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Prognostic value of hematological indexes in endometrioid type endometrial cancer

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Abstract

Endometrial cancer remains a significant health concern, particularly in developed nations where its prevalence is increasing. Reliable prognostic markers are paramount to enhance disease management and patient outcomes. This study explores the prognostic capabilities of various hematological indices, including the eosinophil-lymphocyte ratio (ELR) and the prognostic nutritional index (PNI), in relation to endometrioid type endometrial cancer (ETEC) staging and grading. We retrospectively analyzed data from ETEC patients, categorizing them by tumor grade and stage, and evaluating their hematological indices from preoperative blood samples. Our results indicated that higher ELR and lower PNI levels correlate with more advanced tumor grades and stages. Additionally, the platelet-lymphocyte ratio (PLR) was found to be the most significant marker for staging, with PLT, SII, SIRI, ELR, and PNI also showing significant differences across stages. These findings suggest that hematological indices such as ELR and PNI could be instrumental in predicting tumor grade and stage, offering valuable insights for clinical practice. Future research should focus on prospective studies to confirm these findings and consider the integration of these markers into standard diagnostic protocols.

Keywords: Hematological indices, eosinophil-lymphocyte ratio, prognostic nutritional index, platelet-lymphocyte ratio, endometrial cancer, tumor grade, tumor stage, prognostic markers

Introduction

Endometrial cancer is the most prevalent malignancy of the female reproductive tract in developed countries, with its incidence rising due to factors such as obesity and metabolic syndrome [1,2]. Accurate prognostic tools are critical for effective disease management, particularly for stratifying patients based on tumor aggressiveness and guiding therapeutic decisions [3]. Endometrioid type endometrial cancer (ETEC) is the most common subtype, accounting for approximately 80% of all endometrial cancer cases [4,5].

It is thought that hematological indexes can be analyzed alongside standard acute-phase proteins since recent studies have indicated the importance of the relationship between the overinflamed cells, the tumor, and the tumor's microenvironment, as well as the assessment of what the presence of overinflamed and increased platelets in the tumor should mean.

Survival of patients with ETEC depends on prognostic factors, such as age at diagnosis, comorbidities, tumor diameter, positive lymph nodes, histological grade and subtype, tumor grade, lymphovascular space involvement (LVSI), and FIGO stage [4].

Hematological indices like the eosinophil-lymphocyte ratio (ELR) and the prognostic nutritional index (PNI) have been suggested to predict tumor behavior and patient outcomes in various cancers [6-9]. We chose ETEC due to its high prevalence and the need for better prognostic markers in this specific subtype. This study aims to evaluate the prognostic value of these markers in predicting the grade and stage of ETEC.

Material and Methods

Study Design and Participants

This retrospective study included patients diagnosed with ETEC at a tertiary care center. Participants were categorized based on

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tumor grade and stage. Hematological indices were measured from preoperative blood samples. Key indices analyzed included platelet count (PLT), neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), systemic inflammation index (SII), systemic inflammatory response index (SIRI), ELR, and PNI.

This study utilized the surgical staging results, which were determined based on the TNM classifications of the estimated International Federation of Gynecology, Obstetrics (FIGO), Union for International Cancer Control, and American Joint Committee on Cancer (AJCC). [4].

Ethical Approval

This received approval from the Sivas Cumhuriyet University Ethics Committee. All participants provided written informed consent prior to their inclusion in the study. The study was approved by the ethical committee with the approval number 2024/04-15 on 18.04.2024.

Data Collection and Analysis

Data on hematological indices were collected from patient records. The Kruskal-Wallis test was used to assess the significance of differences across tumor grades and stages, and the association between these indices and tumor grade and stage was evaluated to determine their predictive value.

Results

Significant differences were found in ELR and PNI among different tumor grades. The significant difference in ELR indicates that it can differentiate between grades of ETEC. Specifically, there is a notable difference between grade 1 and grade 3, as well as grade 2 and grade 3. This suggests that higher ELR is associated with more advanced grades of ETEC, suggesting its potential as a predictive marker for more aggressive disease (p=0.005). PNI was also significantly different across tumor grades (p=0.036), indicating its prognostic value (Table 1). Other indices such as NLR, PLR, and platelet count did not show significant differences, highlighting the specificity of ELR and PNI.

Table 1. Hematological indices evaluating prediction of grade of endometrioid type endometrium cancer

	Grade 1	Grade 2	Grade 3	
Indexes	**Median (Q1-Q3)**	**Median (Q1-Q3)**	**Median (Q1-Q3)**	**P**
PLT	271.00 (226.25-310.50)	259.50 (230.00-328.00)	282.00 (232.50-347.00)	0.4
NLR	2.89 (1.80-5.99)	3.37 (2.08-5.84)	2.76 (2.01-4.81)	0.69
PLR	150.11 (117.33-221.30)	184.96 (130.26-256.61)	154.12 (122.80-249.73)	0.436
ELR	0.040 (0.017-0.072)[a]	0.035 (0.010-0.077)[a]	0.07 (0.04-0.11)[b]	**0.005****
PNI	42.70 (39.93-44.93)[a]	41.76 (37.10-43.98)[ab]	40.10 (36.05-43.76)[b]	**0.036***

PLT: platelet count, NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, ELR: eosinophil-lymphocyte ratio, PNI: prognostic nutritional index, *p<0.05, **p<0.005, Kruskal Wallis test

Regarding tumor stages, PLT, PLR, SII, SIRI, ELR, and PNI showed significant differences across various stages of ETEC (Table 2). PLR was found to be the most significant marker for staging, with a notable difference observed between stages 1 and 4 (p=0.003). Additionally, PLT, SII, SIRI, and ELR were also significantly different across stages, indicating their potential prognostic value. Notably, PLR showed a very strong significance with a p-value below 0.005 (p=0.003), highlighting its robust association with tumor staging.

Table 2. Hematological indices evaluating prediction of stage of endometrioid type endometrium cancer

	Stage 1	Stage 2	Stage 3	Stage 4	
Indexes	**Median (Q1-Q3)**	**Median (Q1-Q3)**	**Median (Q1-Q3)**	**Median (Q1-Q3)**	**p**
PLT	268 (224-315)	282 (256-345)	254 (1.96-8.98)	348 (288-431)	**0.033***
NLR	2.84 (1.76-4.62)	2.63 (2.18-8.56)	2.84 (1.96-8.98)	5.88 (3.46-13.02)	0.080
PLR	146.43 (118.67-205.83)	138.92 (124.18-242.96)	207.90 (116.25-332.98)	267.44 (221.47-391.82)	**0.003****
SII	804.57 (490-1306.99)	792.00 (611.26-2954.37)	964.39 (411.18-2546.19)	2069.82 (1202.65-3879.14)	**0.016***
SIRI	1.22 (0.74-2.86)	1.35 (0.95-5.82)	1.03 (0.68-4.13)	3.48 (1.83-9.37)	**0.026***
ELR	0.04 (0.02-0.07)	0.08 (0.02-0.13)	0.06 (0.02-0.10)	0.08 (0.06-0.11)	**0.013***
PNI	42.40 (40.00-45.01)	39.00 (35.91-43.30)	41.05 (36.18-44.00)	40.00 (30.30-43.50)	**0.016***

PLT: platelet count, NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, SII: systemic inflammation index, SIRI: systemic inflammatory response index, ELR: eosinophil-lymphocyte ratio, PNI: prognostic nutritional index, *p<0.05, **p<0.005, Kruskal Wallis test

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Discussion

The findings of our study underscore the potential utility of hematological indices such as ELR and PNI in the prognostic assessment of ETEC. The significant correlation of higher ELR and lower PNI with more advanced tumor grades and stages aligns with previous research emphasizing the role of systemic inflammation and nutritional status in cancer progression [6-9].

Previous studies have explored the prognostic value of various hematological markers in cancer [6-9]. Our study highlighted the predictive value of ELR and PNI in the prognostic evaluation of ETEC grading. However, our study found that staging was more strongly correlated, particularly with PLR, which shows promise for clinical usage. Other indices such as ELR, PNI, SII, SIRI, and PLT were also significant in staging.

Marin et al. (2024) support these results by demonstrating the value of systemic immune-inflammation indices such as NLR and PLR as prognostic tools in endometrial cancer [7]. Similarly, Hishinuma et al. (2023) highlight the importance of pre-operative hematological indices, reinforcing the relevance of ELR and PNI [5].

Further validation is found in Njoku et al. (2022), who identify NLR and PLR as significant prognostic indicators, showing a strong link between inflammation markers and negative outcomes in endometrial cancer cases [7]. This comprehensive approach is mirrored by Marin et al. (2024), who integrate multiple hematological markers into a prognostic framework [8].

Huang et al. (2021) and Mirili & Bilici (2020) have demonstrated that systemic immune-inflammation indices, such as the SII, are more effective prognostic indicators in many types of malignancies, including endometrial cancer [10,11]. These studies support our findings, suggesting that hematological indicators are useful in predicting patient outcomes. Integrating these indices into nomogram models, as proposed by Chen et al. (2020), can enhance prognostic evaluations and tailor treatment approaches [12].

In addition, Leng et al. (2022) highlight the significance of pre-treatment ratios such as NLR and PLR in forecasting cancer outcomes [13]. Although our investigation did not identify any significant variations in NLR and PLR across different tumor grades, the considerable predictive significance of ELR and PNI highlights the unique relevance of these indices in endometrial cancer.

In their study, Han et al. (2021) performed a thorough examination of the predictive significance of hemato-immunological indices in uterine cervical cancer [14]. They proposed that these indicators could also be valuable in predicting the prognosis of endometrial cancer. Our research supports the conclusion that ELR and PNI are dependable indicators for evaluating tumor aggressiveness and predicting patient survival.

Furthermore, Ionică et al. (2024) highlight the predictive role of pre-operative anemia in the early recurrence of endometrial cancer, which complements our study by suggesting that nutritional and hematological status are crucial in cancer prognosis [15].

The significant prognostic value of hematological indices such as ELR (Eosinophil-Lymphocyte Ratio) and PNI (Prognostic Nutritional Index) in endometrial cancer is reinforced by multiple studies. Petric et al. (2023), in their work on hematological and biochemical markers for endometrial cancer, emphasize the diagnostic and staging relevance of these markers [16]. Their findings align with our study, highlighting the importance of integrating these indices into routine clinical assessments for more accurate prognosis and treatment planning.

Furthermore, Cong et al. (2020) demonstrated the combined prognostic value of preoperative ratios such as NLR (Neutrophil-Lymphocyte Ratio), PLR (Platelet-Lymphocyte Ratio), and MLR (Monocyte-Lymphocyte Ratio) in endometrial cancer [17]. Their research suggests that a combination of these markers can provide a superior prognostic framework, supporting our results that ELR and PNI are crucial in assessing tumor aggressiveness and patient survival.

Additionally, Xiong et al. (2023) investigated the predictive value of hemoglobin, albumin, lymphocyte, and platelet indexes for lymph node metastasis and recurrence in endometrial cancer [18]. Their retrospective study underscores the significance of these hematological markers in predicting disease progression, which complements our findings on the prognostic relevance of ELR and PNI. By incorporating these indices into clinical practice, healthcare providers can better stratify patients based on risk and tailor treatment strategies accordingly.

The integration of these markers into nomogram models, as suggested by Chen et al. (2020) and validated in our study, enhances the precision of prognostic assessments [12]. These models can incorporate multiple independent risk factors, providing a comprehensive tool for clinicians to predict patient outcomes and make informed decisions about postoperative management.

Integrating ELR and PNI into routine clinical practice could improve prognostic assessments for ETEC grading. These markers are easily measurable from routine blood tests, making them accessible and cost-effective tools for guiding therapeutic decisions. Subsequent investigations should prioritize bigger, multi-center groups of individuals to confirm these discoveries and investigate the combination of hematological indices with molecular markers to provide a more comprehensive prognostic framework.

Conclusion

Hematological indices, particularly ELR and PNI, show promise as predictive markers for tumor grade in ETEC. Their routine use could enhance prognostic assessments and guide therapeutic decision-making, ultimately improving patient outcomes.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
This study was reviewed and approved by the Sivas Cumhuriyet University Ethics Committee. The approval reference number is 2024/04-15 on 18.04.2024. The study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki.

Patient Informed Consent
All patients participating in this study were informed about the study's purpose, methodology, potential risks, and benefits, and provided written informed consent. The research was conducted in accordance with the ethical principles of the Declaration of Helsinki. All participants completed and signed a written informed consent form prior to their inclusion in the study.

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