Experimental
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Clinical Article

Gynecology; *and Gynecological Oncology*

The Effect of Prognostic Nutritional Index and Systemic Inflammatory Index in Endometrioid Type Endometrial Cancer

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ABSTRACT

OBJECTIVES: The primary goal of the cohort was to show the relationship between systemic inflammatory index (SII) and prognostic nutritional index (PNI) values and the prognostic factors of endometrial cancer (EC), especially lymph node (LN) involvement, and lymphovascular space invasion (LVSI), which can not generally be evaluated preoperatively.

STUDY DESIGN: This is a retrospective cohort study on reviews of patient records who were diagnosed with EC and underwent treatment between January 2014 and 2021. Complete blood counts and albumin level measurements were performed within 2 weeks before treatment.

RESULTS: Two hundred twenty-seven patients with endometrioid type EC were included in the cohort. The mean follow-up was 35.4 ± 19.6 months. LVSI positivity was 8.2% in the presence of low SII and 44.1% in the presence of high SII (p<0.001). LVSI positivity was 23.3% in the presence of low PNI and 11.1% in the presence of high PNI (p=0.025). Low and high PNI values do not affect disease-free (DFS) and overall survival (OS) significantly. 5-year mean DFS and OS differ significantly with low and high SII values.

CONCLUSİON: SII and PNI values can be used to predict the presence of LVSI in the preoperative period, and to determine the extent of LN dissection and the surgical procedure Patients with high SII values had worse survival outcomes.

Keywords: Endometrial cancer; Lymph node; Lymphovascular space invasion; Prognostic nutritional index; Systemic inflammatory index

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Introduction

Endometrial cancer (EC) is the most common gynecological malignancy, especially in developed countries (1). The most prominent prognostic factors that determine the extent of surgical staging and adjuvant treatment choices in endometrial cancer are lymph nodes (LN) status, lymphovascular space invasion (LVSI), depth of myometrial invasion, cervical invasion, and tumor size (2).

Neutrophils, thrombocytes, lymphocytes, and albumin play an important role in cancer-related inflammation and are significant prognostic factors for survival (3-5). Neutrophil/lymphocyte ratio (NLR) and thrombocyte/lymphocyte ratio (PLR) have been investigated as prognostic parameters (6-8). Increased inflammatory indices at the time of diagnosis have been associated with circulating tumor cells and thus probable advanced tumor (9). Various nutritional indexes representing the nutrition and general situation of patients with malignancies have been evaluated as prognostic parameters (3). Hypoalbuminemia is generally considered an indicator of malnutrition and cachexia and is usually seen in patients with advanced tumors (3). The prognostic nutritional index (PNI) (PNI = 10 × albumin concentration + 0.005 × total lymphocyte

count) can serve as a practical indicator of immunity and nutritional status, especially in low resource settings, as it is easily calculated.

However, the impact of the immune system and nutritional status on prognostic factors in these cases has not been well studied. The purpose of this study was to determine the role of systemic inflammatory index (SII) and PNI in predicting prognostic factors in endometrial cancer, especially LN involvement and LVSI, which are often not fully assessed preoperatively.

Material and Method

This retrospective cohort study was based on the records of patients who were diagnosed and treated for EC in the Gynecologic Oncology Clinic between January 2014 and 2021. Patients with EC who were operated on in our institution, and for whom follow-up data were available were included in the study. Patients with hematological disorders, other malignancies, and liver disease that could change the albumin value were excluded from the study. Tumor staging was based on the International Federation of Gynecology and Obstetrics (FIGO) 2009 staging criteria. The study approval was obtained from the Local Ethics Committee (Decision no: 2021/156, Date: 03.03.2021) and was conducted with the principles of the Declaration of Helsinki.

The patient's clinical records and pathological materials were collected. Data contain the patient's age at diagnosis, tumor dimension, histological subtype, LVSI, FIGO stage, and comorbidities (hypertension and diabetes mellitus). All pathological slides were evaluated by the gyneco-pathologist's postoperative period. Histological type and histologic FIGO grade (with respect to the World Health Organization criteria) were evaluated both in the primary tumor and the curettage material. Uterine slide parts were selected from the anterior and posterior courses of the cervix, the lower uterine section, and the uterine corpus. For all specimens, at least 6 sections were provided, including the section showing the deepest tumoral involvement.

All surgical procedures were performed by surgeons experienced in gynecological oncologic surgery. A vertical incision was chosen in all cases to facilitate access during abdominal exploration and organ resection. After entering the peritoneal cavity, a peritoneal washout was performed for cytology. Exploration of the abdominal cavity included systematic examination of the peritoneal surfaces, omentum, gastrointestinal tract, and para-colic, pelvic, mesenteric, and para-aortic regions, and palpation to locate suspicious lesions. Procedures included hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, resection of bulky LNs, and omentectomy. In our clinic, Systematic retroperitoneal lymphadenectomy was performed in patients with (a) myometrial invasion ≥1/2, (b) positive pelvic LNs, (c) non-endometrioid tumors, and (d) grade 3 endometrioid cancer. Pelvic lymphadenectomy is performed to remove the lymphatic tissue over the external and lower half common iliac artery and vein and in the obturator fossa. Para-aortic LN removal was performed with the removal of the lymphatic tissue over the inferior vena cava and aorta if deemed necessary.

After treatment, patients were called for follow-up every 3-4 months for the first 2 years. Then, controls were performed every 6 months until the 5th year. Annual controls were performed for patients who completed five years of age. Computed tomography and magnetic resonance imaging scans were performed annually. Disease-free survival (DFS) refers to the time from initial treatment until relapse occurs. Overall survival (OS) was defined as the time from initial treatment until death or last follow-up.

Complete blood count and albumin levels were analyzed in all patients within two weeks before surgery. Neutrophil, lymphocyte, and platelet counts were evaluated using automated blood cell counters (Bayer HealthCare, Diagnostics Division, Tarrytown, NY, USA). Levels of blood albumin were assessed by latex nephelometry (LT Auto Wako, Osaka, Japan). NLR was defined as absolute neutrophil count (µl) divided by absolute lymphocyte count (µl), and PLR was defined as absolute platelet count (µl) divided by lymphocyte count (µl). PNI was described as 10 × albumin concentration (g/dl) + 0.005 × total lymphocyte count (µl). The SII was calculated as neutrophil × platelet/lymphocyte (9). The PNI was calculated as 10 x albumin concentration + 0.005 × total lymphocyte count (5).

Statistical analysis

Normal distribution analysis was performed with the Shapiro-Wilk test. Normally distributed parameters were reported as mean±SD, while non-normally distributed parameters were reported as median (min-max). Continuous data were expressed as mean ± standard deviation, and frequency data were expressed as percentages. The $\chi 2$ test was used to analyze categorical data and the student's t-test was used to analyze numerical inputs. We calculated the follow-up time as the median time that can be calculated from the frequencies part. The optimal cut-off value for predictive prognostic markers in EC was determined using receiver operating characteristic (ROC) curve analysis. Cox regression analysis was used to determine the factors affecting survival, with the results presented as hazard ratios (HR) and 95% confidence interval (CI). All statistical analyses were performed using SPSS software (ver. 20.0; IBM Corp., Armonk, NY, USA). A p-value <0.05 was considered to indicate statistical significance.

Results

Two hundred twenty-seven patients with endometrioid type EC were included in the study, 48.9% of which had hypertension and 29.1% had diabetes mellitus. The mean follow-up pe-

riod was 35.4 ± 19.6 (median months=34.5, min-max=4-85) months. The mean age of the cases was 58.6 ± 10.1 years. The mean tumor size was measured as 3.7 ± 2.0. One hundred and forty-six (64.3%) patients had histological grade 1 tumors whereas 61 (26.9%) had grade 2 and 20 (8.8%) had grade 3 tumors. Hysterectomy and oophorectomy were performed in all patients. Pelvic LN dissection was applied in 136 (59.9%) cases and paraaortic LN dissection was applied in 112 (49.3%) cases. The average number of pelvic LNs obtained was 20.1 ± 8.5 and the number of paraaortic LNs was 7.1 ± 4.3. Malignant cells were seen in the peritoneal cytology of 11 (4.8%) patients. Cervical involvement was observed in 13 (5.7%), adnexal involvement in 8 (3.5%), and LVSI in 43 (18.9%) of the patients. The uterine tumor was limited to the cavity in 24 (10.6%) patients, <1/2 myometrial involvement in 156 (68.7%) patients, ≥1/2 invasion in 43 (18.9%) patients, and serosal spread was seen in 4 (1.8%). Postoperatively, 85 (37.4%) patients received adjuvant radiotherapy which was vaginal brachytherapy for 77 (33.9%) patients, and external beam radiotherapy for 38 (16.7%). Twenty-seven (11.9%) patients received chemotherapy. Recurrence was observed in 27 (11.9%) patients and the regions were vaginal cuff in 4 patients, pulmonary in 4, colon in 2 livers in 1, lymph nodes in 2, peritoneal in 2, vertebral in 1 and multiple sites in 11 patients. The stages and laboratory data of the cases are given in Table I.

According to the ROC curve, SII and PNI values and the determination of prognostic factors are shown in Figure 1. The ideal cut-off, sensitivity, specificity, and AUC values for PNI and SII values predicting prognostic factors are summarized in Table II according to ROC curve analysis. The highest AUC value (AUC=0.787) was found in the SII parameter used in LVSI estimation, and the cut-off value was >572. Table III shows the rates of prognostic factors according to low and high PNI and SII values. LVSI positivity was 8.2% in the presence of low SII and 44.1% in the presence of high SII (p<0.001), whereas it was 23.3% for low PNI and 11.1% for high PNI values (p=0.025). The mean BMI values of patients with low and high PNI values were calculated as 32.8 ± 2.7 and 33.4 ± 2.3, respectively (p=0.175). While the mean BMI values of patients with low SII were 33.0 ± 2.9, it was 33.0 ± 2.1 in patients with high SII (p=0.864).

The mean 5-year DFS was 85.8% in patients with low PNI and 85.4% in patients with high PNI (0.885) (Figure 2a). The mean 5-year OS was 89.2% in patients with low PNI and 93.7% in patients with high PNI (0.698) (Figure 2b). There was a significant difference in mean 5-year DFS values of patients with low (<572) and high (≥572) SII values (90.7% vs. 77.8%; p=0.010) (Figure 2c). A significant difference was observed between the mean 5-year OS values of patients with low (<572) and high (≥572) SII values (94.4% and 80.1%; p=0.044) (Figure 2d).

Univariate and multivariate analyses of overall survival using Cox Regression are presented in Table IV. Only one stage was found to be an independent risk factor affecting overall survival.

Table I: *The stages and laboratory data of the patients*

Parameters	n=227
Stage; n (%)	
- IA	167 (73.6)
- IB	27 (11.9)
- II	4 (1.8)
- IIIA	4 (1.8)
- IIIB	-
- IIIC1	7 (3.1)
- IIIC2	7 (3.1)
- IVA	-
- IVB	11 (4.8)
Ca125 (U/mL)[a]	14 (2-5000)
Hemoglobin (g/dL)[b]	12.4 ± 1.9
Platelet (µL) (×10³)[b]	288 ± 90
Leukocyte (µL)[b]	8480 ± 2980
Neutrophil (µL)[b]	5790 ± 2890
Lymphocyte (µL)[b]	1900 ± 820
Protein (g/dL)[b]	6.6 ± 0.9
Albumin (g/dL)[b]	3.8 ± 0.7
Prognostic nutritional index[b]	48.1 ± 8.9
Systemic inflammatory index[b]	416 (36-24089)

StD: Standard deviation, a: Median (min-max), b: Mean ± StD

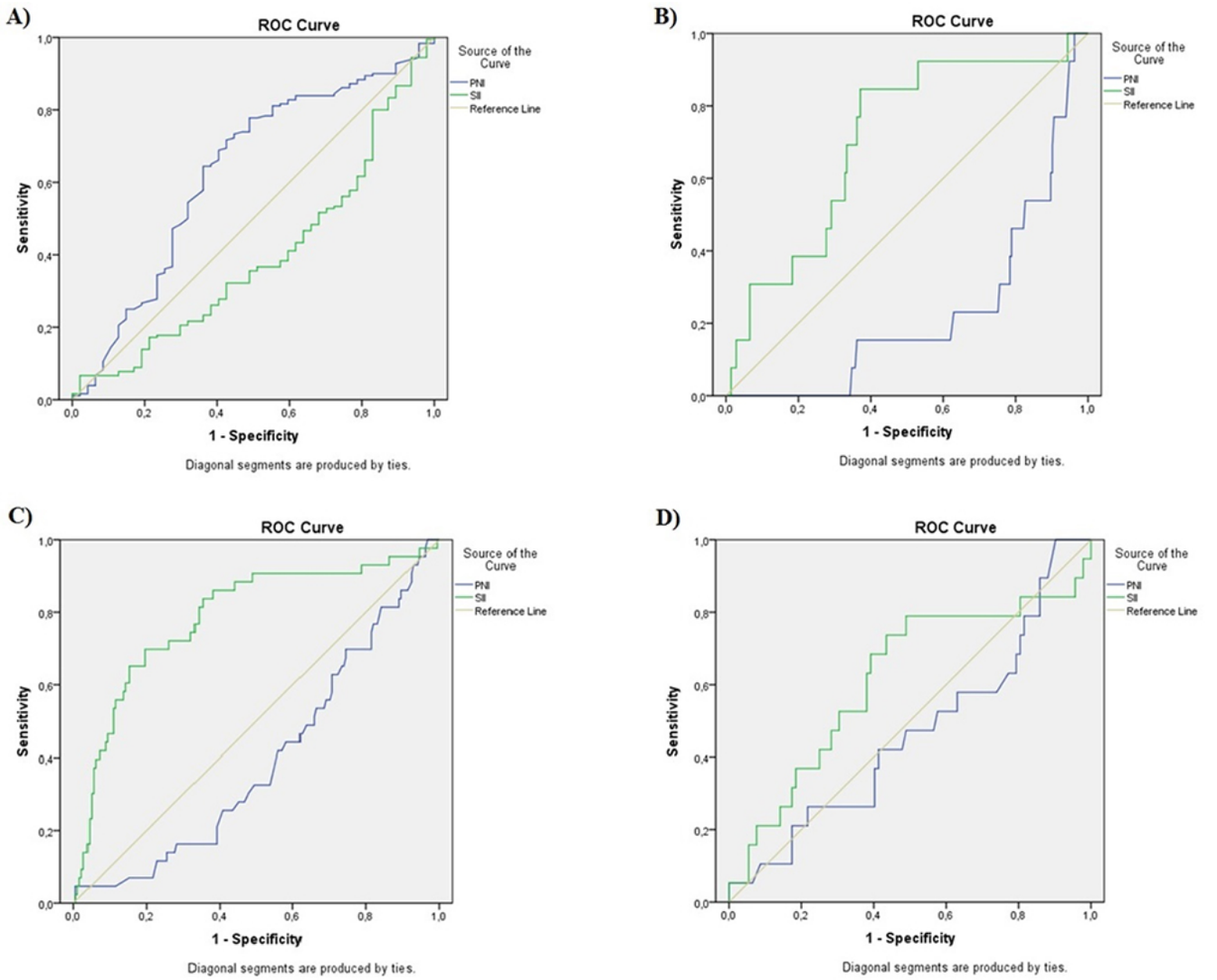

Figure 1: *According to the ROC curve, the determination of the cut-off value of SII and PNI for prognostic factors (a: deep myometrial invasion, b: cervical involvement, c: Lymphovascular space invasion, and d: Lymph node involvement).*

Table II: *According to ROC curve analysis, the ideal cut-off, sensitivity, specificity, and AUC values for PNI and SII values predicting prognostic factors*

	Cut-off	Sensitivity	Specificity	AUC	p
Deep Myometrial invasion					
PNI	>43	71.7%	57.4%	0.628	0.007
SII	>528	61.7%	59.6%	0.393	0.025
Cervical involvement					
PNI	>41	76.9%	75.5%	0.228	0.001
SII	>572	84.6%	63.2%	0.708	0.012
Lymphovascular space invasion					
PNI	>52	83.7%	39.1%	0.395	0.032
SII	>572	69.8%	80.4%	0.787	<0.001
Lymph node involvement					
PNI	>37	36.8%	79.3%	0.463	0.608
SII	>567	73.7%	56.5%	0.614	0.119

AUC=Area under curve, PNI=Prognostic nutritional index, SII=Systemic inflammatory index

Table III: *Prognostic factors according to low and high PNI and SII values*

	Low	High	p
Deep myometrial invasion; (%)			
PNI	35.6	17.0	0.006
SII	14.2	26.4	0.023
Cervical invasion; (%)			
PNI	15.9	1.8	<0.001
SII	1.5	12.4	0.002
Lymphovascular space invasion; (%)			
PNI	23.3	11.1	0.025
SII	8.2	44.1	<0.001
Lymph node involvement; (%)			
PNI	22.7	15.7	0.310
SII	8.9	25.5	0.019

PNI=Prognostic nutritional index, SII=Systemic inflammatory index

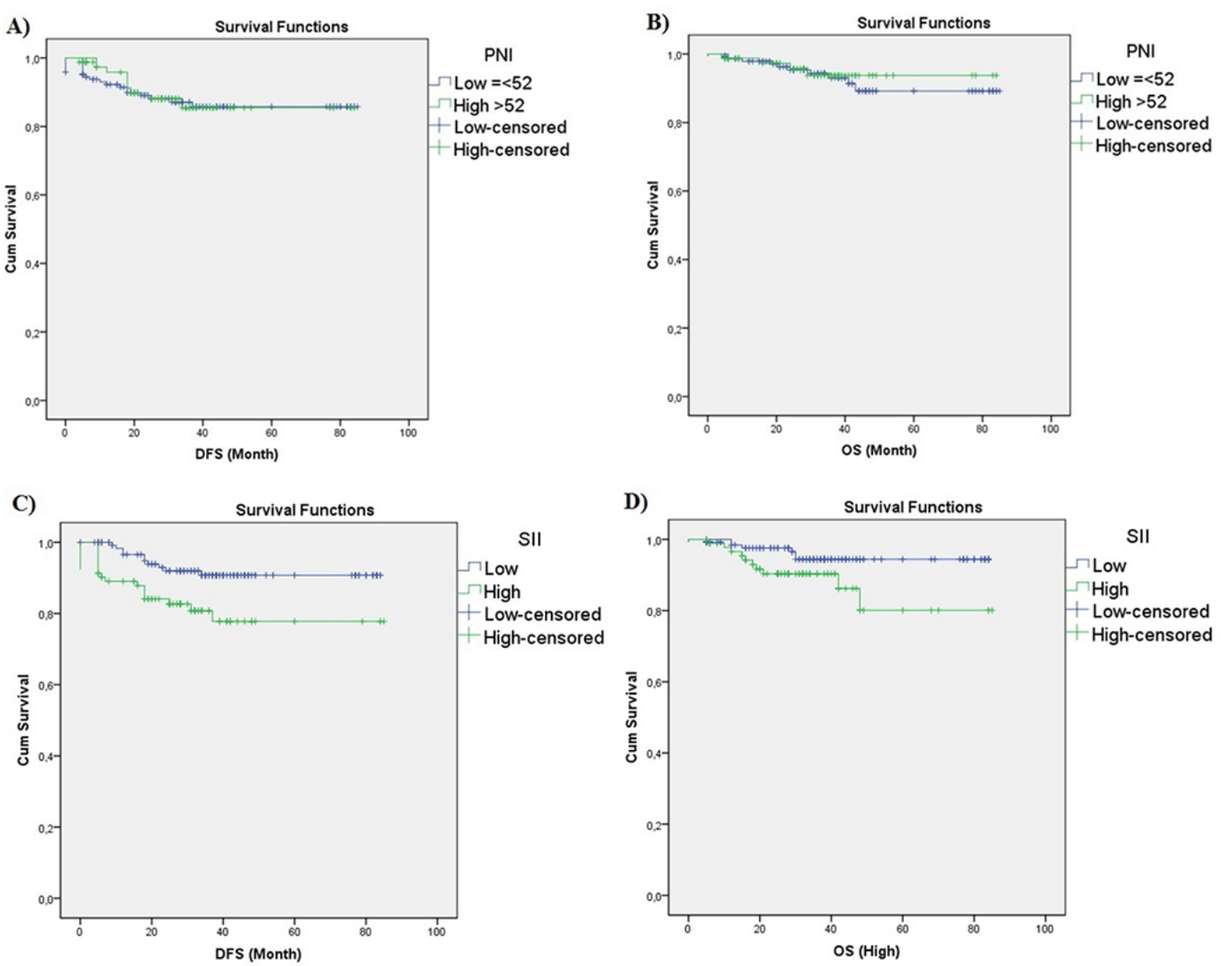

Figure 2: *Disease-free (2a for PNI and 2c for SII) and overall (2b for PNI and 2d for SII) survival curves of low and high PNI & SII values according to Kaplan Meier.*

Table IV: *Results of univariate and multivariate analyses of overall survival*

	Univariate			Multivariate		
	HR	95% CI	p	HR	95% CI	p
Stage	0.7	0.6-0.9	0.006	0.7	0.6-0.9	0.009
CA125	1.0	0.9-1.1	0.828			
Albumin	0.9	0.5-2.0	0.999			
Hemoglobin	0.7	0.6-0.9	0.049	0.7	0.6-1.0	0.063
Platelet (µL)	1.0	1.0-1.0	0.073			
Neutrophil	1.0	0.9-1.0	0.421			
Lymphocyte	1.0	0.9-1.0	0.279			
PNI	0.9	0.9-1.0	0.576			
SII	1.0	0.9-1.0	0.487			

Discussion

We investigated the role of SII and PNI values in the preoperative determination of prognostic factors in endometrial cancer. Statistically significant cut-off values were found for both SII and PNI, especially for myometrial invasion and LVSI. There are studies in the literature evaluating SII and PNI values for various malignancies, to our knowledge, this is the first group to investigate the evaluation of SII and PNI values for endometrial cancer.

In a study conducted with advanced-stage EC patients, NLR, PLR, and PNI values were found to be independent prognostic agents according to regression analysis (10). The median values of prognostic factors were as follows: CA 125: 138 U/mL; NLR: 4.9; PLR: 246.0; and PNI: 43.1 (10). Besides, NLR, PLR, and PNI have been identified as prognostic factors and factors affecting survival in cervical and ovarian cancers (3,4,11,12). Patients with low PNI had a shorter survival (4). In the literature, NLR, PLR, and PNI values were found to be independent risk factors for OS (4,13). PNI values were predictors of response to chemoradiotherapy in locally advanced cervical tumors (5). The optimal threshold value for PNI has been calculated as 44.8 (5). High SII was significantly associated with advanced-stage and recurrence in vulvar cancer but was not found to be associated with grade and nodal involvement (9). Studies are showing that high SII values cause a higher rate of LN metastasis (14). Postoperative SII values were also found to be an independent risk factor for overall survival (15,16). In addition to this information, a prospective study showed that although the SII value was associated with some clinical factors, it did not affect disease-specific survival and overall survival (17). In our study, significant cut-off values were found for SII and PNI, especially in determining LVSI and deep myometrial invasion. PNI could be relatively more effective in predicting patients with poorer prognoses or more advanced-stage tumors with systemic effects and impaired nutritional balance. In our study, the results of SII, in terms of P and AUC values, are relatively more significant than PNI results. This finding may be related to the fact that endometrial cancer is mostly diagnosed at earlier stages with local disease due to its early symptoms. Likewise, despite having no significant difference regarding DFS and OS in patients with low and high PNI, 5-year overall survival rates were inferior in those with higher SII values.

LVSI positivity was 8.2% in the presence of low SII (≤746) and 44.1% in the presence of high SII (>746) ($p<0.001$). In other words, LVSI was found positive in almost half of the patients with high SII values. LVSI is the first step in tumor metastasis and is defined as the invasion of tumor cells in lymphatic and/or blood vessels. Its presence is associated with metastatic spread to lymph nodes and distant sites. Therefore, it is very important to make a preoperative estimation of LVSI, which has an important role in determining the extent of systematic lymphadenectomy and postoperative adjuvant therapy. The presence of LVSI is examined in the hysterectomy specimen, but a negative result does not guarantee its absence in all remaining areas. Recently, the tumor microenvironment has received a great deal of attention, and a variety of inflammatory cells and mediators are known to be the main components of it. While the effects of the systemic inflammatory response can even be seen in localized tumors, changes in nutritional index are more evident in extensive ones. Although PNI and SII values were significant in predicting deep myometrial invasion, cervical involvement, and LVSI, they were not found significant in predicting LN involvement. A low number of advanced-stage patients and the short follow-up periods could be the underlying cause for it. Studies consisting of a larger number of patients with more advanced stages and longer terms of follow-up are needed to re-evaluate this regard.

This cohort had some shortcomings. First, it was retrospective by design and the size of the model was conceptually small. Further cohorts with larger sample sizes and prospective designs could be recommended. The third limitation of this cohort was that systematic LN dissection was not performed in all cases. Despite these shortcomings, the similarities in demographics in the cohort population and the analysis

documentation by expert pathologists increased the timeliness of our outcomes and mitigated these weaknesses.

In conclusion, SII and PNI values can be used to predict the presence of LVSI in the preoperative period and may be useful in determining the need for LN dissection and the surgical procedure. We found that SII and PNI values, evaluated for the first time in endometrial cancer, have prognostic significance. Patients with higher SII values had worse survival outcomes.

Declarations

Ethics approval and consent to participate: Consent for using data was taken. The study was reviewed and approved by the ethics committee of Erciyes University (Ethics approval reference number: 2021/156, Date: 03.03.2021). All procedures were performed according to the Declaration of Helsinki.

Availability of data and materials: The data supporting this study is available through the corresponding author upon reasonable request.

Declaration of conflicts of interest: The authors report no conflicts of interest

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Author Contributions: Concept – Varol Gulseren, Kemal Gungorduk, design, Varol Gulseren, data collection or processing, Mine Daggez, Ertugrul Sen, analysis or interpretation, Fulya Caglı, Literature Search, Mehmet Dolanbay, review & editing- Ibrahim Serdar Serin, Bulent Ozcelik, writing, Varol Gulseren

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References

1. Polterauer S, Khalil S, Zivanovic O, Abu-Rustum NR, Hofstetter G, Concin N, et al. Prognostic value of lymph node ratio and clinicopathologic parameters in patients diagnosed with stage IIIC endometrial cancer. Obstet Gynecol. 2012;119(6):1210-8. Doi: 10.1097/AOG.0b013e318255060c. PMID: 22617586.

2. Ferraioli D, Chopin N, Beurrier F, Carrabin N, Buenerd A, Mathevet P. The incidence and clinical significance of the micrometastases in the sentinel lymph nodes during surgical staging for early endometrial cancer. Int J Gynecol Cancer. 2015;25(4):673-80. Doi: 10.1097/IGC.0000000000000408. PMID: 25902281.

3. Haraga J, Nakamura K, Omichi C, Nishida T, Haruma T, Kusumoto T, et al. Pretreatment prognostic nutritional index is a significant predictor of prognosis in patients with cervical cancer treated with concurrent chemoradiotherapy. Mol Clin Oncol. 2016;5(5):567-74. Doi: 10.3892/mco.2016.1028. PMID: 27900086, PMCID: PMC5103867.

4. Ida N, Nakamura K, Saijo M, Kusumoto T, Masuyama H. Prognostic nutritional index as a predictor of survival in patients with recurrent cervical cancer. Mol Clin Oncol. 2018;8(2):257-63. Doi: 10.3892/mco.2017.1508. PMID: 29435286, PMCID: PMC5774443.

5. Gangopadhyay A. Prognostic Nutritional Index and Clinical Response in Locally Advanced Cervical Cancer. Nutr Cancer. 2020;72(8):1438-42. Doi: 10.1080/01635581.2020.1729820. PMID: 32091264.

6. Ethier JL, Desautels DN, Templeton AJ, Oza A, Amir E, Lheureux S. Is the neutrophil-to-lymphocyte ratio prognostic of survival outcomes in gynecologic cancers? A systematic review and meta-analysis. Gynecol Oncol. 2017;145(3):584-94. Doi: 10.1016/j.ygyno.2017.02.026. PMID: 28222899.

7. Peng HX, Lin K, He BS, Pan YQ, Ying HQ, Hu XX, et al. Platelet-to-lymphocyte ratio could be a promising prognostic biomarker for survival of colorectal cancer: a systematic review and meta-analysis. FEBS Open Bio. 2016;6(7):742-50. Doi: 10.1002/2211-5463.12083. PMID: 27398314, PMCID: PMC4932454.

8. Cummings M, Merone L, Keeble C, Burland L, Grzelinski M, Sutton K, et al. Preoperative neutrophil: lymphocyte and platelet: lymphocyte ratios predict endometrial cancer survival. Br J Cancer. 2015;113(2):311-20. Doi: 10.1038/bjc.2015.200. PMID: 26079303, PMCID: PMC4506386.

9. Bartl T, Bekos C, Postl M, Alexander R, Polterauer S, Stefanie A, et al. The systemic immune-inflammation index (SII) is an independent prognostic parameter of survival in patients with invasive vulvar cancer. J Gynecol Oncol. 2021;32(1):e1. Doi: 10.3802/jgo.2021.32.e1. PMID: 33185042, PMCID: PMC7767659.

10. Kiuchi K, Hasegawa K, Ochiai S, Motegi E, Kuno T, Kosaka N, et al. Prognostic significance of inflammatory parameters and nutritional index in clinical stage IVB endometrial carcinomas. J Obstet Gynaecol. 2019;39(2):237-41. Doi: 10.1080/01443615.2018.1494703. PMID: 30370797.

11. Huang H, Liu Q, Zhu L, Zhang Y, Lu X, Wu Y, et al. Prognostic Value of Preoperative Systemic Immune-Inflammation Index in Patients with Cervical Cancer. Sci Rep. 2019;9(1):3284. Doi: 10.1038/s41598-019-39150-0. PMID: 30824727, PMCID: PMC6397230.

12. Farolfi A, Petrone M, Scarpi E, Gallà V, Greco F, Casanova C, et al. Inflammatory Indexes as Prognostic and Predictive Factors in Ovarian Cancer Treated with Chemotherapy Alone or Together with Bevacizumab. A Multicenter, Retrospective Analysis by the MITO Group (MITO 24). Target Oncol. 2018;13(4):469-479. Doi: 10.1007/s11523-018-0574-1. PMID: 29948780.

13. Ji Y, Wang H. Prognostic prediction of systemic immune-inflammation index for patients with gynecological and breast cancers: a meta-analysis. World J Surg Oncol. 2020;18(1):197. Doi: 10.1186/s12957-020-01974-w. PMID: 32767977, PMCID: PMC7414550.

14. 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. Doi: 10.2147/JIR.S345790. PMID: 34992410, PMCID: PMC8710076.

15. 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. Doi: 10.3389/ fsurg.2021.704235. PMID: 34746222, PMCID: PMC8568766.

16. Holub K, Busato F, Gouy S, Sun R, Pautier P, Genestie C, et al. Analysis of Systemic Inflammatory Factors and Survival Outcomes in Endometrial Cancer Patients Staged I-III FIGO and Treated with Postoperative External Radiotherapy. J Clin Med. 2020;9(5):1441. Doi: 10.3390/jcm9051441. PMID: 32408668, PMCID: PMC7291051.

17. 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):146-53. Doi: 10.1016/j.ygyno. 2021.11.009. PMID: 34802721, PMCID:PMC 8802781.