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Predictive Utility of Systemic Immune Inflammation Index (SII) in Identifying Endometrial Carcinoma in Premalignant Endometrial Lesions

Sistemik İmmün İnflamatuar İndeksin (Sİİ) Premalign Endometrial Lezyonlarda Endometrial Karsinom Tanısında Öngörüsel Kullanımı

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Abstract

Introduction: It is important to detect endometrial cancer (EC) in endometrial intraepithelial neoplasia (EIN) patients. It was aimed to determine the role of systemic immune inflammation index (SII) in predicting concurrent EC in women with EIN.

Materials and Methos: In this retrospective study, 429 women with EIN divided into three groups according to final histopathologic results: benign(n=151), EIN(n=152), and EC(n=126). Demographic and clinical data, pathologic and laboratory result were collected. Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and SII index were calculated and compared among groups.

Results: The SII, PLR and NLR values of benign, EIN and EC groups were compared and all values of EC group were the highest (p<0.001). The ROC analysis showed that although all markers had statistical significance, the AUC of SII was the highest. The SII score>0.67 (95%CI:7.17-37.3, p<0.001) had a 16.35-fold, preoperative platelet count > 287 (95%CI:1.91-6.2, p<0.001) had a 3.45-fold and age >49 years (95%CI:1.97-5.92, p<0.001) had 3.42-fold increased risk for EC.

Conclusion: Although age and preoperative platelet count were found independent risk factors, SII was the strongest predictor for EC in women with EIN. SII can be used as a predictive marker for identifying concurrent EC or having risk for developing EC in women with EIN.

Keywords: Endometrial cancer; endometrial hyperplasia; endometrial neoplasms; inflammation.

Özet

Amaç: Endometriyal intraepitelyal neoplazi (EİN) tanısı alan kadınlarda, eş zamanlı endometriyal kanser (EK) tanısının önemli olması nedeniyle, bu çalışmada EİN olgularında sistemik immün inflamatuar indeksin (Sİİ) EK'nın tahminindeki rolünü incelemeyi amaçlanmıştır.

Gereç ve Yöntem: Bu retrospektif çalışmada, EİN tanısı konulmuş 429 kadın final histopatolojik sonuçlarına göre benign (n=151), EİN (n=152) ve EK (n=126) olmak üzere üç gruba ayrıldı. Demografik ve klinik veriler ile patolojik ve laboratuvar sonuçları hasta dosyalarından toplandı. Nötrofil-lenfosit oranı (NLR), trombosit-lenfosit oranı (PLR) ve Sİİ indeksi hesaplandı ve ilgilenilen özellikler bakımından gruplar karşılaştırıldı.

Bulgular: Benign, EİN ve EK gruplarının Sİİ, PLR ve NLR değerleri hesaplandı ve üç grup arasında karşılaştırıldı. EK grubunun Sİİ, PLR ve NLR değerleri diğer gruplardan yüksek bulundu. ROC analizi, Sİİ, PLR ve NLR'nin istatistik olarak EK için anlamlı olduğunu gösterdi, ancak Sİİ'nin eğri altında kalan (AUC) değeri en yüksek bulundu. Sİİ skoru>0.67 (95%GA: 7.17-37.3), preoperatif trombosit sayısı >287 (95%GA: 1.91-6.2) ve yaş >49 yıl (95%GA: 1.97-5.92) olması, EK riskinde sırasıyla 16.35 kat, 3.45 kat ve 3.42 kat artışla ilişkilendirildi.

Sonuç: Yaş ve preoperatif trombosit sayısı bağımsız risk faktörleri olarak belirlenmiş olmasına rağmen, Sİİ, EİN tanılı kadınlarda EK için en güçlü tahmin edici olarak bulundu. Sİİ, eş zamanlı EK tanımlamak veya EİN tanılı kadınlarda EK geliştirme riskini değerlendirmek için kullanılabilir.

Introduction

Endometrial intraepithelial neoplasia (EIN) is a premalignant lesion, and within one year, approximately 1/3 of newly diagnosed EIN cases develop into endometrial carcinoma (EC) (1). The majority of EIN patients diagnosed at EC are early-stage and low-risk cases (2). Diagnosis and therapeutic treatment of premalignant lesions of the endometrium is central to the prevention ofendometrial cancer (3). Early detection improvesthe chances that the cancer can be successfully treated (4).

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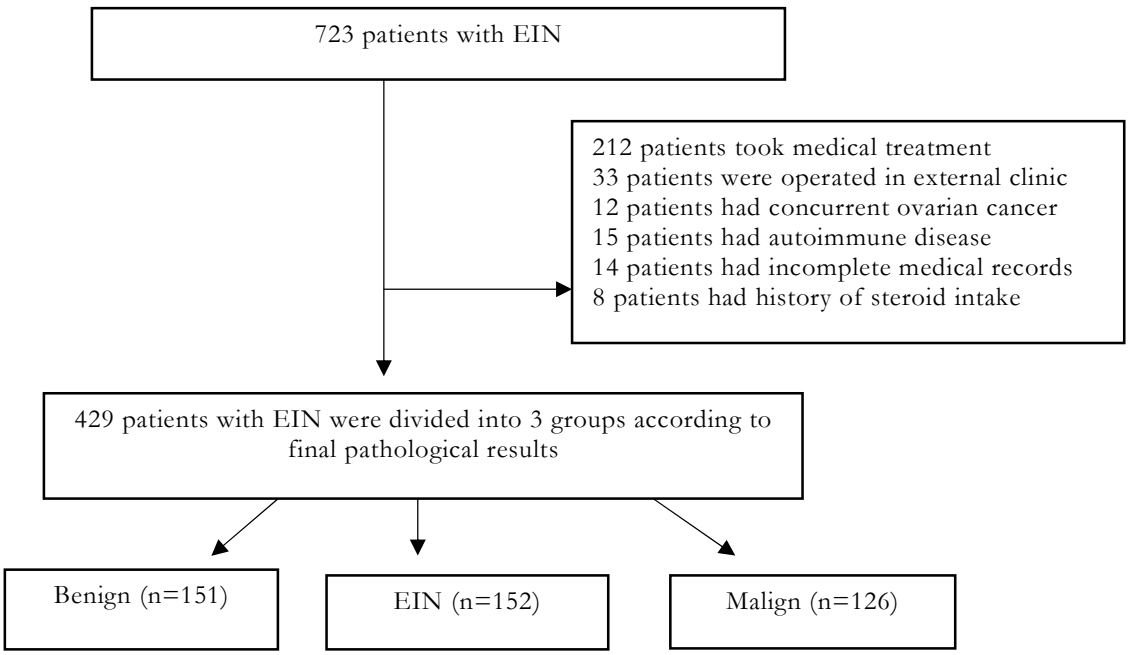

Figure 1. Flow chart of the study

Recently, there has been increased interest in the tumor microenvironment (5). A variety of inflammatory cells and mediators are considered to be major factors of the tumor microenvironment (5,6). Inflammation is involved in tumor development, progression, and metastasis (7,8). Two mechanisms have been identified for the relationship between cancer and inflammation: intrinsic and extrinsic mechanisms. At EC, increased release of inflammatory substances is thought to promote tumor development via the intrinsic pathway (7-10).
Peripheral blood cells (neutrophils, lymphocytes, and monocytes) may reflect the inflammatory microenvironment of cancer. Cancer cells produce growth factors, and these factors induce thrombopoiesis, lymphopoiesis, and granulopoiesis (9-11). Previous studies have shown that leukocytosis, neutrophilia, and thrombocytosis are involved in the development, progression, and prognosis of cancer. Peripheral blood cells can be detected in a simple and convenient manner (12-13). Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and systemic immune inflammation index (SII) can serve as meaningful prognostic indicators in patients with various cancers, including EC (14,15). The SII has been shown to be a useful prognostic indicator in cancer patients. Many studies have shown that systemic inflammatory response markers are associated with postoperative survival in EC patients (16-18). Although the importance of SII in the prognosis of EC has been discussed in previous studies, its role in EIN cases has not been discussed (16-20). Therefore, this study aimed to investigate whether SII is useful for predicting coexisting EC in women with EIN.

Materials and Methods

There were 723 women with diagnosis of EIN according to endometrial curettage samples. In 511 of them hysterectomy was chosen initially for treatment according to the patient's risk of concurrent EC or progression to EC. Medical treatment was chosen alternative to hysterectomy in 212 women who desired fertility, declined hysterectomy and had a high risk of surgical complications. The study enrolled 511 patients diagnosed with EIN and operated at a gynecologic oncology clinic in a tertiary hospital. The study included women who had surgery at the hospital, whose final histopathologic evaluation was performed at the same hospital, and whose blood counts were obtained one week before surgery. All surgical procedures included hysterectomy and salphingoophorectomy by laparotomy or laparoscopy. FIGO Classifications from EC were used for staging and grading. Surgical staging was determined by the surgical team based on tumor size, extent of myometrial invasion, and tumor grade. Exclusion criteria were concurrent ovarian or other malignancies; endometrial cancer that was not of the endometrioid type at the time of final histopathologic evaluation; steroid use; inflammatory, hematologic, and autoimmune diseases; and missing data in medical

records. Women who took medical therapy was excluded from study, also. Demographic characteristics such as age, body mass index (BMI), menopausal status, medical history, smoking habits, ultrasound findings such as endometrial thickness, and pathologic results were obtained by reviewing medical records. After reviewing the patients' medical records, 82 patients were excluded because 33 of them had undergone surgery at another hospital, 12 had concurrent ovarian cancer, 15 had autoimmune disease (Rheumatoid arthritis, Celiac disease, Graves, Hashimoto thyroiditis, etc.) 14 had incomplete medical records, and 8 had taken steroids. Figure 1 shows the flowchart of the study. Four hundred twenty-nine patients who met the inclusion criteria were enrolled in the study. Patients were divided into three groups according to the final pathologic findings: benign, EIN and endometrial cancer. Benign findings included nonatypical hyperplasia, leiomyoma, cervicitis, and proliferative endometrium. In the cancer group, all cancer cases were endometrioid-type endometrial carcinomas. Neutrophil, lymphocyte, and platelet counts were used to calculate NLR, PLR, and SII indices. NLR and PLR were calculated by dividing the total neutrophil or platelet count by the total lymphocyte count. SII was calculated by multiplying the platelet and neutrophil counts and dividing by the lymphocyte count. Formula for SII = (P × N)/ L.

Table 1: Descriptive statistics and comparison results of three groups

	Benign (n=151)	EIN (n=152)	Malign (n=126)	p value
Age (y)	47.8±6.95[a]	49.06±7.43[a, b]	53.76±9.11[c]	0.001
BMI (kg/m^2)	30.53±4.53[a]	31.48±4.88[a, b]	32.17±5.17[b, c]	0.027
Gravidity (median, range)	3(0-7)	3(0-12)	3(0-9)	0.059
Parity (median, range)	2(0-6)	2(0-7)	2(0-7)	0.085
Endometrial thickness (mm)	10.11±5.25[a]	11.81±5.42[b]	12.39±7.19[b, c]	0.004
Preoperative leukocyte (x1/μL)	7.72±2.46	7.55±2.37	7.99±2.21	0.299
Preoperative hemoglobin (x1/μL)	12.25±1.86	12.65±1.63	12.99±1.58	0.002
Preoperative platelet (x1/μL)	288.21±78.16[a]	271.05±54.68[a, b]	329.76±78.21[c]	0.001
SII	6.28±4[a]	6.42±4.6[a, b]	10.27±6.33[c]	0.001
PLR	160.11±88.44[a]	148.78±65.48[a, b]	176.17±83.4[a, c]	0.017
NLR	2.21±1.44[a]	2.36±1.67[b]	2.66±1.29[c]	0.040
SII adjusted for age	6.28±4	6.42±4.6	10.27±6.33	0.001

† ***BMI:*** *Body mass index,* ***SII:*** *Systemic immune inflammation index,* ***PLR:*** *Platelet to Lymphocyte Ratio,* ***NLR:*** *Neutrophil to Lymphocyte Ratio.* ‡^{a,b,c} *groups with different letters are significantly different from each other.*

Ethical approval: In accordance with the Helsinki Declaration study was performed. Ethical approval was obtained from the Clinical Research Ethics Committee of the Ankara Etlik Zubeyde Hanim Women's Health and Research Hospital on 26/05/2022 with decision number 06-14.

Statistical analysis: The SPSS (Statistical Package for the Social Science) version 24 program (SPSS, Chicago, IL, USA) was used for statistical analyzes. Histogram and Shapiro-Wilk normality tests were used to determine the distribution of parameters. Descriptive statistics were presented as mean ± standard deviation. Chi-square test was used to compare determine relationships among categorical variables. Qualitative data were presented as number (n) and percentage (%). For comparison of three groups, the ANOVA test was used, and Bonferroni and Tukey were used as post hoc tests to determine the difference between pairs. Receiver operating characteristic analysis (ROC) was used to determine the predictive value of PLR, NLR, and SII for distinguishing endometrial cancer from other cases. Cutoff values and area under the curve (AUC), sensitivity, and specificity were calculated according to the ROC curve. Univariate analysis was performed to determine the risk factors for EC. After univariate analysis, a model for multiple logistic regression analysis was formed. 95% confidence interval and a p value of < 0.05 were considered significant.

Results

Four hundred and twenty-nine patients were enrolled in the study. 151 (35.2%) of the women were postmenopausal, and laparotomy was preferred in 258 (60.1%) and laparoscopy in 170 (39.6%) women. Patients were divided into three groups according to the final pathologic findings: benign (n=151), EIN (n=152), and EC (n=126). Table 1 shows the comparison of demographic, clinical, and blood outcomes in the three groups. Age, BMI, and endometrial thickness were statistically significant (p< 0.001, p=0.027, p=0.004, respectively). There were no statistically significant differences among groups in terms of chronic disease, smoking status, and menopausal status. In the cancer group, all women were stage I, n=103 (81.7%) were stage IA, and n=23 (18.3%) were stage IB. The SII was calculated by multiplying the platelet and neutrophil counts and dividing by the lymphocyte count.

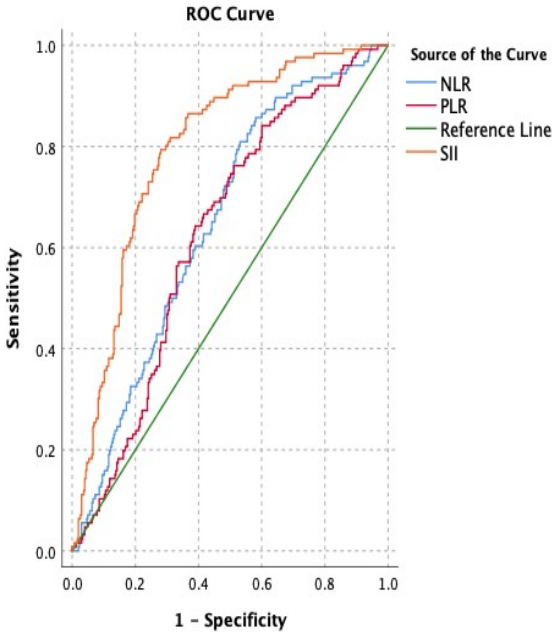

Figure 2: ROC analysis of SII, PLR and NLR for predictability of Endometrial Cancer

(**AUC**=0.795, an optimal cutoff point of **SII=0**.67, **sensitivity=**80.2%, **specificity=**70.3%; AUC=0.628, an optimal cutoff point of **PLR=**153.881, **sensitivity=**65.1%, **specificity=**60%; **AUC=**0.647, an optimal cutoff point of **NLR=**2.105, **sensitivity=**62.7%, **specificity=**58.4%)

Formula for SII = (P × N)/L. SII, PLR, and NLR values of the groups were compared. There was no statistically significant difference between the SII, PLR, and NLR values of benign and EIN groups; the SII (6.28±4, 6.42±4.6, 10.27±6.33), PLR (160.11±88.44, 148.78±65.48, 176.17±83.4) and NLR values (2.21±1.44, 2.36±1.67, 2.66±1.29) (benign, EIN, and EC, respectively) of EC were higher than the other groups (p < 0.001). Figure 3 shows the comparison of SII values of three groups. The predictive value of SII, PLR, and NLR for EC was calculated using ROC analysis (Figure 2).

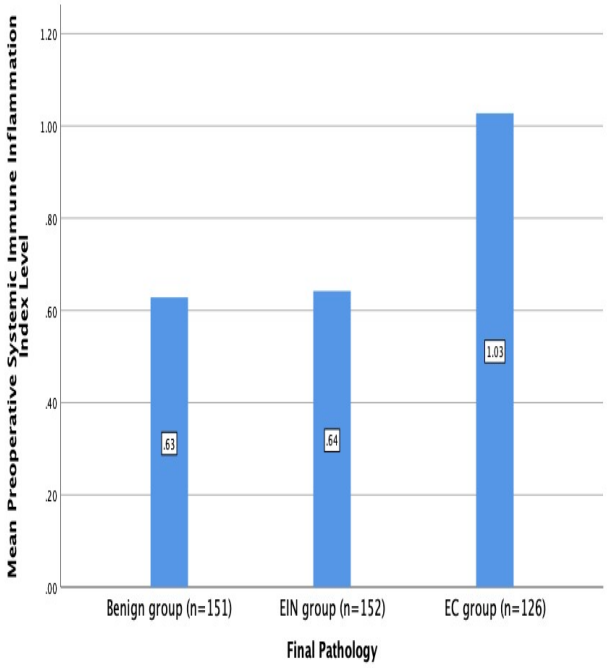

Figure 3. Comparison of SII values of three groups

Cut-off values were calculated. The ROC analysis showed that although all markers had statistical significance, the AUC of SII was the highest. Patients were divided into two groups based on the cut-off values from the ROC analysis and the median values of age, BMI, and endometrial thickness. After univariate logistic regression analysis, age, endometrial thickness, preoperative platelet count, PLR, NLR, and SII were determined as risk factors. After univariate analysis, a multiple logistic regression model was constructed; age, preoperative platelet count, and SII were found significant risk factors for EC. Patients with an SII score > 0.67 (95% CI: 7.17-37.3, p < 0.001) had a 16.35-fold increased risk of EC, 3.45-fold increased risk in patients with a preoperative platelet count > 287

Table 2: Multiple logistic regression analysis of the variables for endometrial cancer

Factor		Univariate logistic regression Odds ratio (95% CI)	p*	Muliple logistic regression Odds ratio (95% CI)	p*
Age (years)	≤49 (n=223)	1 (reference)			
	>49 (n=206)	2.69 (1.74-4.14)	0.001	3.42 (1.97-5.92)	0.001
BMI (kg/m²)	≤30.82 (n=214)	1 (reference)			
	>30.82 (n=215)	1.49 (0.98-2.26)	0.061	-	
Endometrial thickness (mm)	≤10 (n=221)	1 (reference)			
	>10 (n=208)	1.56 (1.02-2.37)	0.036	1.43 (0.84-2.43)	0.178
Preoperative Platelet	≤287 (n=217)	1 (reference)			
	>287 (n=212)	5.8 (3.59-9.37)	0.001	3.45 (1.91-6.2)	0.001
PLR	≤153.881 (n=223)	1 (reference)			
	>153.881 (n=206)	3.82 (2.44-5.98)	0.001	0.91 (0.46-1.79)	0.79
NLR	≤2.105 (n=226)	1 (reference)			
	>2.105 (n=203)	2.94 (1.9-4.54)	0.001	0.69 (0.34-1.42)	0.324
SII	≤0.67 (n=238)	1 (reference)			
	>0.67 (n=191)	15.9 (9.09-27.8)	0.001	16.35 (7.17-37.3)	0.001

(95% CI: 1.91-6.2, p < 0.001) and 3.42-fold in patients older than 49 years (95% CI: 1.97-5.92, p< 0.001) (Table 2).

Discussion

EIN is a precancerous lesion that can progress into EC. It is important to detect concurrent endometrial cancer in EIN patients to ensure successful treatment and surveillance. However, there are studies in the literature investigating the predictive markers for EC, but there is no reliable test for usage. The contribution of inflammatory cells and cytokines to tumor growth has been reported in previous studies.[11-13] The relationship between the systemic inflammatory response and malignancies, including gynecologic malignancies, has been demonstrated (14-15). The prognostic value of systemic inflammatory markers before treatment in patients with endometrial cancer and their influence on prognosis have also been investigated (16-20). This study aimed to investigate whether the SII is useful for predicting coexisting EC in women with EIN. In a study that investigated the relationship between pretreatment systemic inflammatory markers and prognosis in stage I EC, it was found that poor clinical outcome was significantly related to elevate MLR (16). Matsubara et al. found that elevated SII was associated with shorter survival EC. SII was more valuable than PLR or NLR for estimating survival (17). In a prospective study by Njoku et al. the predictive power of pretreatment systemic inflammatory markers including CRP, NLR, SII for survival was investigated in EC patients. Only women with pretreatment CRP > 5.5 mg/L had higher mortality than women with < 5.5 mg/L (18). But CRP is not a specific test. It can detect any inflammation in any part of the body. The role of CRP in predicting mortality in EC patients is controversial. Lei et al. investigated the predictive value of preoperative SII for lymph node metastases (LNM) in EC patients. It was found that elevated SII was associated with LNM (19). Huang et al. investigated the preoperative and postoperative SII to predict the prognosis of patients with EC after surgery. Preoperative SII, NLR, and PLR were found to be not significant for prognosis. Postoperative SII was found to be an independent risk factor for survival and contributed to poor outcome (20). NLR and PLR values were associated with poor prognosis at EC (21-22). These studies mainly investigated the

predictability of inflammatory markers for survival and prognosis of endometrial cancer. It can be said that systemic inflammatory markers are useful for predicting prognosis after EC. Our study investigated the role of inflammatory markers in detecting EC or predicting progression to EC in EIN. The SII value of EC patients was higher than that of the benign and EIN groups, and SII was found to be the strongest risk factor for EC. The risk for EC was increased 16.35-fold in patients with an SII value > of 0.67. However, the effect of SII on survival and outcome could not be evaluated in our study because of all EC patients were at stage I and recurrence occurred in only 8 patients in the study population. Selen et al compared the preoperative PLR, NLR, and PDW values of patients with EIN and EC. NLR was different between groups but had no diagnostic predictive value. A low PLR score was associated with EC (23). In studies comparing NLR and PLR values of patients with normal endometrial pathology, EIN and EC, no significant difference was found between the groups (24-27). In our study, NLR and PLR values differed significantly between groups, with the highest values in the cancer groups. The ROC analysis showed that NLR, PLR, and SII were statistically significant, but the AUC of SII was higher than NLR and PLR. NLR and PLR were associated with EC in univariate analysis. However, in multiple analysis, they were not found to be an independent risk factor for EC. In a study by Vetter et. al, high endometrial thickness and older age were found to be the strongest predictors of EC in EIN cases (28). Another study found an association between age greater than 60 years and a BMI ≥ 40 kg/m^2 and endometrial cancer (29). A recent study found no statistical differences in endometrial thickness and BMI among benign, EIN and EC patients. This study suggests that in diabetic women with EIN, preoperative HgA1c level could be used as a predictor for EC (30). In our study, age, BMI, and endometrial thickness were found to be significantly different among the groups. In the multiple model, age > 49 years had a 3.42-fold increased risk for EC. Although retrospective studies contribute greatly to the literature. The retrospective design and single-center conduct may be the limitations of the study. Performing at a single center has the advantage that the histopathologic material is examined by the same pathologists. The sufficient number of patients and the homogeneity of the groups were the strengths of the study. In addition, to our knowledge, this is the first study to investigate whether SII is useful for predicting coexisting EC in women with EIN. Future larger studies with prospective designs are needed to substantiate these data.

Study limitations: The study has several limitations. First, its retrospective design and reliance on historical data from a single medical center may limit the generalizability of the findings. The sample size, although considered sufficient, may not be representative of the broader population, potentially affecting the study's statistical power. Additionally, the lack of data on survival and long-term outcomes restricts the assessment of the inflammatory markers' impact on prognosis.

Conclusion

Age, preoperative platelet count and SII were found independent risk factors for EC in women with EIN. SII was found the strongest predictive marker for EC. It is calculated easily from blood tests and it can be used as a predictive marker for identifying concurrent EC or having risk for developing EC in women with EIN.

Ethical approval: Ethical approval was obtained from the Clinical Research Ethics Committee of the Ankara Etlik Zübeyde Hanım Women's Health and Research Hospital on 26/05/2022 with decision number 06-14.

Conflict of interest: The authors have no conflicts of interest related to this study.

Financial support: No financial support was received for this study.

Author contributions: Concept (CK, BK, VK), Design (VK, HK, ZK), Data Collection and/or Processing (CK, BK), Analysis and/or Interpretation (CK, BK, VK, ZK).

References

1. Hecht JL, Ince TA, Baak JP, Baker HE, Ogden MW, Mutter GL. Prediction of endometrial carcinoma by subjective endometrial intraepithelial neoplasia diagnosis. Mod Pathol 2005;18(3):324-330.
2. Weiderpass E, Antoine J, Bray FI, Oh JK, Arbyn M. Trends in corpus uteri cancer mortality in member states of the European Union. Eur J Cancer 2014;50(9):1675-1684.
3. Baak JP, Mutter GL, Robboy S, van Diest PJ, Uyterlinde AM, Orbo A, et al. The molecular genetics and morphometry-based endometrial intraepithelial neoplasia classification system predicts disease progression in endometrial hyperplasia more accurately than the 1994 World

Health Organization classification system. Cancer 2005;103(11):2304-2312.
4. Auclair MH, Yong PJ, Salvador S, Thurston J, Colgan TTJ, Sebastianelli A. Guideline No. 390-Classification and Management of Endometrial Hyperplasia. J Obstet Gynaecol Can 2019;41(12):1789-1800.
5. Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow? Lancet 2001;357(9255):539-545.
6. Quail DF, Joyce JA. Microenvironmental regulation of tumor progression and metastasis. Nat Med 2013;19(11):1423-1437.
7. Mantovani A, Cassatella MA, Costantini C, Jaillon S. Neutrophils in the activation and regulation of innate and adaptive immunity. Nat Rev Immunol 2011;11(8):519-531.
8. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell 2011;144(5):646-674.
9. Weis SM, Cheresh DA. Tumor angiogenesis: molecular pathways and therapeutic targets. Nat Med 2011;17(11):1359-1370.
10. Shiao SL, Ganesan AP, Rugo HS, Coussens LM. Immune microenvironments in solid tumors: new targets for therapy. Genes Dev 2011;25(24):2559-2572.
11. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. Cell 2010;140(6):883-899.
12. Sangiovanni A, Del Ninno E, Fasani P, De Fazio C, Ronchi G, Romeo R, et al. Increased survival of cirrhotic patients with a hepatocellular carcinoma detected during surveillance. Gastroenterology 2004;126(4):1005-1114.
13. Beaugerie L, Svrcek M, Seksik P, Bouvier AM, Simon T, Allez M,et al. Risk of colorectal high-grade dysplasia and cancer in a prospective observational cohort of patients with inflammatory bowel disease. Gastroenterology 2013;145(1):166-175.
14. Cong R, Kong F, Ma J, Li Q, Wu Q, Ma X. Combination of preoperative neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and monocyte-lymphocyte ratio: a superior prognostic factor of endometrial cancer. BMC Cancer 2020;20(1):464.
15. Raungkaewmanee S, Tangjitgamol S, Manusirivithaya S, Srijaipracharoen S, Thavaramara T. Platelet to lymphocyte ratio as a prognostic factor for epithelial ovarian cancer. J Gynecol Oncol 2012;23(4):265-273.
16. Ahn JH, Lee SJ, Yoon JH, Park DC, Kim SI. Prognostic value of pretreatment systemic inflammatory markers in patients with stage I endometrial cancer. Int J Med Sci 2022;19(14):1989-1994.
17. Matsubara S, Mabuchi S, Takeda Y, Kawahara N, Kobayashi H. Prognostic value of pre-treatment systemic immune-inflammation index in patients with endometrial cancer. PLoS One 2021;16(5):1-11.
18. Njoku K, Ramchander NC, Wan YL, Barr CE, Crosbie EJ. Pre-treatment inflammatory parameters predict survival from endometrial cancer: A prospective database analysis. Gynecol Oncol 2022;164(1):146-153.
19. Lei H, Xu S, Mao X, Chen X, Chen Y, Sun X, et al. Systemic Immune-Inflammatory Index as a Predictor of Lymph Node Metastasis in Endometrial Cancer. J Inflamm Res 2021;14:7131-7142.
20. Huang Y, Chen Y, Zhu Y, Wu Q, Yao C, Xia H, et al. Postoperative Systemic Immune-Inflammation Index (SII): A Superior Prognostic Factor of Endometrial Cancer. Front Surg 2021;8:704235.
21. Ni L, Tao J, Xu J, Yuan X, Long Y, Yu N, et al. Prognostic values of pretreatment neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in endometrial cancer: a systematic review and meta-analysis. Arch Gynecol Obstet 2020;301(1):251-261.
22. Haruma T, Nakamura K, Nishida T, Ogawa C, Kusumoto T, Seki N, et al. Pre-treatment neutrophil to lymphocyte ratio is a predictor of prognosis in endometrial cancer. Anticancer Res 2015;35(1):337-343.
23. Selen S, Kilic F, Kimyon Comert G, Unsal M, Kilic C, Karalok A, et al. Can preoperative inflammatory markers differentiate endometrial cancer from complex atypical hyperplasia/endometrial intraepithelial neoplasia? J Obstet Gynaecol Res 202;46(7):1148-1156.
24. Ural ÜM, Şehitoğlu İ, Tekin YB, Şahin FK. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in patients with endometrial hyperplasia and

endometrial cancer. J Obstet Gynaecol Res 2015;41(3):445-448.
25. Acmaz G, Aksoy H, Unal D, Ozyurt S, Cingillioglu B, Aksoy U, et al. Are neutrophil/lymphocyte and platelet/lymphocyte ratios associated with endometrial precancerous and cancerous lesions in patients with abnormal uterine bleeding? Asian Pac J Cancer Prev 2014;15(4):1689-1692.
26. Kurtoglu E, Kokcu A, Celik H, Sari S, Tosun M. Platelet Indices May be Useful in Discrimination of Benign and Malign Endometrial Lesions, and Early and Advanced Stage Endometrial Cancer. Asian Pac J Cancer Prev 2015;16(13):5397-5400.
27. Cakmak B, Gulucu S, Aliyev N, Ozsoy Z, Nacar M, Koseoglu D. Neutrophil-lymphocyte and platelet-lymphocyte ratios in endometrial hyperplasia. Obstet Gynecol Sci. 2015;58(2):157-161.
28. Vetter MH, Smith B, Benedict J, Hade EM, Bixel K, Copeland LJ, et al. Preoperative predictors of endometrial cancer at time of hysterectomy for endometrial intraepithelial neoplasia or complex atypical hyperplasia. Am J Obstet Gynecol 2020;222(1):601-607.
29. Giannella L, Delli Carpini G, Sopracordevole F, Papiccio M, Serri M, Giorda G, et al. Atypical Endometrial Hyperplasia and Unexpected Cancers at Final Histology: A Study on Endometrial Sampling Methods and Risk Factors. Diagnostics (Basel) 2020;10(7):474.
30. Kose C, Korpe B, Korkmaz V, Engin-Ustun Y. Is hemoglobin A1c valuable for predicting concurrent endometrial cancer in diabetic women with endometrial intraepithelial neoplasia? Gynecol Endocrinol. 2022;38(11):1003-1007.