Relation between femoral bone mineral density and aortic calcifications in a cohort of renal transplanted patients

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Background

Bone and cardiovascular disorders are relevant problems during kidney transplantation (KTx), and have their major expression during the first year of KTx. High interest in bone mineral density (BMD) anomalies and in their relation with vascular calcifications and cardiovascular risk is nowadays present. The aim of our study is to evaluate, in a cohort of KTx patients: 1) the prevalence of femoral osteopenia and osteoporosis; 2) the factors related to femoral bone mineral density (F-BMD) 3) the relationship between F-BMD and aortic calcifications (ACI); 4) the role of F-BMD in predicting cardiovascular events (CV) during the first year of KTx.

Material and Methods

293 patients (M=170; mean age 48±11 years – table I) transplanted in our Department between 2004 and 2013 were randomly evaluated. Clinical parameters, fasting blood and urinary samples were collected at 1st and 12th mth after KTx. In addition, at the same time, in 170 of them plasmatic FGF-23, Fetuin and 25OH-VitD were dosed. At 1 and 12 months after KTx F-BMD, assessed by dual energy X-ray absorption (DEXA), was performed. F-BMD was expressed as g/cm^2. Patients with T-score -1>T>-2.5 were considered osteopenic whereas those with T-score<-2.5 osteoporotic. In 115 patients, at 1 and 12 months of KTx, a Lumbar X-Ray for the ACI evaluation was performed. ACI were quantified using Kauppila score. ACI progression was determined by their simple increase. CV was defined by a major disease affecting heart (f.i. stroke, arrhythmia) or vascular (f.i. stenosis/thrombosis) system.

Results

At baseline and after 12 mths osteopenia was present in 53% and 52% of patients resp., whereas osteoporosis in 15% and 12% resp (table II). At baseline, F-BMD correlated directly with BMI, alkaline phosphatase (ALP), fetuin, FGF-23 and 25OH-VitD (p=0.003; p=0.01; p=0.02 and p=0.005 resp.) and inversely with the age, time of dialysis and s-P (p<0.0001; p=0.01; p=0.03 resp). Twelve mths later, a direct correlation with BMI, FGF-23 and fetuin (p=0.001; p=0.04, p=0.003 resp.) and an inverse one with age and time of dialysis (p<0.0001 and p=0.001 resp) were found. In multivariate analysis, age and fetuin resulted able in determining F-BMD, at 1st mth in addition to ALP and P. At baseline and after 12 mths ACI were present in 55% and in 61% of patients. Both at baseline and at 12 mths number of ACI was higher in patients with F-BMD not normal (p=0.06 – p=0.01 resp), without differences between osteoporotic and osteopenic patients. During the year of follow up, in 26% of patients a progression of ACI was detected (ACI-Prog). In ACI-Prog patients, F-BMD was significantly lower both at baseline (and at 12th mth of KTx (p=0.01 and p=0.03 resp – Figure 1 A-B). Using ROC curve, F-BMD showed a discriminatory role of ACI-Prog (1st mth: AUC 0.62 – p=0.02; 12th mth: AUC 0.69 p=0.005 – Figure 1 C-D). During the year of follow up, 8 patients experienced a cardiovascular event (CV). In those patients, F-BMD in the two time points were not different with those of CV free patients.

Table I: *Characteristics of the cohort*

Parameter	***Mean ± SD***	
Age (yrs)	48±11	
Time of Dialysis (mths)	57±53	
Parameter	***1st mth***	***12th mth***
BMI (kg/m^2)	23±3	24±3
Creatinine (mg/dl)	1.41±0.47	1.40±0.39
eGFR (ml/min)	57±20	55±17
Hb (mg/dl)	11.1±1.4	12.8±1.6
Glucose (mg/dl)	83±22	82±18
PTH (pg/ml)	157±140	143±165
Ca (mg/dL)	9.95±0.8	10±0.7
P (mg/dL)	2.47±0.9	3.1±0,65
ALP (U/L)	111±74	97±68
U-Prot (g/24h)	0.29±0.7	0.24±0.5
FETUIN (g/L)	0.32±0.2	0.31±0.08
FGF-23 (pg/ml)	37±50	35±52
25OH-VitD (ng/mL)	13±6	16±8

Patients (n)	293
Gender (M/F)	170/123
Type of dialysis (HD/PD) (%)	70/21
Type of KTx (Deceased/Living) (n)	226/47
Previous Steroid Therapy (%)	38
Cya / FK (%)	12/88
MMF therapy (%)	95
mTOR inhibitor therapy (%)	2
Steroids in the 1° year (mg)	2860±1050
Vit.D Therapy at baseline (Calcifediol/Calcitriol) (%)	0/11
Vit.D Therapy at 12 mths (Calcifediol/Calcitriol) (%)	7/19

Footnotes.: *BMI: Body mass index, eGFR: estimated glomerular filtration rate estimated using MDRD formula; PTH: Paratormone; ALP: Alkaline Phosphatase; FGF-23: Fibroblas grouth factor 23, U-Prot: protein urinary excretion. HD: Hemodialysis; PD: Peritoneal Dialysis; Cya: Ciclosporine; MMF:mycophenolate*

Table II: *DEXA and Aoric Calcification Index of the cohort*

Parameter	***Mean ± SD***		***p***
	1° mth	***12° mth***	
Femoral Bone mineral density (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
Femoral Osteopenia (%) Femoral Osteoporosis (%)	53 15	52 12	-
Aortic Calcification Index (n/ % of patients positve)	3.94±5.3 / 55	5.18±6.19 / 61	<0.0001
ACI-Prog (%)	-	26	-

Footnotes: *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.*

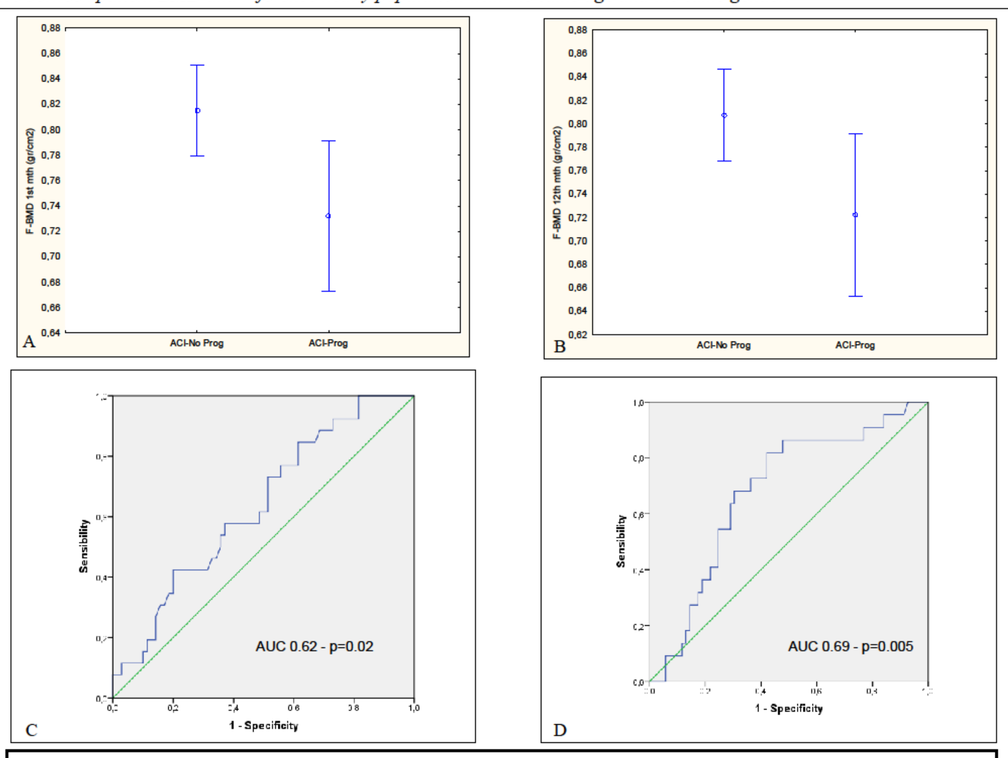

Figure 1:*ANOVA test: baseline F- BMD distribution at 1st (A) and 12th mth (B) among patients who increased ACI during the first year of KTx. ROC Curve: discriminatory power of ACI-Prog for F-BMD at 1st (C) and 12th mth (D)*

Conclusions

According to our results: 1) the prevalence of osteopenia and osteoporosis is quite high in KTx patients. Fetuin and age are the variables that influence independently F-BMD 2) aortic calcifications are present approximately in half of patients. A small degree of ACI progression was found during the first year of KTx. F-BMD could represent a good and indirect indicator of aortic calcification and of ACI-progression. 3) F-BMD seems not able to predict CV events during the first year of KTx. In any case, our results confirm a cross-link between bone mineralization and vascular calcification in KTx patients.

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