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Prognostic Nutritional Index in Patients with Both Vertebral and Non-Vertebral Osteoporotic Fractures

Vertebral ve Non-Vertebral Osteoporotik Kırığı Olan Hastalarda Prognostik Nutrisyonel İndeks

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Abstract

Objective: The prognostic nutritional index (PNI) is an index used to evaluate the basic nutritional status of patients with osteoporosis. However, it is not yet clear whether PNI can be used as an indicator of osteoporotic fracture. This study aimed to investigate whether the PNI is different in osteoporotic patients with and without fragility fractures.

Materials and Methods: This retrospective study included 58 female patients with osteoporosis. The first group included 28 patients with osteoporotic fractures and 30 patients without fractures. The primary outcome measure was PNI calculated using albumin and lymphocyte values. The secondary outcome measures were bone mineral density (BMD), albumin, lymphocyte, calcium, phosphorus, alkaline phosphatase, parathyroid hormone, calcium/creatine ratio in spot urine, 25-hydroxy vitamin D values, and FRAX® scores.

Results: The mean age and body mass index (BMI) were similar in both groups (1st group: age: 67.60±9.78 years; BMI: 27.63±3.89 kg/m^2, 2nd group: age: 66.83±7.91 years; BMI: 27.04±4.50 kg/m^2). Patients with fragility fractures had a significantly higher risk of FRAX® major osteoporotic fracture (p=0.002) and lower phosphorus levels (p=0.002). There were no significant differences in the PNI and blood albumin levels. Among patients with fragility fractures, albumin levels were significantly lower in patients with vertebral fractures (p=0.049), and corrected calcium values were significantly lower in patients with non-vertebral fractures (p=0.002). Correlation analysis showed that in patients with fragility fractures, there was no correlation between PNI, albumin levels, BMD, and FRAX®.

Conclusion: Our results showed no association between PNI and fragility fractures in patients with osteoporosis.

Keywords: Osteoporosis, osteoporotic fractures, prognostic nutritional index

Öz

Amaç: Prognostik nutrisyonel indeks (PNI), temel beslenme durumunu değerlendirmek için kullanılan bir indekstir ve osteoporozlu hastaların beslenme durumunu değerlendirmek için kullanılabilir. Ancak PNI'nın osteoporotik kırık için bir gösterge olarak kullanılıp kullanılamayacağı henüz belli değildir. Bu çalışmanın amacı kırılganlık kırığı olan ve olmayan osteoporotik hastalar arasında PNI'da fark olup olmadığını araştırmaktır.

Gereç ve Yöntem: Bu araştırma, osteoporoz tanısı almış 58 kadın hastanın dahil edildiği retrospektif bir çalışmadır. Birinci grupta osteoporotik kırığı olan 28 hasta, ikinci grupta ise kırığı olmayan 30 hasta yer aldı. Birincil sonuç ölçüsü albümin ve lenfosit değerleri kullanılarak hesaplanan PNI idi. İkincil sonuç ölçütleri kemik mineral dansitometrisi (BMD), albümin, lenfosit, kalsiyum, fosfor, alkalen fosfataz, paratiroid hormonu, spot idrarda kalsiyum/kreatin oranı, 25-hidroksi D vitamini değerleri ve FRAX® skorlarıdır.

Bulgular: Ortalama yaş ve vücut kitle indeksi (VKİ) her iki grupta da benzerdi (1. grup: yaş: 67,60±9,78 yıl; VKİ: 27,63±3,89 kg/m^2, 2. grup: yaş: 66,83±7,91 yıl; VKİ: 27,04±4,50 kg/m^2). Osteoporotik kırığı olan hastalarda FRAX majör osteoporotik kırık riski anlamlı derecede yüksek (p=0,002) ve fosfor düzeyleri daha düşüktü (p=0,002). PNI ve kan albümin düzeylerinde anlamlı bir fark yoktu. Osteoporotik kırığı olan hastalardan vertebra kırığı olanlarda albümin anlamlı olarak daha düşük (p=0,049), vertebral dışı kırığı olanlarda ise düzeltilmiş kalsiyum değeri anlamlı olarak daha düşüktü (p=0,002). Kırılganlık kırığı olan hastalarda PNI, albümin seviyeleri, BMD ve FRAX® arasında herhangi bir korelasyon bulunmadığı görüldü.

Sonuç: Sonuçlarımız osteoporotik hastalarda PNI ile kırılganlık kırıkları arasında bir ilişki bulunmadığını gösterdi.

Anahtar kelimeler: Osteoporoz, osteoporotik kırıklar, prognostik nutrisyonel indeks

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Introduction

A fragility fracture is a fracture that occurs as a result of mechanical forces known as low-energy trauma that would not normally produce a fracture. Osteoporotic fragility fractures occur mainly in bones with low density, such as the vertebral column, hip, forearm, and shoulder (1). Additionally, they may occur in other bones such as tibia and ribs (1,2). Fragility fractures are a strong predictor of future fragility fractures. Within 3 years of a vertebral fracture, half of patients will experience another, with most occurring in the first year (3). Patients who have experienced a previous fracture at any site, have almost a two times greater risk of a future fracture. Besides that, patients with a fragility fracture of radius, femur, humerus and ankle have a four times greater risk for a future fracture (4).

According to the Fracturk study, Turkish men over 50 years old have a 3.5% risk of hip fracture, while Turkish women in the same age group have a higher risk of 14.6% (5). In the ageing population, increasingly frequent osteoporotic fractures not only result in increased morbidity and mortality but also a serious economic burden for countries (6,7). Therefore, it becomes important to reveal the relevant factors in terms of preventing osteoporotic fracture.

Many studies have evaluated the relationship between nutrition and bone density, and significant differences in bone density values have been observed between patients with and without malnutrition (8,9). Saito et al. (10) showed that protein malnutrition reduces bone density measurement independently of other factors. Insufficient calcium intake is another factor that causes a decrease in bone density in older ages (11).

There are various methods of evaluating malnutrition, including body mass index (BMI) and laboratory parameters such as albumin, prealbumin, and transferrin. Prognostic nutritional index (PNI) is a laboratory index calculated using serum albumin and total lymphocyte count (12). Low PNI is associated with increased morbidity and mortality due to malnutrition and poor postoperative outcomes for various malignancies (13,14). Additionally, recent studies have shown that it may be associated with postoperative outcomes in patients with fractures (15,16). However, the relationship between PNI and osteoporotic fragility fractures is not yet well understood.

In previous studies, it has been shown that the PNI is an indicator in determining the nutritional needs of patients with osteoporosis (17). However, in osteoporotic patients with fragility fractures, PNI has not been investigated whether. This study aims to investigate whether the PNI is different in osteoporotic patients with and without fragility fractures.

Materials and Methods

The file records of female patients, aged 45 years and over, who were registered to the "Osteoporosis Clinic" within the Eskişehir Osmangazi University Faculty of Medicine, Physical Medicine and Rehabilitation Outpatient Service, between August 2022 and 2023, and diagnosed with osteoporosis, were reviewed retrospectively. Patients with secondary osteoporosis, using steroids, having any comorbidity that may cause cancer or malnutrition, or using any protein-containing drug and also missing variables in patient files were excluded. Bone mineral densitometry (BMD) (lumber L1-4, femur total, femur neck), radiographic data (thoracolumbar spine lateral radiographs and extremity radiographs), laboratory parameters including albumin, lymphocyte, calcium, alkaline phosphatase, phosphorus, parathyroid hormone (PTH), calcium/creatine ratio in spot urine, 25-hydroxy vitamin D values were recorded.

The reference range for albumin is between 3.4 and 5.4 g/dL at blood level in adults. Using total serum calcium concentration is not recommended, calcium needs to be corrected with serum albumin level. Corrected calcium= total calcium (mg/dL) +0.8 × (4-albumin value g/dL).

According to the World Health Organization (WHO) international reference standard, low bone mass (osteopenia) is defined as -2.5< T-score in BMD <-1.0 and osteoporosis as T-score ≤-2.5, in the total hip, femoral neck, or lumbar spine. The criteria for classification apply to postmenopausal women and men aged 50 and older (18).

FRAX® is a computer-based algorithm that is a 10-year fracture risk calculation method created by entering the data of BMD and patient characteristics such as age, weight, height, smoking and alcohol history (19,20). WHO recommends FRAX® to detect fracture risk in patients.

BMI was calculated from these equations: BMI: body weight / height²

The PNI was calculated using the values of albumin and lymphocyte count of patients.

The PNI was Calculated from the Following Equations

PNI= 10× serum albumin (g/dL) 0.005+ × total lymphocyte count (per mm³). If the PNI value is ≥50, it indicates normal malnutrition. A PNI value of less than 50 indicates mild malnutrition, while a value of less than 45 indicates moderate to severe malnutrition. Severe malnutrition is indicated by a PNI value of less than 40 (17).

This study was performed in line with the principles of the Declaration of Helsinki. Ethics approval was granted by Eskişehir Osmangazi University Presidency Non-Interventional Clinical Research Ethics Committee (number: E-25403353-050.04-2400002818, date: 04.01.2024).

Statistical Analysis

The distribution of each continuous variable was tested for normality using the Shapiro-Wilk test. Non-normally distributed variables were compared using the Mann-Whitney U test and expressed as median values (25-75%). Normally distributed variables were performed using the t-test and they were expressed as mean ± standard deviation. Categorical variables are expressed as frequencies and percentages and they were compared using the chi-square test. The Spearman correlation coefficient was used as the correlation analysis. A p-value of

<0.05 was considered significant. All analyses were performed using the SPSS version 22.0 software (SPSS Inc, Chicago, IL, USA).

We conducted a post-hoc power analysis to determine the expected effect power of our study. We used G*power 3.1.9.7 software to perform post-hoc power analysis. The analysis was performed with an effect size of 0.79, an alpha error rate of 5% and a sample size of 58 participants. A previous comparable study of serum calcium and phosphorus concentration in patients with osteoporotic vertebral fractures yielded a moderate effect size (18). Post-hoc power analysis showed that our study had a 91% probability of detecting the determined effect size.

Results

A total of 112 female patient files were evaluated. Thirty-four files were excluded due to secondary osteoporosis, 8 patients were excluded due to collagen supplement usage, 10 patients were excluded due to having cancer history, and 2 patients were excluded due to missing variables. Twenty-eight patients with fragility fractures according to radiography and file examinations were accepted as the 1st group. Thirty patients who did not have any fragility fractures were accepted as 2nd group (Figure 1).

Out of 28 patients, 11 (39.2%) had vertebral column fragility fractures and 17 (60.7%) had fractures in extremities (wrist fracture in 8 patients, humerus fracture in 4 patients, ankle in 2 patients, costa/tibia/hip fractures were each in one patient).

Comparing the two groups showed that, patients with fragility fractures have a risk of major vertebral fracture (p=0.002) and significantly lower phosphorous value (p=0.002). Both groups showed similar levels of PNI. PNI values of all patients above 45, none of the patients had moderate or higher malnutrition risk (Table 1).

Patients with fragility fractures were divided into 2 groups: those with vertebral fractures (n=11) and those with non-vertebral fractures (n=17). The average age of individuals with vertebral fractures was significantly higher (p=0.016). Comparing the two groups showed that in patients with a fragility fracture, the corrected calcium value was significantly higher (p=0.002) and the albumin value was significantly lower (p=0.049). Both groups of patients with fragility fractures showed similar levels of PNI and lymphocytes (Table 2).

Correlation analysis showed that, in patients with fragility fractures, there was no correlation between PNI, albumin levels, BMD values, and FRAX® values (Table 3).

Discussion

This study investigated whether PNI and albumin levels play a role in the development of fragility fractures in osteoporotic patients. However, we did not detect a significant relationship between PNI and osteoporotic fracture. Although we found lower albumin levels in the group with vertebral osteoporotic fractures, there was no significant difference between those with and without fractures.

According to reviews of the literature, it appears that there are limited studies that investigate the relationship between osteoporosis and PNI. Studies have shown that PNI may be a useful indicator in predicting the development of osteoporosis and the prognosis of osteoporotic fracture (16,17). He et al. (22) found PNI superior to albumin alone in evaluating perioperative outcomes of femur fracture. According to our study results, PNI which is one of the malnutrition indicators, were similar between osteoporotic patients with or without fragility fractures. Also, PNI values did not correlate with BMD and FRAX® in patients with fragility fractures. These results may be because PNI and albumin values of all patients were approximately normal range. After all, none of the patients had malnutrition risk in our study population. Contrary to our study, in previous studies, Kul et al. (17) found that patients with a low PNI score had lower total lumbar BMD T-scores.

Calcium and phosphorus are the main elements of bone mineral building. Sufficient amounts of calcium and phosphorus are needed not only to support the mineralization of bone but also to suppress excessive and persistent elevations of circulating PTH, hypothesized as a potential mechanism responsible for low bone mass (23,24). Our study results showed that vitamin D and PTH levels were similar between groups. In addition, in our study, people with osteoporotic fractures had significantly lower phosphorus levels than those without. The use of regular

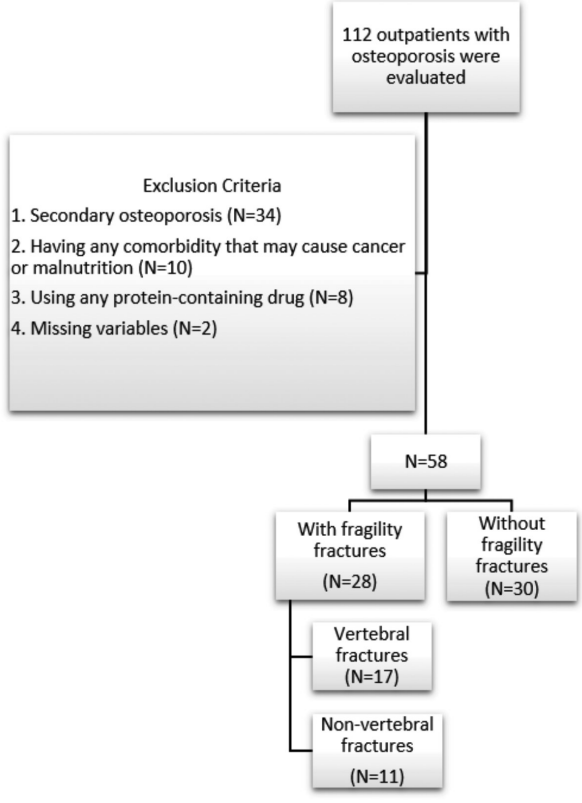

Figure 1. Flowchart of the study

Table 1. Comparison of osteoporosis patients with and without fragility fracture

		Osteoporosis with fragility fracture (n=28) (Mean ± SD)	Osteoporosis without fragility fracture (n=30) (Mean ± SD)	p-value
Age		67.60±9.78	66.83±7.91	0.741
Weight		68.68±10.14	65.88±10.44	0.337
Height		157.68±6.88	156.26±7.42	0.485
BMI		27.63±3.89	27.04±4.50	0.618
PNI		53.84±3.98	55.70±4.59	0.110
BMD	L1-4	-2.35±0.82	-2.22±0.76	0.621
	Femur neck	-2.09±0.56	-2.18±0.77	0.721
	Femur total	-1.74±0.58	-1.85±0.78	0.815
FRAX®	Major osteoporotic fracture	19.74±7.69	12.74±6.45	0.002**
	Hip fracture*	4.00 (2.70-6.95)	2.70 (1.05-5.40)	0.246
Laboratory results				
Lymphocyte		1.90±0.59	2.15±0.66	0.150
Creatine		0.71±0.12	0.70±0.11	0.627
Calcium		9.55±0.40	9.67±0.36	0.244
Corrected calcium		9.24±0.42	9.27±0.34	0.774
Phosphorus		3.27±0.44	3.69±0.50	0.002**
ALP*		71.00 (51-95)	63.50 (50.50-84.25)	0.631
Calcium/creatinine ratio in spot sample of urine*		0.12 (0.06-0.20)	0.11 (0.05-0.18)	0.873
Albumin		4.43±0.35	4.49±0.23	0.451
PTH*		46.20 (35.80-57.50)	34.20 (30.25-55.25)	0.085
25-OH vitamin D		30.80±10.77	35.90±10.46	0.421

*: Median (25-75%), **: p<0.05
n: Number, SD: Standard deviation, BMI: Body mass index, PNI: Prognostic nutritional index, BMD: Bone mineral density, ALP: Alkaline phosphatase, PTH: Parathyroid hormone

and high amounts of citrate and carbonate salts of calcium may have caused the decrease in dietary phosphorus by binding (25). Furthermore, low dietary intake of phosphorus may not support the effect of high calcium intake on bone growth, thus limiting the benefit of treatment (26).

FRAX® scoring is an important tool to detect fracture risk in osteoporosis and low BMI is one of the risk factors (20,21). However, the FRAX® calculation does not use the serum albumin value, which is commonly used in nutritional indexes to detect malnutrition. As an expected result, in our study, the risk of FRAX® major osteoporotic fracture was significantly higher in patients with fragility fracture. Additionally, out of the two groups observed, the risks of hip fractures were similar in both groups. Supporting the results obtained from the FRAX® analysis, when 28 patients with osteoporotic fractures were examined, it was found that only 1 person had a hip fracture.

The effect of albumin evaluated in PNI on BMD and osteoporotic fracture is controversial in the literature. Serum albumin level is a marker of nutritional status, and poor nutritional status may result in increased osteoporosis and bone fragility (27). Afshinnia et al. (28) found an independent and highly significant relationship between the duration of low albumin and osteoporosis. Other researchers have also suggested that low serum albumin levels increase the risk of future fractures (29,30). However, in our study, we did not detect any difference in albumin levels between those with and without osteoporotic fractures. Also, albumin levels did not correlate with BMD and FRAX®. Similar to our study, Lunde et al. (31) did not find a relationship between low-energy fracture history and albumin levels. Evaluation of a population with different categorical levels of albumin and repeated measurements of albumin levels may better elucidate the relationship between albumin and osteoporotic fracture risk. In our study, we found lower albumin levels in those with vertebral fractures compared to the non-vertebral fracture group. However, the average age was significantly higher in the group with vertebral fractures and we think that the low albumin level may be related to older age.

Study Limitations

The main limitation of our study was the small sample size, also PNI and albumin values of all patients were in the normal range. None of the patients had malnutrition risk in our study

Table 2. Comparison of patients with vertebral fragility fractures and patients with non-vertebral fragility fractures

		Fragility fractures in vertebrae (n=11)	Non-vertebral fragility fractures (n=17)	p-value
Age		73.00±9.06	64.11±8.78	0.016**
Weight		70.27±10.67	67.42±9.92	0.498
Height		156.45±5.44	158.64±7.89	0.402
BMI		28.62±3.59	26.86±4.07	0.270
PNI		52.56±4.14	54.67±3.76	0.176
BMD	L1-4	-2.05±0.94	-2.57±0.84	0.148
	Femur neck	-1.97±0.78	-2.09±0.36	0.578
	Femur total	-1.61±0.65	-1.88±0.58	0.274
FRAX®	Major osteoporotic fracture	19.44±6.71	19.97±8.64	0.880
	Hip fracture*	6.50 (1.40-7.15)	3.20 (2.92-4.72)	0.554
Laboratory results				
Lymphocyte		1.97±0.79	1.85±0.45	0.618
Creatine		0.74±0.11	0.69±0.13	0.304
Calcium		9.71±0.33	9.45±0.41	0.096
Corrected calcium		9.54±0.32	9.05±0.37	0.002**
Phosphorus		3.40±0.48	3.18±0.41	0.207
ALP*		64 (54-92)	71.00 (46.00-99.50)	0.535
Calcium/creatinine ratio in spot sample of urine*		0.09 (0.06-0.15)	0.15 (0.06-0.23)	0.863
Albumin		4.27±0.43	4.53±0.25	0.049**
PTH*		38.85 (28.25-47.12)	50.70 (39.90-83.25)	0.076
25-OH vitamin D		35.20±14.23	27.53±6.50	0.093

*: Median (25-75%), **: p<0.05
n: Number, SD: Standard deviation, BMI: Body mass index, PNI: Prognostic nutritional index, BMD: Bone mineral density, ALP: Alkaline phosphatase, PTH: Parathyroid hormone

Table 3. Correlation analysis between prognostic nutritional index, albumin levels, bone mineral density and FRAX® in patients with fragility fractures

	Fragility fractures in vertebrae (n=11)		Non-vertebral fragility fractures (n=17)		All patients with fragility fractures (n=28)	
	PNI	**Albumin**	**PNI**	**Albumin**	**PNI**	**Albumin**
BMD						
L1-4	p=0.627 r=-0.176	p=0.603 r=-0.188	p=0.569 r=0.149	p=0.817 r=0.061	p=0.935 r=-0.017	p=0.801 r=0.051
Femur neck	p=0.983 r=-0.008	p=0.907 r=0.043	p=0.381 r=-0.227	p=0.493 r=-0.179	p=0.243 r=-0.233	p=0.475 r=-0.143
Femur total	p=0.627 r=-0.176	p=0.365 r=-0.321	p=0.623 r=0.128	p=0.279 r=0.278	p=0.906 r=-0.024	p=0.657 r=0.090
FRAX®						
Major osteoporotic fracture	p=0.651 r=-0.176	p=0.932 r=0-.033	p=0.871 r=-0.053	p=0.584 r=-0.176	p=0.893 r=0.031	p=0.929 r=-0.021
Hip fracture	p=0.559 r=-0.226	p=0.431 r=-0.301	p=0.201 r=-0.397	p=0.357 r=-0.292	p=0.197 r=-0.293	p=0.196 r=-0.294

BMD: Bone mineral density, PNI: Prognostic nutritional index

population. We believe this limitation affected our results. There is a need for studies with a large number of osteoporotic patients, including patients with malnutrition and low albumin levels. In future, in the light of future studies, albumin can also be added to the FRAX® tool.

Another limitation is that the average age in the group with vertebral fractures is significantly higher than in the non-vertebral fracture group.

Conclusion

In conclusion, "PNI" and albumin levels were similar in osteoporotic patients with or without fragility fractures.

Ethics

Ethics Committee Approval: The present study is retrospective and its permission was obtained from Eskişehir Osmangazi University Presidency Non-Interventional Clinical Research Ethics Committee (number: E-25403353-050.04-2400002818, date: 04.01.2024).

Informed Consent: This study reviewed retrospectively.

Footnotes

Authorship Contributions

Concept: F.B., G.S., Design: F.B., G.S., Data Collection or Processing: F.B., G.S., Analysis or Interpretation: F.B., G.S., Literature Search: F.B., G.S., Writing: F.B., G.S.

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