Basal Bone Mineral Density Status predicts the worsening of femoral and vertebral BMD during the first year of kidney transplantation

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Background

Bone disorder is a relevant problem during kidney transplantation (KTx), and has it major expression during the first year of KTx. The aim of our study was to evaluate the prevalence of osteopenia and osteoporosis at femoral and vertebral levels in KTx patients and the factors implicated in their worsening during the first year after KTx.

Material and Methods

We evaluated 284 patients (M=165; mean age 48±11 years) over the 470 patient transplanted in our Department between April 2004 and July 2013. Clinical parameters, blood and urinary samples were collected after an overnight fast at 1, 6 and 12 months after KTx (Table I). In addition, at the same time, in 150 of these patients plasmatic levels of FGF-23, Fetuin-A, 25OH-Vitamin D and Osteoprotegerin were also evaluated. At 1st and 12th month after KTx femoral and vertebral BMD (F-BMD and V-BMD), assessed by dual energy X-ray absorption (DEXA), was performed. The results were expressed as g/cm^2. T and Z-scores were also calculated. Patients with T-score -1>T>-2.5 were considered osteopenic whereas those with T-score<-2.5 osteoporotic (Table II).

Parameter	***Mean ± SD***		
Age (yrs)	48±11		
Time of Dialysis (mths)	58±51		
Parameter	***1st mth***	***6th mth***	***12th mth***
BMI (kg/m^2)	23±3	-	24±3
Creatinine (mg/dl)	1,41±0,47	1,46±0,49	1,40±0,39
eGFR (ml/min)	57±20	54±17	55±17
Hb (mg/dl)	11,1±1,4	12,3±1,5	12,8±1,6
Glucose (mg/dl)	83±22	87±19	82±18
PTH (pg/ml)	157±140	148±156	143±165
Ca (mg/dL)	9,95±0,8	10,0±0,8	10±0,7
P (mg/dL)	2,47±0,9	3,1±0,8	3,1±0,65
ALP (U/L)	111±74	114±95	97±68
U-Prot (g/24h)	0,29±0,7	0,28±1,0	0,24±0,5
FETUIN (g/L)	0,32±0,2	0,46±0,2	0,31±0,08
FGF-23 (pg/ml)	37±50	62±70	35±52
OPG (pmol/L)	5,2±2,3	5,1±2,2	5,0±1,8
25OH-VitD (ng/mL)	13±6	13±8	16±8

Patients (n)	284
Gender (M/F)	165/119
Type of dialysis (HD/PD)	70/21
Type of KTx (Deceased/Living)	226/47
Previous Steroid Therapy (%)	38
Cya / FK (%)	12/88
MMF therapy (%)	95
mTOR inhibitor therapy (%)	2
Steroids in the 1° year (mg)	2853±1038
Vit.D Therapy at baseline (Calcifediol/Calcitriol) (%)	0/11
Vit.D Therapy at 12 mths (Calcifediol/Calcitriol) (%)	7/19
Restart of dialysis (%)	6

***Table I**: Characteristics of the cohort.: BMI: Body mass index, eGFR: estimated gòlomerular filtration rate estimated using MDRD formula; PTH: Paratormone; ALP: Alkaline Phosphatase; FGF-23: Fibroblas grouth factor 23, OPG: Osteoprotegerin, U-Prot: protein urinary excretion. HD: Hemodialysis; PD: Peritoneal Dialysis; Cya: Ciclosporine;*

Parameter	***Mean ± SD***		***p***
	1° mth	***12° mth***	
Femoral BMD (g/cm^2)	0,75±0,17	0,77±0,15	0,54
Femoral T-score	-1,49±1	-1,43±0,9	0,05
Femoral Z-score	-0,9±0,97	-0,84±0,9	0,01
Vertebral BMD (g/cm^2)	0,91±0,18	0,91±0,14	0,0008
Vertebral T-score	-1,58±1,6	-1,62±1,3	0,01
Vertebral Z-score	-1,08±1,6	-1,07±1,4	0,005
Femoral Osteoporosis (%) Femoral Osteopenia (%)	16 54	13 53	-
Vertebral Osteoporosis (%) Vertebral Osteopenia (%)	31 33	29 33	-
Worsening of Femoral BMD (%)	55		-
Worsening of Vertebral BMD (%)	39		-

***Table II:** DEXA Characteristics of the cohort.: BMD: Bone mineral density; T-score: difference between patient BMD and reference general healty population; Z-score: difference between patient BMD and reference healty population with the same age and the same gender.*

Results

Femoral osteopenia was present at baseline and after 12 mths in 54% and 53% of patients respectively, whereas vertebral osteopenia in 33% at both evaluation times. Osteoporosis was present in 16% and in 13% of patients in femur and 31 % and 29% in vertebrae, at baseline and after 12 mths resp. Both at baseline and at 12th mth a direct correlation was found between femoral and vertebral bone mineral density (p<0.0001 – figure 1A). At baseline, F-BMD correlated directly with BMI and FGF-23 at baseline (p=0.004; p=0.02 respectively) and inversely with the age at KTx (p<0.0001), time of dialysis (p=0.03) and fetuin at 1st mth (p=0.01). At the second evaluation it correlated directly with BMI, FGF-23, Fetuin and U-Prot/24h at 12 mths (p=0.02; p=0.005, p=0.03 and p=0.05 resp.) and inversely with age at KTx and months of dialysis (p=0.0003 and p=0.03 resp). V-BMD was directly correlated at baseline with BMI at 1st mth (p=0.01), whereas at 12th mth directly with BMI at 12 mths and inversely with cumulative steroid dosage in the first year (both p=0.01). During the year of follow up, a worsening of F-BMD was detected in 55% of patients. These patients had significantly higher BMD at baseline (p=0.004 – Figure 1B). V-BMD worsted in 39% of patients, these patients had significant higher VBMD at baseline (p=<0,0001- Figure 1C) and U-Prot/24h and blood glucose at 12 mths (p= 0,006 and 0,02 respectively). Using multiple (table III), baseline F- and V-BMD resulted the most important independent factors in predicting BMD worsening during the first year of KTx.

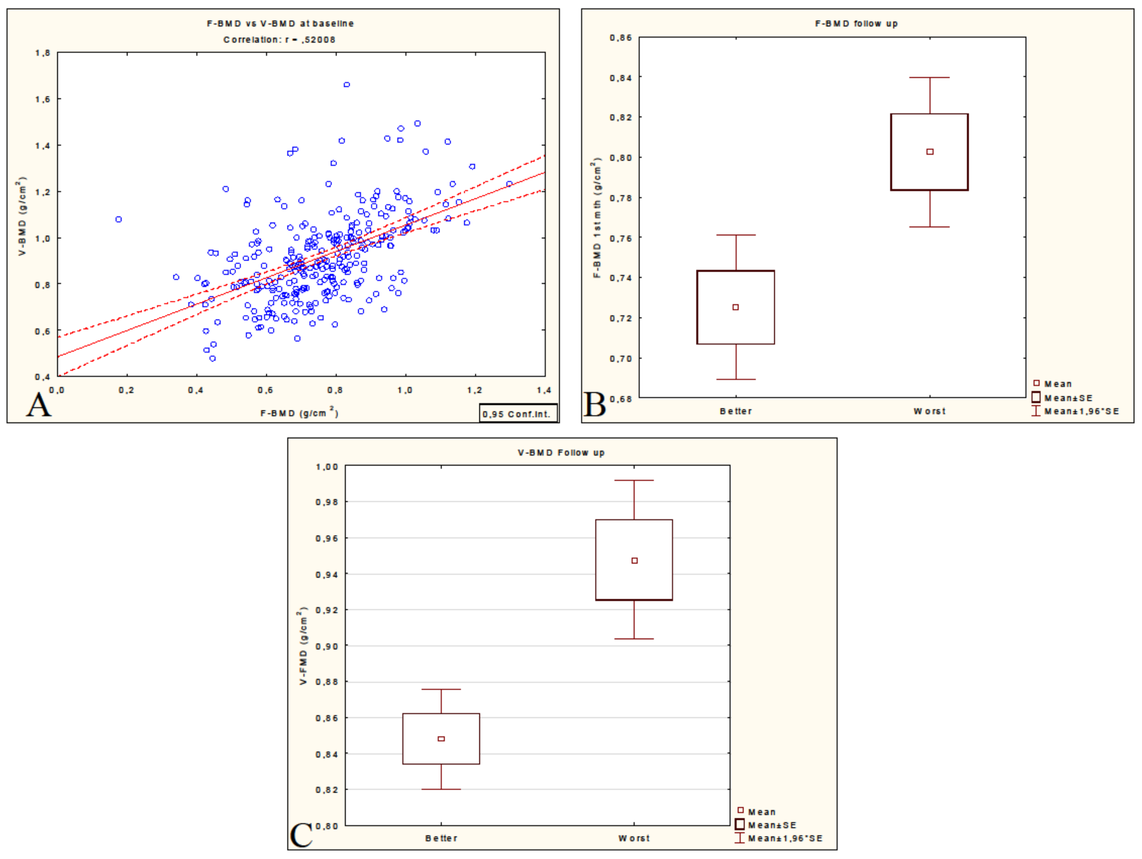

***Figure 1:** A) Univariate regression between F-BMD and V-BMD at baseline. B) ANOVA test: baseline F- BMD distribution among patients who worsened and increased F-BMD during the first year of KTx. C) ANOVA test: baseline V- BMD distribution among patients who worsened and increased V-BMD during the first year of KTx.*

Parameter	Coefficient	t-value	p-value
Age	-0,27	-1,24	0,21
F-BMD	-69,7	-4,46	<0,0001
BMI	0,61	0,81	0,41
FGF-23	0,05	1,52	0,13

% of variation of F-BMD

Parameter	Coefficient	t-value	p-value
Age	-0,37	-0,65	0,51
V-BMD	-23,24	-5,62	<0,0001
BMI	0,26	1,42	0,15
Blood Glucose	-0,07	-2,07	0,03
Cumulative Steroids	-0,001	-1,67	0,09

% of variation of V-BMD

***Table III:** Multiple regression: evaluation of the factors implicated in F-BMD and VBMD variation during the first year of KTx*

Conclusions

The prevalence of Osteopenia and Osteoporosis is high in KTx patients and, according to our results, age, time of dialysis and the basic BMD seem to be both in femur and in vertebrae the strongest predictive factor of its worsening. This underscore the beneficial effects of KTx in bone metabolism. A strong correlation between F-BMD and V-BMD is present. An important role, especially in V-BMD seems to be played by steroid therapy. Interesting, no role for mineral metabolism parameters was evident.

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