



Osteoporosis after renal transplantation

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SUMMARY

This study was performed to determine risk factors associated with osteoporosis that develops after renal transplantation. Sixty-five kidney graft recipients were included in this study. They were divided into four groups according to the time since transplantation : Group 1 (< 1 year ; n = 26), group 2 (1 – 3 years ; n = 16), group 3 (3-5 years ; n = 12) and group 4 (> 5 years ; n = 11). These groups were matched according to probable risk factors for osteoporosis, findings of serum biochemistry, biochemical markers of bone turnover and measurements of bone mineral density. One way ANOVA test and Kruskal-Wallis test were used for statistical analysis. Osteoporosis was found in 22 recipients (33.8%). There were significant differences in recipient age, cumulative steroid dose, and episodes of acute rejection between the four groups. Increasing age, cumulative steroid dose and episodes of acute rejection were found to be risk factors for osteoporosis in our study.

Key words: Renal transplantation. Osteoporosis. Risk factors.

OSTEOPOROSIS DESPUÉS DEL TRASPLANTE RENAL

RESUMEN

Este estudio tuvo como objetivo determinar factores de riesgo asociados a osteoporosis que se desarrolla después del trasplante renal. En este estudio se incluyeron 65 pacientes portadores de un trasplante renal. Se dividieron en 4 grupos de acuerdo al tiempo desde el trasplante: Grupo 1 (< 1 año; n = 26), grupo 2 (1-3 años; n = 16), grupo 3 (3 a 5 años = 12) y grupo 4 (> 5 años; n = 11). Todos los grupos se ajustaron de acuerdo a probables factores de riesgo de osteoporosis, marcadores bioquímicos, marcadores de recambio óseo y densidad mineral ósea. El análisis estadístico se realizó por medio de ANOVA y mediante el test Kruskal-Wallis. Se encontró osteoporosis en un total de 22 receptores de trasplante de riñón (33,8%). La edad de recepción del trasplante, la dosis acumulada de esteroides y los episodios de rechazo agudo de trasplante renal fueron estadísticamente significativos entre los cuatro grupos. El aumento de la edad, la dosis acumulada de esteroides y los episodios de rechazo agudo fueron factores de riesgo de osteoporosis en nuestro estudio.

Palabras clave: Trasplante renal. Osteoporosis. Factores de riesgo.

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INTRODUCCIÓN

Osteoporosis occurs commonly after renal transplantation and contributes to post-transplant morbidity by increasing the risk of bone fractures¹. Many studies have demonstrated that bone mass is reduced in transplant patients²⁻⁴. The bone loss is most pronounced during the first six months after renal transplantation and predominantly confined to the trabecular bone of the spine. It has been shown that during the first six months after transplantation, the spinal bone mineral density (BMD) decreases by a mean of 6.8 percent and an additional decrease of 2.6 percent occur between 6 and 18 months after transplantation².

In kidney graft recipients, the most important cause of osteoporosis is corticosteroid treatment⁵. Additionally, kidney transplant recipients are exposed to other potential factors that lead to osteoporosis after transplantation, such as renal osteodystrophy, hyperparathyroidism, heparin therapy before transplantation, and probably therapy with cyclosporin or tacrolimus after transplantation⁶.

In this study, we aimed to determine the prevalence of osteoporosis and the independent risk factors influencing the development of osteoporosis after renal transplantation.

PATIENTS AND METHODS

Between January 2001 and October 2001, 65 consecutive kidney graft recipients (22 females and 43 males) who had stable allograft function (defined by serum creatinine < 2 mg/dl) were recruited in this cross-sectional study in our out-patient clinic.

Postmenopausal women or those on estrogen replacement therapy and patients with secondary osteoporosis due to type I or II diabetes mellitus, hyperthyroidism, primary or tertiary hyperparathyroidism, hypogonadism, hyperprolactinemia, Cushing's syndrome, acromegaly, chronic diarrhoea and malabsorption syndromes were excluded.

The following risk factors for low BMD were obtained from patient records: age, gender, smoking, existence of pre-transplant steroid therapy, hyperparathyroid bone disease, duration of chronic renal failure, time on dialysis, donor source, cumulative steroid dose, doses of steroid bolus therapy, episodes of acute rejection, osteonecrosis and persistent hyperparathyroidism. Cumulative steroid and pulse steroid doses were calculated starting from date of transplantation to the time of evaluation of BMD.

At the time of the bone examination, serum creatinine, albumin, alkaline phosphatase, calcium,

phosphorus, creatinine clearance and intact parathyroid hormone levels were measured. The levels of daily urinary calcium and phosphorus, and tubular reabsorption of phosphate were also measured. Biochemical assessment of bone-turnover was performed by using serum bone alkaline phosphatase and serum osteocalcin as indices of bone formation, and urine deoxypyridinoline as an index of bone resorption.

BMD of the first, second, third, and fourth lumbar vertebrae and left femoral neck was measured using dual-energy x-ray absorptiometry (DEXA-Hologic, model QDR-4500 W). Osteoporosis was defined as T scores below 2.5 SD^{7,8}.

Patients were divided into four groups according to the duration of transplantation: Group 1: < 1 year; group 2: 1-3 years; group 3: 3-5 years and group 4: > 5 years. The groups were compared for the probable risk factors of osteoporosis, serum biochemistry, biochemical markers of bone turnover and BMD.

Data were expressed as mean \pm SD. One way ANOVA test and Kruskal-Wallis test were used for statistical analysis. P values < 0.05 were accepted as significant.

RESULTS

Osteoporosis was found in 22 recipients (33.8%). The prevalence of osteoporosis varied significantly during different time periods after transplantation; it was, respectively, 15.3% within the first year after transplantation, 37.5% between 1 and 3 years, and 41.6% between 3 and 5 years. Osteoporosis was observed in as many as 63.6% of patients with transplants lasting longer than five years.

There were significant differences in recipient age, cumulative steroid dose, and episodes of acute graft rejection between the four groups. Patients in group 1 and 2 (the mean age 30.3 ± 8.9 and 29.1 ± 8.5 , respectively) were significantly younger than those in group 4 (the mean age 42.4 ± 11) ($p = 0.004$ and $p = 0.004$, respectively). Group 4 had received the highest cumulative steroid doses. There was significant difference in episodes of acute rejection between groups 1 and 2 (3 patients versus 8 patients, respectively) ($p = 0.007$). There were no significant differences in the other variables between the four groups (table I).

When we evaluated the bone formation and resorption markers, we found no significant difference in the mean concentrations of bone alkaline phosphatase, osteocalcin and deoxypyridinoline between the groups. Levels of bone alkaline phosphatase and osteocalcin were found to be higher in groups 1, 2

Table I. Comparison of four groups with respect to the probable risk factors and biochemical parameters

	Group 1 (< 1 year) (n = 26)	Group 2 (1-3 years) (n = 16)	Group 3 (3-5 years) (n = 12)	Group 4 (> 5 years) (n = 11)	p
Age (Year)	30.3 ± 8.9	29.1 ± 8.5	35.0 ± 10.1	42.4 ± 11.0	0.002
Female / Male	11/15	3/13	3/9	5/6	NS
Smoking	8	3	2	1	NS
Pre Tx steroid use	4	2	0	0	NS
Pre Tx bone disease	8	2	4	0	NS
Duration of CRF (month)	43.5 ± 29.5	44.9 ± 43.7	45.5 ± 41.8	31.3 ± 26.5	NS
Time on dialysis (month)	17.8 ± 12.3	26.1 ± 27.2	27.0 ± 31.9	16.4 ± 18.9	NS
Cadaveric/Living donors	7/19	2/14	4/8	3/8	NS
Cumulative steroid dose (g)	3.8 ± 2.2	11.6 ± 6.2	17.5 ± 5.0	42.5 ± 9.9	0.000
Total pulse steroid dose (g)	2.4 ± 2.2	4.1 ± 2.9	4.5 ± 2.5	1.1 ± 0.4	NS
Number of recipients with acute rejection	3	8	5	4	0.046
Osteonecrosis	4	2	0	1	NS
Persistent hyperparathyroidism	3	1	2	0	NS
Serum creatinine (mg/dl)	1.3 ± 0.3	1.4 ± 0.2	1.3 ± 0.4	1.1 ± 0.4	NS
Serum albumin (g/dl)	4.4 ± 0.4	4.8 ± 0.4	4.6 ± 0.3	4.2 ± 0.4	NS
Serum alkaline phosphatase (IU/L)	180 ± 101	167 ± 74	154 ± 55	122 ± 45	NS
Serum calcium (mg/dl)	9.9 ± 0.7	10.1 ± 0.5	9.5 ± 0.4	9.8 ± 0.5	NS
Serum phosphorus (mg/dl)	3.1 ± 0.7	3.4 ± 0.6	3.2 ± 0.5	3.4 ± 0.8	NS
Creatinine clearance (ml/min)	49 ± 17	52 ± 14	48 ± 18	54 ± 13	NS
IPTH (pg/ml)	164 ± 132	107 ± 61	139 ± 61	115 ± 56	NS
Daily urinary calcium (mg)	131 ± 71	116 ± 79	72 ± 43	107 ± 47	NS
Daily urinary phosphorus (mg)	735 ± 359	699 ± 281	655 ± 136	491 ± 195	NS
Tubular reabsorption of phosphate	0.61 ± 0.16	0.64 ± 0.14	0.68 ± 0.18	0.73 ± 0.20	NS

CRF: chronic renal failure, IPTH: intact parathyroid hormone, NS: nonsignificant.

and 3 than in group 4; but this difference was not statistically significant. Level of deoxypyridinoline was higher in group 4 than in groups 1, 2 and 3 although this difference was not statistically significant. Also, the values of BMD and T-score were not different between the groups (table II).

DISCUSSION

Osteoporosis is a frequent complication after renal transplantation. Julian et al. prospectively studied renal transplant recipients receiving CsA and prednisone and showed that 18 of the 20 patients had a decrease in spinal BMD within 6 months of transplantation². Moreover, Grotz et al. measured BMD in 115 patients after renal transplantation. Of the patients examined, 49% displayed a significant decrease in BMD. Lowest mean values were observed between 12 and 24 months after transplantation⁶. Some authors documented the partial recovery or stability of BMD values between 2 and 20 years after transplantation^{3,6}. In our study, osteoporosis was found in 22 of the 65 recipients (33.8%). Our findings indicate that the prevalence of osteoporosis seems to increase with time since transplantation.

According to some recent studies, increasing age is a risk factor for osteoporosis after renal transplantation^{6,9}. Indeed, increasing age was also found to be a predisposing factor in our study.

High cumulative steroid dose was suggested as an important risk factor for bone loss in renal transplant recipients^{1,3}. However, a correlation between the degree of bone loss and the cumulative steroid dose has not been observed in some studies^{2,10,11}. In our study, cumulative steroid dose was found as expected, to be significantly different between all the groups. This difference became striking with prolonged transplantation duration. On the other hand, in our study there was no significant difference in total pulse steroid dose between the groups.

It is known that poor nutrition is a predisposing factor responsible for the bone loss in renal transplant recipients¹². In our study, serum albumin level although relatively lower in group 4 was within normal limits in all groups.

In conclusion, the results of our study indicate that increasing age and cumulative steroid dose are the most important risk factors of bone loss in renal transplant recipients. Moreover, episodes of acute rejection may contribute to bone loss partially. It is important to identify the recipients who have the pre-

Tabla II. Comparison of four groups with respect to mean values of bone formation and resorption markers, and bone mineral density

	Group 1 (< 1 year) (n = 26)	Group 2 (1-3 years) (n = 16)	Group 3 (3-5 years) (n = 12)	Group 4 (> 5 years) (n = 11)	p
BALP (IU/L)	62.0 ± 38.4	59.0 ± 34.3	52.3 ± 16.8	33.0 ± 10.8	NS
Osteocalcin (ng/ml)	39.8 ± 31.6	43.1 ± 31.2	32.3 ± 20.4	16.9 ± 9.9	NS
DOP (nM/mMcr)	4.3 ± 1.6	4.2 ± 2.2	3.9 ± 1.6	4.5 ± 2.6	NS
BMD of femoral neck (g/cm ²)	0.860 ± 0.159	0.819 ± 0.127	0.776 ± 0.159	0.746 ± 0.147	NS
BMD of lumbar spine (g/cm ²)	0.953 ± 0.119	0.905 ± 0.168	0.863 ± 0.253	0.939 ± 0.198	NS
Femoral neck T-score	-1.43 ± 1.0	-1.50 ± 1.06	-1.91 ± 1.43	-2.36 ± 0.82	NS
Lumbar T-score	-1.38 ± 0.97	-2.18 ± 1.1	-2.14 ± 1.75	-2.16 ± 1.29	NS

BALP: bone alkaline phosphatase, DOP: deoxypyridinoline, BMD: bone mineral density, NS: nonsignificant.

disposing risk factors for osteoporosis and take the necessary measurements without delay, since this may improve the expected quality of life after renal transplantation.

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