ENDOCRINOLOGY RESEARCH AND PRACTICE

SOCIETY OF ENDOCRINOLOGY AND METABOLISM OF TÜRKİYE

ORIGINAL ARTICLE
Endocrinol Res Pract. 2024;28(3):143-150

Association Between Prognostic Nutritional Index and Bone Mineral Density, Fracture Risk Assessment (FRAX) Tool, and Disability in Patients with Postmenopausal Osteopenia/Osteoporosis: A Cross-Sectional Study

ABSTRACT

Objective: To evaluate the relationship between prognostic nutritional index (PNI) and bone mineral density (BMD) values and disability in patients with osteopenia/osteoporosis.

Methods: Between January 2022 and January 2023, 106 postmenopausal women with osteopenia (n = 54) and osteoporosis (n = 52) were included in the study. Patients with a disease or medication causing secondary osteoporosis were excluded. Bone mineral density was evaluated using dual-energy X-ray absorptiometry. Nutritional status was measured using the PNI, which was calculated using total lymphocyte count and serum albumin levels. The Health Assessment Questionnaire Disability Index (HAQ-DI) was used to evaluate disability.

Results: The mean age of the participants was 63.78 ± 7.53 years. Prognostic nutritional index was positively correlated with total hip BMD values ($r = 0.217$, $P = .029$) and total hip T-scores ($r = 0.207$, $P = .037$) and negatively correlated with Fracture Assessment Tool Model (FRAX)-major fracture risk ($r = -0.399$, $P < .001$), FRAX-hip fracture risk ($r = -0.300$, $P = .002$), and HAQ-DI scores ($r = -0.474$, $P < .001$). The mean PNI was lower in patients with a history of falls than in those without falls ($P < .001$). The mean PNI was lower in patients with a history of osteoporotic fractures than in those without a fracture history ($P = .007$). Multivariate linear regression analyses showed that PNI was the only independent variable for HAQ-DI ($B = -0.040$, $P < .001$) ($R2 = 0.17$).

Conclusion: Using PNI in clinical practice may be beneficial because of its association with BMD values and for predicting the independence of patients with osteopenia/osteoporosis. If a disability is detected, a multidisciplinary approach should be considered, including rehabilitation and improvement of nutritional condition.

Keywords: Bone mineral density, Ca metabolism, osteoporosis and metabolic bone diseases, disability, FRAX, prognostic nutritional index

Introduction

Osteoporosis is the most common metabolic bone disorder.[1] It is characterized by low bone mass, microarchitectural bone deterioration, and increased bone fragility.[1,2] It may be asymptomatic until osteoporotic fractures occur.[1] Fractures have significant medical and personal consequences, including morbidity, mortality, disability, reduced health-related quality of life, and economic burden.[1,3]

The amount of bone acquired at the end of skeletal maturation in adults is called peak bone mass.[4] Peak bone mass is explained by genetic and environmental factors, including dietary intake, lifestyle, and other factors.[4,5] After reaching peak bone mass, bone mass reduces with age, and loss of bone mass accelerates with menopause because of decreasing sex hormones, particularly estrogen.[4,5] Previous studies indicated that the loss of estrogen promoted increased production of proinflammatory cytokines and persistent inflammation and might lead to osteoporosis and other comorbidities.[5] On the other hand, proteins constitute approximately 50% of bone volume and one-third of bone mass and provide the structural matrix of bone.[6] Collagen and various non-collagen proteins form the organic matrix of bone, and calcium is the main mineral in this matrix.[6] Accordingly, adequate dietary proteins are essential for obtaining and maintaining optimal bone mineral mass in adults.[6]

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Received: February 10, 2024
Revision Requested: March 13, 2024
Last Revision Received: March 15, 2024
Accepted: March 21, 2024
Publication Date: May 27, 2024

Cite this article as: Baday-Keskin D, Hepşen S, Uz C. Association between prognostic nutritional index and bone mineral density, fracture risk assessment (FRAX) tool, and disability in patients with postmenopausal osteopenia/osteoporosis: A cross-sectional study. *Endocrinol Res Pract.* 2024;28(3):143-150.

DOI: 10.5152/erp.2024.24438

The prognostic nutritional index (PNI), first used to predict complications in patients undergoing gastrointestinal surgery, is used as an immune-nutritional index.[7] Prognostic nutritional index is calculated by using total lymphocyte count and serum albumin levels.[8] Albumin is a negative acute phase reactant related to nutritional status.[7,9] Low levels of lymphocytes are associated with a poor immune response.[9] In addition, the monocyte-to-lymphocyte ratio (MLR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) are novel indicators of systemic inflammation severity in various conditions.[7,9,10]

Prognostic nutritional index may be a good indicator of osteoporosis because it reflects nutrition and immune response, which are important for bone health. To our knowledge, this is the first study evaluating the relationship between PNI and disability in patients with osteo penia/osteoporosis. This study aimed to determine the relationship between PNI, MLR, NLR, PLR, and bone mineral density (BMD) values, Fracture Risk Assessment Tool (FRAX), and disability in patients with osteopenia and osteoporosis.

Materials and Methods

Data Collection

This cross-sectional study included 106 consecutive postmenopausal women with osteopenia (n = 54) and osteoporosis (n = 52) who visited physical medicine and rehabilitation outpatient clinics between January 2022 and January 2023. Patients who have a disease or medication causing secondary osteoporosis, ischemic heart disease, chronic kidney disease, liver failure, diabetes mellitus, active infection, history of major trauma or surgery within 6 months, autoimmune disorders [e.g., rheumatoid arthritis (RA), multiple sclerosis], cancer, and neurologic and psychological disorders causing physical disability, were excluded. This study was approved by the Local Clinical Research Ethics Committee of Kırıkkale University (date: January 20, 2022; number: 22/01), and written informed consent was obtained from all participants.

Sociodemographic variables including age (years), height (cm), weight (kg), body mass index (BMI) (kg/m^2), education duration (years), occupation, marital status, cigarette smoking status, cigarette consumption (peak/year), alcohol use, history of osteoporotic fractures, and history of falls (within 1 year) were recorded. Bone mineral density was evaluated using dual-energy X-ray absorptiometry (Lunar Prodigy, GE Healthcare, Madison, Wis, USA). Bone mineral density values and T-scores of total lumbar spine, femoral neck, and total hip were noted. The T-score of the total lumbar spine, femoral neck, or total hip of ≤ -2.5 was defined as osteoporosis, and the T-score of $-2.5 < T < -1.0$ was defined as osteopenia according to the World Health Organization diagnostic criteria.[11] Laboratory test results of patients [lymphocyte (mm^3), neutrophil (mm^3), monocyte (mm^3), albumin (g/dL), and vitamin D (ng/mL) levels] were recorded. Nutritional status was measured using PNI, which was calculated with the following formula: [10 × blood albumin (g/dL)] + [0.005 × total lymphocyte count (/mm^3)].[8,12] Higher PNI levels indicated better nutritional status.[12] Neutrophil-to-lymphocyte ratio, MLR, and PLR were calculated. The estimated 10-year risk of a major (a clinical vertebral fracture, proximal humerus, hip, or forearm fracture) and hip osteoporotic fracture risks were calculated using the FRAX Model (FRAX®) program, including BMD values via (https://www.sheffield.ac.uk/FRAX), which was recommended by the International Osteoporosis Foundation and National Osteoporosis Foundation.[2,11,13]

The Health Assessment Questionnaire Disability Index (HAQ-DI) was used to evaluate disability. The total HAQ-DI score ranges between 0 and 3. Higher scores indicate more severe disability.[14]

The participant's physical activity level was determined using the International Physical Activity Questionnaire (IPAQ) (Short Form). This questionnaire comprises questions about walking, moderate activity, and vigorous activity durations. The durations of each activity are multiplied by metabolic equivalents (METs). The sum of all activity scores represents the total score of IPAQ.[15]

The validation and reliability of the HAQ-DI and IPAQ questionnaires in Turkish have been previously completed and published.[14,15]

Statistical Analysis

Descriptive variables are presented as a number of cases with percentage (%), mean ± standard deviation (SD) and median [interquartile range (IQR)]. The normality of continuous variable distributions was determined using the Shapiro–Wilk test. Student's *t*-test was used for the comparison of PNI, femoral neck BMD, and femoral neck T-scores and the Mann–Whitney *U*-test was used for the comparison of total lumbar spine BMD, total hip BMD, total lumbar spine T-scores, total hip T-scores, NLR, PLR, MLR, HAQ-DI scores, IPAQ scores, FRAX-major fracture risk, and FRAX-hip fracture risk between the osteopenia and osteoporosis groups. One-way analysis of variance was used for normally distributed variables, and the Kruskal–Wallis test was used for non-normally distributed variables when comparing more than 2 independent groups. The chi-squared test or Fisher's exact test was used to compare proportions between groups. Correlation coefficients between normally and non-normally distributed/ordinal variables were determined using Pearson's and Spearman's correlation tests, respectively. To determine the final predictive factors of total lumbar spine BMD, total lumbar spine T-scores, femoral neck BMD, femoral neck T-scores, total hip BMD, total hip T-scores, and HAQ-DI, multivariate linear regression analyses were used. The age, cigarette consumption, BMI, IPAQ score, vitamin D levels, PNI, NLR, PLR, and MLR of all participants were included in the multivariate linear regression analysis for determining independent variables for total lumbar spine BMD, total lumbar spine T-scores, femoral neck BMD, femoral neck T-scores, total hip BMD, and total hip T-scores. In addition, age, education duration, BMI, cigarette smoking status, history of falls, history of fragility fracture, vitamin D levels, PNI, MLR, NLR, total lumbar spine BMD, femoral neck BMD, total hip BMD, and IPAQ score variables were included in the multivariate linear regression analysis for investigating predictors for disability. *P*-values less than .05 were considered statistically significant.

MAIN POINTS

- Prognostic nutritional index (PNI) was positively correlated with total hip bone mineral density and total hip T-scores.
- Prognostic nutritional index was negatively correlated with Fracture Assessment Tool Model (FRAX)-major fracture risk and FRAX-hip fracture risk.
- Prognostic nutritional index was negatively correlated with disability level.
- The mean PNI was lower in patients with a history of falls and osteoporotic fractures.
- Prognostic nutritional index was a predictive variable for disability in patients with osteopenia/osteoporosis.

Results

A total of 106 postmenopausal patients with osteopenia/osteoporosis were included in the study. The mean age of the participants was 63.78 ± 7.53 years. Fifty-two (49.1%) patients had osteoporosis, and 54 (50.9%) had osteopenia. Eight patients with osteopenia (14.8%) and 14 patients with osteoporosis (26.9%) had a history of falling within one year ($P = .124$). All seven patients with a history of osteoporotic fracture had osteoporosis ($P = .006$). The mean PNI was 55.73 ± 6.21. The difference in PNI scores was not statistically significant between the osteoporosis (55.13 ± 5.49) and osteopenia (56.31 ± 5.93) groups ($P > .05$). The median HAQ score of the participants was 0.125 (IQR, 0-0.725). The demographic variables, BMD values and T-scores, laboratory data, and questionnaire scores of the patients with osteopenia and osteoporosis are presented in Table 1.

Prognostic nutritional index was positively correlated with total hip BMD values ($r = 0.217$, $P = .029$) and total hip T-scores ($r = 0.207$, $P = .037$), and negatively correlated with FRAX-major fracture risk ($r = -0.399$, $P < .001$), FRAX-hip fracture risk ($r = -0.300$, $P = .002$), HAQ-DI scores ($r = -0.474$, $P < .001$), MLR ($r = -0.461$, $P < .001$), PLR ($r = -0.515$, $P < .001$), and NLR ($r = -0.410$, $P < .001$) in all participants. There was no statistically significant correlation between PNI and age, education duration, BMI, IPAQ scores, and vitamin D levels ($P > .05$). The correlations between PNI and demographic variables, BMD values and T-scores, laboratory data, and questionnaire scores are presented in Table 2. The mean PNI was lower in patients with a history of falls compared to those without a history of falls (51.54 ± 6.67 and 56.83 ± 5.62, respectively) ($P < .001$). In addition, the mean PNI was lower in patients with a history of osteoporotic fractures than in those without a fracture history (49.66 ± 7.06 vs. 56.13 ± 5.97) ($P = .007$). Prognostic nutritional index was not related to smoking status, occupation, and marital status ($P > .05$). Also, there was no relationship between a history of osteoporotic fractures and NLR, PLR, and MLR ($P > .05$).

Total lumbar spine T-scores were positively correlated with femoral neck T-scores ($r = 0.280$, $P = .004$), total hip T-scores ($r = 0.433$, $P < .001$), and BMI ($r = 0.240$, $P = .013$), and negatively correlated with FRAX-hip fracture risk ($r = -0.259$, $P = .008$), MLR ($r = -0.270$, $P = .006$), and PLR ($r = -0.217$, $P = .029$). Femoral neck T-scores were positively correlated with BMI ($r = 0.320$, $P = .001$), and negatively correlated with FRAX-major fracture risk ($r = -0.601$, $P < .001$), FRAX-hip fracture risk ($r = -0.787$, $P < .001$), cigarette consumption ($r = -0.195$, $P = .045$), MLR ($r = -0.218$, $P = .028$), and PLR ($r = -0.225$, $P = .023$). Total hip T-scores were positively correlated with BMI ($r = 0.405$, $P < .001$), and PNI ($r = 0.207$, $P = .037$), and negatively correlated with cigarette consumption ($r = -0.203$, $P = .041$), FRAX-major fracture risk ($r = -0.484$, $P < .001$), FRAX-hip fracture risk ($r = -0.602$, $P < .001$), MLR ($r = -0.342$, $P < .001$), PLR ($r = -0.264$, $P = .007$), and NLR ($r = -0.234$, $P = .018$). The total lumbar spine, femoral neck, and total hip T-scores were not related to marital status, smoking, and history of falls ($P > .05$).

Health Assessment Questionnaire Disability Index scores were negatively correlated with PNI ($r = -0.474$, $P < .001$), and education duration ($r = -0.260$, $P = .009$), and positively correlated with NLR ($r = 0.216$, $P = .027$), FRAX-major fracture risk ($r = 0.424$, $P < .001$), FRAX-hip fracture risk ($r = 0.287$, $P = .003$), and IPAQ ($r = 0.260$, $P = .007$) scores. The median HAQ-DI score was 0.5 (IQR, 0.25-1.0) in patients with a history of falls, and 0.0 (IQR, 0-0.5) in patients without a history of falls ($P = .002$). The median HAQ-DI score was higher in patients with a history of osteoporotic fracture than in those without a fracture history [1.0 (IQR, 0.50-1.10) vs. 0.13 (IQR, 0-0.63)] ($P = .004$). There were no correlations between HAQ-DI scores and age, cigarette consumption, vitamin D levels, BMI, MLR, PLR, total lumbar spine BMD, femoral neck BMD, total hip BMD, and T-scores of the total lumbar spine, femoral neck, and total hip ($P > .05$). There were no relationships between HAQ-DI scores and marital status, occupation, and smoking ($P > .05$).

Multivariate linear regression analyses showed that NLR ($B = -0.026$, $P = .012$), ($B = -0.261$, $P = .001$), and MLR ($B = -0.002$, $P = .024$), ($B = -0.012$, $P = .012$) were independent variables for total lumbar spine BMD ($R^2 = 0.10$) and total lumbar spine T-scores ($R^2 = 0.16$), respectively. Age ($B = -0.005$, $P = .006$) ($B = -0.033$, $P = .023$) and BMI ($B = 0.007$, $P = .010$) ($B = 0.057$, $P = .006$) were predictive variables for femoral neck BMD ($R^2 = 0.11$) and femoral neck T-scores ($R^2 = 0.10$), respectively. Body mass index was an independent variable for total hip BMD ($B = 0.011$, $P < .001$) ($R^2 = 0.13$). Platelet–to-lymphocyte ratio ($B = -0.004$, $P = .006$) and BMI ($B = 0.078$, $P < .001$) were predictive variables for total hip T-scores ($R^2 = 0.26$). Prognostic nutritional index was the only independent variable for HAQ-DI in patients with osteo penia/osteoporosis ($B = -0.040$, $P < .001$) ($R^2 = 0.17$). Multivariate regression analysis results are presented in Table 3.

Discussion

The current study showed that PNI was positively correlated with total hip BMD and total hip T-scores and negatively correlated with FRAX-major fracture risk, FRAX-hip fracture risk, and HAQ-DI scores. Moreover, PNI was lower in patients with a history of falls and osteoporotic fractures. In addition, PNI was the only predictive variable for disability in patients with osteopenia/osteoporosis.

Various factors such as age, sex, maturation, genetics, population ancestry, lifestyle, immune system, nutrition, physical activity, and environmental factors play a role in bone health.[5,16,17] The skeletal system grows rapidly after birth and reaches peak bone mass approximately in the mid- to late 20s.[5] Bone mass reduces gradually with age in both men and women.[5] Besides age, T helper (Th) cells and various immune cells majorly affect bone homeostasis.[16] Srivastava et al[16] termed the role of the immune system in osteoporosis as "immunoporosis." Natural killers and innate lymphoid cells in the lymphoid lineage and neutrophils, eosinophils, and mast cells in the myeloid lineage contribute to osteoporosis by producing proinflammatory mediators.[18] In addition, sex hormones, especially estrogen, are very important in bone homeostasis.[5] Previous studies showed that the immune system and inflammation had a critical pathogenic role in bone loss in the context of estrogen loss. Wu et al[5] reported that loss of estrogen might cause chronic low-grade proinflammatory cytokine (tumor necrosis factor-alpha and interleukin 17) production by converting memory T cells (Tm) to effector Tm. On the other hand, malnutrition, which is a modifiable risk factor and is common in older patients, may promote the development of osteoporosis and lead to osteoporotic fractures.[19,20] A healthy diet is essential for adequate bone mass.[21] Body mass index is commonly used for evaluating nutrition.[20] Low BMI is reported as a risk factor for bone loss and hip fracture in previous studies.[20,22] Coin et al[20] signified that BMI in both sexes, serum albumin in women, and protein intake in men were independent variables for BMD. Shangguan et al[19] reported that malnutrition was common in patients with osteoporosis and was

Table 1. Demographic Variables, Bone Mineral Density Values and T-scores, Laboratory Data, FRAX Fracture Risk Scores, and Questionnaire Scores of Participants

	Patients with Osteopenia (n = 54)	Patients with Osteoporosis (n = 52)	*P*
Age (mean ± SD)	64.26 ± 7.06	63.29 ± 8.02	.509
BMI (kg/m^2) (median, IQR)	30.44 (IQR, 25.64-33.33)	28.12 (IQR, 24.77-32.23)	.072
Education duration (year) (median,IQR)	5.0 (IQR, 5.0-11.0)	5.0 (IQR, 5.0-9.5)	.819
Occupation (%)			.268
Employed	2 (3.7%)	4 (7.7%)	
Housewife/unemployed	46 (85.2%)	46 (88.5%)	
Retired	6 (11.1%)	2 (3.8 %)	
Marital status (%)			.894
Married	42 (77.8%)	41 (78.8 %)	
Single	12 (22.2 %)	11 (21.2 %)	
Cigarette smoking (%)			.842
Yes	8 (14.8%)	7 (13.5%)	
No	46 (85.2%)	45 (86.5%)	
Cigarette consumption (packs/year) (mean ± SD)	3.35 ± 9.51	3.87 ± 13.0	.949
Alcohol use (%)			
Yes	0 (0 %)	0 (0%)	
No	54.0 (100%)	52 (100%)	
History of fall (within 1-year) (%)			.124
Yes	8 (14.8%)	14 (26.9%)	
No	46 (85.2%)	38 (73.1%)	
History of osteoporotic fracture (%)			**.006***
Yes	0 (0%)	7 (13.5%)	
No	54 (100%)	45 (86.5%)	
PNI (mean ± SD)	56.31 ± 5.93	55.13 ± 5.49	.330
Albumin level (g/dL)	4.43 ± 0.43	4.40 ± 0.37	.710
Serum lymphocyte level (mm^3)	2403.28 ± 716.58	2225.19 ± 888.85	.258
MLR (median,IQR)	0.21 (IQR, 0.17-024)	0.24 (IQR, 0.20-0.29)	**.016**
PLR (median, IQR)	113.74 (IQR, 88.97-138.24)	131.39 (IQR, 104.56-155.85)	**.044**
NLR (median, IQR)	1.43 (IQR, 1.24-1.92)	1.79 (IQR, 1.37-2.58)	**.004**
Vitamine D level (ng/mL) (median, IQR)	22.80 (IQR, 14.10-27.60)	20.0 (IQR, 13.0-32.10)	.694
Total lumbar spine BMD (gr/cm^2) (median, IQR)	0.89 (IQR, 0.86-0.95)	0.73 (IQR, 0.69-0.78)	**<.001**
Femoral neck BMD (mean ± SD)	0.83 ± 1.11	0.71 ± 0.14	**<.001**
Total hip BMD (median, IQR)	0.94 (IQR, 0.84-1.02)	0.82 (IQR, 0.74-0.90)	**<.001**
Total lumbar spine T-score (median, IQR)	-1.60 [IQR, (-1.80)-(-0.40)]	-3.00 [IQR, (-3.30)-(-2.60)]	**<.001**
Femoral neck T-score (mean ± SD)	−0.78 ± 0.86	−1.63 ± 1.05	**<.001**
Total hip T-score (median, IQR)	−0.40 [IQR, (−1.10)-(0.10)]	−1.50 [IQR, (−2.00)-(−1.00)]	**<.001**
FRAX-major fracture risk (%) (median, IQR)	6.0 (IQR, 4.3-7.6)	6.2 (IQR, 4.5-11.2)	.078
FRAX-hip fracture risk (%) (median, IQR)	0.6 (IQR, 0.2-1.5)	1.1 (IQR, 0.6-3.1)	**.006**
HAQ-DI (median,IQR)	0.13 (IQR, 0.0-0.63)	0.13 (IQR, 0.0-1.0)	.506
IPAQ (METs, min/wk.), (median, IQR)	610 (IQR, 198-1124)	297 (IQR, 0-919)	.137

Values in bold indicate statistical significance.
BMD, bone mineral density; BMI, body mass index; FRAX, Fracture Risk Assessment Tool; HAQ-DI, Health Assessment Questionnaire Disability Index; IPAQ, International Physical Activity Questionnaire; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index.
*Fisher's exact test was used because of 2 cells (50.0%) having expected count less than 5.

associated with an increased risk of all-cause mortality compared with normal nutritional status. Consistent with the literature, age was a predictive variable for femoral neck BMD and femoral neck T-scores in the current study. Body mass index was an independent variable for femoral neck BMD, femoral neck T-scores, total hip BMD, and total hip T-scores. In addition, physical activity levels were positively correlated with total lumbar spine and femoral neck BMD.

Prognostic nutritional index is an immuno-nutritional index calculated using total lymphocyte count and serum albumin levels.[8] Recent studies found it useful for predicting the prognosis of chronic inflammatory diseases.[7] In addition, it was found useful for identifying disease activity in rheumatologic diseases.[7,8] To our knowledge, this is the first cross-sectional study to evaluate PNI in patients with postmenopausal osteopenia/osteoporosis. Prognostic nutritional

Table 2. The Correlations between Demographic Variables, Laboratory Data, Bone Mineral Density Values and T-Scores, Fracture Risk Assessment Tool Fracture Risk Scores, and Questionnaire Scores

	Age	Education Duration	BMI	Vitamin D Level	IPAQ	PNI	MLR	PLR	NLR	Albumin	Lymphocyte
Total lumbar spine BMD	*r* = 0.044 *P* = .653	*r* = −0.100 *P* = .317	*r* = 0.192 *P* = .051	*r* = 0.008 *P* = .939	***r* = 0.238** ***P* = .015**	*r* = −0.026 *P* = .791	*r* = −0.185 *P* = .064	*r* = −0.149 *P* = .134	*r* = −0.170 *P* = .082	*r* = −0.043 *P* = .661	*r* = 0.063 *P* = .523
Femoral neck BMD	***r* = −0.270** ***P* = .006**	*r* = 0.033 *P* = .746	***r* = 0.288** ***P* = .003**	*r* = −0.023 *P* = .820	***r* = 0.211** ***P* = .032**	*r* = 0.045 *P* = .647	*r* = −0.056 *P* = .583	*r* = −0.123 *P* = .219	*r* = −0.115 *P* = .245	*r* = 0.037 *P* = .707	*r* = −0.015 *P* = .878
Total hip BMD	*r* = −0.019 *P* = .850	*r* = 0.044 *P* = .664	***r* = 0.407** ***P* < .001**	*r* = −0.003 *P* = .973	*r* = 0.110 *P* = .274	***r* = 0.217** ***P* = .029**	***r* = −0.198** ***P* = .047**	***r* = −0.250** ***P* = .011**	***r* = −0.220** ***P* = .026**	*r* = 0.144 *P* = .148	*r* = 0.171 *P* = .086
Total lumbar spine T-score	*r* = 0.132 *P* = .177	*r* = −0.056 *P* = .578	***r* = 0.240** ***P* = .013**	*r* = 0.066 *P* = .516	*r* = 0.147 *P* = .135	*r* = 0.091 *P* = .354	***r* = −0.270** ***P* = .006**	***r* = −0.217** ***P* = .029**	***r* = −0.231** ***P* = .017**	*r* = 0.017 *P* = .861	***r* = 0.210** ***P* = .031**
Femoral neck T-score	*r* = −0.185 *P* = .057	*r* = 0.062 *P* = .537	***r* = 0.320** ***P* = .001**	*r* = −0.012 *P* = .908	*r* = 0.162 *P* = .099	*r* = 0.071 *P* = .469	***r* = −0.218** ***P* = .028**	***r* = −0.225** ***P* = .023**	*r* = 0.191 *P* = .050	*r* = −0.007 *P* = .945	*r* = 0.091 *P* = .356
Total hip T-score	*r* = 0.004 *P* = .968	*r* = 0.052 *P* = .608	***r* = 0.405** ***P* < .001**	*r* = −0.061 *P* = .549	*r* = 0.099 *P* = .322	***r* = 0.207** ***P* = .037**	***r* = −0.342** ***P* < .001**	***r* = −0.264** ***P* = .007**	***r* = −0.234** ***P* = .018**	*r* = 0.099 *P* = .321	***r* = 0.211** ***P* = .033**
FRAX major fracture risk	***r* = 0.406** ***P* < .001**	***r* = −0.251** ***P* = .012**	*r* = −0.010 *P* = .923	*r* = −0.109 *P* = .287	*r* = 0.071 *P* = .477	***r* = −0.399** ***P* < .001**	***r* = 0.264** ***P* = .008**	***r* = 0.256** ***P* = .010**	***r* = 0.237** ***P* = .015**	***r* = −0.311** ***P* = .001**	***r* = −0.247** ***P* = .011**
FRAX hip fracture risk	***r* = 0.346** ***P* < .001**	*r* = −0.120 *P* = .234	***r* = −0.205** ***P* = .037**	*r* = −0.038 *P* = .707	*r* = −0.121 *P* = .219	***r* = −0.300** ***P* = .002**	***r* = 0.308** ***P* = .002**	***r* = 0.289** ***P* = .004**	***r* = 0.290** ***P* = .003**	*r* = −0.190 *P* = .053	***r* = −0.252** ***P* = .010**
IPAQ	*r* = −0.145 *P* = .141	*r* = −0.048 *P* = .634	*r* = 0.025 *P* = .798	*r* = −0.107 *P* = .291	–	*r* = −0.164 *P* = .095	*r* = −0.114 *P* = .258	*r* = −0.025 *P* = .807	*r* = −0.151 *P* = .125	*r* = −0.091 *P* = .355	*r* = −0.121 *P* = .218
HAQ-DI	*r* = 0.174 *P* = .076	***r* = −0.260** ***P* = .009**	*r* = 0.021 *P* = .831	*r* = −0.177 *P* = .081	***r* = 0.260** ***P* = .007**	***r* = −0.474** ***P* < .001**	*r* = 0.128 *P* = .203	*r* = 0.141 *P* = .159	***r* = 0.216** ***P* = .027**	***r* = −0.461** ***P* < .001**	***r* = −0.254** ***P* = .009**
PNI	*r* = −0.101 *P* = .304	*r* = 0.121 *P* = .229	*r* = 0.061 *P* = .535	*r* = 0.153 *P* = .128	*r* = −0.164 *P* = .095	–	***r* = −0.461** ***P* < .001**	***r* = −0.515** ***P* < .001**	***r* = −0.410** ***P* < .001**	***r* = 0.745** ***P* < .001**	***r* = 0.718** ***P* < .001**
MLR	*r* = 0.128 *P* = .201	*r* = 0.010 *P* = .923	*r* = −0.121 *P* = .230	*r* = −0.065 *P* = .528	*r* = −0.114 *P* = .258	***r* = −0.461** ***P* < .001**	–	***r* = 0.620** ***P* < .001**	***r* = 0.563** ***P* < .001**	*r* = −0.138 *P* = .169	***r* = −0.634** ***P* < .001**
PLR	*r* = 0.059 *P* = .558	*r* = 0.027 *P* = .792	*r* = −0.124 *P* = .215	*r* = 0.011 *P* = .911	*r* = −0.025 *P* = .807	***r* = −0.515** ***P* < .001**	***r* = 0.620** ***P* < .001**	–	***r* = 0.674** ***P* < .001**	*r* = −0.125 *P* = .211	***r* = −0.684** ***P* < .001**
NLR	*r* = 0.077 *P* = .430	*r* = 0.051 *P* = .614	*r* = −0.054 *P* = .583	*r* = −0.089 *P* = .381	*r* = −0.151 *P* = .125	***r* = −0.410** ***P* < .001**	***r* = 0.563** ***P* < .001**	***r* = 0.674** ***P* < .001**	–	*r* = −0.071 *P* = .467	***r* = −0.606** ***P* < .001**

Values in bold indicate statistical significance.

BMD, bone mineral density; BMI, body mass index; FRAX, Fracture Risk Assessment Tool; HAQ-DI, Health Assessment Questionnaire Disability Index; IPAQ, International Physical Activity Questionnaire; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index.

Table 3. Multivariate Regression Models for Total Lumbar Spine Bone Mineral Density (BMD), Total Lumbar Spine T-Scores, Femoral Neck BMD, Femoral Neck T-Scores, Total Hip BMD, Total Hip T-Scores, and Health Assessment Questionnaire

	B	Standard Error	*P*
Dependent variable: total lumbar spine BMD			
NLR	−0.026	0.010	.012
MLR	−0.002	0.001	.024
Dependent variable: total lumbar spine T-score			
NLR	−0.261	0.073	.001
MLR	−0.012	0.005	.012
Dependent variable: femoral neck BMD			
Age	−0.005	0.002	.006
BMI	0.007	0.003	.010
Dependent variable: femoral neck T-score			
Age	−0.033	0.014	.023
BMI	0.057	0.020	.006
Dependent variable: total hip BMD			
BMI	0.011	0.003	<.001
Dependent variable: total hip T-score			
BMI	0.078	0.016	<.001
PLR	−0.004	0.001	.006
Dependent variable: HAQ-DI			
PNI	−0.040	0.009	<.001

BMD, bone mineral density; BMI, body mass index; HAQ-DI, Health Assessment Questionnaire; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index.

index was positively correlated with total hip BMD values and total hip T-scores and negatively correlated with FRAX-major fracture risk, FRAX-hip fracture risk, HAQ-DI scores, MLR, PLR, and NLR in our study. Also, patients with lower PNI scores may have a higher risk of osteoporotic fractures because the mean PNI score was lower in patients with a history of falls and in patients with a history of osteoporotic fractures than in those without a history of falls or osteoporotic fractures.

Furthermore, PNI was negatively correlated with FRAX-major and FRAX-hip fracture risk scores. A retrospective study showed that although the mean PNI was higher in patients with osteoporosis than in controls, the difference in PNI was not statistically significant between osteopenia and osteoporosis groups.[23] Wang et al[24] demonstrated that the Geriatric Nutritional Risk Index was positively correlated with BMD in patients with type 2 diabetes mellitus. In light of these data, the nutritional condition of patients with osteopenia and osteoporosis should be considered and evaluated in a multidisciplinary manner, including appropriate osteoporosis treatment, lifestyle recommendations, and diet.

Previous studies showed that neutrophils and lymphocytes affected bone resorption and remodeling.[25] Platelet-to-lymphocyte ratio, NLR, and MLR are known as systemic inflammatory biomarkers and are reported as prognostic in various conditions such as cancer, infectious disease, cardiovascular disease, and thrombosis-related diseases.[26] Few studies evaluate the relationship between PLR, NLR, MLR, and BMD in the literature.[10,25,26-28] These markers are simple, easily measurable, and inexpensive to assess.[10] In our study, NLR and MLR were predictive variables for total lumbar spine BMD and total lumbar spine T-scores, and PLR was an independent variable for total hip T-scores. In addition, PLR, NLR, and MLR were positively correlated with FRAX-major fracture risk and FRAX-hip fracture risk scores. Previous studies demonstrated that higher NLR values were associated with osteoporosis.[25,26] A meta-analysis showed that higher preoperative and postoperative NLR values were associated with greater long-term mortality risk in older patients undergoing surgery for hip fractures.[27] Song et al[10] conducted a retrospective cohort study reporting that higher NLR and PLR values were significantly associated with hip osteoporosis in patients with RA. Moreover, they signified that a high PLR, NLR, and MLR baseline were associated with an increased risk of incident vertebral fractures. Supporting our data, an observational study revealed that MLR and PLR levels were higher in the osteoporosis group than in the osteopenia group.[28]

Although previous studies showed that quality of life was poor in patients with osteopenia or osteoporosis, there is a lack of knowledge in the literature in terms of disability.[29,30] Health Assessment Questionnaire scores were negatively correlated with PNI and education duration and positively correlated with NLR, FRAX-major fracture risk, and FRAX-hip fracture risk scores in the current study. Moreover, higher HAQ-DI scores were associated with a history of falls and a history of osteoporotic fractures. Lower PNI was the only predictor for disability. A cross-sectional study including self-reported questions showed that patients with osteoporosis had more physical health limitations in moderate activities, stair climbing, and shopping than patients without osteoporosis.[21] Lin et al[31] conducted a 3-year longitudinal observational cohort study of 477 patients with RA to investigate the risk factors for fragility fractures. They reported higher HAQ-DI scores associated with new incident fracture risk. A retrospective cohort study compared RA patients with or without osteoporosis in terms of disability and demonstrated that patients with RA with osteoporosis had greater disability than those without osteoporosis in the second and third visits.[32]

Interestingly, our study found a positive correlation between IPAQ and HAQ-DI scores. This result may be explained by the fact that physical activity includes leisure or occupation domains with different profiles of frequency, intensity, time, type, and repetition of muscular activity.[33] Physical activity involving static load, repetitive movement, and high peak forces may cause musculoskeletal pain.[33] In contrast, planned physical exercise training is beneficial for muscular strength, endurance, and resilience.[33] In our study, most patients did not perform regular physical exercise. Thus, they might perform high peak force or repetitive activities, which cause greater disability. Further studies comparing patients with osteoporosis performing different types of physical activities may provide greater insight into the relationship between physical activity levels and disability.

The strengths of the study were the exclusion of patients with secondary osteoporosis, inflammatory diseases, and disorders affecting disability, and the evaluation of other systemic inflammatory biomarkers, such as NLR, PLR, and MLR, besides PNI for investigating the role of the immune system in patients with osteopenia/osteoporosis. The study's limitations were that it did not include a control group,

it did not include dietary intake content and habits, and the prognostic role of PNI could not be determined because of the cross-sectional study design. The fact that the study group was selected only from osteopenia and osteoporosis patients means that the findings are valid only for this patient group, but there is no reason why the results obtained should be invalid in the population outside the study group.

In conclusion, higher PNI values were associated with higher total hip BMD and T-scores and lower FRAX-major and FRAX-hip fracture risk scores. Moreover, the current study demonstrated that a lower PNI score is the only predictor for greater disability in patients with osteopenia/osteoporosis. Thus, using PNI in clinical practice may be beneficial for its association with BMD values, FRAX-major, and hip fracture risk scores, as well as for predicting the independence of patients with osteopenia/osteoporosis. If disability or higher fracture risk is detected, a multidisciplinary approach, including osteopenia /osteoporosis treatment, rehabilitation, and improvement of nutritional condition, should be considered.

Ethics Committee Approval: This study was approved by the Ethics Committee of Kırıkkale University (approval no: 22/01; date: January 20, 2022).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – D.B.K., S.H.; Design – D.B.K., S.H.; Data Collection and/or Processing – D.B.K., C.U.; Analysis and/or Interpretation – D.B.K., S.H., C.U.; Literature Search – D.B.K., S.H., C.U.; Writing – D.B.K., S.H.; Critical Review – D.B.K., S.H., C.U.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: This study received no funding.

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