

Bone Microarchitecture in Renal Osteodystrophy Patients

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Aims

Renal Osteodystrophy (ROD) is a systemic disorder that develops early with loss of kidney functions and is manifested by abnormalities in bone metabolism, mineralization and volume. Phosphate binders are a major constituent in chronic kidney disease management. Previous Aluminum and calcium containing phosphate binders were thought to be of detrimental effect on bone histology¹. The aim of this study was to investigate whether Micro-CT imaging can spot the deterioration in bone morphology (if it exists) with the use of calcium based phosphate binders. It was also our aim to evaluate the effect of the recently introduced non-calcium based phosphate binders on bone microarchitecture using quantitative Micro-CT scanning. Comparison and correlation between Micro-CT and quantitative histomorphometry for this type of bone disorder was also to be investigated.

Methods

Sixty-three pairs of transiliac bone core biopsies were taken from patients undergoing kidney dialysis. Biopsies were harvested at base line, one, and two years after the beginning of treatment. Patients were randomized to receive either calcium or non-calcium based phosphate binders. All specimens were scanned using SkyScan desktop Micro-CT machine (Model 1072; SkyScan, Aartselaar, Belgium). Source voltage was set at 100 KV, and source current at 98 μ A. Image pixel size of 11.2 μ m was generated using a rotation step of 45 degrees and a rotation angle of 180 degrees. Exposure time of 4500 ms was used with a 0.5 mm external aluminum filter. About 416 images were created and hence reconstructed using SkyScan's volumetric reconstruction software "Nrecon". CTAn was used for image analysis (Skyscan, version 1.10.0.2) using global thresholding for bone segmentation.

Bone alignment was adjusted in all specimens using DataViewer (SkyScan, version 1.4.3) to standardize and facilitate creating the ROI. Two Regions of interest were created to delineate the cortical and the trabecular bone areas separately. The slice inclusion/exclusion from the ROI was dependant on the slice enclosure of both bone types. All Regions of interest were created by the same researcher.

Statistical Analysis

Comparison of mean values was analysed using the t-test for independent as well as for paired variables. For each pair of parameters, Pearson's correlation coefficient was also performed to examine the degree of correlation between the Micro-CT and the quantitative histomorphometry in this type of bone disease. The level of significance was set at 0.05.

Results

The base line bone biopsies showed similar morphological parameters between both treatment groups with no statistically significant differences as measured by both

histomorphometric and Micro-CT techniques. At base line, the mean trabecular bone volume as measured by histomorphometry (TBVH) was 26.9 ± 8 for the calcium and 19.8 ± 7 for the non-calcium group. The mean trabecular bone volume as measured by the Micro-CT (TBVC) was 28.7 ± 9 and 26.3 ± 12 for the same groups respectively. Highly significant correlation was observed between the parameters measured by both methods (Table 1).

%	Histomorph	SD	Micro-CT	SD	r=	Histomorph	SD	Micro-CT	SD	r=
Ct.BV. 1	86.2	10.1	92.3	6.2	0.7*	83.98	10.1	87.81	11.2	0.8**
Ct.BV. 2	85	8.6	85.4	8.8	0.8*	83.33	11.7	88.78	9.1	0.4
Tb.BV. 1	19.8	7.7	26.3	12	0.8*	26.90*	8.2	28.71**	9.4	0.7*
Tb.BV. 2	18.2	7.2	25.5	8.1	0.5	22.86*	7.8	24.78**	13.8	0.4

Table 1: Percentage cortical and trabecular bone volume at base line (first biopsy) and after one year follow up (second biopsy) for non-calcium (left) and calcium based (right) phosphate binders. Pearson correlation coefficient (r value) correlating Histomorphometrical and Micro-CT results is given. Significance was evident at 0.05* and 0.01** levels.

Significant reduction was observed in TBVH and TBVC between base line and first follow up specimens in the calcium group while TBV was preserved in the non-calcium treated patients (Table 1. P= 0.018). The TBV continued to drop in the second bone sample in the calcium group patients; however, the reduction was not significant when compared with the second bone sample (Figure 1).

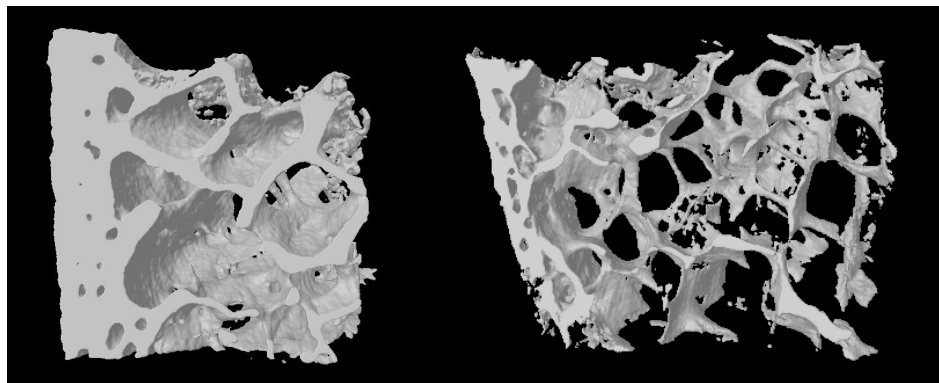


Figure 1: A paired transiliac bone biopsies taken at base line (left) and at one year after treatment (right). The Patient was in the calcium group. The deterioration in the bone architecture is well demonstrated.

Conclusions

Our results suggests that non-calcium based phosphate binders are of more favorable effect on bone microarchitecture than the calcium containing preparations which have negative effects on bone morphological parameters.

It was also possible to show that high resolution Micro-CT analysis is a non-invasive technique that is highly comparable to quantitative bone histomorphometry in analyzing bone samples from ROD patients.

References:

1. Malluche, H., Mawad, H., Monier-Faugere, M-C. "Effects of Treatment of Renal Osteodystrophy on Bone Histology", Clin J Am Soc Nephrol, 3, 157-63, 2008