BONE TURNOVER MARKERS, BONE DENSITY AND FRAGILITY FRACTURES IN RENAL TRANSPLANT CANDIDATES

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INTRODUCTION

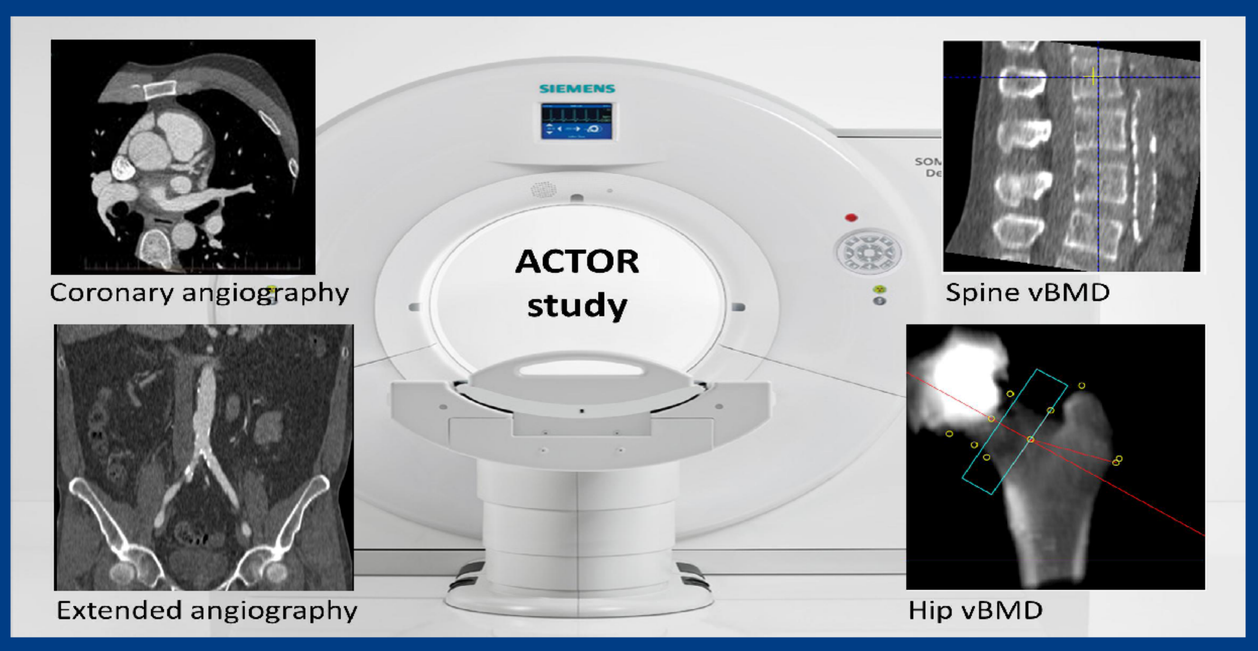
Fracture risk is increased 2-4-fold in chronic kidney disease (CKD) and remains high after renal transplantation. Bone disease in renal failure involves both decreased bone density and disturbed bone remodeling which may affect bone strength. Biochemical markers of bone turnover may be used to assess bone remodeling, but their utility in renal failure is unclear. We investigated the association between bone turnover markers, bone mineral density (BMD) and previous fragility fractures in renal transplant candidates with CKD4-5D.

AIMS

→ Are biochemical markers of bone turnover associated with bone mineral density and/or fragility fractures in renal transplant candidates?

CONCLUSIONS

- Bone density of spine and hip were significantly lower in patients with previous fragility fractures -> Figure 1
- Biochemical markers of bone turnover as well as PTH were negatively associated with bone density at total hip, but not lumbar spine –> Table 2
- Bone turnover markers were not associated with previous fragility fractures -> Figures 3



METHODS

Adult renal transplant candidates were recruited from four Danish centers from 2011-13. Of 167 included, twenty were excluded due to: Withdrawn consent (*n* = 5), major cardiovascular event (*n* = 4), renal transplantation (*n* = 1), incomplete CT-scan (*n* = 6) or incomplete CT analysis (*n* = 4). CT scan images were analyzed by dedicated software *QCT Pro* (Mindways Inc.) yielding volumetric BMD (vBMD) of lumbar spine (L1-L3), total hip and femoral neck. Fracture status were determined by previous non-vertebral fragility fracture, confirmed by chart review, or prevalent vertebral fracture diagnosed by Genants method on CT scan of total spine. Blood samples were drawn in the morning in the fasting state. All statistial analyses were performed in STATA/IC13.1 (Statacorp LP). Data given as mean with standard deviation (SD) or median with interquartile range [IQR]. Students' ttest, linear and logistic regression were used for data analyses.

RESULTS

Demographic data

A total of 147 patients were included in analyses. Median age was 54.4 [45.3, 63.6] years, and two thirds were men (66.7%). Sixty-six (44.9%) had received renal replacement therapy (RRT) for a median of 18 [3, 48] months, while the remaining 81 (55.1%) had a median estimated glomerular filtration rate (eGFR) of 11 [9,14] ml/min. Diabetic nephropathy was the cause of renal failure in 27.2%.

Bone density and fractures

Mean vBMD of lumbar spine was 122.5 (39.5) mg/cc and femoral neck 233.6 (51.8) mg/cc with no significant differences between CKD4-5 and CKD5D. There were 53 fragility fractures in 26 patients (11 with VF, 10 with clinical fractures, 5 with both). vBMD was significantly lower in patients with fragility fractures, both at lumbar spine and total hip, and remained so in adjusted analyses (Figure 1, Table 1).

Calcium metabolism

Markers of calcium-metabolism – plasma intact parathyroid hormone (p-iPTH), p-phosphate (p-PO_4) and p-calcium (p-Ca^{2+}) – did not differ between CKD4-5 and CKD5D (data not shown). None were associated with previous fragility fracture. P-iPTH was negatively associated with BMD of total hip and remained so after multivariate adjustement.

Bone turnover markers

Plasma C- and N-terminal telopeptides of type I collagen (CTX and NTX), procollagen type-1 N-terminal propeptide (P1NP), bone-specific alkaline phosphatase (B-AP) and tartrate-resistant acid phosphatase (TRAP-5b) – were higher in patients receiving renal replacement therapy, which was signifiant for all but TRAP-5b (Figures 3).

All markers were negatively associated with vBMD at total hip, while neither were associated with vBMD of lumbar spine (Table 2). There were no differences in markers of bone turnover according to fracture status, considering patients together or stratified on renal replacement therapy (Figures 3).

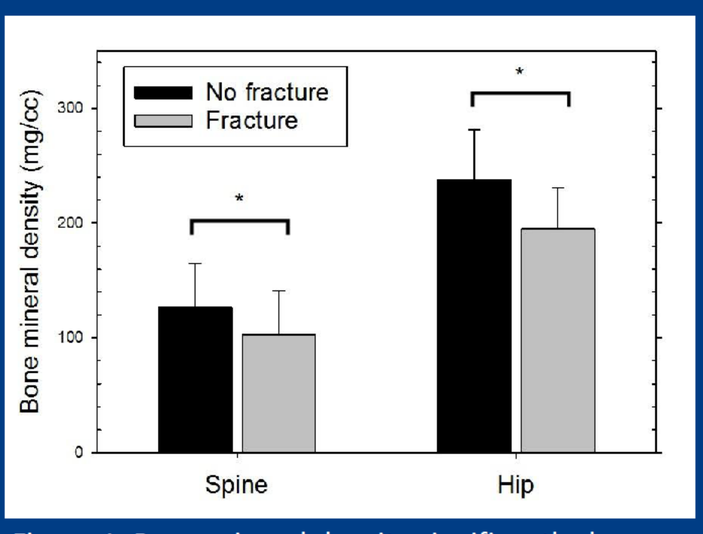


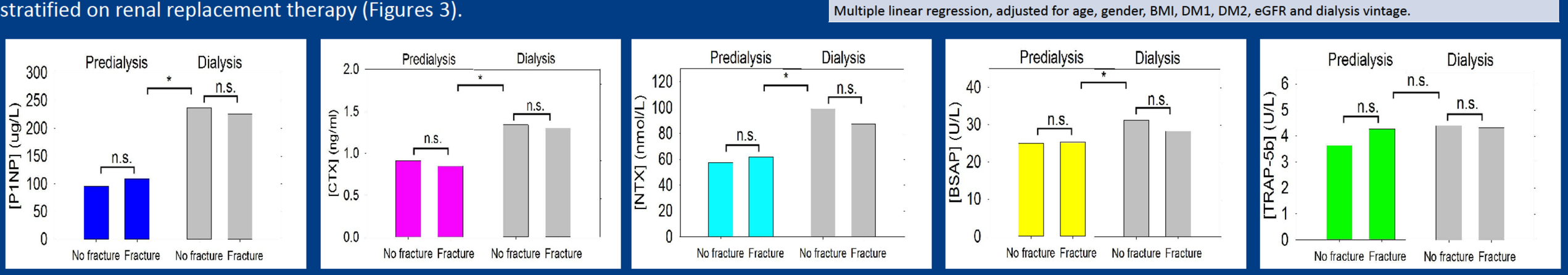
Figure 1: Bone mineral density significantly lower in patients with previous fracture.*p<0.05

Table 1	No fracture	Fracture	Students' t-test	Adjusted *
Lumbar spine vBMD	126.5 (38.4)	102.5 (38.6)	**p < 0.01**	**p = 0.001**
Total hip vBMD	237.5 (44.1)	194.8 (35.7)	**p < 0.001**	**P < 0.001**

Mean (SD). * Multiple logistic regression adjusted for age, gender, BMI, diabetes and RRT.

Table 2	B-AP		P1NP		Trap-5b		CTX		NTX	
Total hip vBMD	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*
Simple	-18.88	**<0.05**	-2.58	0.59	-17.81	**<0.01**	-3.14	0.62	-6.18	0.26
Adjusted	-25.00	**<0.01**	-10.89	**<0.05**	-20.00	**<0.01**	-15.34	**<0.05**	-17.67	**<0.01**
Lumbar spine vBMD										
Simple	4.12	0.61	3.88	0.348	-6.76	0.26	2.56	0.64	-0.16	0.97
Adjusted	-5.40	0.48	-0.31	0.944	-8.32	0.13	-4.11	0.46	-7.37	0.13

Multiple linear regression, adjusted for age, gender, BMI, DM1, DM2, eGFR and dialysis vintage.



Figures 3: Biochemical markers of bone turnover: No difference depending on fracture status, but significantly higher levels in patients on RRT. * p < 0.05, n.s.: Not significant

CONFLICTS OF INTEREST

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