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Evaluation of the Prognostic Role of the Systemic Immune Inflammation Index in Postmenopausal Osteoporosis

Postmenopozal Osteoporozda Sistemik İmmün İnflamasyon İndeksinin Prognostik Rolünün Değerlendirilmesi

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ABSTRACT Objective: The aim of this study is to evaluate the prognostic role of the systemic immune inflammation index (SII) in postmenopausal osteoporosis and to examine the SII, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), mean platelet volume (MPV), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), femur and lumbar bone mineral densitometry (BMD) T scores and their relationships with each other. **Material and Methods:** A total of 139 patients were included in this retrospective case-control study. Lumbar vertebra 1-4 and femoral neck BMD T scores, ages, ESR, CRP, MPV values were recorded. NLR, PLR, and SII values were calculated. Patients with lumbar and femoral T scores ≥-1 constituted the control group (n=31); with lumbar or femoral T scores between -1 and -2.5 constituted the osteopenia group (n=38), ≤-2.5 constituted the osteoporosis group (n=37), ≤-2.5 and one or more fragility fractures constituted the severe osteoporosis group (n=33). **Results:** SII value was significantly higher in the osteoporosis group compared to the osteopenia group (p=0.004). SII value had a diagnostic value in predicting osteoporosis in patients with osteopenia (area under curve: 0.686, %95 confidence interval: 0.565-0.806, p<0.006); the cut-off value for the SII was calculated as 458.46. ESR value was significantly higher in the severe osteoporosis group compared to the osteopenia group and the control group (p<0.001, p=0.0080). There was no significant difference between the groups in terms of other variables (p>0.05). **Conclusion:** SII value can be a prognostic predictor that can be used to predict the development of osteoporosis in postmenopausal osteopenic patients.

Keywords: Osteoporosis; postmenopausal; inflammation

ÖZET Amaç: Bu çalışmanın amacı, postmenopozal osteoporozda sistemik immün inflamasyon indeksinin (SII) prognostik rolünün değerlendirilmesi ve SII, nötrofil-lenfosit oranı (NLO), platelet-lenfosit oranı (PLO), ortalama platelet hacmi (OPH), eritrosit sedimentasyon hızı (ESH), C-reaktif protein (CRP), femur ve lomber vertebra kemik mineral dansitometri (KMD) T skorlarının ve birbirleriyle ilişkilerinin incelenmesidir. **Gereç ve Yöntemler:** Bu retrospektif vaka-kontrol çalışmasına 139 hasta dâhil edildi. Lomber vertebra 1-4, femur boynu KMD T skorları, yaş, ESH, CRP, OPH değerleri kaydedildi. NLO, PLO ve SII değerleri hesaplandı. Lomber ve femoral T skoru ≥-1 olan hastalar kontrol grubunu (n=31); lomber veya femoral T skoru -1 ve -2,5 arasında olan hastalar osteopeni grubunu (n=38), ≤-2,5 olan hastalar osteoporoz grubunu (n=37), ≤-2,5 ve 1 ya da daha fazla frajilite kırığı olanlar şiddetli osteoporoz grubunu (n=33) oluşturdu. **Bulgular:** SII değeri osteoporoz grubunda osteopeni grubuna göre anlamlı olarak daha yüksekti (p=0,004). SII değerinin osteopenik hastalarda osteoporozu öngörmede tanısal değeri vardı (eğri altındaki alan: 0,686, %95 güven aralığı: 0,565-0,806, p<0,006); SII için kestirim değeri 458,46 olarak hesaplandı. ESH değeri şiddetli osteoporoz grubunda osteopeni ve kontrol gruplarına kıyasla anlamlı olarak daha yüksekti (p<0,001, p=0,0080). Gruplar arasında diğer değişkenler açısından anlamlı farklılık yoktu (p>0,05). **Sonuç:** SII değeri, postmenopozal osteopenik hastalarda osteoporoz gelişimini öngörmede kullanılabilecek prognostik bir prediktör olabilir.

Anahtar Kelimeler: Osteoporoz; postmenopozal; inflamasyon

Osteoporosis is a multifactorial, systemic skeletal disease characterized by changes in the microarchitecture structure of the bone and low bone mineral density, in which bone fragility and the risk of fracture development after low-energy traumas are increased.[1-3] Postmenopausal osteoporosis is the most common form of osteoporosis. Estrogen deficiency associated with menopause affects negatively periosteal bone formation and increases endosteal bone resorption, bone turnover, and consequently trabecular bone loss.[4]

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Osteoporosis is an important public health concern.[1] Symptomatic or radiographic osteoporotic fractures lead to increased morbidity, mortality, disability, and decreased quality of life.[1-3] When patients with osteoporosis are not treated early, the social and personal costs associated with the disease increase, and fractures also cause serious financial and psychosocial consequences.[1,2] Early prevention can be effective in reducing morbidity associated with osteoporosis.[1]

Although it is known that densitometric measurement is the most used method in the diagnosis of osteoporosis and determining the risk of osteoporotic fractures, it is known that many clinical factors may increase the fracture risk.[1,2] For this reason, not only densitometric measurement but also clinical evaluations should be taken into consideration while making the diagnosis.[4]

The opinion that osteoporosis is a disease in which changes are observed not only in bone but also in whole-body homeostasis has been accepted in recent years.[3] New evidence supports the existence of immune dysfunction and pro-inflammatory response in osteoporosis pathogenesis.[3,5] The decrease in endogenous estrogen after menopause can lead to an increase in pro-inflammatory cytokines, and this increase can lead to postmenopausal osteoporosis through oxidative stress damage and triggering of osteoclasts.[5,6]

Recently, neutrophil-lymphocyte (NLR) and platelet-lymphocyte ratio (PLR) and mean platelet volume (MPV) values are frequently used in studies as new markers reflecting systemic inflammatory response.[7] In addition, in the literature, it was stated that NLR, PLR, and MPV values are associated with low bone mineral densitometry (BMD) values and osteoporosis.[6,8-11] For these reasons, it is thought that systemic inflammatory biomarkers can be used in the early diagnosis of postmenopausal osteoporosis.[5]

Systemic immune inflammation index (SII) is a new index related to systemic inflammation calculated by the numbers of lymphocytes (L), neutrophils (N), and platelets (PLT) in peripheral blood defined in 2014. The index is calculated with the formula "SII=PLTx N/L."[12] In the literature, it has started to be used in studies of some diseases with systemic inflammation, especially in cancer research; there are studies indicating that high SII values may be associated with worse prognosis and can be used as a prognostic biomarker as well as a helpful marker for diagnosis.[5,12-19] Since it has been shown in studies that pro-inflammatory processes have a role in the pathogenesis of postmenopausal osteoporosis, it has been suggested that the SII value can be used as a systemic inflammatory biomarker in the early diagnosis of the postmenopausal osteoporosis and determination of fracture risk.[5,20-22]

Our goal is to examine the systemic immune inflammation index' prognostic role in postmenopausal osteoporosis and to examine the SII, NLR, PLR, MPV, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), femur and lumbar BMD values and their relationships with each other.

MATERIAL AND METHODS

This study is a retrospective case-control study. In the study, the data of 304 patients evaluated between January 2017-January 2020 with a pre-diagnosis or diagnosis of postmenopausal osteoporosis were retrospectively reviewed. Patients with risk factors for secondary osteoporosis, acute or chronic infection, malignancy, rheumatic disease, or systemic diseases that may cause changes in hematological inflammation parameters and those who were missing one or more of the parameters planned to be investigated among the available data were excluded from the study. Finally, 139 patients were included in the study.

Lumbar vertebra 1-4 and femoral neck BMD values T scores, ages, ESR, CRP, neutrophil, leukocyte, platelet levels, and MPV of the patients were recorded. The NLR was calculated by dividing the neutrophil count by the lymphocyte count, and the PLR was calculated by dividing the platelet count by the lymphocyte count. The SII was calculated with the "SII=platelet count Xneutrophil count/lymphocyte count" formula.[12]

By the World Health Organization (WHO) criteria, the grouping in terms of BMD values was done as follows; patients with L1-4 vertebra and femoral

neck T scores greater than -1 standard deviation were the control group (n=31), between -1 and -2.5 were the osteopenia group (n=38), below -2.5 were the osteoporosis group (n=37), below -2.5 and one or more fragility fractures were the severe osteoporosis group (n=33).[23]

Ethics committee approval was obtained for the study (date: December 30, 2020, no: 2020-4-26), and the Helsinki Declaration principles were followed.

STATISTICAL ANALYSIS

Statistical analyzes were performed using the SPSS (Statistical Package for Social Sciences, SPSS Inc, Chicago Ill, USA) version 20 program. The conformity of the variables to the normal distribution was examined by visual (histogram and probability charts) and analytical methods (Kolmogorov Smirnov/Shapiro-Wilk's tests), and the homogeneity of variances was examined using the Levene test. In the descriptive analysis, all data were expressed as mean and standard deviation. In the intergroup comparisons, one-way variance analysis was used for data that conform to the normal distribution; the Kruskal-Wallis test was used for those that did not. In the double-group comparisons to determine which 2 groups have a significant difference, post-hoc analysis (Tukey corrected) was used for data that conform to the normal distribution, and the Mann-Whitney U test (Bonferroni corrected) was used for those that did not. To examine the relationships between variables, Pearson correlation analysis (2-tailed) was used for variables that both conformed to the normal distribution, and the Spearman test (2-tailed) was used for at least one which did not. Receiver operating characteristic (ROC) curve analysis was used for diagnostic decision-making features of the SII value in predicting osteoporosis in osteopenic patients. The numbers and percentages were used to express the categorical data. In the comparison of the categorical data, the chi-square test was used. The statistical significance level was p=0.008 when Bonferroni correction was applied. In all other analyzes, it was p=0.05.

RESULTS

In the comparisons between the groups, there were significant differences between the groups in terms of femoral T score ($p<0.001$), lumbar vertebra 1-4 T score ($p<0.001$), ESR ($p=0.01$), and SII ($p=0.03$) values. No significant difference was found between the groups in terms of variables other than these ($p>0.05$). Age was found similar between the groups ($p=0.71$). Table 1 shows the descriptive statistics for the variables in the study.

The data regarding the comparison results of the variables between groups are shown in Table 1 also. While the ESR value was significantly higher in the severe osteoporosis group compared to the osteopenia group and the control group ($p<0.001$, $p=0.0080$), there were no statistically significant differences in other pairwise group comparisons ($p>0.0083$). While the SII value was significantly higher in the osteoporosis group compared to the osteopenia group ($p=0.004$), there were no statistically significant differences in other pairwise group comparisons ($p>0.0083$).

The results of the ROC analysis performed to examine the diagnostic decision-making feature of SII value in predicting osteoporosis in osteopenic patients are given in Figure 1 and Table 2. As a result of the evaluation made by ROC analysis, it was seen that the SII value has a diagnostic value in predicting osteoporosis in osteopenic patients ($p<0.006$). The cut-off value for SII was calculated as 458.46.

The comparison between osteopenia and osteoporosis groups according to the calculated cut-off value is given in Table 3. In the osteoporosis group, the number of patients with the SII value was equal to and greater than the calculated cut-off value of 458.46 was more than in the osteopenia group ($p=0.008$).

Table 4 shows the correlations between the variables in the study. There was a significant, positive, and excellent correlation between NLR and SII variables ($r=0.88$ $p<0.001$). There was a statistically significant, positive, very good correlation between PLR and SII variables ($r=0.72$, $p<0.001$). There were statistically significant, positive, moderate correlations between femur T score and lumbar T score variables ($r=0.49$, $p<0.001$), PLR and NLR variables ($r=0.54$, $p<0.001$). There was a statistically significant, negative, low-moderate correlation between MPV and PLR variables ($r=-0.37$, $p<0.001$). There were low or insignificant and statistically significant correlations

TABLE 1: The descriptive statistics and comparison of variables between the groups.

	Total (n=139)	Severe osteoporosis (n=33)	Osteoporosis (n=37)	Osteopenia (n=38)	Control (n=31)	p value
Age-year (mean±SD) (minimum/maximum)	64.02±8.48 (43/89)	63.91±8.18 (50/86)	65.16±7.64 (49/82)	62.87±8.70 (47/89)	64.19±9.62 (43/77)	0.71
Femur BMD T score-sd (mean±SD) (minimum/maximum)	-1.45±1.17 (-4.1/3.7)	-2.10±0.86 (-3.8/-0.6)	-2.17±0.80 (-4.1/-0.6)	-1.29±0.62 (-2.2/0.2)	-0.08±1.07 (-1.0/3.7)	**<0.001***
Lumbar BMD T score-sd (mean±SD) (minimum/maximum)	-1.84±1.24 (-4.7/2.7)	-2.85±0.92 (-4.7/0.5)	-2.47±0.93 (-4.4/0.3)	-1.62±0.43 (-2.2/-0.6)	-0.31±0.92 (-1.0/2.7)	**<0.001***
Lymphocyte-k/µl (mean±SD) (minimum/maximum)	2.16±0.62 (1/4.3)	2.09±0.64 (1/3.6)	2.12±0.55 (1.3/3.7)	2.22±0.56 (1.4/3.4)	2.20±0.77 (1.2/4.3)	0.79
Neutrophil-k/µl (mean±SD) (minimum/maximum)	3.94±1.27 (1.6/7.9)	3.75±0.99 (2.21/5.8)	4.37±1.41 (2.03/7.9)	3.64±1.17 (1.9/6.8)	4.02±1.37 (1.6/7.3)	0.06
Platelet-k/µl (mean±SD) (minimum/maximum)	266.22±69.805 (136/643)	248.15±58.01 (136/386)	285.19±69.25 (193/564)	257.92±49.07 (158/356)	272.97±95.716 (150/643)	0.12
ESR-mm/h (mean±SD) (minimum/maximum)	19.73±12.34 (2/58)	26.12±14.24 (2/58)	22.24±13.38 (5/53)	13.74±7.01 (2/33)	17.26±10.20 (4/47)	**0.001***
CRP-mg/L (mean±SD) (minimum/maximum)	1.62±2.02 (0.01/11)	1.93±2.08 (0.01/7)	1.81±2.21 (0.01/11)	1.06±1.14 (0.01/4,6)	1.77±2.47 (0.01/11)	0.41
MPV-fl (mean±SD) (minimum/maximum)	7.77±1.49 (5.4/13.4)	7.89±1.47 (5.44/11.8)	7.41±1.22 (5.4/11)	7.73±1.51 (5.6/13.4)	8.10±1.72 (5.5/13.3)	0.30
PLR (mean±SD) (minimum/maximum)	131.85±47.13 (63.93/363.57)	127.45±41.92 (67.92/237.86)	140.64±38.65 (77.23/226.21)	122.74±37.86 (63.93/213.75)	137.22±67.31 (63.95/363.57)	0.26
NLR (mean±SD) (minimum/maximum)	1.99±0.96 (0.71/6.08)	1.99±1.00 (0.9/5.8)	2.23±1.11 (1.05/6.08)	1.72±0.69 (0.76/4.21)	2.03±0.97 (0.71/4.17)	0.16
SII (mean±SD) (minimum/maximum)	534.53±321.8 (166/2235)	483.87±236.94 (189/1284)	629.90±325.62 (248/1787)	448.43±217.15 (166/1096)	580.16±453.33 (194/2235)	0.03*

*Statistical significance level p=0.05; SD: Standard deviation; BMD: Bone mineral densitometry; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; MPV: Mean platelet volume; PLR: Platelet-lymphocyte ratio; NLR: Neutrophil-lymphocyte ratio; SII: Systemic immune-inflammation index.

between age and ESR, age and CRP, age and NLR, age and SII variables (r=0.20, p=0.02; r=0.25, p=0.003; r=0.26, p=0.002; r=0.2, p=0.02), lumbar T score and ESR variables (r=-0.2, p=0.02), ESR and CRP variables (r=0.24, p=0.004), CRP and MPV variables (r=-0.21, p=0.01), CRP and PLR, CRP and NLR, CRP and SII variables (r=0.25, p=0.003; r=0.20, p=0.02; r=0.23, p=0.01), MPV and SII variables (r=-0.23, p=0.01).

DISCUSSION

In this study, in which we purpose to examine the prognostic role of the SII value in osteoporosis, we found that the SII value was significantly higher in

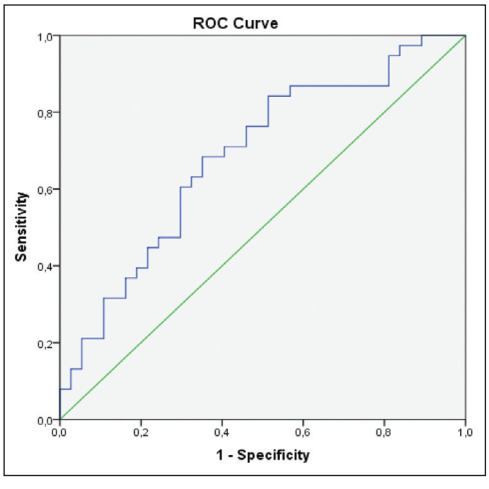

FIGURE 1: ROC curve for the SII value.
ROC: Receiver operating characteristic.

TABLE 2: The ROC curve for the SII value.

Risk factor	AUC (%95 CI)	Cut-Off	p value	Sensitivity (%)	Specificity (%)
SII	0.686 (0.565-0.806)	458.46	0.006*	65.8	64.9

*Statistical significance level p=0.05; SII: Systemic immune-inflammation index; ROC: Receiver operating characteristic; AUC: Area under the curve; CI: Confidence interval.

TABLE 3: Comparison between the groups according to the SII cut-off value.

	SII≥458.46 (n=38)	SII<458.46 (n=37)	Total (n=75)	p value
Osteopenia	13 (35.1%)	24 (64.9%)	37 (100%)	0.008*
Osteoporosis	25 (65.8%)	13 (34.2%)	38 (100%)	

*Statistical significance level p=0.05; SII: Systemic immune-inflammation index.

TABLE 4: Correlations between the variables.

	Age	Femur T score	Lumbar T score	ESR	CRP	MPV	PLR	NLR	SII
Age		r: -0.09	r: 0.08	r: 0.20*	r: 0.25**	r: 0.05	r: 0.10	r: 0.26**	r: 0.20*
		p: 0.28	p: 0.33	p: 0.02	p: 0.003	p: 0.53	p: 0.23	p: 0.002	p: 0.02
Femur BMDT score	r: -0.09		r: 0.49**	r: -0.06	r: -0.02	r: 0.03	r: -0.01	r: -0.10	r: -0.11
	p: 0.28		p:<0.001	p: 0.45	p: 0.81	p: 0.72	p: 0.91	p: 0.25	p: 0.21
Lumbar BMD-T score	r: 0.08	r: 0.49**		r: -0.2*	r: -0.08	r: 0.07	r: 0.03	r: 0.08	r: 0.05
	p: 0.33	p:<0.001		p: 0.02	p: 0.38	p: 0.44	p: 0.72	p: 0.35	p: 0.58
ESR	r: 0.20*	r: -0.06	r: -0.20*		r: 0.24**	r: -0.15	r: 0.13	r: 0.13	r: 0.16
	p: 0.02	p: 0.45	p: 0.02		p: 0.004	p: 0.08	p: 0.13	p: 0.13	p: 0.06
CRP	r: 0.25**	r: -0.02	r: -0.08	r: 0.24**		r: -0.21*	r: 0.25**	r: 0.20*	r: 0.23**
	p: 0.003	p: 0.81	p: 0.38	p: 0.004		p: 0.01	p: 0.003	p: 0.02	p: 0.01
MPV	r: 0.05	r: 0.03	r: 0.07	r: -0.15	r: -0.21*		r: -0.37**	r: 0.002	r: -0.23**
	p: 0.53	p: 0.72	p: 0.44	p: 0.08	p: 0.01		p:<0.001	p: 0.98	p: 0.01
PLR	r: 0.10	r: -0.01	r: 0.03	r: 0.13	r: 0.25**	r: -0.37**		r: 0.54**	r: 0.72**
	p: 0.23	p: 0.91	p: 0.72	p: 0.13	p: 0.003	p: <0.001		p:<0.001	p:<0.001
NLR	r: 0.26**	r: -0.10	r: 0.08	r: 0.13	r: 0.20*	r: 0.002	r: 0.54**		r: 0.88**
	p: 0.002	p: 0.25	p: 0.35	p: 0.13	p: 0.02	p: 0.98	p: <0.001		p: <0.001
SII	r: 0.20*	r: -0.11	r: 0.05	r: 0.16	r: 0.23**	r:-0.23**	r: 0.72**	r: 0.88**	
	p: 0.02	p: 0.21	p: 0.58	p: 0.06	p: 0.01	p: 0.01	p: <0.001	p: <0.001	

*Statistical significance level of correlation p=0.05 (2-tailed); **Statistical significance level of correlation p=0.01 (2-tailed); BMD: Bone mineral densitometry; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; MPV: Mean platelet volume; PLR: Platelet-lymphocyte ratio; NLR: Neutrophil-lymphocyte ratio; SII: Systemic immune-inflammation index.

the patient group with osteoporosis compared to the patient group with osteopenia and had a diagnostic value in predicting osteoporosis in patients with osteopenia. In other pairwise group comparisons, it was observed that there was no significant difference in terms of SII value. In the evaluation of other hematological parameters related to inflammation, the ESR value was found to be significantly higher in the severe osteoporosis group compared to the normal group and the osteopenia group; there was no significant difference between the groups in terms of NLR, PLR, MPV, CRP values. No statistically significant correlation was observed between SII and T scores. It was observed that the only statistically significant relationship between T scores and inflammation-related parameters was the negative low or insignificant correlation between Lumbar T score and ESR.

In osteoporosis, which is a major public health problem and its incidence increases with age, it is a common opinion to start screening at the age of 65 in healthy individuals without risk factors for osteoporosis. It is recommended to start screening earlier in patients with risk factors.[1] The WHO reported that the best test for measuring bone mineral density is

scanning the central skeleton with dual X-ray absorptiometry (DEXA).[1] However, some reservations, such as high cost or not being available in all health centers, may reduce the compliance of postmenopausal women to screenings with this method.[5] It is known that densitometric measurement is the most used method in the diagnosis of osteoporosis and determining the risk of osteoporotic fractures, but it is known that many clinical factors can have important effects also.[1,2,4] It is known that individuals with a T score below -2.5 according to the DEXA test have an increased fracture risk. However, there are more individuals with osteopenia than individuals with osteoporosis. Therefore, the absolute number of fractures observed in osteopenic patients is higher than in osteoporotic patients.[24-26] For these reasons, it is thought that treatment strategies based solely on densitometric measurement may cause individuals who are at risk of developing osteoporosis and fracture and who may benefit from early interventions to be overlooked.[5,24-26] Therefore, it has become important to define easy and effective biomarkers that can be used to diagnose postmenopausal osteoporosis early.[5]

The role of pro-inflammatory systemic response in the pathogenesis of postmenopausal osteoporosis has been shown in studies.[5,20-22] The increased incidence of osteoporosis in many rheumatic diseases with systemic inflammation supports the presence of inflammatory processes in osteoporosis.[27] Therefore, it has been suggested that systemic inflammatory biomarkers can be used in the early diagnosis of postmenopausal osteoporosis.[5]

In recent years, there have been studies in the literature that use NLR, PLR, and MPV values to evaluate systemic inflammation in osteoporosis, as in many diseases, with conflicting results. In our study, there was no significant difference between the groups in terms of NLR values. Similar to our study, in the Eroglu et al.'s study, it was reported that there was no significant difference between the groups in terms of NLR values.[9] On the other hand, there are studies in the literature reporting that the NLR value in osteoporosis is significantly higher compared to the osteopenic and normal groups and that it is a clinical method that can be used as an aid in diagnosis.[5,6,8,11,28]

There was no statistically significant difference between the groups in terms of PLR and MPV values in our study. Similarly, Önalan et al. reported in their cross-sectional study in 2019 that there was no significant difference between the groups in terms of MPV and PLR values in the osteoporosis group compared to the osteopenic and normal groups.[8] Lee et al. stated that there was no relationship between PLR values and BMD values in their study examining the relationships between PLR and BMD values.[6] Eroglu et al. reported that the PLR value was significantly higher in the osteoporosis group compared to the osteopenia and normal groups, and it was an independent prognostic factor for postmenopausal osteoporosis and that there was no significant difference between the groups in MPV values.[9] On the contrary, the studies of Yildirim et al. indicated that MPV values were significantly more in osteoporosis and osteopenia compared to controls and reversely correlated with BMD values.[10]

In our study, the ESR value was found to be significantly higher in the osteoporosis group compared to the osteopenia and normal group, but there was no significant difference between the groups in terms of CRP values. The results of studies evaluating ESR and CRP values in osteoporosis in the literature are also contradictory. Findings similar to our study were reported in the study of Önalan et al. and Öztürk et al.[8,28] On the contrary, Lee et al. reported that there was a significant relationship between postmenopausal osteoporosis and CRP values, and the same situation was not observed with ESR.[6]

The SII was defined by Hu et al. in 2014 to be used in predicting prognosis in hepatocellular carcinomas. In their study, it was stated that a high SII value in hepatocellular carcinomas is a strong poor prognostic indicator.[12] SII began to be used in various fields in the literature, especially in cancer studies, in later periods. Especially in studies conducted with different types of cancer patients, it was stated that high SII values are associated with bad prognosis and low survival rates, and it has been stated that it can be used as a noninvasive predictor in predicting prognosis.[13,15-17] There are also recent studies in the literature on various diseases other than cancer, which are thought to involve systemic inflammation in pathogenesis, and the prognostic role of

the SII value has been investigated. Most notably, in their study by Fois et al. in 2020, where they evaluated survival after the novel coronavirus disease-2019 (COVID-19), they showed that the SII value was significantly lower in surviving patients; and they stated that it is a much more important prognostic biomarker in predicting survival in COVID-19 than hematological inflammatory indices (e.g., NLR, PLR) widely used in research.[19] In various rheumatic diseases with systemic inflammation, there are also studies reporting SII value elevations and their correlations with disease activities.[29-33] Since the SII value is based on the platelet, neutrophil, and lymphocyte counts; it is thought that it can integrate other inflammatory indices and reflect a more comprehensive and stable picture.[5]

In our study, we found the SII value significantly higher in the osteoporosis group compared to the osteopenia group, and we found that the SII value had a diagnostic value in predicting osteoporosis in osteopenic patients (cut-off value 458). There are a limited number of studies in the literature evaluating SII in osteoporosis. In a prospective cohort study conducted by Fang et al. and published in 2019, it was stated that a high SII value is an important predictor of the diagnosis of postmenopausal osteoporosis and the risk of osteoporotic fractures in postmenopausal osteoporosis patients.[5] Wang et al., in their study examining the relationship between mortality after hip fractures, which is one of the well-known conditions associated with osteoporosis, and SII, reported that SII value is an independent predictor associated with a higher mortality rate.[34] Unlike, we did not find a significant difference in SII values between the severe osteoporosis group with a history of osteoporotic fractures and the osteoporosis group. We think that the reason why this finding is different from the studies mentioned may be the retrospective design of our study and the relatively small sample size. In the study of Du et al., it was reported that SII value and NLR value had a strong negative correlation with BMD. They stated that, unlike NLR, this relationship with SII was independent of covariates such as age, body mass index, and sex hormone levels.[35] The authors suggested that oxidative stress and chronic inflammation, which are well-known to be associated with platelet function, and the role of PLT in bone formation may be the reason for the difference in the predictive effects of SII and NLR values.[35] While no significant difference was observed between the groups in NLR values in our study, we think that the difference in SII values can be explained from this point of view.

One of the superior aspect of our study is that the SII value is presented as a valuable and practical method that can be used to identify patients with a high risk of developing osteoporosis in the early period and thus mediate the emergence of earlier and effective treatment approaches. We think that our study is also important in terms of showing that the data obtained with the measurements that are frequently used in routine evaluation (which can be accessed in almost every health center, will not impose an additional burden on the health system, will not tire the patient in the examinations, and will not waste time) can be used to predict osteoporosis. There are some limitations of this study. The first is that the study is retrospective and the number of patients is relatively small, and its generalizability is relatively low for these reasons. These limitations were tried to be overcome by conducting the study design as a case-control study. Another limitation is that the menopause duration, accompanying systemic diseases, and treatments for osteoporosis were not evaluated. More comprehensive information on the subject will be obtained through prospective studies conducted with larger patient groups in which these parameters are also evaluated. In addition, we think that prospective studies that can be planned in the future, in which patients with a high SII cut-off value are followed and evaluated in terms of osteoporosis development and fracture risk, may provide important contributions to the literature and clinical practice.

CONCLUSION

SII value is a prognostic predictor that can be used to predict the development of osteoporosis in postmenopausal osteopenic patients. Its use in clinical practice will enable early diagnosis of patients with a high risk of developing postmenopausal osteoporosis, planning earlier and effective treatments, and preventing or delaying the development of osteoporosis.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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