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Araştırma Makalesi

Böbrek Nakilli Hastalarda Düşük Kemik Yoğunluğuna Etki Eden Faktörlerin ve FRAX (Fracture Risk Assessment Tool) Risk Skorununun Değerlendirilmesi

Evaluation of Factors Affecting Low Bone Density and Fracture Risk Assessment Tool (FRAX) Risk Score in Kidney Transplant Patients

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ÖZET

Amaç: Kemik mineral hastalıkları böbrek nakilli hastalarda sık görülmektedir. Osteopeni ve osteoporoz daha fazla olmakla birlikte osteonekroz daha az görülen komplikasyonlardır. Çalışmamızda düşük kemik mineral yoğunluğu (LBD) risk faktörlerini, femoral osteonekroz sıklığını ve FRAX skorunu araştırmayı amaçladık.

Materyal ve Metot: 90 hastanın verileri retrospektif olarak incelendi. Hastaların nakil öncesi, nakil sonrası ve güncel klinik bulguları, demografik özellikleri, kan tetkikleri, Dual Energy X-Ray Absorbsiyometri ile kemik yoğunlukları kaydedildi. Hastaların FRAX skorları hesaplandı. Osteonekroz tanısı alan hastaların verileri ayrıca analiz edildi.

Bulgular: Kırk iki hasta (%46,7) kadındı. 53 (%58) hastada LBD saptandı. Beş hastada (%5,5) osteonekroz gelişti. Majör osteoporotik kırık için ortalama FRAX Skoru riski %6,5 ± 3,9, kalça kırığı için ortalama FRAX Skoru riski %1,2 ± 1,9 idi. Erkek cinsiyet, yüksek alkalen fosfataz düzeyleri, ameliyat öncesi hiperfosfatemi ve ameliyat sonrası hipofosfatemi osteonekrozlu 5 hastada (%5,5) daha sık bulundu. Kadınlarda menopoz, ek intravenöz steroid dozu uygulaması, nakil sonrası hipofosfatemi, düşük ağırlık ve vücut kitle indeksi, LBD'li hastalarda anlamlı olarak daha yaygındı. Kadınlarda düşük kilo ve menopoz, LBD risk faktörleri olarak belirlendi.

Sonuç: Çalışmamızda önceki çalışmalarda kanıtlanmış olan postmenopozal duruma ek olarak düşük kilonun da LBD için bir faktör olduğu belirlenmiştir. Risk faktörü olmamakla birlikte ameliyat sonrası fosfor seviyesi faydalı olabilir.

Anahtar Kelimeler: Hipofosfatemi, osteonekroz, osteoporoz, böbrek nakli.

ABSTRACT

Aim: Metabolic bone disorders are seen as common in kidney transplant (KT) patients. Osteopenia and osteoporosis are more but osteonecrosis is a less commonly seen complication. In our study, we aimed to investigate low bone mineral density (LBD) risk factors, the FRAX (Fracture Risk Assessment Tool) score and the frequency of femoral osteonecrosis in KT patients.

Materials and Methods: The data of 90 patients were analyzed retrospectively. The patients' pre-transplant, post-transplant and current clinical findings, demographic characteristics, blood tests and bone mineral density (BMD) with current Dual Energy X-Ray Absorbsiometry were recorded. FRAX scores of the patients were calculated. The data of patients with a diagnosis of osteonecrosis were analyzed.

Results: Forty-two patients (46.7%) were female. LBD was detected in 53 (58%) patients. Osteonecrosis developed in 5 patients (5.5%). The mean FRAX Score risk for major osteoporotic fracture was 6.5% ± 3.9, mean FRAX Score risk for hip fracture was 1.2% ± 1.9. Male gender, high alkaline phosphatase levels, pre-operative hyperphosphatemia and post-operative hypophosphatemia were found more frequently in 5 patients (5.5%) with osteonecrosis. Menopause in women, additional intravenous steroid dose administration, post-transplant hypophosphatemia, lower weight and body mass index were significantly more frequent in patients with LBD. Low weight and menopause in women were found as risk factors.

Conclusion: In our study, it is determined that low weight was also a factor for LBD in addition to the postmenopausal status proven in previous studies. Although it is not a risk factor, the post-operative phosphorus level may be useful.

Keywords: Hypophosphatemia, osteoporosis, osteonecrosis, kidney transplantation.

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INTRODUCTION

Renal transplantation is an effective treatment for end-stage kidney disease. A successful transplant can reverse many complications of kidney disease; but, disturbances in bone and mineral metabolism may persist and be associated with fracture, morbidity and mortality [1]. The causes of progressive loss of bone mineral density (BMD) and fracture risk in kidney transplant (KT) patients are a variety of posttransplant factors, such as immunosuppressive drugs, hyperparathyroidism, vitamin D deficiency, and loss of renal graft function over time [2]. KDIGO 2017 CKD-MBD guide recommends use of Dual-energy x-ray absorptiometry (DEXA) for diagnosis of the bone mineral disorder in renal transplant patients and also recommends vitamin D, calcium supplementation, or antiresorptive therapy, especially in low bone density detected in the first 12 months of post-transplant [3]. A T-score of 2.5 SD or more below (more than -2.5 SD), entire hip or lumbar spine on DEXA; previous vertebral/ hip fractures; a 20% or greater probability of hip or vertebral fractures and a 10-year probability of major osteoporotic fracture (MOF) 20% or greater, or a 10-year probability of hip fracture 3% or more are considered as an indication for treatment in the general population [4].

Osteonecrosis of the femoral head (ONFH) is well-known as a skeletal complication after kidney transplantation [5]. With advances in immunosuppressive therapy, it has been reported that the improvement of renal function and reduced corticosteroid dose after transplantation lead to a decrease in the incidence of ONFH. [6]. The risk factors that have been reported for the development of ONFH, include cumulative steroid dose [7], calcineurin inhibitors (CNI) [8] and delayed graft function [6]. In our study, firstly we investigated the frequency of osteonecrosis and the more common findings in these patients.

Iliac crest bone biopsy is the most accurate method for assessing bone metabolism, but it is an invasive procedure and requires specific expertise. Bone quantity for assessment of BMD can also be measured using regional DEXA. Increasing evidence indicates that reduced BMD is useful for predicting fractures in transplant recipients [9-11]. In addition, fracture risk assessment with the Fracture Risk Assessment Tool (FRAX) for 10-year hip and MOF risk has not been validated in transplant recipients, and clinical trials are needed to determine the usefulness of these tools. In our study, we planned to determine low bone mineral density and risk factors that affect it, we also aimed to calculate the FRAX score MOF and hip fractures.

MATERIALS AND METHOD

Our study was carried out with KT patients followed up in the transplantation outpatient clinic between February 01, 2019, and August 31, 2022. Exclusion criteria included systemic illness (apart from chronic diseases such as diabetes, hypertension, coronary artery disease; cancer and systemic active infection, which may predispose to malnutrition and osteoporosis), malnutrition, transplant time for less than 6 months, failure to achieve laboratory parameters for data collection, additional comorbidities (cancer and systemic active infection) that would affect the laboratory parameters. Data from 90 patients were reviewed retrospectively. The following data were recorded from patient charts: sex, age, height, weight, comorbidities, etiology of kidney disease, duration of renal replacement treatment, menopausal status in women and current medications. Pre-transplant, post-transplant and current blood tests (calcium, phosphorus, creatinine, parathormone, vitamin D, magnesium, alkaline phosphatase (ALP), albumin, hemogram), current bone mineral measurement with DEXA were recorded. Intravenous additional steroid therapy was considered as 250 mg methylprednisolone and above for at least 1 day. All of the laboratory results were obtained from the electronic archive system.

BMD measurements were obtained by DEXA using a Hologic scanner (DMS Stratos DR). Vertebral bone density values were recorded by calculating the average of the first four lumbar vertebrae. The hip bone density was measured at the femoral neck level. Results were expressed as T-scores for gender-matched young adults. Patients were divided into two groups according to hip and spine T-scores: normal bone mineral density (T-Score ≥ -1.0) and low bone mineral density (LBD) (osteopenia: T-Score between -1.0 and -2.5, and osteoporosis: T-Score ≤ -2.5). FRAX (FRAX Web, version 4.1. Turkish FRAX tool) is the software that provides a 10-year percentage of hip fracture (HF) and MOF risk in osteoporosis management. More than 20% calculated risk of MOF and more than 3% of the risk of hip fracture are described as high risk. Patients who started bisphosphonate therapy due to osteoporosis; Fragility fracture, hip or vertebral fracture (detected clinically or by imaging), T score $\leq$-2.5 SD in the femoral neck, total hip or lumbar spine, Low bone mass (T-score at the femoral neck or vertebra of -1 SD to -2.5 SD) and 10-year risk of hip fracture $\geq$3% or 10-year osteoporosis-related fracture risk $\geq$20% or additional risk factor (long-term steroid use). Bisphosphonates could not be started in patients who met these criteria but were found to be below eGFR 30 and did not approve for treatment.

Orthopedic clinic consultation was requested for patients with hip pain or mobility deficits. Aseptic necrosis of the femoral head was diagnosed in patients with a necrotic area surrounded by a wavy border (demarcation line) in the subarticular region of the femoral head on hip magnetic resonance (MR) images, and typical “double line sign” on T2-weighted images. These patients were referred to in the text as patients with osteonecrosis.

SPSS (Chicago, IL, U.S.A., version 23.0) program was used for statistical analysis. As the descriptive methods; mean

± standard deviation was used for continuous numerical variables and numbers, and % for categorical variables. In the comparison of the two groups (LBD/ Normal BMD); the Independent Sample T test was used for normally distributed numerical variables, Mann Whitney U test for abnormally distributed variables, chi-square and Fisher's test were used for categorical variables. Parameters that were significant in univariate analysis and that did not show multicollinearity were analyzed using the statistical method of binary logistic regression. Backward LR Strategy was applied in multiple regression analysis.

All procedures were carried out under the ethical standards of the Clinical Research Ethics Committee, which approved the protocols in this study (Approval No. HNEAH-KAEK 2022/232), and with the 1964 Helsinki Declaration.

RESULT

Forty-two patients (46.7%) were female. The mean age of men was 46.3 ± 12 years and the mean age of women was 45.8 ± 11.9. Mean height levels were 164.9 ± 11.4 cm, mean weight was 72 ± 15 kg and mean body mass indexes were 26 ± 4.8. The BMI of the eighteen patients was compatible with obesity (%20).

In 69 patients with known etiology of chronic kidney disease, the frequency according to the etiology was as follows: hypertension %33, glomerulonephritis %13, vesicoureteral reflux %10, polycystic kidney disease %8. 76% of the patients had a living donor KT. The average time elapsed since transplantation was 94.8 ± 56.4 months. About 50% of the females were in their post-menopause stage.

%94 of the patients were using CNI, %9 azatiopurine, %82 mycophenolate mofetil, %14 mTOR inhibitors. None of the patients received a steroid-free regimen. %28 of the patients were given extra steroid dosage for delayed graft function, treatment of rejection, or as a recurrence therapy of the primary disease. Ten patients had a rejection attack. Approximately half of the patients (n:67, %55) had hypophosphatemia (phosphorus level <2 mg/dl) and 31 per 58 patients had hypomagnesemia (%53) after transplantation. Other test results and mean values according to low or normal bone density had been shown in Table 1 and Table 2.

Time to evaluation from transplantation to BMD measurement was 7.94 ± 4.7 (Mean ± SD) years. Low bone density was detected in 53 (58%) patients (femur or vertebral T score < -1). Osteonecrosis was detected in 5 patients (5.5%). Bisphosphonate treatment was started in 9 (10%) of the patients (1 patient with ibandronic acid and 9 patients with alendronate). In male patients, the mean femur T score was 0.9 ± 0.2, the mean femur BMD was 0.97 ± 0.17 gr/cm2, the mean vertebral T score was -0.7 ± 0.2, the mean vertebral BMD was 1 ± 0.2 gr/cm2, in female patients, the mean femur T score was -0.9 ± 0.14, the mean femur BMD was 0.91 ± 0.13 gr/cm2, the mean vertebral T score was -1.2 ± 0.2, the mean vertebral BMD was 0.92 ± 0.19 gr/cm2.

Table 1. Comparison of the patients' demographic parameters regarding BMD status

Parameters	Patient (n:90)	Normal BMD (n=37)	Low BMD (n=53)	P value (p<0.05)
Categorical Variables n (%), Numeric Variables (Mean ± SD)				
Female	42 (46.7)	14 (33.3)	28 (66.7)	0.1
Male	48 (53.3)	23 (47.9)	25 (52.1)	0.1
Menopausal status (n:42)	**21 (50)**	**3 (14.3)**	**18 (85.7)**	**0.009**
Age, year	46 ± 11	43.5 ± 11.9	47.9 ±11.7	0.12
Height, cm	164 ± 11.4	167 ± 11	162 ± 11	0.15
Weight, kg	**72 ± 15**	**77 ± 16**	**68 ± 14**	**0.001**
BMI, kg/m2	**26 ± 4.8**	**27.4 ± 4.4**	**25.7 ± 5**	**0.03**
Hypertension	56 (62)	22 (39.3)	34 (60.7)	0.6
Diabetes Mellitus	12 (13)	7 (58.3)	5 (41.7)	0.22
Living donor KT	69 (76)	28 (40.6)	41 (59.4)	0.8
CNI (yes)	85 (94)	35 (41.2)	50 (58.8)	0.6
AZA (yes)	8 (9)	3 (37.5)	5 (62.5)	0.5
MMF (yes)	74 (82)	29 (39.2)	45 (60.8)	0.2
mTOR inhibitors (yes)	13 (14)	7 (53.8)	6 (46.2)	0.3
Preop vitamin D use (n:61)	51 (83)	20 (39.2)	31 (60.8)	0.3
Postop active vitamin D use	22 (24)	7 (31.8)	15 (62.2)	0.3
Delayed Graft Function (n:21)	11 (52)	4 (36.4)	7 (63.6)	0.3
Rejection	10 (11)	2 (20)	8 (80)	0.18
Additional steroid	**28 (31)**	**7 (25)**	**21 (75)**	**0.03**
Desensitization (n: 69)	5 (7)	1 (20)	4 (80)	0.2

BMD: Bone mineral density, CNI: Calcineurin inhibitors, AZA: Azatiopurine, Mtor: Mammalian target of rapamycin, BMI: Body mass index,

Within ten years, the mean FRAX Score risk for MOF was 6.5% ± 3.9, the mean FRAX Score risk for HF was 1.2% ± 1.9. The mean FRAX Score risk for MOF was 6.3% ± 0.5 in men and 6.7% ± 4.3 in women. The mean FRAX Score risk for HF was 1.42% ± 0.3 in men and 1% ± 1.5 in women. In terms of FRAX risk, no significant difference was found between men and women. According to FRAX, a high risk of MOF (20% risk of fracture) was found in 1.1% and hip fracture risk (≥3% risk of hip fracture) was found in 10% of patients.

Femoral aseptic necrosis which of them mostly occurred within the first year was developed in 5 (5.5%) of the patients. All patients were male and the mean year of transplantation was 5.4 ± 3.7. Two of the 5 patients had polycystic kidney disease. Two of the patients had a cadaveric KT. Four patients were on tacrolimus and one was on everolimus immunosupresive regimen. There was no patient taking cyclosporine. An additional dose of steroid (250 mg methylprednisolone and above for at least 1 day) was administered to 3 (60%) of the patients (29% in remaining patients). While the mean ALP level of the patients was 134 ± 23 IU/l , the mean value of the remaining patients was 75 ± 30 IU/l. Postoperative hypophosphatemia was observed in all patients and hypomagnesemia was observed in 3 patients. The mean preoperative phosphorus level was 6.3 ± 0.1 mg/dl , which was higher than the mean values of the other patients (5.4 ± 0.1 mg/dl).

Menopause in women (14.3% - 85.7%, p:0.009), additional intravenous steroid administration despite routine

dosage (25% - 75%, p:0.03), early post-transplant hypophosphatemia (32.4% - 67.6%, p:0.046), low weight (77 ± 16 vs. 68 ± 14, p: 0.001) and low body mass index (27.4 ± 4.4 vs. 25.7 ± 5, p: 0.03) were found to be significantly more common in patients with low bone density. Age, duration of transplantation, immunosuppressive drugs other than steroids, and other biochemical tests except postoperative hypophosphatemia did not differ significantly between the two groups (Table 1-2).

Data that were significant according to univariate analysis and non-collinearity were included in the regression analysis (Table 3). Low weight (OR 0.882; 95% CI 0.813–1.057; p<0.01) and menopausal status in women (OR 6.28; 95% CI 1.111–48.843; p<0.01) were found as a risk factors for LBD

Table 2. Comparison of the patients' laboratory parameters and bone mineral measurement results parameters regarding BMD status

Parameters	Patient (n:90)	Normal BMD (n:37)	Low BMD (n:53)	P value (p<0.05)
Categorical Variables n (%), Numeric Variables (Mean ± SD)				
Femur T score	**-0.9 ± 1.2**	**-0.1 ± 1.2**	**-1.5 ± 0.7**	**0.001**
Vertebra T score	**-0.9 ± 1.5**	**0.2 ± 1.1**	**-1.8 ± 1.2**	**0.001**
BMD (Femur)	**0.94 ± 0.15**	**1.06 ± 0.12**	**0.8±0.1**	**0.001**
BMD (Vertebra)	**0.97 ± 0.19**	**1.1 ± 0.17**	**0.8 ± 0.14**	**0.001**
Preop PTH, pg/ml, (n:62)	427 ± 265	463 ± 277	398 ± 256	0.3
Preop Phosphorus, mg/dl, (n:63)	5.4 ± 1.16	5.4 ± 1.2	5.4 ± 1.1	0.7
Preop Calcium, mg/dl, (n:63)	8.94 ± 0.73	9.07 ± 0.7	8.7 ± 0.7	0.14
Preop D vit, ng/ml, (n:63)	13.1 ±7.8	14.3 ± 9	12.1 ± 6.9	0.4
Postop hypophosphatemia (n:67)	**37 (55)**	**12 (32.4)**	**25 (67.6)**	**0.046**
Postop hypomagnesemia (n:58)	31 (53)	13 (41.9)	18 (58.1)	0.3
***Creatinine, mg/dl**	1.4 ± 1.2	1.5 ± 1.7	1.2 ± 0.8	0.2
***Calcium, mg/dl**	9.5 ± 0.6	9.6 ± 0.6	9.4 ± 0.5	0.5
***Hemoglobin, g/dl**	12.8 ± 2.1	13.1 ± 1.6	12.5 ± 2.4	0.3
***Phosphorus, mg/dl**	3.1 ± 0.6	3 ± 0.6	3.2 ± 0.6	0.3
***Magnesium, mg/dl**	1.69 ± 0.2	1.6 ± 0.17	1.6 ± 0.23	0.9
***PTH, pg/ml**	112 ± 73	107 ± 75	115 ± 72	0.4
***Albumin, g/dl**	4.4 ± 0.3	4.4 ± 0.2	4.3 ± 0.3	0.4
***D vit, ng/ml, (n:78)**	16.9 ± 10	18.3 ± 0.3	16.1 ± 0.9	0.3
***ALP, IU/L, (n:78)**	79 ± 32	83.6 ± 28	76 ± 35	0.08

BMD: Bone mineral density, PTH: Parathormone, vit: Vitamin, ALP: Alkaline phosphatase, Preop: preoperative, Postop: postoperative, SD: Standart deviation, KT: Kidney transplantation, * current laboratory value

Table 3. Risk factors for low BMD according to multiple regression analyse

Parameters	p value	β (S.E)*	Exp(B)**	95% CI***	
				Upper	Lower
Menopausal status	**0.024**	**1.82 (0.8)**	**6.28**	**1.111**	**48.843**
Weight	**0.046**	**-0.02 (0.03)**	**0.882**	**0.813**	**1.057**
Hypophosphotemia	0.16	1.1 (0.8)	3.142	0.62	15.7
Additional steroid	0.94	0.06 (0.9)	1.095	0.164	7.596

* Beta and standard errors, ** The odds ratio, *** The 95% confidence interval

DISCUSSION

In our study, in which the factors affecting low bone mineral density are examined, it is determined that low weight and postmenopausal status in women are risk factors for LBD.

Overweight and obesity are defined as abnormal or excessive fat accumulation that poses a health risk. The most plausible mechanism for the increased BMD in obese individuals is mechanical loading and strain. This leads not only to passive loading but also increased muscle tension with positive effects on bone geometry and modeling.. These findings may partially explain the positive relationship between BMD and BMI [12-14]. Whether there is a sustained positive association with increased BMI is less certain. In the context of bone health, a low BMI and weight are associated with an increased risk of fractures in CKD, particularly in renal transplant patients [11, 15, 16]. In our study, it is found that low weight is significant in predicting LBD. Besides the predisposition to malnutrition in these patients, LBD may have developed more frequently since drugs such as steroids that predispose to osteoporosis are often given in standard doses regardless of weight.

Estrogens are steroid hormones that play a key role in maintaining skeletal homeostasis, promoting bone formation, reducing osteoporosis and maintaining bone. Low estradiol and high luteinizing hormone levels have previously been shown to correlate with the annual degree of BMD loss in postmenopausal women [17]. In our study, the osteoporosis rate was found to be significantly higher (85.7%) in postmenopausal women compared to the group with normal bone mineral density. Our study results are consistent with the literature findings in KT patients [18].

Hypophosphatemia causes osteoblast apoptosis in the early post-transplantation period. Lower phosphorus levels have been reported in patients with delayed mineralization 2 years after kidney transplantation [19]. A normal physiological response to hypophosphatemia is to increase renal phosphorus reabsorption, which effectively eliminates phosphorus in the urine, but KT recipients have high urinary phosphorus excretion, possibly due to effects on the ongoing hyperparathyroidism and hyperphosphatoninism on the renal graft. [20]. The most important causes of hypophosphatemia are phosphaturia due to the persistence of pre-transplant Fibroblast growth factor 23 (FGF 23) and PTH elevation. Although hypophosphatemia has been associated with better long-term outcomes after transplantation and a reduced risk of cardiovascular events and graft failure, its potentially detrimental effects on bone and the possibility of causing fractures have been demonstrated [21, 22]. Calcineurin inhibitors may decrease the expression of type II sodium/phosphorus (Na/Pi) cotransporter in the renal tubules and cause phosphaturia [23]. Posttransplant early-period hypophosphatemia deviated with a frequency of 90% in other studies, and we found at a rate of 55% [22]. In our study,

hypophosphatemia, which is thought to be related to the mechanisms described above, is detected more frequently in patients with LBD, but it is not found as a risk factor. However, we think to follow-up postoperative phosphorus level is important.

Osteonecrosis is well-recognised as a skeletal complication after kidney transplantation [5]. In our study, male gender, high ALP levels, preoperative hyperphosphatemia and postoperative hypophosphatemia are found more frequently in patients with osteonecrosis. High preoperative serum phosphorus levels have been associated with vascular calcification [24, 25]. Previous studies have reported an increased incidence of ONFH in male patients [26] and in those with high cumulative steroid doses [7]. High ALP levels are due to increased osteoblastic activity to repair the necrotic area [27, 28]. In our study, the number of patients was not sufficient to determine the statistical significance of the results described for ONFH. However, we think that these findings may help clinicians in the differential diagnosis. More studies are needed to understand the relationship between P, ALP, male gender, and ONFH after kidney transplantation.

The FRAX score is a simple risk score tool that can be used to predict fracture risk. In a previous study in transplant patients, the probability of predicting fracture risk using the FRAX score was similar to that of the normal population [29]. In a study conducted in our country, high MOF and HF risk were found (1.9% and 23.5% respectively) in transplant patients [4]. In our study, high MOF risk is 1.1%, hip fracture risk is 10%, and it is found at a rate similar to the literature

(Naylor et al. found that %1.5 of patients had high MOF probability and %6.5 of patients had high hip fracture probability, Malakoutian et al. found that %1.4 of patients had high MOF probability and %15 of patients had high hip fracture probability) [29, 30]. In the study of Naylor et al., the FRAX tool was found to be successful in predicting fracture in transplant patients, while the study of Malakoutian et al. revealed the opposite. We did not examine fracture outcomes associated with FRAX in our study. More studies are needed to routinely use FRAX in KT recipients.

The most important limiting factor in our study is the lack of data specific to retrospective studies. In addition, the limited number of patients, the inability to measure bone-specific ALP, and since there is no research in terms of bone fractures in patients, the lack of a clear evaluation of the effectiveness of the FRAX score may be other study limitations. The cumulative dose of additional steroid therapy could not be calculated for the reasons explained below: There is no routine steroid dose protocol in our clinic and different doses are decided for each patient in the light of clinical findings, some additional steroid treatments are applied daily in outpatient follow-ups and dose records are not kept clear, clinical follow-ups of a few patients are carried out in other hospitals and dose duration data cannot be accessed. Due to a lack of data, cumulative steroid dose could not be calculated. Finally, the small number of patients with a diagnosis of osteonecrosis is another study limitation that makes it difficult to interpret the findings.

In conclusion, it is determined that postmenopausal status and low weight are risk factors for low bone mineral density. Although it is not a risk factor, it is thought that postoperative phosphorus levels may be useful in clinical practice. High ALP levels, preoperative hyperphosphatemia and postoperative hypophosphatemia are found more frequently in patients with osteonecrosis. Further and longitudinal studies are needed to evaluate the effectiveness of FRAX in the transplant population.

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