve analysis. **A** K-M survival curves of PFS between the high and low PNI subgroups in early patients. **B** K-M survival curves of PFS between the high and low PNI subgroups in advanced patients. **C** K-M survival curves of OS between the high and low PNI subgroups in early patients. **D** K-M survival curves of OS between the high and low PNI subgroups in advanced patients. **E** K-M survival curves of PFS between the high and low SII subgroups in early patients. **F** K-M survival curves of PFS between the high and low SII subgroups in advanced patients. **G** K-M survival curves of OS between the high and low SII subgroups in early patients. **H** K-M survival curves of OS between the high and low SII subgroups in advanced patients. OS, Overall survival; PFS, Progression-free survival; PNI, Prognostic Nutritional Index; SII, Systemic immune-inflammation index

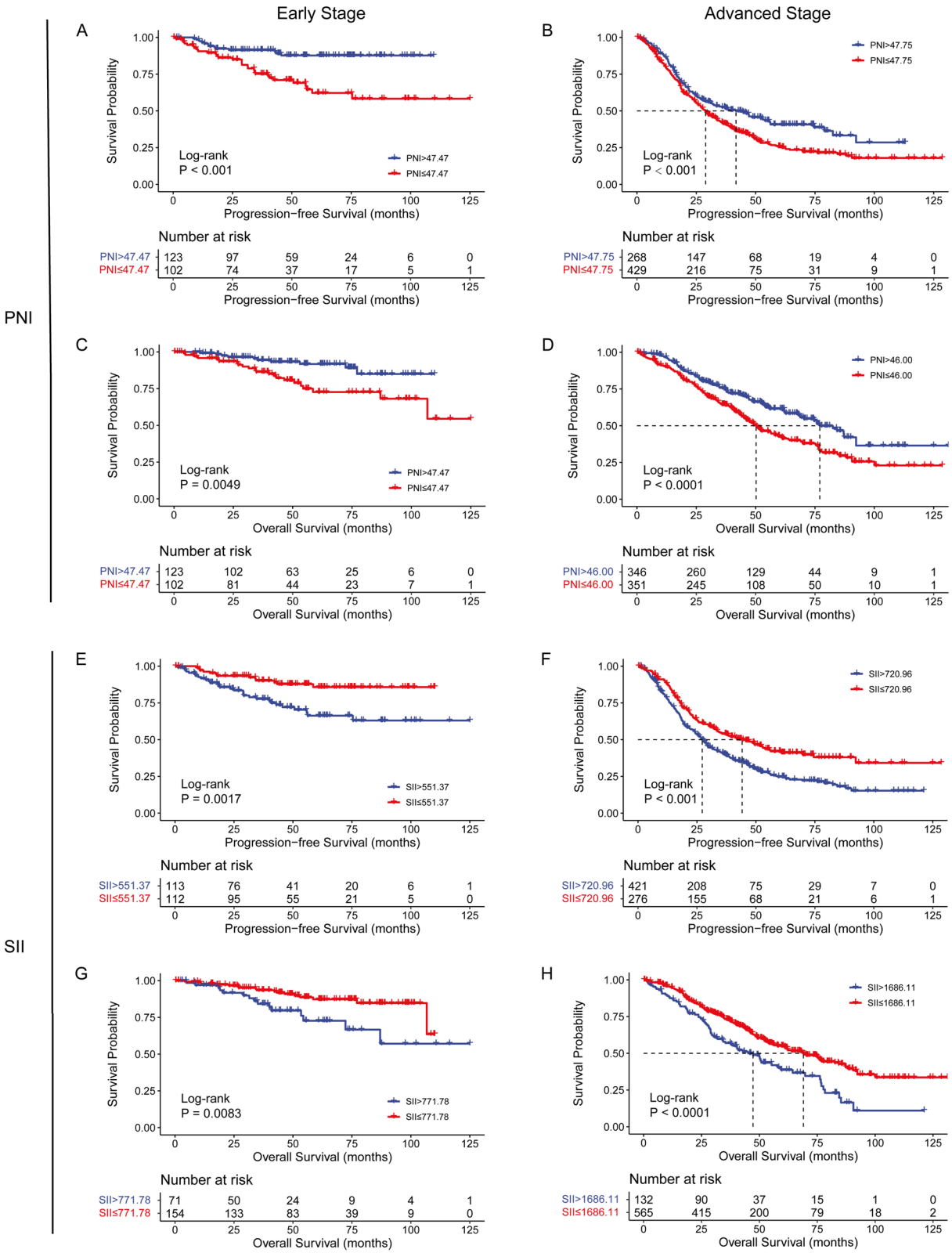

Fig. 2 (See legend on previous page.)

Table 3 Univariate and multivariate Cox regression analysis for PFS and OS in early stage epithelial ovarian patients

	PFS				OS			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age								
≤ 53	Ref		Ref		Ref		Ref	
> 53	1.31 (0.72–2.39)	0.372	0.95 (0.48–1.90)	0.895	1.61 (0.80–3.22)	0.180	1.47 (0.67–3.22)	0.335
PNI								
Low	Ref		Ref		Ref		Ref	
High	0.31 (0.16–0.59)	< 0.001	0.39 (0.20–0.76)	0.006	0.36 (0.17–0.76)	0.007	0.44 (0.20–0.97)	0.042
SII								
Low	Ref		Ref		Ref		Ref	
High	2.72 (1.42–5.22)	0.003	2.43 (1.23–4.81)	0.011	2.43 (1.21–4.89)	0.013	2.05 (0.96–4.39)	0.064
Histology								
HGSC	Ref		Ref		Ref		Ref	
Others	0.71 (0.38–1.36)	0.304	0.71 (0.35–1.42)	0.335	1.08 (0.49–2.42)	0.843	1.27 (0.52–3.08)	0.599
FIGO stage								
I	Ref		Ref		Ref		Ref	
IIA	1.42 (0.66–3.07)	0.371	1.26 (0.56–2.84)	0.570	1.57 (0.68–3.64)	0.295	1.34 (0.55–3.26)	0.520
Comorbidities								
No	Ref		Ref		Ref		Ref	
Yes	1.77 (0.89–3.52)	0.101	1.63 (0.75–3.56)	0.217	2.39 (1.13–5.07)	0.022	2.13 (0.94–4.83)	0.071
Family history of cancer								
No	Ref		Ref		Ref		Ref	
Yes	0.84 (0.33–2.13)	0.713	0.58 (0.22–1.53)	0.268	0.68 (0.21–2.24)	0.525	0.58 (0.17–1.96)	0.379
Lymphadenectomy								
No	Ref		Ref		Ref		Ref	
Yes	0.50 (0.25–1.03)	0.059	0.63 (0.28–1.38)	0.244	0.51 (0.24–1.05)	0.068	0.59 (0.28–1.25)	0.170

PNI Prognostic Nutritional Index, *SII* Systemic immune-inflammation index, *FIGO* International Federation of Gynecology and Obstetrics, *HGSC* High-grade serous carcinoma

time to relapse. The observation that decreased PNI effectively predicted platinum resistance further substantiates this viewpoint [22, 25].

In addition to preoperative nutritional status, inflammatory and related cells are vital to cancer formation and progression, thus affecting the survival outcomes. Inflammatory cells secrete cytokines and chemokines, stimulate angiogenesis and proliferation, and promote metastasis [13]. High SII (including neutrophil, platelet, and lymphocyte counts), was observed to be related to higher levels of circulating tumor cells in the cancer patients, suggesting an increased risk of metastasis and recurrence [32]. In study by Nie et al., they revealed that high SII was an independent risk factor for PFS (HR 7.61(95% CI 3.34–17.35), $P<0.001$) and OS (HR 6.36(95% CI 2.64–15.33), $P<0.001$) [19]. This study did not differentiate between early and late-stage SII, nor did it separate SII based on PFS and OS, applying a uniform SII across all populations. In early-stage ovarian cancer (stage I-IIIA1), increased SII was associated with worse disease-free survival (DFS) and OS [33]. However, Borella et al. found a significantly negative association between high SII and DFS (HR 6.84 (95% CI 1.30–35.9), $P=0.023$), but no association between high SII and DSS in stage I epithelial ovarian cancer [21]. In our study, SII were both independent prognostic factors for PFS and OS in the early-stage patients (FIGO stage I-IIA). Differences in results among early-stage patients may be due to inconsistencies in the included populations. In advanced cohort (FIGO stage IIB-IV), we found that PNI and SII were significantly associated with OS but had no impact on PFS. Unfortunately, we have not found any study on the efficacy of SII in patients with advanced ovarian disease. Beyond the primary treatment population, elevated SII was also an independent risk factor for prognosis in patients with platinum-sensitive recurrent epithelial ovarian cancer [34]. Moreover, SII has been identified as a predictor of the therapeutic efficacy of neoadjuvant chemotherapy and bevacizumab. High SII was a predictor of inefficacy of neoadjuvant chemotherapy and a risk

Table 4 Univariate and multivariate Cox regression analysis for PFS and OS in advanced stage epithelial ovarian patients

	PFS				OS			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age								
≤ 53	Ref		Ref		Ref		Ref	
> 53	0.88 (0.73–1.06)	0.181	0.91 (0.75–1.11)	0.366	1.04 (0.83–1.29)	0.758	1.09 (0.86–1.39)	0.475
PNI								
Low	Ref		Ref		Ref		Ref	
High	0.71 (0.58–0.87)	< 0.001	0.87 (0.70–1.07)	0.185	0.62 (0.50–0.78)	< 0.001	0.77 (0.60–0.99)	0.043
SII								
Low	Ref		Ref		Ref		Ref	
High	1.56 (1.27–1.90)	< 0.001	1.16 (0.93–1.43)	0.188	1.66 (1.29–2.15)	< 0.001	1.34 (1.01–1.78)	0.041
Stage								
IIB	Ref		Ref		Ref		Ref	
III	3.40 (2.26–5.10)	< 0.001	3.02 (1.98–4.60)	< 0.001	3.38 (2.01–5.69)	< 0.001	3.17 (1.85–5.44)	< 0.001
IV	3.99 (2.51–6.36)	< 0.001	3.08 (1.90–4.99)	< 0.001	4.49 (2.52–8.01)	< 0.001	3.78 (2.09–6.86)	< 0.001
Histology								
HGSC	Ref		Ref		Ref		Ref	
Others	1.26 (1.01–1.58)	0.040	1.72 (1.37–2.17)	< 0.001	1.46 (1.14–1.88)	0.003	2.03 (1.56–2.64)	< 0.001
Comorbidities								
No	Ref		Ref		Ref		Ref	
Yes	0.86 (0.66–1.12)	0.255	0.98 (0.74–1.29)	0.862	1.10 (0.82–1.47)	0.538	1.31 (0.96–1.79)	0.090
Family history of cancer								
No	Ref		Ref		Ref		Ref	
Yes	0.89 (0.68–1.16)	0.400	0.84 (0.64–1.10)	0.198	0.86 (0.62–1.18)	0.339	0.77 (0.56–1.06)	0.113
Lymphadenectomy								
No	Ref		Ref		Ref		Ref	
Yes	0.58 (0.48–0.71)	< 0.001	0.87 (0.70–1.08)	0.214	0.53 (0.42–0.67)	< 0.001	0.82 (0.64–1.06)	0.134
Residual disease								
R0	Ref		Ref		Ref		Ref	
R1	1.84 (1.44–2.34)	< 0.001	1.69 (1.32–2.16)	< 0.001	2.15 (1.60–2.89)	< 0.001	1.98 (1.46–2.67)	< 0.001
R2	3.22 (2.50–4.13)	< 0.001	2.62 (2.00–3.44)	< 0.001	3.48 (2.56–4.72)	< 0.001	2.85 (2.05–3.94)	< 0.001

PNI Prognostic Nutritional Index, *SII* Systemic immune-inflammation index, *FIGO* International Federation of Gynecology and Obstetrics, *HGSC* High-grade serous carcinoma

factor for death in patients with stage III ovarian cancer [20]. High SII also impaired the efficacy of bevacizumab, resulting in no survival benefit in the chemotherapy plus bevacizumab group compared with the chemotherapy alone group [35].

There are several advantages to our research. To the best of our knowledge, this is the largest multicenter study to comprehensively investigate the effect of preoperative immunonutritional status on prognosis in ovarian cancer patients. The data required for the PNI and SII indices can be easily obtained from routine blood and liver function tests, and both indices are cost-effective, practical, and reliable. Furthermore, PNI and SII are better predictors of nutritional status and inflammatory immunity than other nutritional and immune indicators [19, 22]. Ultimately, the cutoff values for PNI and SII were determined through early-late stratification of PFS and OS, providing a more accurate representation of the immunonutritional status across various populations and enhancing prognostic predictions.

Several limitations in our study should be noted. Our investigation centered on the association between preoperative PNI and SII (baseline PNI and SII) and patient survival outcomes. However, given that cancer progression and recurrence are dynamic, multistage processes, consistently low levels of PNI and high levels of SII may be more robust indicators of poor prognosis. Although our study is the largest multicenter study to

comprehensively investigate the effect of preoperative immunonutritional status on prognosis in ovarian cancer patients, only 922 patients were included in our study. Larger sample sizes are needed to allow for internal validation of cutoff values and to eliminate potential model overfitting. Variations in instruments or kits across hospitals can result in slight differences in laboratory test results, such as routine blood tests. However, since we included all top tertiary hospitals in China, these differences are relatively minor and within acceptable limits. In our study, HGSC patients made up the majority (64.8%), and the survival differences between high and low PNI and SII groups may largely stem from the HGSC patients. Histologic stratification further revealed that these survival differences were present in both HGSC and other histologic types (data not shown), indicating that varying immunonutritional status may affect survival across all histologic types, not just specific ones. Previous studies indicated PNI cutoff values between 42.9 and 50.4 [22, 25, 30, 36] which aligns with the values used in our study. Similarly, SII cutoff values were no greater than 1000 [19, 33, 34], with most of our study's SII cutoff values falling within this range, except for those related to OS in advanced patients. The SII cutoff value for overall survival in advanced patients appears to be high. However, we obtained the same cutoff value using Xtile software, another recognized method for determining optimal survival cutoff values [37–40]. To investigate if the survival difference arises from the unequal group sizes of high and low SII, we analyzed survival using the median SII from the advanced stage population. Significant differences in PFS and OS were observed between high and low SII groups (All $P < 0.05$, data not shown).

Conclusions

In conclusion, Poor preoperative immunonutritional status has a deleterious effect on the prognosis of patients with ovarian cancer. The combination of PNI and SII can be used as simple and useful markers for predicting short-term and long-term survival of ovarian cancer patients. When patients show a poor preoperative immunonutritional status, timely intervention should be implemented to enhance their immunonutritional condition, thereby mitigating adverse prognostic outcomes.

Abbreviations

CI	Confidence interval
DSS	Disease-specific survival
FIGO	International Federation of Gynecology and Obstetrics
HR	Hazard ratio
IQR	Interquartile range
PNI	Prognostic nutritional index
PFS	Progression-free survival
SII	Systemic immune-inflammation index
OS	Overall survival

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13048-025-01607-4.

Supplementary Material 1: Supplementary Table S1. List of Study Sites.

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Not applicable.

Authors' 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, D.M and YG.C 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) in accordance with the Declaration of Helsinki. As a real-world retrospective study, the informed consent was waived, and the results were used for scientific research only.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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