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Article

Multidimensional Analysis of Clinicopathological Features on the Prognosis of Epithelial Ovarian Cancer Patients Who Received Neoadjuvant Chemotherapy

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Simple Summary: As long as the prognosis of epithelial ovarian cancers is poor, estimation of such a mortal disease is very valuable and may direction to the intense of therapy and follow-up.

Abstract: Background/Objectives: Epithelial ovarian cancer (EOC) has one of the highest mortality rates among cancers affecting women. Herein we aimed to describe how to estimate the prognosis for EOC with clinicopathological features. **Methods:** This study included 86 patients with stage III and IV epithelial ovarian cancer who received neoadjuvant chemotherapy and who had been followed up at least one year. Prognostic factors and their impact on survival were evaluated. FIGO staging of the disease, body mass index (BMI), histological subtype, menopause status, ECOG performance status, genetic testing with variations, residual disease, ascites, serum Ca125 levels, platelets, MPV, neutrophils, lymphocytes, monocytes, lymphocyte/monocyte ratio, CRP, protein, LDH levels, albumin, CRP/albumin ratio, modified Glasgow prognostic score (mGPS), prognostic nutritional index (PNI), systemic inflammatory response index (SIRI), systemic inflammation index (SII), pan-immune inflammation value (PIV), relapse status, type and number of neoadjuvant chemotherapy were evaluated. **Results:** The median age of the patients was 60.0 years. Median overall survival (OS) was 55.1±8.7 months and median disease-free survival (DFS) was 36,8±5,0 months. No significant differences in survival were observed based on age, BMI, or menopausal status. However, patients with an ECOG score of 0 had significantly longer OS compared to those with an ECOG score of 1 ($p<0.001$). Inflammatory markers, including the neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), SII, SIRI, PIV, and mGPS, were found to be significant predictors of progression, relapse, and mortality. Elevated NLR, PLR, SII, SIRI, and PIV values were associated with shorter OS and DFS and higher risks of adverse outcomes. In terms of the prediction of the mortality NLR with a cut-off value of 2.37 and SIRI with a cut-off value of 1.72 showed sensitivity of greater than 70%. Patients with lower LMR and poor mGPS also demonstrated worse survival outcomes. **Conclusions:** ECOG score and immune-inflammatory markers are significant prognostic indicators in epithelial ovarian cancer, providing valuable insights for predicting survival and guiding clinical decision-making.

Keywords: epithelial ovarian cancer; prognostic factors; neoadjuvant chemotherapy; immune markers; inflammatory markers; NLR; LMR; SIRI; SII; mGPS

1. Introduction

In 2022, ovarian cancer was responsible for circa 325,000 new cases and 207,000 deaths globally. It is the fifth most common cause of cancer-related mortality among women [1]. The majority (90%) of ovarian cancers originate from epithelial cells, with approximately 75% of cases being diagnosed

at advanced stages [2]. The 5-year survival rate for early-stage ovarian cancer is 90%, but it declines dramatically to 15% for those diagnosed at metastatic disease [3]. It is crucial to identify prognostic factors to gain a deeper understanding of the underlying mechanisms of this fatal disease.

The prognosis of ovarian cancer is primarily determined by disease stage, with additional significant factors including ECOG performance status, age, histological subtype, CA-125 levels, presence of ascites, and the amount of residual tumor after surgery [4,5]. Inflammatory markers, such as neutrophil, lymphocyte, monocyte, and platelet counts, along with CRP, albumin levels, and composite indices like SIRI, SII, mGPS, PIV, and PNI, have been shown to impact survival and overall prognosis.

In cancer pathogenesis, genetic damage induced by the inflammatory process is implicated, with approximately 25% of cancers regarded as developing through this mechanism. During inflammation, the increase in local cytokines, along with the elevated platelet count in the affected area and the active roles of neutrophils, macrophages, and lymphocytes, disrupt the balance between pro-inflammatory and anti-inflammatory responses [6,7]. In the case of ovarian cancer, chronic inflammation caused by repeated ovulation is thought to contribute to carcinogenesis.

This study investigates the effects of these prognostic factors through multidimensional analysis on survival outcomes in patients with advanced-stage ovarian cancer (Stages III and IV) who have undergone neoadjuvant chemotherapy. Due to the comprehensive interactions between the tumor and the host's immune-inflammatory responses, these indicators contribute to accurately predicting the prognosis.

2. Materials and Methods

In this study, the impact of prognostic factors on survival in patients diagnosed with epithelial ovarian cancer who underwent neoadjuvant chemotherapy between 2011 and 2021 at Tepecik Training and Research Hospital, Health Sciences University was examined. This was a retrospective, single-center study employing a cross-sectional sampling approach. Patients who died within one year of follow-up, discontinued follow-up, or had concurrent malignancies were excluded.

The indicator parameters using the formula are as follows:

NLR: neutrophil ($10^9/L$) / lymphocyte ($10^9/L$) ratio

LMR: lymphocyte ($10^9/L$) / monocyte ($10^9/L$) ratio

PLR: platelet ($10^9/L$) / lymphocyte ratio

mGPS (modified glasgow prognostic score): combines the indicators of decreased plasma albumin and elevated CRP

PNI (prognostic nutritional index): serum albumin (g/L) + $0.005 \times$ lymphocyte count (per mm³)

SIRI (systemic inflammation response index): neutrophil ($10^9/L$) $\times$ monocyte ($10^9/L$) / lymphocyte ($10^9/L$) ratio

SII (systemic immune-inflammation-index): platelet count ($10^9/L$) $\times$ neutrophil count ($10^9/L$) / lymphocyte count ($10^9/L$).

PIV (pan-immune inflammation value): neutrophil count ($10^9/L$) $\times$ platelet count ($10^9/L$) and monocyte count ($10^9/L$), then divided by lymphocyte count ($10^9/L$).

Statistical analyses were conducted using SPSS version 22.0. Descriptive statistics were initially calculated, followed by assessment of the normality of continuous variables using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For comparing non-normally distributed continuous-ordinal variables between the mortality and progression groups, the non-parametric Mann-Whitney U test was applied. Student's t-test was used for normally distributed continuous-ordinal variables. Categorical variables were compared using Chi-square and Fisher's exact tests. The predictive values of immune-inflammatory markers for mortality and progression/recurrence were determined by ROC analysis. The Youden index (YI) was calculated for parameters with p-values <0.05 for the area under the curve (AUC). Cut-off values corresponding to the highest YI for each parameter were identified, and sensitivity and specificity values for these cut-off points were calculated. Patients were categorized into low and high-risk groups based on these cut-off values. Survival analyses for these

groups were performed using Kaplan-Meier analysis. Mean OS (overall survival), PFS (progression free survival), and DFS (disease free survival) values for each parameter's risk groups were compared using the Log-rank test. Cox regression analysis was used to identify risk factors for mortality and progression. All results were presented with 95% confidence intervals. Statistical significance was defined as $p < 0.05$ for all tests.

A total of 86 patients who had ECOG performance status of 0 or 1, were included in the analysis. The neoadjuvant chemotherapy regimen consisted of a combination of carboplatin (5 AUC) and paclitaxel (150 mg/m²) administered every 3 weeks.

The following genes were investigated in the germline genetic analysis for ovarian cancer: BRCA 1, BRCA 2, ATM, PALB2, other.

Ethics approval for the study was obtained from the Health Sciences University Tepecik Training and Research Hospital Clinical Research Ethics Committee (2023/06-07), adhering to the terms of the Declaration of Helsinki.

3. Results

The median age of the 86 patients included in the study was 60.0 years (31.0-83.0 years), and the median BMI was 27.0 kg/m² (16.6-41.0 kg/m²). Among the patients, 80.2% were postmenopausal. Demographic, clinical, genetic, histopathologic and laboratory characteristics of the patients are presented in **Table 1** with progression status.

Table 1. Demographic and clinical characteristics of the patients with median laboratory values according to progression status.

	Progressed (n=51)	Non-progressed (n=35)	p value
Age	57,3±10,3	62,2±11,3	0,039
BMI	26,5±5,2	28,8±5,5	0,057
Menopause	38 (74,5)	31 (88,6)	0,108
ECOG			0,001
ECOG 0	8 (15,7)	17 (48,6)	
ECOG 1	43 (51,4)	18 (51,4)	
Stage			0,890
Stage 3	24 (47,1)	17 (48,6)	
Stage 4	27 (52,9)	18 (51,4)	
Ascites	50 (98,0)	32 (91,4)	0,300
Histopathological subtype			0,163
Serous, high grade	50 (98,0)	33 (94,3)	
Clear cell	-	-	
Endometrioid	0 (0,0)	2 (5,7)	
Mucinous	1 (2,0)	0 (0,0)	
Resection status			0,077
R0	46 (90,2)	35 (100,0)	
R1	-	-	
R2	5 (9,8)	0 (0,0)	
Tumor grade			0,633
G1	1 (2,0)	1 (2,9)	
G2	2 (3,9)	3 (8,6)	

G3	48 (94,1)	31 (88,6)	
mGPS			0,046
Good	19 (41,3)	22 (64,7)	
Intermediate	16 (34,8)	10 (29,4)	
Poor	11 (23,9)	2 (5,9)	
Thrombocytosis	31 (60,8)	16 (45,7)	0,168
Genetical evaluation			0,748
Not available	35 (68,6)	21 (60,0)	
BRCA 1	4 (7,8)	3 (8,6)	
BRCA 2	0 (0,0)	1 (2,9)	
ATM	-	-	
PALB2	1 (2,0)	1 (2,9)	
Others*	11 (21,6)	9 (25,7)	
CA-125	1018,0 (7,8-6532,0)	1599,0 (22,5-5160,0)	0,125
Neutrophils	6,0 (2,9-13,7)	5,3 (2,2-11,2)	0,038
Lymphocytes	1,6 (0,7-3,4)	1,8 (0,7-3,2)	0,123
MPV	8,4±1,0	8,2±1,2	0,320
Platelets	434,0 (202,0-924,0)	387 (121,0-744,0)	0,048
Monocyte	0,6 (0,3-1,2)	0,6 (0,3-1,5)	0,326
LDH	221,0 (81,0-1843)	238,0 (109,0-1394,0)	0,542
Total Protein	7,0 (3,4-8,2)	7,0 (3,3-5,3)	0,741
Albumin	3,4±0,7	3,5±0,6	0,292
CRP	14,0 (0,5-181,6)	4,4 (0,2-114,6)	0,009
NLR	4,0 (1,9-14,6)	2,9 (1,3-9,9)	0,006
LMR	2,5 (0,7-5,2)	3,0 (0,8-6,0)	0,020
PLR	289,6 (115,7-667,5)	202,8 (52,6-718,6)	0,001
PNI	42,4±7,9	45,0±7,0	0,112
SIRI	2,6 (0,9-10,2)	1,7 (0,4-8,9)	0,014
SII	1835,0 (603,7-4802,2)	1051,9 (173,6-4958,2)	0,001
PIV	1038,5 (280,3-4322,0)	776,1 (69,4-4462,3)	0,006
MPV/PLT ratio	0,2 (0,1-3,3)	0,2 (0,1-0,7)	0,316
CRP/Albumin ratio	2,9 (0,0-71,8)	2,0 (0,0-26,6)	0,127
LDH/Albumin ratio	70,5 (36,8-586,9)	70,0 (30,8-343,4)	0,651

The median follow-up duration was 45.2 ± 25.3 months, with a median PFS of 36,8±5,0 months (%95 CI: 27,1-46,5 months) and with a median overall survival (OS) of 55.1 ± 8.7 months (95% CI: 38.1–72.1 months). The progression rate among the patients was 59.3%, and the mortality rate was 53.5%. The mean age of patients with progression (n=51) was 57.3 ± 10.3 years, compared to 62.2 ± 11.3 years in those without progression (n=35), with the difference between the groups being statistically significant (p=0.039). Age was found to influence PFS, whereas no significant association was observed between age and OS. Similarly, BMI and menopausal status showed no significant differences in OS or PFS across subgroups. However, patients with an ECOG score of 0 had significantly higher OS and PFS compared to those with an ECOG score of 1 (p<0.001 and p=0.002,

respectively; median PFS was 89.7±11,6 months vs 32,0±5,1 months). The progression rate was 32.0% in patients with an ECOG score of 0 and 70.5% in those with an ECOG score of 1. The difference between the groups was statistically significant (p<0.001). Notably, patients with an ECOG score of 1 exhibited a 5.3-fold higher risk of mortality and 3.1-fold higher risk of progression compared to those with an ECOG score of 0. (**Table 1 and Table 2**) The mean and median values of the laboratory parameters and immune-inflammatory markers calculated from these parameters, as well as genetic analysis results, are shown in these tables.

Based on the mGPS classification, 47.7% of patients were classified with a good prognosis, 30.1% with an intermediate prognosis, and 15.1% with a poor prognosis. Progression rates also differed significantly between mGPS groups (p=0.046). Patients with poor mGPS were observed to have a 3.1-fold higher risk of progression compared to those with favorable mGPS (HR=3.1, 95% CI: 1.6–6.7, p=0.003). There was also a clear difference in progression rates between the mGPS patient groups, which was statistically significant (p=0.046). Germ-line genetic analyses were driven only in 26% of the patients.

Table 2. Demographic and clinical characteristics of the patients with median laboratory values according to survival status.

	Exitus n=46	Alive n=40	p value
Age	57,9±10,3		0,199
BMI	26,6±5,4	28,4±5,4	0,143
Menopausal	36 (78,3)	33 (82,5)	0,622
ECOG score			
ECOG 0	6 (13,0)	19 (47,5)	<0,001
ECOG 1	40 (87,0)	21 (52,5)	
Stage of disease			
Stage 3	21 (45,7)	20 (50,0)	0,687
Stage 4	25 (54,3)	20 (50,0)	
Ascites present	45 (97,8)	37 (92,5)	0,334
Histopathological subtype			
Serous, high grade	45 (97,8)	38 (95,0)	0,213
Clear cell	-	-	
Endometrioid	0 (0,0)	2 (5,0)	
Mucinous	1 (2,2)	0 (0,0)	
Resection status			
R0	42 (91,3)	39 (97,5)	0,221
R1	-	-	
R2	4 (8,7)	1 (2,5)	
Tumor grade			
G1	1 (2,2)	1 (2,5)	0,829
G2	2 (4,3)	3 (7,5)	
G3	43 (93,5)	36 (90,0)	
mGPS			
Good	17 (40,5)	24 (63,2)	0,067
Intermediate	15 (35,7)	11 (28,9)	

Poor	10 (23,8)	3 (7,9)	
Thrombocytosis present	27 (58,7)	20 (50,0)	0,419
Genetic analysis			
Not available	34 (73,9)	22 (55,0)	
BRCA 1	2 (4,3)	5 (12,5)	
BRCA 2	0 (0,0)	1 (2,5)	0,315
ATM	-	-	
PALB2	1 (2,2)	1 (2,5)	
Others*	9 (19,6)	11 (27,5)	
Neoadjuvant chemotherapy cycles	3,5 (3,0-13,0)	4,0 (3,0-14,0)	0,610
CA-125	867,8 (7,8-6532,0)	1855 (22,5-5160,0)	0,019
Neutrophils	6,1 (2,9-13,7)	5,3 (2,2-11,2)	0,034
Lymphocytes	1,5 (0,7-3,4)	1,8 (0,7-3,2)	0,079
MPV	8,5±1,0	8,1±1,1	0,088
Thrombocytes	423,5 (202,0-924,0)	400,5 (121,0-744,0)	0,206
Monocytes	0,6 (0,3-1,2)	0,6 (0,3-1,5)	0,578
LDH	238,5 (81,0-1843,0)	216,0 (109,0-1394,0)	0,631
Total Protein	7,0 (3,9-8,0)	7,0 (3,0-8,3)	0,762
Albumin	3,4±0,7	3,5±0,6	0,377
CRP	16,5 (0,5-181,6)	5,0 (0,1-158,6)	0,016
NLR	4,0 (1,9-14,6)	2,8 (1,3-9,9)	0,003
LMR	2,4 (0,7-5,2)	3,0 (0,8-5,0)	0,024
PLR	290,4 (115,7-667,5)	219,0 (52,6-718,6)	0,005
PNI	42,3±8,2	44,8±6,8	0,131
SIRI	2,6 (0,9-10,2)	1,8 (0,4-8,9)	0,016
SII	2010,0 (603,7-4802,2)	1200,0 (173,6-4958,1)	0,002
PIV	1026,0 (280,3-432,0)	795,0 (69,4-4462,3)	0,020
MPV/PLT ratio	0,2 (0,1-3,3)	0,2 (0,1-0,7)	0,859
CRP/Albumin ratio	3,3 (0,1-69,9)	2,0 (0,0-71,8)	0,177
LDH/Albumin ratio	70,5 (36,8-586,9)	68,6 (30,8-343,4)	0,822

Risk groups created based on the cut-off values of immuno-inflammatory markers showed significant differences in progression-free survival (PFS). Patients with lower NLR, LMR, PLR, SIRI, SII and PIV values generally had significantly longer PFS compared to those with higher values. Additionally, higher marker values were associated with an increased risk of progression and higher progression rates. However, no significant differences were found for other immunoinflammatory parameters, including MPV/PLT, LDH/Albumin, and CRP/Albumin ratios. These findings highlight the predictive value of these markers for progression, with detailed statistical results provided in **Table 3**.

Table 3. Evaluation of factors influencing prediction of progression (ROC analysis).

	AUC	%95 GA	P value	Cut-off	Sensitivity	Specificity
AAge	0,623	0,501-0,746	0,056	-	-	-
BMI BMI	0,618	0,495-0,741	0,070	-	-	-
NLR	0,677	0,558-0,796	0,005	2,37	88,2	42,9
LMR	0,648	0,523-0,774	0,020	2,69	66,7	62,9
PLR	0,688	0,575-0,802	0,003	255,28	60,8	77,1
PNI	0,606	0,486-0,726	0,097	-	-	-
SIRI	0,657	0,536-0,779	0,014	1,22	96,1	34,3
SII	0,709	0,597-0,822	0,001	1392,47	66,7	74,3
PIV	0,676	0,561-0,791	0,006	1148,90	47,1	82,9
MPV/PLT	0,436	0,313-0,559	0,316	-	-	-
CRP/ALB	0,600	0,476-0,725	0,127	-	-	-
LDH/ALB	0,471	0,344-0,598	0,651	-	-	-

According to the ROC analysis, age and BMI did not show significant predictive value for mortality. However, patients with lower NLR, PLO, SII, and PIV values demonstrated significantly longer OS compared to those with higher values. Higher marker values were associated with an increased risk of mortality and higher mortality rates. For instance, patients with NLR > 2.37, PLO > 256.91, SII > 1983.89, and PIV > 1589.69 were found to have 2.2- to 3.2-fold higher risks of mortality compared to those with lower marker values. Detailed statistical comparisons and results are provided in **Table 4**.

Table 4. Evaluation of factors influencing prediction of mortality (ROC analysis).

	AUC	%95 CI	P value	Cut-off	Sensitivity	Specificity
Age	0 0,572	0,449- 0,696	0,250	-	-	- -
BMI	0.589	0,466- 0,713	0,164	-	-	-
NLR	0,688	0,575-0,802	0,003	2,37	91,3	42,5
LMR	0,641	0,522-0,760	0,024	2,69	67,4	60,0
PLR	0,674	0,559-0,790	0,005	256,91	60,9	75,0
PNI	0,595	0,475-0,716	0,130	-	-	-
SIRI	0,652	0,535-0,769	0,016	1,72	76,1	50,0
SII	0,690	0,578-0,802	0,002	1983,89	52,2	85,0
PIV	0,646	0,529-0,762	0,020	1588,69	41,3	90,0
MPV/PLT	0,489	0,365-0,613	0,859	-	-	-
CRP/ALB	0,588	0,463-0,713	0,177	-	-	-
LDH/ALB	0,514	0,389-0,639	0,822	-	-	-

According to the ROC analysis, age or BMI, and PNI, MPV/PLT, LDH/Albumin or CRP/Albumin ratios, did not show predictive values for progression. However, NLR, LMR, PLR, SIRI, SII, and PIV demonstrated predictive value for disease progression with varying cut-off values, sensitivities, and specificities. Detailed results, including cut-off values and AUC scores, are provided in **Table 5**.

Table 5. Predictive values of age, BMI, and immunoinflammatory markers for progression.

	AUC	%95 GA	P value	Cut-off	Sensitivity	Specificity
Age	0,623	0,501-0,746	0,056	-	-	-
BMI	0,618	0,495-0,741	0,070	-	-	-
NLR	0,677	0,558-0,796	0,005	2,37	88,2	42,9
LMR	0,648	0,523-0,774	0,020	2,69	66,7	62,9
PLR	0,688	0,575-0,802	0,003	255,28	60,8	77,1
PNI	0,606	0,486-0,726	0,097	-	-	-
SIRI	0,657	0,536-0,779	0,014	1,22	96,1	34,3
SII	0,709	0,597-0,822	0,001	1392,47	66,7	74,3
PIV	0,676	0,561-0,791	0,006	1148,90	47,1	82,9
MPV/PLT	0,436	0,313-0,559	0,316	-	-	-
CRP/ALB	0,600	0,476-0,725	0,127	-	-	-
LDH/ALB	0,471	0,344-0,598	0,651	-	-	-

Patients with worse inflammatory markers had significantly higher progression risks and shorter PFS:

- NLO>2.37: 3-fold higher risk (HR=3.0, p=0.012), progression rate %64.6 vs %19.0 (p<0.001).
- LMO<2.69: 2-fold higher risk (HR=2.0, p=0.020), progression rate %72.3 vs %43.6 (p=0.007).
- PLO>255.28: 2.5-fold higher risk (HR=2.5, p=0.002), progression rate %79.5 vs %42.6 (p=0.001).
- SIRI>1.22: 6.6-fold higher risk (HR=6.6, p=0.009), progression rate %67.1 vs %15.4 (p<0.001).
- SII>1392.47: 2.7-fold higher risk (HR=2.7, p=0.001), progression rate %79.1 vs %39.5 (p<0.001).
- PIV>1148.90: 2.1-fold higher risk (HR=2.1, p=0.009), progression rate %80.0 vs %48.2 (p=0.004).

4. Discussion

In the aspect of tumorigenesis, neutrophils, lymphocytes, macrophages, and dendritic cells initially act to inhibit the growth of neoplastic cells. However, as the tumor microenvironment develops and metastasizes, these cells undergo changes that ultimately promote tumor progression [8]. CD4 and CD8 T lymphocytes exert a cytotoxic effect by inhibiting tumor cell proliferation and migration; thus, a decrease in lymphocyte count indicates a weakened and inadequate anti-tumor immune response. Monocytes, through cytokine release (e.g., IL-1, IL-6), promote tumor cell migration and contribute to tumor-associated macrophage transformation, enhancing angiogenesis, proliferation, and metastasis. Consequently, markers such as the neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR) or systemic immune-inflammation index (SII) provide valuable prognostic information [9].

Where inflammation plays a major role in cancer development, neutrophils suppress the cytolytic effects of cytotoxic T cells, NK cells, and lymphocytes while promoting tumor growth by releasing mediators like IL-1, IL-6, tumor necrosis factor, and vascular endothelial growth factor. An imbalance between neutrophils and other immune cells has been found to affect prognosis [10,11]. Increased IL-6 levels, triggered by tumor growth, lead to hepatic thrombopoietin production, causing

paraneoplastic thrombocytosis, which has been linked to advanced disease and shorter survival in studies [12].

In the current study prognostic value of several immunoinflammatory markers are assessed in advanced stage epithelial ovarian cancer patients using real world data, some of those support the existing literature but some of those contribute to it. Williams et al. and subsequent meta-analyses have shown that elevated NLR levels are associated with advanced disease, aggressive features, and shorter survival in ovarian cancer patients for those we demonstrated a cut of value of 2.37 for this ratio [13,14]. A meta-analysis of seven studies found that low LMR levels were associated with shorter OS and PFS [15] we also established a cut-off value of 2.69 for it. The platelet-to-lymphocyte ratio (PLR) is a significant prognostic marker in epithelial ovarian cancer, with predictive value for identifying advanced-stage or residual disease post-surgery which our study demonstrated a cut-off value of 255.28 to predict disease progression and impact survival [16].

Elevated levels of CRP, an acute-phase reactant, are regarded has been associated with poor prognosis in ovarian cancer patients. This association may be attributed to CRP's role in promoting angiogenesis through increased circulating vascular growth factors and interleukin levels in cancer patients [17]. The CRP/albumin ratio has a stronger prognostic impact than inflammation-related indices like mGPS and PNI, and it serves as an independent marker of poor prognosis in ovarian cancer patients, showing superior prognostic performance compared to these indices [18]. Studies have shown that the CRP/albumin ratio is associated with prognosis in patients with hepatocellular carcinoma, gastric carcinoma, and esophageal squamous cell carcinoma [19–21]. In a meta-analysis of eight retrospective studies including ovarian cancer patients, high mGPS values were associated with lower OS and PFS [22]. In our study, mGPS did not show a significant effect on OS, but it was found to influence PFS and DFS.

Several studies investigating the prognostic factors in ovarian cancer have identified different variables. One study associates postoperative residual tissue, ascites, thrombocytosis, ECOG >1, and menopausal status with outcomes, while another emphasizes the FIGO stage and the presence of residual tissue after surgery [23,24]. In contrast, our study found that postoperative residual tissue did not have an impact on PFS or OS. This suggests that the predictive factors are multifactorial when considering the other parameters.

CA125 is the most widely used biomarker for assessing chemotherapy response, monitoring recurrence, and evaluating disease severity in ovarian cancer patients. Elevated CA125 levels, those were extremely high in our study population, correlate with advanced cancer stages, poor differentiation, ascites, lymph node metastasis, and tumor burden [25]. High preoperative CA-125 levels have been also associated with poorer survival outcomes [26].

The SIRI index, which is calculated using neutrophil, monocyte, and lymphocyte counts, was found to be more comprehensive than NLR and LMR for distinguishing between benign and malignant ovarian masses [27]. While our study found that the SIRI index influenced OS, DFS, and PFS, with predictive value for mortality, the limited research on its impact in ovarian cancer emphasizes the significance of our findings.

Systemic immune-inflammation index (SII), which reflects thrombocytosis, neutrophilia and lymphopenia within the tumor microenvironment, has been associated with poor prognosis and decreased efficacy in ovarian cancer patients [28]. In our study, we calculated a cut of value of 1983 for distinguishing high and low SII levels, which was predictive of poor progression and increased mortality rates. Notably, this threshold is substantially higher than those reported in previous ovarian cancer studies, where cut-off values of 730 and 612 were identified [29,30]. Prognostic nutritional index (PNI), reflecting nutritional and immune status, has been linked to survival outcomes, though it was not predictive of progression or mortality in this study but influenced PFS and OS [31,32]. Platelet-to-lymphocyte ratio (PIV) shows a strong association with survival, with higher levels indicating shorter survival times, as shown in breast cancer and colon cancer patients [33,34].

Our study has some limitations. First, retrospective observational design inherently introduces biases. Second, although a comprehensive analyze was conducted, the number of patients was limited due to the exclusion of cases with missing parameters. Third, this was a single center study, and the cut-off values representing this specific cohort may not be generalizable to other populations, as they could vary across different groups.

5. Conclusions

Ovarian cancer's high mortality is linked to advanced-stage diagnosis and treatment failures. This study found inflammatory markers like NLR, PLR, SII, and PIV to significantly impact prognosis and survival, while thrombocytosis and CRP-related ratios did not. The findings highlight the potential for underexplored markers to guide personalized treatments and reduce mortality. This approach enables clinicians to develop tailored and personalized treatment plans with multi dimentions of these metrics.

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Abbreviations

The following abbreviations are used in this manuscript:

EOC	Epithelial Ovarian Cancer
BMI	Body Mass Index
mGPS	modified Glasgow Prognostic Score
PNI	Prognostic Nutritional Index
SIRI	Systemic Inflammatory Response Index
SII	Systemic Inflammation Index
PIV	Pan-immune Inflammation Value
NLR	Neutrophil-to-Lymphocyte Ratio
LMR	Lymphocyte-to-Monocyte Ratio
PLR	Platelet-to-Lymphocyte Ratio
OS	Overall Survival
PFS	Progression Free Survival
CRP	C-Reactive Protein

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