Successful Renal Transplantation, Bone Mineral Densitometry, and Affecting Factors

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ABSTRACT

Background. Successful renal transplantation corrects many disorders of bone and mineral metabolism owing to the normalization of serum levels of calcium and phosphorus and restoration of calcitriol production. However, successful transplantation does not guarantee complete resolution of the pre-transplantation osteopathy.

Methods. This study evaluated 100 patients who underwent successful renal transplantation. We determined the possible risk factors for osteoporosis among 72 male and 28 female renal transplant patients of mean age 32.3 ± 10.0 years with 81% of them recipients of living-related grafts. Bone mineral densitometry (BMD) was performed in all patients before and ≥1 year after transplantation. Routine test results and demographic data were recorded.

Results. At the time of transplantation 76% of the patients had osteoporosis or osteopeni and only 24% of them had normal BMD in 4 regions (femur neck, lumber, radius, and ultradistal). After transplantation, 70% of them had osteopororosis or osteopeni and 30% were normal. After renal transplantation, BMD scores increased ($P > .05$) although the diagnosis of the bone disease did not change ($P < .05$). Only preexisting osteodystrophy and smoking were found to be important risk factors for post-transplantation osteoporosis.

Conclusions. After renal transplantation, BMD scores increased whereas the diagnosis of bone disease did not change statistically. We found that medical management of osteopenia/osteoporosis before transplantation and smoking habit are the main factors to prevent post-transplantation osteoporosis. Further long-term studies may be more helpful for evaluating the risk factors of post-transplantation osteoporosis.

SECONDARY hyperparathyroidism, adynamic bone disease, osteomalacia, the use of corticosteroids, and chronic acidosis may all decrease bone density and increase the risk of fractures in patients with end-stage renal disease (ESRD) [1,2]. Compared with dialysis, renal transplantation may be more beneficial in improving the problems that develop due to uremia in patients with ESRD, although the success rate declines in disorders of the bone metabolism. Histologic evidences of osteodystrophy and osteopenia are commonly detected in most patients with successful kidney transplants. Osteoporosis may also develop in early phases owing to the loss of the bone mass. Moreover, many patients experience the risk of avascular necrosis within the 1st 2 years after transplantation [3].

Ongoing hyperparathyroidism, hypercalcemia, and hyperphosphatemia after renal transplantation also are risk factors for the deterioration of existing bone diseases [4]. Various studies in renal transplant patients with osteopenia indicated the existence of many histologic structures that were not related to hyperparathyroidism. Low-turnover bone lesions similar to osteoporosis [5] and even osteomalacia were detected in bone biopsies [6].

High doses of tacrolimus in patients with kidney transplants, as well as cyclosporine, which is known to reduce osteoclast formation and inhibit osteoclastic bone resorption, enhance the loss of bone mass [7]. A consensus on the reduction of

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Table 1. Descriptive Characteristics of the Patients

Characteristic	%*
Median age at transplantation: 32.3 ± 10.0 y	
Sex	
Female	28.0
Male	72.0
Etiology of renal failure	
Hypertension	13.0
Glomerulonephritis	27.0
VUR	5.0
PCKD	2.0
FMF	5.0
Unknown	48.0
Pre-transplantation dialysis modality	
Hemodialysis	87.0
Peritoneal dialysis	13.0
Donation	
Living donation	81.0
Cadaver	19.0
Familial status	
1st degree	83
2nd degree	4
3rd degree	2
Marriage	11
Acute rejection history	
Yes	11.0
No	89.0
Immunsuppression protocols	
Azathioprine + prednisolone + tacrolimus	5
Azathioprine + prednisolone + sirolimus	2
MMF + prednisolone + cyclosporine	40
MMF + prednisolone + tacrolimus	42
MMF + prednisolone + sirolimus	11
Hepatitis B virus	
Positive	10.0
Negative	90.0
Hepatitis C virus	
Positive	10.0
Negative	90.0
Smoking	
Yes	27.0
No	73.0
Body mass index (kg/m^2)	
Underweight (<18.5)	2
Healthy weight (18.5–24.9)	48.0
Overweight (25.0–29.9)	36.0
Obese (≥30)	14.0

Abbreviations: VUR, vesicoureteral reflux; PCKD, polycystic kidney disease; FMF, familial Mediterranean fever; MMF, mycophenolate mofetil.

*The number of patients is 100, so the percentages are the same as the numbers.

osteoblast formation and precipitation of the loss of the bone mass by the use of glucocorticoids after renal transplantation has recently been achieved [8]. The increase in osteocalcin levels due to the effects of cyclosporine after renal transplantation contributes to the low-turnover bone disease developing under the action of glucocorticoids [9].

Rapid loss of the bone mass in patients with kidney transplants can not yet be prevented. Post-transplantation osteodystrophy (mostly osteoporosis) and osteonecrosis are among the most important causes of long-term morbidity in patients with kidney transplants. Therefore, we investigated the factors that influence bone mineral density (BMD) after successful renal transplantation.

METHODS

One hundred patients who received kidney transplants in Baskent University, Ankara, Turkey, were randomly included in this study (72 men, 28 women). The descriptive characteristics of the patients are summarized in Table 1. Pre- and post-transplantation BMD scores as well as the means of some biochemical parameters are presented in Table 2.

Inclusion criteria were: absence of hyperparathyroidism at the time of transplantation (intact parathyroid hormone [PTH] <600 ng/mL); no history of parathyroidectomy; and absence of a comorbid disease that affects bone metabolism, such as hyperthroidism, Cushing syndrome, or advanced liver disease. Patients were excluded if they displayed poor renal function, namely, serum creatinine value >2 mg/dL or proteinuria >1,000 mg/d. None of the patients received vitamin D or analogues during the post-transplantation period. Bone mineral densitometry was performed on all patients at the 1st year after renal transplantation with the use of dual-energy x-ray absorptiometry (DEXA-Hologic, model QDR 1500A, Watham, Massachusetts). Osteoporosis was defined by the World Health Organization criteria as a T score of −2.5 or more below the SD. Osteopenia and normal values were defined as T scores from 1.5 to −2.5 SD and over −1.5 SD, respectively. Patients were divided into 3 groups according to BMD results: group 1 with normal values (T score greater than −1.5 SD), group 2 with osteopenia (T score from −1.5 to −2.5 SD), and group 3 with osteoporosis (T score less than −2.5 SD). We analyzed differences in pre- and post-transplantation T score values, as well as clinical, laboratory, and demographic data.

Patients received prednisone, azathioprine, mycophenolate mofetil, and cyclosporine for maintenance immunosuppression. Cyclosporine was initiated at a dose of 8–10 mg/kg/d orally in 2 divided doses and then adjusted to maintain whole-blood levels of 100–200 ng/mL with the use of a modular ISE 900 machine (Cedia Cyclosporine Assay; Roche Diagnostic Corp, Indianapolis, Indiana) with a homogeneous enzyme immunoassay system. Prednisolone was initiated at 1–2 mg/kg/d orally and tapered over 6 months to a maintenance dosage of 10 mg/d. An acute rejection episode was suspected based on clinical and biochemical parameters and confirmed by means of renal allograft biopsy. It was initially treated with intravenous pulse methylprednisolone. Steroid-resistant acute rejection episodes were treated with OKT3. Laboratory parameters were performed with the use of standard laboratory techniques.

Statistical analyses were performed with the use of SPSS software (Statistical Package for the Social Sciences, version 15.0; SPSS, Chicago, Illinois). All numeric variables, such as biochemical parameters and BMD scores, are expressed as mean ± SD. The values of categoric variables (history of smoking, sex, menopausal status, body mass index [BMI] scores, dialysis modality, the presence of hepatitis B virus [HBV] or hepatitis C virus [HCV] seropositivity, BMD-associated diagnoses, donor of transplantation, acute rejection, immunosuppressive protocol) are presented as n (%). McNeamar test was used for showing the differences of pre- and post-transplantation BMD-associated diagnoses. We analyzed the values of variables such as age, alkaline phosphatase (ALP), phosphorus, and duration of dialysis with the use of Pearson correlation analysis technique. All numeric variables are expressed as mean ± SD. Intergroup differences were compared by means of the Student *t*, Mann-Whitney *U*, 1-way analysis of variance, or