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ORIGINAL RESEARCH

The Predictive Role of Neutrophil Percentage-to-Albumin Ratio (NPAR) in Endometrial Carcinoma: A Novel Prognostic Marker

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Background: Endometrial carcinoma, EC is the most common gynecologic malignancy in developed countries, and identifying accessible prognostic markers remains critical for guiding treatment strategies. Systemic inflammatory markers have emerged as promising tools in cancer prognosis.

Objective: This study aimed to investigate the predictive value of the neutrophil percentage-to-albumin ratio, NPAR in patients diagnosed with endometrial carcinoma and to compare its utility with other systemic inflammatory indices.

Methods: This retrospective study included 194 patients who underwent surgical treatment for endometrial carcinoma between January 2020 and May 2025 at a tertiary care center. Preoperative blood samples were used to calculate neutrophil percentage-to-albumin ratio, NPAR, neutrophil-to-lymphocyte ratio, NLR, platelet-to-lymphocyte ratio, PLR, systemic immune-inflammation index, SII, and other related markers. Patients were analyzed according to final pathological outcomes, and the relationship between inflammatory indices and prognostic parameters such as tumor grade, histologic type, depth of myometrial invasion, lymphovascular space invasion, LVSI and FIGO stage was evaluated. Receiver operating characteristic, ROC analysis was performed to determine optimal cutoff values for NPAR.

Results: NPAR did not show a statistically significant association with lymphovascular space invasion (LVSI) or deep myometrial invasion. However, it was significantly associated with advanced stage (FIGO ≥ Stage II). High NPAR, elevated SIRI, high PLR, low NLR, elevated MLR, and increased immature granulocyte count were significant predictors of advanced stage. The regression model demonstrated strong predictive ability for advanced disease (Nagelkerke $R^2 = 0.79$; $p < 0.001$).

Conclusion: NPAR is a novel, simple, and cost-effective prognostic biomarker in endometrial carcinoma. Its preoperative evaluation may help identify high-risk patients and contribute to more individualized treatment planning. Further prospective studies are warranted to validate these findings.

Keywords: endometrial carcinoma, neutrophil percentage-to-albumin ratio, NPAR, systemic inflammatory markers, pathology, prognostic biomarker

Introduction

Endometrial carcinoma is one of the most prevalent gynecological malignancies, ranking as the sixth most common cancer among women globally.[1] Its incidence has shown a steady increase, particularly in developed countries, which is partially attributed to rising obesity rates and aging populations.[2] Despite advancements in diagnostic and therapeutic modalities, early and precise prognostic indicators remain crucial for improving patient outcomes. The rising burden of this malignancy necessitates a comprehensive approach to understand its biology and progression to improve diagnostic, therapeutic, and prognostic strategies.[3]

Systemic inflammatory markers have emerged as potential tools for understanding tumor biology and predicting cancer outcomes. Among these, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and C- reactive

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protein (CRP) have been extensively studied in various malignancies. Elevated levels of these markers have been linked to poorer survival rates and advanced disease stages, reflecting the interplay between systemic inflammation and tumor progression.[4,5]

Systemic immune-inflammation index (SII), which integrates platelet, neutrophil, and lymphocyte counts, has been investigated in endometrial carcinoma and found to be a superior prognostic factor compared to traditional inflammatory markers. SII has been shown to correlate with critical pathological features such as tumor stage, lymphatic invasion, and overall survival, further highlighting the role of systemic inflammation in cancer progression.[6]

Additionally, the neutrophil percentage-to-albumin ratio (NPAR) has recently gained attention as a novel biomarker, demonstrating prognostic value across multiple cancers, including bladder and oral cavity cancers.[7,8] These markers are easily accessible and cost-effective, making them practical for routine clinical use.

Beyond oncology, NPAR has demonstrated value in systemic conditions such as nonalcoholic fatty liver disease (NAFLD) and advanced liver fibrosis, where it is significantly correlated with disease severity and progression.[9] Elevated NPAR levels have also been shown to predict mortality in peritoneal dialysis patients, where its prognostic value surpasses that of other systemic inflammatory indices like NLR and PLR.[10]

In the context of endometrial carcinoma, the role of NPAR remains unexplored. To our knowledge, this study represents the first investigation into the potential of NPAR as a prognostic marker in endometrial carcinoma. By establishing its relevance in this malignancy, we aim to provide novel insights into the inflammatory mechanisms underlying tumor progression and prognosis. This study seeks to evaluate the relationship between preoperative NPAR levels and critical pathological findings such as tumor grade, stage, and lymphovascular invasion, thereby offering a comprehensive understanding of its predictive value in clinical practice.

Materials and Methods

This retrospective study was conducted at a tertiary hospital and included patients who underwent surgery for endometrial carcinoma between January 1, 2020, and May 15, 2025. The preoperative systemic inflammatory indices of the patients, including the neutrophil percentage-to-albumin ratio, NPAR, neutrophil-to-lymphocyte ratio, NLR, systemic immune-inflammation index, SII, and platelet-to-lymphocyte ratio PLR, were calculated. Additionally, preoperative CA-125 levels were included in the study for analysis.

Inclusion and Exclusion Criteria

Patients were included in the study if their medical records contained complete and accurate data necessary for calculating inflammatory markers and CA-125 levels. Patients with insufficient or missing data, concurrent malignancies, or significant inflammatory conditions unrelated to endometrial carcinoma were excluded. Systemic inflammatory markers could be influenced by other systemic diseases, ongoing infections, or autoimmune disorders; therefore, patients with these conditions were also excluded from the study. Efforts were made to ensure that all included patients had reliable and verifiable data.

Data Collection and Parameters Assessed

Postoperative final pathology results were analyzed to evaluate key pathological features, including:

- Histological type and stage of endometrial cancer
- Tumor size
- Presence of lymphovascular space invasion (LVSI)
- Peritoneal fluid cytology results
- Depth of myometrial invasion
- Lymph node involvement

In addition, patient demographics such as age and survival status were recorded. The type of treatments received, including adjuvant therapies like chemotherapy or radiotherapy, was also documented.

Staging was performed according to the 2023 FIGO classification system for endometrial carcinoma. However, due to institutional limitations, molecular parameters were not used in the staging process, and the staging was based solely on clinicopathological features.

Study Outcomes

The primary outcome of the study was to evaluate the association between preoperative systemic inflammatory markers (with a focus on NPAR) and final pathological features in patients with endometrial carcinoma, including tumor stage, histological subtype, myometrial invasion, lymphovascular space invasion (LVSI), and lymph node metastasis.

The secondary outcomes included:

- A comparative analysis of NPAR with other inflammatory markers (NLR, SII, PLR, SIRI) in terms of their predictive ability for the above pathological outcomes.
- An assessment of the correlation between these markers and preoperative CA-125 levels.

This approach aimed to determine the clinical utility of these markers in preoperative risk stratification.

Calculation and Units of Systemic Inflammatory Indices

To calculate systemic inflammatory indices, the following hematological parameters were used with their respective units:

- Neutrophil percentage (%)
- Neutrophil count ($\times 10^9$/L)
- Lymphocyte count ($\times 10^9$/L)
- Monocyte count ($\times 10^9$/L)
- Platelet count ($\times 10^9$/L)
- Immature granulocyte count ($\times 10^9$/L)
- Serum albumin level (g/L)

Based on these parameters, the indices were calculated as follows:

- NPAR = Neutrophil percentage (%)/Albumin (g/L)
- NLR = Neutrophil count ($\times 10^9$/L)/Lymphocyte count ($\times 10^9$/L)
- PLR = Platelet count ($\times 10^9$/L)/Lymphocyte count ($\times 10^9$/L)
- SII = (Platelet count × Neutrophil count)/Lymphocyte count
- SIRI = (Neutrophil count × Monocyte count)/Lymphocyte count

All indices were calculated from preoperative blood samples taken within one week before surgery.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Since the continuous data were not normally distributed, they were presented as median (minimum–maximum), and comparisons between groups were conducted using the Mann–Whitney *U*-test. Categorical variables were expressed as frequencies and percentages, and differences between groups were analyzed using Pearson's chi-square test or Fisher's exact test, as appropriate.

Binary logistic regression analyses were performed to identify independent predictors of lymphovascular space invasion (LVSI), deep myometrial invasion (≥50%), and advanced FIGO stage (Stage ≥ II). Subsequently, receiver operating characteristic (ROC) curves were constructed to evaluate the predictive performance of the regression models. In addition, Spearman correlation analysis was conducted to examine the relationships between individual hematologic

and inflammatory parameters. These correlations were visualized using a heatmap generated with JASP software (version 18.3) to illustrate the strength and direction of associations among variables.

Ethical Considerations

Approval for the study was obtained from the Ethics Committee of the Necmettin Erbakan University Faculty of Medicine Ethics Committee, and all procedures were conducted in compliance with institutional and international ethical standards. Informed consent was obtained from all patients prior to their inclusion in the study. The study was designed and conducted in accordance with the principles outlined in the Declaration of Helsinki.

Results

Patient Demographics and Clinical Characteristics (Table 1)

The study included 194 patients with endometrial cancer diagnoses. The average age at diagnosis was 58.51 ± 10.84 years, and it is currently 61.79 ± 8.98 years. Eight patients (4.1%) had passed away at the time of data collection, while 186 patients (95.9%) were still alive. Every patient received surgery. In 37.6% (n = 73), 52.1% (n = 101), and 4.6% (n = 9) of the cases, adjuvant therapy consisted of chemotherapy, external beam radiation, and brachytherapy.

Table 1 Clinical, Pathological, and Treatment Characteristics of Endometrial Cancer Patients

Variables		**Mean ± SD/Median (min–max)/n (%)**
Age at diagnosis (years)		58.51 ± 10.84
Current age (years)		61.79 ± 8.98
Vital status	Died	8 (4.1%)
	Alive	186 (95.9%)
Surgical procedure	Performed	194 (100%)
Chemotherapy	Took	73 (37.6%)
	Did not take	121 (62.4%)
Radiotherapy	Took	101 (52.1%)
	Did not take	93 (47.9%)
Brachytherapy	Took	9 (4.6%)
	Did not take	185 (95.4%)
Pathological diagnosis	Endometrioid	161 (83.0%)
	Serous	16 (8.2%)
	Mix	8 (4.1%)
	Clear cell	3 (1.5%)
	Mucinous	2 (1.0%)
	Leiomyosarcoma	2 (1.0%)
	Sertoli-Leydig	1 (0.5%)
	Granulosa cell	1 (0.5%)

(*Continued*)

Table 1 (Continued).

Variables		Mean ± SD/Median (min–max)/n (%)
Histological subtype	Endometrioid	161 (83.0%)
	Non-endometrioid	33 (17.0%)
FIGO stage	IA	104 (53.6%)
	IB	52 (26.8%)
	IC	3 (1.5%)
	IIA	5 (2.6%)
	IIB	8 (4.1%)
	IIC	2 (1.0%)
	III	19 (9.8%)
	IV	1 (0.5%)
Stage categories (1 vs ≥2)	Stage 1	159 (82.0%)
	Stage ≥2	35 (18.0%)
Stage categories (1–2 vs ≥3)	Stage 1–2	174 (89.7%)
	Stage ≥3	20 (10.3%)
Lymph node status	Carcinoma infiltration	37 (19.1%)
	Reactive lymph node	157 (80.9%)
Tumor grade		2.00 (1–3)
Longest diameter of the tumor (cm)		4.00 (1.00–18.00)
LVSI presence	Present	36 (18.6%)
	Absent	158 (81.4%)
Myometrial invasion	<1/2 invasion	119 (61.3%)
	≥1/2 invasion	75 (38.7%)
Peritoneal fluid cytology	Benign	176 (90.7%)
	Malignant	18 (9.3%)

Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; LVSI, Lymphovascular Space Invasion.

According to histopathological analysis, 83.0% (n = 161) had endometrioid carcinoma, whereas 17.0% (n = 33) had non-endometrioid histology, which included tumours of the serous (8.2%), mixed (4.1%), clear cell (1.5%), mucinous (1.0%), leiomyosarcoma (1.0%), Sertoli-Leydig (0.5%), and granulosa cell (0.5%). Just 18.0% of patients were categorised as stage ≥II, while the majority (82.0%) received a FIGO stage I diagnosis. 19.1% of patients had lymph node cancer infiltration, and 18.6% had lymphovascular space invasion (LVSI). In 38.7% of cases, there was deep myometrial invasion (≥50%). Tumour diameter ranged from 1.00 to 18,00 cm, with a median of 4.00 cm. 9.3% of patients had malignant peritoneal cytology.

Hematologic and Inflammatory Biomarkers (Table 2)

Descriptive statistics of laboratory parameters showed a median WBC count of 8.00 $\times 10^9$/L, neutrophils 5.01 $\times 10^9$/L, lymphocytes 2.27 $\times 10^9$/L, and platelets 288.00 $\times 10^9$/L. The mean albumin level was 40.65 ± 4.29 g/L. Inflammatory indices showed the following medians: NPAR 1.59, NLR 2.24, PLR 138.62, SII 725.10, and SIRI 1.16. The median CA-125 level was 18.20 U/mL.

Predictors of Lymphovascular Space Invasion (Table 3)

A number of independent predictors of LVSI were found using binary logistic regression analysis. Significant correlations were found between the presence of LVSI and older age at diagnosis (OR = 1.06, 95% CI not shown, p = 0.013), non-endometrioid histology (OR = 3.63, p = 0.010), larger tumour diameter (OR = 1.16, p = 0.042), and elevated immature granulocyte count (IG; OR = 26.82, p = 0.025). NPAR, NLR, SII, and SIRI were among the other inflammation-based biomarkers that did not show statistically significant predictive power. The overall logistic model showed moderate discriminative power (McFadden's $R^2 = 0.21$; Nagelkerke $R^2 = 0.30$), acceptable fit indices (AIC = 174.43, BIC = 220.18), and was significant (χ^2 (13) = 39.71, p <0.001). Figure 1 displays the ROC curve.

Predictors of Myometrial Invasion (Table 4)

Age at diagnosis (OR = 1.04, p = 0.011) and tumour size (OR = 1.19, p = 0.018) were significant predictors in the prediction model for myometrial invasion ≥50%. Statistical significance was not attained by any of the inflammatory markers. Overall, the model had a modest explanatory power (McFadden's R2 = 0.11; Nagelkerke R2 = 0.18), and it was statistically significant (χ^2 (13) = 28.06, p = 0.009). Figure 2 displays the ROC curve used to evaluate model performance.

Table 2 Descriptive Statistics of Hematologic and Inflammatory Markers in Patients with Endometrial Cancer

Variables	Mean ± SD/Median (min–max)
WBC ($\times 10^9$/L)	8.00 (4.09–20.60)
Hemoglobin (g/dL)	13.20 (7.76–16.50)
Neutrophil ($\times 10^9$/L)	5.01 (2.07–18.80)
Lymphocyte ($\times 10^9$/L)	2.27 (0.44–5.58)
Monocyte ($\times 10^9$/L)	0.51 (0.14–1.22)
Platelet ($\times 10^9$/L)	288.00 (104–693)
Immature granulocyte (IG) ($\times 10^9$/L)	0.04 (0.01–0.80)
Albumin (g/L)	40.65 ± 4.29
CA-125 (U/mL)	18.20 (2.00–1035.00)
NPAR	1.59 (0.95–2.96)
NAR	0.12 (0.04–0.46)
NLR	2.24 (0.84–26.59)
PLR	138.62 (39.34–693.42)
MLR	0.23 (0.06–1.49)
SII	725.10 (142.80–7791.23)
SIRI	1.16 (0.37–27.92)

Abbreviations: WBC, White Blood Cell; CA-125, Cancer Antigen 125; NPAR, Neutrophil Percentage to Albumin Ratio; NAR, Neutrophil-to-Albumin Ratio; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; SII, Systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index.

Table 3 Binary Logistic Regression Analysis of Factors Associated with Lymphovascular Space Invasion in Endometrial Cancer Patients

Predictor	Estimate	SE	Z	p-value
Intercept	−3.95	4.57	−0.86	0.387
Age at diagnosis	0.06	0.02	2.49	**0.013**
Non-endometrioid (vs Endometrioid)	1.29	0.50	2.59	**0.010**
Longest tumor diameter	0.15	0.08	2.03	**0.042**
IG	10.19	4.55	2.24	**0.025**
Albumin	−0.05	0.07	−0.73	0.463
CA-125	−0.00	0.00	−0.76	0.448
NPAR	−0.41	1.29	−0.32	0.753
NAR	0.72	9.75	0.07	0.941
NLR	0.04	0.24	0.18	0.854
PLR	0.00	0.01	0.41	0.683
MLR	−5.24	4.28	−1.22	0.221
SII	0.00	0.00	0.09	0.929
SIRI	0.20	0.42	0.48	0.629

Notes: Bold values indicate statistically significant results ($p < 0.05$). The binary logistic regression model used to identify predictors of LVSI was statistically significant (χ^2 (13) = 39.71, $p < 0.001$), indicating that the model successfully differentiates between patients with and without lymphovascular space invasion. The model demonstrated an acceptable fit, with a deviance of 146.43, AIC of 174.43, and BIC of 220.18. The pseudo R^2 values were McFadden's $R^2 = 0.21$ and Nagelkerke $R^2 = 0.30$, suggesting moderate explanatory power.

Abbreviations: IG, Immature Granulocyte; CA-125, Cancer Antigen 125; NPAR, Neutrophil Percentage to Albumin Ratio; NAR, Neutrophil-to-Albumin Ratio; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; SII, Systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index.

Predictors of Advanced FIGO Stage (Stage ≥2) (Table 5)

Non-endometrioid histology (OR = 23.37, p = 0.006), increased immature granulocyte counts (OR = 862,274.42, p = 0.001), high NPAR (OR = 208,939.21, p = 0.001), high SIRI (OR = 239.86, p = 0.001), elevated PLR (OR = 1.07, p = 0.003), decreased NLR (OR = 0.04, p = 0.001), and MLR (OR = 2.95×10^{-18}, p = 0.001) were all significant indicators of advanced stage disease (≥FIGO stage II). Advanced stage had a negative correlation with CA-125 (p = 0.042). The regression model had good goodness-of-fit metrics (McFadden's $R^2 = 0.69$; Nagelkerke $R^2 = 0.79$) and strong predictive ability (χ^2 (15) = 126.82, $p < 0.001$). Figure 3 shows the ROC curve.

Correlation Between Biomarkers and Inflammatory Indices

Spearman correlation analysis demonstrated that neutrophil count correlated strongly with NLR (ρ = 0.72), NPAR (ρ = 0.68), and SIRI (ρ = 0.63). Lymphocyte count showed inverse correlations with NLR (ρ = –0.80) and PLR (ρ = –0.69). Platelet count was positively associated with SII (ρ = 0.76), while albumin was negatively correlated with NPAR (ρ = –0.56) and NAR (ρ = –0.48). Immature granulocyte count showed moderate correlation with SIRI (ρ = 0.42) and CA-125 (ρ = 0.31). These correlations are visually illustrated in Figure 4.

Discussion

Lymphovascular space invasion (LVSI) is a significant prognostic factor that reflects the biological aggressiveness and metastatic potential of endometrial cancer.[11] In this study, LVSI was found to be significantly associated with older age, non-

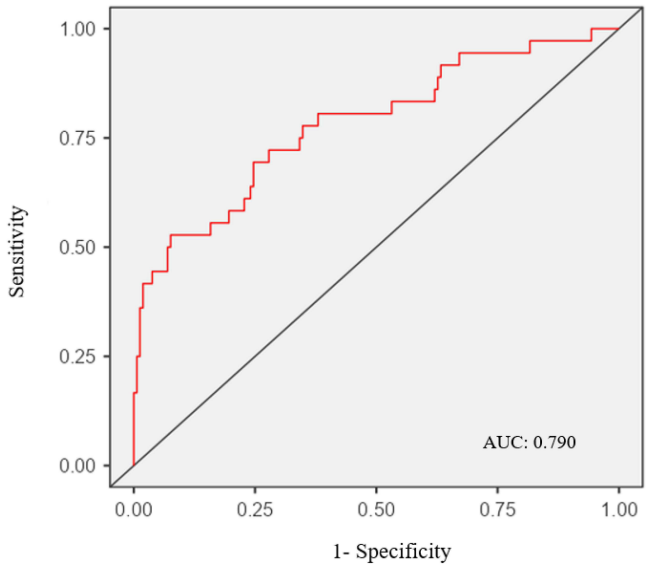

Figure 1 ROC curve illustrating the diagnostic performance of the logistic regression model for predicting lymphovascular space invasion (LVSI) in patients with endometrial cancer.

endometrioid histological type, increased tumor size, and particularly elevated levels of immature granulocytes. These findings are consistent with previous studies suggesting that immature granulocytes may contribute to the tumor microenvironment.[5,12] Although systemic inflammatory indices such as NPAR, SIRI, and SII were not directly associated with LVSI, their correlation with IG levels suggests that these markers may indirectly play a role in the process of vascular invasion. As reported in previous literature, elevated neutrophil levels have been shown to promote neoangiogenesis and endothelial cell migration within the tumor stroma.[6,13] Therefore, the observed association between LVSI and IG levels may serve as an important indicator of the role of inflammation in tumor spread.[14]

Deep myometrial invasion (MI) is a significant feature that increases the risk of recurrence even in early-stage endometrial cancer.[15] In this study, older age and larger tumor size were found to be significantly associated with invasion equal to or greater than 50%. Although inflammatory indices such as NPAR and SIRI demonstrated borderline

Table 4 Binary Logistic Regression Analysis of Factors Associated with Myometrial Invasion in Endometrial Cancer Patients

Predictor	Estimate	SE	Z	p-value
Intercept	−6.16	3.46	−1.78	0.075
Age at diagnosis	0.04	0.02	2.54	**0.011**
Non-endometrioid (vs Endometrioid)	−0.32	0.44	−0.72	0.471
Longest tumor diameter	0.17	0.07	2.36	**0.018**
IG	0.21	2.35	0.09	0.930
Albumin	0.00	0.05	0.02	0.981
CA-125	−0.00	0.00	−0.89	0.373
NPAR	0.68	1.01	0.67	0.505
NAR	8.59	7.24	1.19	0.235
NLR	0.04	0.17	0.25	0.804

(*Continued*)

Table 4 (Continued).

Predictor	Estimate	SE	Z	p-value
PLR	0.01	0.01	1.46	0.144
MLR	−3.07	3.60	−0.85	0.394
SII	−0.00	0.00	−1.15	0.249
SIRI	0.19	0.45	0.42	0.674

Notes: Bold values indicate statistically significant results (p <0.05). The logistic regression model designed to predict deep myometrial invasion was statistically significant (χ^2 (13) = 28.06, p = 0.009), indicating that the selected variables contributed meaningfully to distinguishing between patients with <50% and ≥50% myometrial invasion. Model performance metrics included a deviance of 230.81, an AIC of 258.81, and a BIC of 304.56. The model's explanatory power was modest, with McFadden's R^2 = 0.11 and Nagelkerke R^2 = 0.18.

Abbreviations: IG, Immature Granulocyte; CA-125, Cancer Antigen 125; NPAR, Neutrophil Percentage to Albumin Ratio; NAR, Neutrophil-to-Albumin Ratio; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; SII, Systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index.

p-values in this group, several studies have reported significant associations between MI and markers such as PLR and NLR. For instance, Muangto et al[16] reported that NLR ≥1.93 and PLR ≥134.95 had meaningful sensitivity and specificity in predicting deep myometrial invasion. Similarly, Petrić et al[12] suggested that inflammatory markers may reflect the biological behavior underlying tissue invasion. In this context, the depth of myometrial invasion may be considered not only an anatomical feature but also a manifestation of the systemic inflammatory response.[17]

Advanced FIGO stage (≥2) is one of the key parameters that determines both treatment approach and prognosis in endometrial cancer.[18] In our study, advanced stage was found to be significantly associated with non-endometrioid histology, elevated levels of immature granulocytes (IG), and increased NPAR, SIRI, and PLR values. These findings suggest that the systemic inflammatory response plays a role in tumor progression. Similarly, the study by Lin et al[19] reported that elevated levels of NLR, MLR, PLR, SII, and CA125 were significantly associated with advanced stage, indicating that these markers may contribute to the staging process. Furthermore, the inverse relationship between low NLR and MLR levels and advanced stage, as shown by Bharti et al,[4] suggests that despite increasing neutrophil counts,

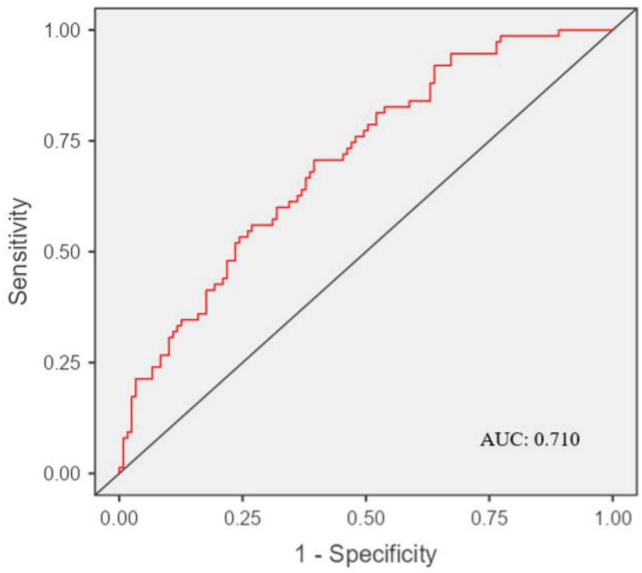

Figure 2 ROC curve of the predictive model for identifying deep myometrial invasion (≥50%) in endometrial carcinoma cases.

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Table 5 Binary Logistic Regression Analysis of Factors Associated with Advanced Stage (Stage ≥2) in Endometrial Cancer Patients

Predictor	Estimate	SE	Z	p-value
Intercept	−14.87	8.12	−1.83	0.067
Age at diagnosis	0.03	0.03	0.91	0.365
Non-endometrioid (vs Endometrioid)	3.15	1.15	2.75	**0.006**
Longest tumor diameter	−0.19	0.17	−1.12	0.264
IG	13.67	3.99	3.42	**0.001**
Albumin	−0.07	0.13	−0.53	0.594
CA-125	−0.01	0.00	−2.04	**0.042**
NPAR	12.25	3.13	3.91	**0.001**
NAR	−38.06	19.79	−1.92	0.054
NLR	−3.12	0.92	−3.40	**0.001**
PLR	0.07	0.02	2.99	**0.003**
MLR	−40.24	11.47	−3.51	**0.001**
SII	−0.00	0.00	−1.42	0.154
SIRI	5.48	1.58	3.47	**0.001**

Notes: Bold values indicate statistically significant results ($p < 0.05$). The logistic regression model constructed to predict FIGO Stage ≥2 in endometrial cancer patients was statistically significant (χ^2 (15) = 126.82, $p < 0.001$), indicating that the model reliably distinguishes between early and advanced stage cases. The model demonstrated a good fit, with a deviance of 56.32, an AIC of 88.32, and a BIC of 140.61. The explanatory power of the model was high, with McFadden's $R^2 = 0.69$ and Nagelkerke $R^2 = 0.79$, suggesting strong discriminative capacity.
Abbreviations: IG, Immature Granulocyte; CA-125, Cancer Antigen 125; NPAR, Neutrophil Percentage to Albumin Ratio; NAR, Neutrophil-to-Albumin Ratio; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; SII, Systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index.

a more prominent decline in lymphocytes may occur as the disease progresses. In conclusion, inflammatory markers may serve as complementary biomarkers in the diagnosis of advanced-stage endometrial cancer.[20]

In our study, significant correlations were observed among inflammatory indices. In particular, neutrophil count showed strong positive correlations with NLR (ρ = 0.72), NPAR (ρ = 0.68), and SIRI (ρ = 0.63), while lymphocyte count was negatively correlated with these indices (ρ = –0.80 for NLR, ρ = –0.69 for PLR). These findings indicate that these indices, calculated based on hematological parameters, have strong structural integrity and reflect the systemic inflammatory response. Furthermore, the negative correlation of albumin levels with NPAR and NAR supports the association of hypoalbuminemia with increased inflammation and poor prognosis.[12] The significant correlation between platelet count and SII (ρ = 0.76) also highlights the potential of SII to reflect tumor progression mediated particularly by platelet-driven inflammation. Overall, these correlations demonstrate the complementary and supportive nature of inflammatory indices.

This study's findings reveal that systemic inflammatory markers are closely associated with prognostic parameters of endometrial cancer. Recent studies on prognostic markers in endometrial cancer have particularly focused on L1 cell adhesion molecule (L1CAM). Vizza et al reported that while vaginal cuff length did not independently affect recurrence in low-risk endometrial carcinoma, L1CAM positivity was more frequently associated with distant relapse.[21] Similarly, a systematic review and meta-analysis by Giannini et al demonstrated that L1CAM expression in stage I endometrial cancer was an unfavorable prognostic factor for both disease-free survival and overall survival.[22] These findings suggest that biomolecular markers may provide prognostic value beyond traditional clinicopathological parameters and should be

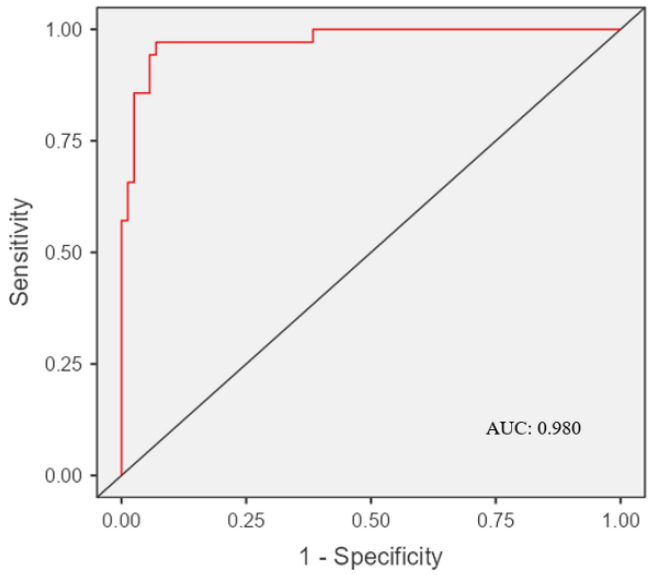

Figure 3 ROC curve evaluating the model performance in predicting advanced FIGO stage (stage ≥ II) among patients.

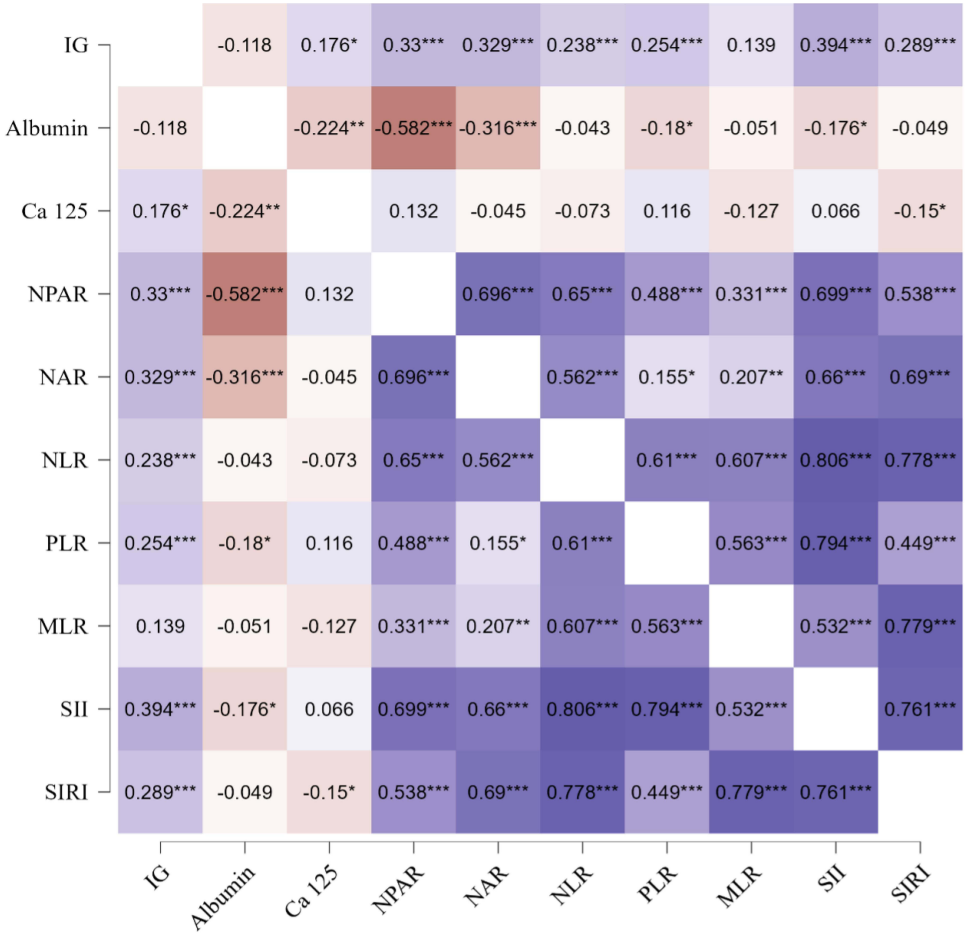

Figure 4 Spearman correlation matrix showing the relationships between systemic inflammatory indices (NPAR, NLR, PLR, SIRI, SII) and laboratory/clinical parameters in patients with endometrial cancer. *Indicates $p < 0.05$, **indicates $p < 0.01$, ***indicates $p < 0.001$.

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integrated into novel risk stratification models. In this context, the prognostic role of NPAR observed in our study, together with previous evidence on L1CAM, indicates that systemic inflammatory indices may complement molecular biomarkers in predicting outcomes in endometrial cancer.

In particular, complex indices such as NPAR, SIRI, and SII provide signals consistent with the biological behavior of the tumor and show significant associations with critical parameters such as stage, depth of invasion, and vascular dissemination.[23,24] Similarly, an increasing number of studies in the literature report associations between these indices and prognosis, recurrence, and overall survival.[5,6,19] In this context, these markers, which are easily calculated from complete blood count and biochemical tests, may offer valuable contributions to preoperative risk stratification and individualized treatment planning for patients with endometrial cancer.

Limitations

This study has some limitations that should be acknowledged. First, the retrospective nature of the design and the single-center dataset may introduce selection bias and limit generalizability. Second, although systemic inflammatory markers such as NPAR, SIRI, and PLR demonstrated significant associations with advanced-stage disease, the predictive models for LVSI and myometrial invasion showed limited discriminative power, reducing their clinical utility in these specific outcomes. Third, molecular classification parameters outlined in the 2023 FIGO staging system were not incorporated due to the unavailability of routine molecular profiling at our institution during the study period. Future multicenter prospective studies including molecular data are warranted to validate and expand upon these findings.

Conclusion

This study demonstrated that systemic inflammatory markers—particularly NPAR, SIRI, and PLR—are significantly associated with adverse pathological features in endometrial cancer, including lymphovascular space invasion, deep myometrial invasion, and advanced FIGO stage. Among these, NPAR emerged as a consistently strong predictor across multiple parameters. These findings suggest that preoperative evaluation of inflammatory indices may offer a practical, cost-effective tool to support risk stratification and surgical decision-making. Further prospective and multicenter studies are warranted to validate the predictive power of these markers and to explore their integration into clinical management algorithms.

Use of AI Assistance

In the preparation of this manuscript, the authors utilized OpenAI's ChatGPT-4 for assistance with English language refinement, structural organization, and formatting of references. The AI tool was employed strictly to enhance clarity, grammar, and consistency, without contributing to the study design, data analysis, or scientific interpretation. All intellectual and analytical content remains the sole responsibility of the authors.

Data Sharing Statement

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

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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