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Osteoporosis and Related Risk Factors in Renal Transplant Recipients

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ABSTRACT

Decreased bone mineral density is a common problem after kidney transplantation. Osteoporosis has a major role in morbidity in these patients. We evaluated the incidence of osteoporosis and determined risk factors in 77 patients aged 17 to 50 years who had undergone renal transplantation 6 months to 2 years previously. Bone mineral densitometry was performed using dual-energy x-ray absorptiometry. The incidence of osteoporosis was 26% (20 of 77 patients). Mean (SD) age of affected patients was 34.6 (8.7) years. The most common sites of osteoporosis were the hip (osteoporotic in 19 patients [24.7%] and osteopenic in 42 [54.5%]) and the spine (osteoporotic in 6 patients [7.8%] and osteopenic in 52 [67.5%]). There was a significant relationship between posttransplantation creatinine concentration and hip osteoporosis ($P = .01$). No relationship was observed between osteoporosis and age, sex, body mass index, duration of hemodialysis therapy, cumulative dosage of any drugs, or use of pulsed methylprednisolone therapy. A hip or spine z score of 1 or less had no relationship to the number of steroid pulse sessions but was significantly related to the total dosage of cyclosporine ($P < .001$), prednisolone ($P < .001$), and mycophenolate mofetil ($P < .05$). A hip z score of less than 1 was related to the posttransplantation period ($P = .02$). In conclusion, osteoporosis is a frequent complication that requires detection and treatment to reduce morbidity.

OSTEOPOROSIS is a frequent complication after renal transplantation,[1,2] and fractures from osteoporosis are a principle cause of morbidity and death.[3] Transplantation can successfully correct many uremia-related impairments in bone structure.[4] However, many studies have demonstrated that kidney transplantation increases the risk of fragility fractures.[3,5–8] Factors that have been suggested to have a role in the pathogenesis of osteoporosis after transplantation include high daily and cumulative dosage of corticosteroids, other immunosuppressant drugs, persistent hyperparathyroidism, and preexisting bone disorders.[4] Long-term administration of glucocorticoid and possibly cyclosporine therapy may chronically activate osteoclasts in the spongy or cortical bone while inhibiting osteoblast activity.[9]

Several studies have demonstrated reduction in bone mass in graft recipients, more frequently in the first year posttransplantation.[2] The incidence of bone fractures increases to 10% to 20%, which is equal to or greater than the incidence in postmenopausal women.[6,8] In renal transplant recipients, the adjusted incidence ratio for fractures is 4.59 (95% confidence interval, 3.29–6.31). Age, sex, duration of dialysis therapy, steroid dosage, and persistent hyperparathyroidism have the greatest effects on the skeleton.[10] The objectives of the present study were to determine the incidence of osteoporosis in renal transplant recipients and to evaluate risk factors.

MATERIALS AND METHODS

The study included 85 patients aged 17 to 50 years who had undergone renal transplantation 6 months to 2 years previously. Patients with a history of thyroid disease before or after transplantation were excluded. Baseline data included age, sex, height, and weight; duration of dialysis therapy before transplantation; days posttransplantation; immunosuppression regimen; cumulative dosages of prednisolone, cyclosporine, and mycophenolate mofetil (MMF) (CellCept; Roche Laboratories Inc, Lisle, Illinois); number

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Table 1. Comparison of Results of the Present Study and 4 Other Studies

Variable	Present Study	El-Agroudy et al,[11] Egypt	Grotz et al,[12] Germany	Mahadavi et al,[13] Iran	Sudhagar et al,[14] India
No. of patients	77	83	56	61	200
Age, mean (SD), y	34.68 (8.71)	31.4 (10.1)	NA	42.28	39.41
Osteoporosis, %	26.0	31.0	22.0	29.5	19.5
Hip	24.7	25.6	18.5	19.7	14.5
Spine	7.8	11.0	6.8	14.8	8.5
Correlation					
Age	No	No	No	No	Yes
BMI	No	No	No	Yes	No
Post-Tx Cr	Yes	Yes	ND	No	ND
Cumulative CsA dosage	No	Yes	ND	No	ND
Cumulative steroid dosage	No	Yes	Yes	No	ND
Pre-Tx dialysis	No	No	ND	No	ND
Calcium or vitamin D supplementation	No	No	Yes	ND	ND

BMI, body mass index; Cr, creatinine concentration; NA, data not available; ND, not done; Tx, transplantation.

of steroid pulse sessions; and use of supplemental calcium and cholecalciferol (vitamin D).

After giving informed consent, all patients underwent bone mineral densitometry (BMD) at the hip (neck of the femur) and lumbar spine using dual-energy x-ray absorptiometry (DPX-MD bone densitometer; Lunar Corp, Madison, Wisconsin). As recommended by the World Health Organization, we classified patients into 3 diagnostic groups, as follows: group 1, normal (T score +1 to −1); group 2, osteopenia (T score −1 to −2.5); and group 3, osteoporosis (T score −2.5).

Statistical analysis was performed using commercially available software (SPSS version 11.5; SPSS Inc, Chicago, Illinois). Correlations were analyzed using the χ^2 test and Fisher exact test. Numerical results are given as mean (SD).

RESULTS

Seventy-seven renal transplant recipients underwent BMD. Twenty-eight (36.4%) were women and 49 (63.6%) were men. Overall mean (SD; range) age was 34.68 (8.71; 17–51) years. Osteoporosis in the hip or spine regions was observed in 20 patients (26%). Hip BMD revealed normal findings in 16 patients (20.8%), osteopenia in 42 (54.5%), and osteoporosis in 19 (24.7%). Spine BMD revealed normal findings in 19 patients (24.7%), osteopenia in 52 (67.5%), and osteoporosis in 19 (24.7%). T test scores demonstrated no significant relationship between body mass index and osteoporosis ($T = 0.54$).

Age and sex; duration of dialysis therapy; cumulative dosages of cyclosporine, prednisolone, and MMF; and number of pulsed steroid sessions demonstrated no significant relationship to osteoporosis in any region. In addition, calcium and cholecalciferol (vitamin D) supplementation before transplantation had no relationship to osteoporosis ($P = .59$). Pretransplantation creatinine concentration was not related to osteoporosis in any region. However, posttransplantation creatinine concentration was significantly correlated with hip osteoporosis ($P = .01$) but not spine osteoporosis ($P = .50$).

Patients were evaluated according to z score. A score of 1 or less in the hip or spine had to relationship to numbers of methylprednisolone pulses but a significant relationship to total dosage of cyclosporine ($P < .001$), prednisolone ($P < .001$), and MMF ($P < .05$). A score of 1 or less was also related to days posttransplantation ($P < .02$).

DISCUSSION

Osteoporosis was common in our patients. More than 90% of patients with osteoporosis had hip osteoporosis, which demonstrates the importance of diagnosis and initiation of treatment to reduce associated morbidity. Our patients were younger than 50 years, which may explain the prevalence of osteoporosis in a relatively young population and underscores the risk of fracture in subsequent years.

Cumulative dosage of cyclosporine was not predictive of bone loss in our study, although it has been related to a high degree of bone loss in previous studies in animals.[4,11] Cumulative dosage of prednisolone and number of pulsed steroid sessions were not predictive of bone loss, which is in accord with some reports[11,12] but not all previous studies[3,8,13] (Table 1).

Osteoporosis develops in as many as half of transplant recipients, and vertebral fractures are present in almost one-third of patients at some centers in the United States.[15] Several factors have been suggested for development of osteoporosis in renal transplant recipients. In our study, there was no significant relationship between most of these factors and osteoporosis, which confirms the controversy. Additional prospective studies with large sample sizes are needed to determine risk factors for osteoporosis in this population. However, osteopenia and osteoporosis were common in our study patients, which may warrant screening and therapeutic intervention for osteoporosis in renal transplant recipients.

REFERENCES

1. Cruz DN, Brickel HM, Wysolmerski JJ, et al: Treatment of osteoporosis and osteopenia in long-term renal transplant patients with alendronate. Am J Transplant 2:62, 2002

2. Sezer S, Ozdemir FN, Ibis A, et al: Risk factors for osteoporosis in young renal transplant recipients. Transplant Proc 37:3116, 2005

3. Abbott KC, Oglesby RJ, Hypolite IO, et al: Hospitalizations for fractures after renal transplantation in the United States. Ann Epidemiol 11:450, 2001

4. Monier-Faugere MC, Mawad H, Qi Q, et al: High prevalence of low bone turnover and occurrence of osteomalacia after kidney transplantation. J Am Soc Nephrol 11:1093, 2000

5. Braga Júnior JW, Neves RM, Pinheiro MM, et al: Prevalence of low trauma fractures in long-term kidney transplant patients with preserved renal function. Braz J Med Biol Res 39:137, 2006

6. Braun WE, Yadlapalli NG: The spectrum of long-term renal transplantation: Outcomes, complications, and clinical studies. Transplant Rev 16:22, 2002

7. Raisz LG: Clinical practice: screening for osteoporosis. N Engl J Med 353:164, 2005

8. Toro J, Gentil MA, García R, et al: Osteoarticular pain and bone mineral density in renal transplantation. Transplant Proc 35:1769, 2003

9. Sperschneider H, Stein G: Bone disease after renal transplantation. Nephrol Dial Transplant 18:874, 2003

10. Brandenburg VM, Westenfeld R, Ketteler M: The fate of bone after renal transplantation. J Nephrol 17:190, 2004

11. El-Agroudy AE, El-Husseini AA, El-Sayed M, et al: Preventing bone loss in renal transplant recipients with vitamin D. J Am Soc Nephrol 14:2975, 2003

12. Grotz WH, Mundinger FA, Rasenack J, et al: Bone loss after kidney transplantation: a longitudinal study in 115 graft recipients. Nephrol Dial Transplant 10:2096, 1995

13. Mahdavi M, Hamidi Z, Soltani A, et al: Bone mineral density in Iranian kidney graft recipients and its relation to biochemical and PTH serum levels. Iran J Publ Health Supplementary issue on Osteoporosis 2004:70.

14. Sudhagar K, Chandrasekar S, Rao S, et al: Bone densitometry in post renal transplant patients. Indian J Nephrol 11:58, 2001

15. Cohen A, Shane E: Osteoporosis after solid organ and bone marrow transplantation. Osteoporosis Int 14:617, 2003