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Changes in bone microarchitecture following kidney transplantation – beyond bone mineral density

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Abstract

Bone disease in kidney transplant recipients (KTRs) is characterised by bone mineral density (BMD) loss but bone microarchitecture changes are poorly defined. In this prospective cohort study, we evaluated bone microarchitecture using non-invasive imaging modalities; high-resolution magnetic resonance imaging (MRI), peripheral quantitative computed tomography (pQCT), dual energy X-ray absorptiometry (DXA) and the trabecular bone score (TBS) following kidney transplantation. Eleven KTRs (48.3 ± 11.2 years) underwent MRI (tibia), pQCT (radius) and DXA at baseline and 12 months post-transplantation. Transiliac bone biopsies, performed at transplantation, showed 70% of patients with high/normal bone turnover. Compared with baseline, 12-month MRI showed deterioration in indices of trabecular network integrity - surface to curve ratio (S/C; -15% , $p=0.03$) and erosion index (EI; $+19\%$, $p=0.01$). However, cortical area increased ($+10.3\%$, $p=0.04$), with a non-significant increase in cortical thickness ($+7.8\%$, $p=0.06$). At 12 months, parathyroid hormone values (median 10.7 pmol/L) correlated with improved S/C ($r=0.75$, $p=0.009$) and EI ($r=-0.71$, $p=0.01$) while osteocalcin correlated with cortical thickness ($r=0.72$, $p=0.02$) and area ($r=0.70$, $p=0.02$). TBS decreased from baseline (-5.1% , $p=0.01$) with no significant changes in BMD or pQCT. These findings highlight a post-transplant deterioration in trabecular bone quality detected by MRI and TBS, independent of changes in BMD, underlining the potential utility of these modalities in evaluating bone microarchitecture in KTRs.

Introduction

Fractures are a common and serious clinical complication of the mineral and bone disorder (MBD) that is almost ubiquitous in patients with chronic kidney disease (CKD). A number of epidemiological studies have highlighted that CKD predisposes to a dramatic increase in fracture risk and resultant morbidity and mortality when compared to an age and gender-matched population without CKD [1-4]. Kidney transplantation is the optimal treatment for end-stage kidney disease (ESKD) but does not attenuate the susceptibility to fracture. Indeed, fracture risk has been reported up to 34% higher in the first two years post transplantation

1 compared to the preceding period on dialysis [5], with a fracture incidence up to 22.5% over
2 the first five years post transplantation [6]. In addition, kidney transplant recipients (KTRs)
3 have higher rates of hospitalization and mortality after fracture than do people in the general
4 population [7]. Although reductions in bone mineral density (BMD) after transplantation
5 have been extensively reported, there is a paucity of post-transplant data regarding modifiable
6 risk factors for fracture [8]. Improved graft and patient survival has further emphasized the
7 importance of optimising long-term clinical outcomes including risk of fracture and
8 cardiovascular disease in KTRs.

9
10 Post-transplant bone disease is multifactorial, and includes effects of immunosuppressive
11 therapy, persisting hyperparathyroidism, 'hyperphosphatoninism' and the consequences of
12 post-transplant impairment of renal function (CKD-T) superimposed on pre-existing renal
13 bone abnormalities [9]. The diagnosis and management of post-transplant bone disease is
14 therefore difficult, with limited validation of available diagnostic tools to evaluate changes in
15 bone structure or predict fracture risk. Although accelerated loss of BMD in the first year
16 after transplantation has been described as the hallmark of post-transplant bone disease [10-
17 12], recent studies have demonstrated a more conservative estimate of early BMD loss with
18 long term values nearer to average for age and gender [13]. The focus of contemporary
19 research has been on change in bone microarchitecture post kidney transplantation and its
20 potential relationship to bone fragility and biomarkers [14-18]. A few studies based on
21 histomorphometry have addressed this issue [18-21] and, more recently, studies involving
22 non-invasive imaging, such as high-resolution peripheral quantitative computed tomography
23 (HR-pQCT) [15], high-resolution magnetic resonance imaging (MRI) [14, 22] and the
24 Trabecular Bone Score (TBS) [23-26] have focused on defining changes in bone
25 microarchitecture.

26
27 In this prospective, observational study over the first 12 months following transplantation, we
28 report changes in bone microarchitecture and bone mass that were assessed using non-
29 invasive techniques: high-resolution MRI (tibia), dual-energy X-ray absorptiometry (DXA) to
30 assess BMD and the TBS, peripheral quantitative computed tomography (pQCT, radius) and
31 changes in biochemical markers.

32 33 **Materials and Methods**

34 *Study participants*

All patients referred for a living donor kidney transplant at The Royal Melbourne Hospital between December 2014 and January 2016 were eligible for this study, providing they had no contraindication to MRI, and were not participating in another trial. The protocol was approved by the local ethics committee and all patients provided informed consent. A total of 27 patients planned for living donor kidney transplantation were approached for this study. Five transplant surgeries were rescheduled or cancelled for clinical or logistical reasons. Fourteen of the remaining 22 patients were recruited and underwent kidney transplantation. Eleven of these patients completed follow up at 12 months. Among the exclusions, two patients moved to a different state for post-transplant care and one patient had to undergo nephrectomy after transplantation and was not included in analysis.

Immunosuppressive therapy

Patients received induction with basiliximab and methylprednisolone (500mg) and subsequently maintenance immunosuppression comprising tacrolimus, mycophenolate mofetil and prednisolone. Initial prednisolone dose was 25mg daily, tapered over 3-months to a maintenance dose of 5 mg/day. Beyond three months, triple immunosuppression was continued in the absence of any abnormal findings on protocol transplant biopsies (at 3 and 12 months post-transplant) or a clinical indication to the contrary determined by the treating team.

Bone histomorphometry

Transiliac biopsies were performed using a modified Bordier trephine (Landanger) in 10 of 11 participants at the time of transplantation. The transiliac cores measuring 7mm in diameter were analyzed by histomorphometry and micro computed tomography (micro-CT) and were classified by Turnover (T), Mineralisation (M) and Volume (V) using the Kidney Disease Improving Global Outcomes (KDIGO) recommended classification [27]. Methodology relating to bone biopsies has been described previously [28].

Noninvasive Assessment of Bone

MRI

MRI images were obtained within 2 weeks preceding transplantation (baseline) with a commercial 3.0-Tesla whole-body imager (Siemens Trio, Germany) and at 12 months after kidney transplantation. Participants were imaged in a feet-first prone position. MRI acquisitions were performed at the left tibial metaphysis using a three dimensional (3D) 'fast

spin echo' pulse sequence readily available on any clinical MRI system requiring a scan time of 12 minutes. This was undertaken utilizing a commercially available eight-channel radiofrequency (RF) extremity coil used in clinical practice. MRI parameters include 0.273 mm x 0.273 mm x 0.6 mm voxel size, 70 mm x 70 mm x 19.2 mm field-of-view, 53ms repetition time, 16ms echo time, 12 averages, and echo train length of two. Raw MRI data was pre-processed via bone volume fraction (BVF) mapping and segmentation of the bone into trabecular and cortical compartments for structural measurements and topological analysis using published algorithms [29]. Topological analysis of the trabecular network was performed and two composite parameters, reported to be sensitive to microstructure of bone [30, 31], were calculated. The first of these, surface/curve ratio (S/C) is the ratio of all surface voxels to all curve voxels with the former representing plate-like elements and the latter being a marker of rod-like elements of the trabecular network. Age and disease related deterioration of trabecular bone involves conversion of plate (surface) like trabeculae to rod (curve) like trabeculae. A higher S/C therefore indicates improved trabecular structure and strength. Trabecular deterioration also involves erosion of trabecular elements, which is measured by the Erosion Index (EI), defined as the ratio of all topological parameters (image voxel parameters representing various trabecular elements) expected to increase, to those parameters likely to decrease with network erosion caused by osteoclastic resorption. A higher ratio is consistent with greater deterioration. Both S/C and EI are derived parameters which have been validated and used in previous studies [30, 31].

DXA-derived BMD and TBS

Participants underwent baseline and 12-month BMD measurements by DXA (QDR-4500 Discovery, Hologic, Waltham, MA), at the lumbar spine, femoral neck and total proximal femur. BMD values were expressed in g/cm^2 and as T -scores. TBS is a novel indirect index of trabecular microarchitecture derived from pixel greyscale texture variations in the lumbar spine images acquired by DXA [32]. TBS iNsight Software (version 3.0.2.0; Medimaps) was used to calculate TBS values for the lumbar spine (L1-L4). A higher TBS score is consistent with better trabecular connectivity and a reduced risk for microarchitectural damage, while a lower TBS is consistent with increased risk for microarchitectural damage. Based on results of two recent studies [23, 24], a TBS cut point of 1.37 was used to stratify patients to reduced or increased fracture risk.

Peripheral quantitative computed tomography (pQCT).

Three dimensional pQCT tomographic images can be used to assess cross-sectional structure and volumetric density. We used pQCT (Stratec XCT-300, Germany) at the distal radius to derive total, cortical and trabecular volumetric BMD (vBMD), cortical thickness (CtTh) and cortical area (CtA) at baseline and 12 months. All DXA and pQCT scans and TBS measurements were performed at one center by a single operator not involved in the care of study participants and blinded to other study measurements.

Laboratory Measurements

Blood samples for routine biomarkers were obtained before transplantation and at 3, 6 and 12 months post transplantation. Serum concentrations of intact parathyroid hormone (iPTH) were determined using Architect Intact PTH (Abbott Laboratories, USA) chemiluminescent microparticle immunoassay (CMIA). Bone turnover markers and serum 1,25-dihydroxyvitamin D (1,25[OH]₂D) were also measured at baseline, 6 and 12 months. Osteocalcin (OC) and procollagen type 1 N-terminal propeptide (P1NP), markers of osteoblast activity, and the osteoclastic resorption marker beta-cross linked telopeptide (β-CTx) were assayed by an electrochemiluminescence immunoassay (Elecsys®, Roche, Switzerland). Serum 1,25[OH]₂D was measured by radioimmunoassay (Immunodiagnostic Systems Ltd).

Statistical methods

Results are presented as mean (+/- standard deviation) for normally distributed continuous variables and as median (and interquartile range) for continuous variables with skewed distributions. Wilcoxon signed-rank test was used to assess changes in parameters between baseline and at 12 months post transplantation. Correlation analyses using Spearman correlation coefficient were conducted to investigate associations between longitudinal changes in parameters obtained by various modalities. A two-tailed *p* value <0.05 was considered statistically significant. Stata statistical software package (version 11.0, Stata Corporation, College Station, TX) was used for analysis.

Results

Participant characteristics

Baseline demographic characteristics and potential bone modulating medications prior to and after transplantation are shown in Table 1 and Table 2 respectively. The mean age of participants was 48 ± 11 years, 72.7% were male and mean body mass index of the cohort

was $26.4 \pm 4.1 \text{ kg/m}^2$. Glomerulonephritis (36.3%) was the most common cause of ESKD followed by reflux nephropathy (27.2%) and diabetes mellitus (18.1%). Seven (63.6%) participants were on dialysis (mean duration 19.4 ± 16.7 months) and 4 underwent pre-emptive kidney transplantation. None of the participants received anti-resorptive therapy prior to or after transplantation. There was one episode of biopsy proven acute cellular rejection treated with methylprednisolone and increased tacrolimus and mycophenolate. The remainder of participants continued on maintenance immunosuppression, including prednisolone 5 mg daily, after their respective 3-month protocol biopsies. The mean cumulative dose of prednisolone over 12 months per patient was $3244 \pm 68.6 \text{ mg}$.

Bone histomorphometry

Ten patients had baseline bone histomorphometry with 4 (40%) having evidence of high bone turnover, 3 normal and 3 low turnover, Mineralisation was abnormal in 4 and trabecular bone volume was normal in 7 and low in 3. By micro-CT mean cortical thickness was reduced and cortical porosity was increased in all patients [28].

Longitudinal changes in bone microarchitecture by MRI

At 12 months there was deterioration in MRI-derived parameters of integrity of the trabecular network. S/C, indicating the plate to rod ratio of trabeculae, decreased by 16% ($p=0.03$) from baseline. EI, which increases with trabecular deterioration, increased by 23% ($p=0.01$) (Table 4, Figure 2). There were no statistically significant differences between pre and post transplantation trabecular bone volume, trabecular number and trabecular separation. Post transplantation cortical area increased significantly by 10.3% ($p=0.04$) while there was a non-statistically significant 7.8% increase in cortical thickness ($p=0.06$).

Longitudinal changes in pQCT

By pQCT at the radius there was a non-significant increase in cortical thickness. There were no longitudinal changes in pQCT derived cortical or trabecular area or in total, cortical or trabecular volumetric BMD.

Longitudinal changes in DXA-derived BMD and the TBS

At the time of transplantation, 80% of the study participants met BMD criteria for osteopenia or osteoporosis at the femoral neck. The median T-score at the femoral neck was -1.6 (-2.4 to -0.6), whereas T-scores at the total proximal femur and lumbar spine were in the normal range (Table 3). At 12 months, there was a 2.2% decrease in lumbar spine BMD (mean change -0.22 g/cm² [-0.56, 0.12], a 2.7% decrease in femoral neck BMD (mean change -0.10 g/cm² [-0.39, 0.19]) and a 1.1% increase in BMD at the total hip (mean change 0.1 g/cm² [-0.14, 0.34]), with none of these changes reaching statistical significance.

Prior to transplantation the mean TBS was 1.27 ± 0.11 , with 9 of 11 (81.8%) patients having a TBS below 1.37. The mean TBS decreased at 12 months to 1.21 ± 0.12 ($p = 0.02$) with 10 out of 11 (90.9%) patients having a TBS lower than 1.37. The TBS at baseline and follow-up, was not significantly related to BMD or any structural parameter derived by MRI.

Changes in Biochemical Markers

Baseline and 12-month follow up biochemical parameters and bone turnover markers are presented in Table 3. Immediately before transplantation, the median serum iPTH was 43.6 (16.5 – 57.5) pmol/L, which is within the target range recommended by the KDIGO Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) guidelines. At 12 months, 54.5% of patients had mild persistent hyperparathyroidism with median PTH 10.7 (7.4 – 17.0) pmol/L. With return of renal function, values of 1,25[OH]₂D rose by 78% from baseline to 6 months and remained stable within the normal reference range to 12 months. Values of bone turnover markers affected by renal function (OC, β -CTx and P1NP) fell from the pre-transplant period to 12 months as expected. On the other hand, alkaline phosphatase (ALP), which reflects osteoblast activity and is not influenced by renal function, did not change significantly from pre-transplant to 12 months. As indicated in Figure 1, mean values of serum P1NP, β -CTX and OC had all fallen towards the upper normal range by 6 months, with no statistically significant change from 6 to 12 months.

Associations of Laboratory Variables to Structural Parameters

Pre-transplant values of serum PTH, P1NP, β -CTx and OC were not significantly associated with any structural MRI parameters. However, at 12-months, levels of PTH correlated to S/C ($r = 0.75$; $p = 0.009$) and EI ($r = -0.71$; $p = 0.01$) but not to other structural parameters (Figure 3). OC levels at 12 months correlated to MRI derived cortical thickness ($r = 0.72$; $p = 0.02$) and area ($r = 0.70$; $p = 0.02$) at the tibia. OC also correlated to pQCT parameters of cortical

1 thickness ($r=0.70$; $p=0.03$) and area ($r=0.67$; $p=0.05$) at the radius. On the other hand, values
2 of serum PTH and the assayed bone turnover markers were not correlated to any BMD value
3 or the TBS at baseline or 12 months.

4 5 ***Clinical outcomes***

6 One patient (with type 2 diabetes mellitus and PTH 65 pmol/L at baseline) was diagnosed
7 with avascular necrosis of both hips after the study period completed, and subsequently
8 sustained a spontaneous trochanteric fracture requiring total hip replacement. There were no
9 clinically detected incident fractures during the 12-month study period.

10 11 **Discussion**

12 After kidney transplantation, factors contributing to deterioration in bone quality include
13 immunosuppressive therapy, abnormalities in mineral homeostasis and remodelling
14 superimposed upon pre-existing renal osteodystrophy. Although post transplantation loss of
15 bone mass or BMD has been well documented, changes in bone microarchitecture are not
16 well described. In this study, we aimed to define changes in bone microarchitecture over the
17 first post-transplant year using a combination of high-resolution imaging techniques and
18 biochemical markers of bone turnover.

19
20 In this cohort study of 11 KTRs with predominantly high or normal turnover at baseline,
21 changes in some MRI parameters and the TBS were consistent with deterioration in
22 trabecular network and connectivity, while MRI suggested an improvement in cortical
23 microarchitecture over 12 months post transplantation. Notably, there were no statistically
24 significant changes in BMD by DXA, despite a significant decline in the TBS to values
25 associated with an increased fracture risk [24]. These changes in bone were accompanied by
26 changes in biomarkers of mineral metabolism, which were concordant with published data
27 [33, 34].

28
29 Progressive deterioration in trabecular connectivity and microarchitecture after
30 transplantation is clinically relevant because it may increase bone fragility without
31 quantifiable changes in bone volume. It has previously been reported that the conversion of
32 trabecular structure from plate-like to rod-like and disruption of network connectivity
33 adversely impacts mechanical strength of bone [35], is associated with aging and
34 osteoporosis [36-38] and discriminates between participants with or without fractures in

1 imaging studies [30, 39]. The observed relationship of post-transplantation PTH values to
2 improvements in the S/C and EI measurements, likely reflects an anabolic effect of mild
3 hyperparathyroidism on trabecular bone [40].

4
5 The MRI-derived longitudinal improvement in cortical microarchitecture in our study is
6 contrary to changes reported by contemporary imaging studies in kidney transplantation [14,
7 15]. The only other MRI study to longitudinally evaluate cortical and trabecular
8 microarchitecture in KTRs reported a decline in cortical, trabecular, and whole-bone stiffness
9 at 6 months after transplantation in the absence of any significant corresponding changes in
10 microarchitecture or BMD [14]. However, Iyer *et al*, investigated bone structure changes in
11 KTRs on an early corticosteroid withdrawal regimen and demonstrated a decrease in HR-
12 pQCT-derived cortical area (-3.9%, radius; -2.7% tibia) and thickness (-3.1%, radius; -1.9%
13 tibia) and an increase in cortical porosity at one-year post transplantation [15]. This decrease
14 in cortical thickness and area was related to higher PTH levels. In comparison to the study by
15 Iyer *et al*, the participants in our study had higher baseline PTH (43.7 pmol/L vs 27 pmol/L),
16 were generally more osteopenic (mean T-score -1.5 vs -0.8) and were on traditional
17 corticosteroid regimen. The overall results should be interpreted in the context of these
18 differences. Participants in the present study were also significantly younger with only two
19 (of 11) over 55 years of age compared to 27 (of 47, 57%) patients above 55 years of age in
20 the study by Iyer *et al*. Notably cortical deterioration occurs with advancing age and is more
21 common in people above 60 years of age. Few other studies have described longitudinal
22 changes in cortical bone post kidney transplantation.

23
24 In contrast to previously published data about the predominance of low bone turnover in
25 ESKD patients [41, 42], 70% of our participants had features of high or normal bone turnover
26 at the time of transplantation, accompanied by universally thin cortices on micro-CT but with
27 relatively preserved trabecular bone volume – an overall picture suggestive of moderate to
28 severe secondary hyperparathyroidism. We postulate that the improvement in MRI-assessed
29 cortical microarchitecture in our study is likely a result of suppression of excessive bone
30 resorption and unmasking of bone modelling due to a decline in PTH levels and represents a
31 partial correction of hyperparathyroidism-related bone changes after kidney transplantation.
32 This release from excess remodelling and endocortical resorption may lead to net adaptive
33 periosteal apposition and a stabilisation or increase in cortical surface area and thickness [43,
34 44]. In our study, the relationship between post transplantation osteocalcin levels and cortical

1 thickness and area at both the tibia (MRI) and the radius (pQCT) are suggestive of net bone
2 formation. Similar to these conclusions, a recent study of paired bone biopsies at baseline and
3 one-year post transplant reported significant declines in parameters of bone resorption at one
4 year, with no changes in other static parameters [18]. Trabecular bone volume was also
5 normal in most patients at baseline and only decreased minimally after transplantation. Julian
6 *et al*, in an early prospective histomorphometry study, also reported similar normalisation of
7 osteoclast resorption markers and resolution of hyperparathyroidism at 6 months post
8 transplantation [10].

9
10 Currently, there is no reference range for TBS for individuals with CKD because of the
11 relative lack of studies investigating its utility in CKD [26, 45] and renal transplantation [24,
12 25]. Two studies have proposed values of the TBS to discriminate between subjects with and
13 without fracture in CKD stages 3-4 (TBS less than 1.27) [45] and in KTRs shortly after
14 kidney transplantation (TBS less than 1.37) [24]. In the current study we observed a
15 significant decline in mean TBS at 12 months post transplantation from a baseline score
16 already consistent with an increased fracture risk. It is possible that the TBS is reduced early
17 after transplantation with recovery over the longer term [25]. The longitudinal decline in TBS
18 paralleled the MRI-derived deterioration in trabecular architecture and was unrelated to areal
19 or volumetric BMD changes. By comparison, we observed no significant decline in BMD
20 over 12 months. This is consistent with contemporary data showing more stable BMD long
21 term after transplantation [13, 18] and may represent a recovery after loss of bone mass early
22 after transplant [10].

23
24 Our study has several limitations. The small sample size limits its statistical robustness and
25 restricts the ability to apply regression analysis to evaluate predictors of changes in bone
26 microarchitecture. This includes the effects of bone-modifying treatments on changes in bone
27 structure. Also, being a single-center study, the relevance of our findings to other centers is
28 limited. Despite these limitations, our study is one of very few to explore longitudinal
29 changes in bone structure after transplantation using high-resolution imaging.

30
31 In summary, using MRI and DXA-derived TBS in a small sample of relatively young living
32 donor KTRs, we identified changes consistent with a progressive deterioration in trabecular
33 bone quality and an increased fracture risk. The lack of significant interval changes in BMD
34 or pQCT parameters accentuates the potential importance of assessing bone health post

transplantation by alternate means. The preservation of cortical structure in our cohort, although different to available data, may represent a partial correction of bone abnormalities related to secondary hyperparathyroidism. Overall, our study highlights the heterogeneous nature of bone microarchitecture changes in post-transplant bone disease and supports further investigation of non-invasive imaging modalities in larger prospective trials to assess the evolution of histologic and structural changes in bone after transplantation. Changes in MRI parameters and the TBS may be of particular interest for detecting changes that may increase post-transplant fracture risk.

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Disclosures

The authors of this manuscript have no conflicts of interest to disclose.

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Tables

Table 1. Demographic parameters at the time of transplantation (n = 11)

Variable	Values
Age at surgery (years)	48.3 ± 11.2
Gender (n of males)	8
Body mass index (kg/m ²)	26.4 ± 4.1
Cause of ESKD (n)	
- Glomerulonephritis	4
- Reflux nephropathy	3
- Diabetes mellitus	2
- Hypertension	1
- Polycystic kidney disease	1
Dialysis: HD / PD / None (n)	3/4/4
Parathyroidectomy (n)	1

Abbreviations: ESKD, end-stage kidney disease; HD, hemodialysis; PD, peritoneal dialysis

Table 2. Bone modulating therapy prior to and after transplantation (n = 11)

Bone Modulating Therapy	At transplantation (n)	Post-transplantation (n)
Cinacalcet	1	1
Phosphate binder (CCB/NCCB)	3/5	0
Calcitriol	4	3
Cholecalciferol	3	5
Prednisolone	3	11

Abbreviations: CBB, calcium containing binders; NCCB, non-calcium containing binders

Table 3. Biochemical parameters at the time of transplantation and at 12 months follow-up

Biomarker	Baseline	12 months	P value
Creatinine (mmol/L)*	501 ± 54.3	106.2 ± 21.5	0.003
eGFR*	10.4 ± 2.0	67.1 ± 11.2	0.003
Calcium (mmol/L)	2.45 ± 0.13	2.47 ± 0.11	0.82
Phosphate (mmol/L)	1.98 ± 0.39	1.00 ± 0.16	0.003
iPTH (pmol/L)	43.6 (16.5 – 57.5)	10.7 (7.4 – 17.0)	0.01
ALP (IU/L)	79.0 (66.0 – 111.0)	84.0 (68.0 – 109.0)	0.79
25[OH]D (nmol/L)	63.7 ± 24.0	86.0 ± 29.4	0.14
1,25[OH] ₂ D (nmol/L)	38.5 (20.0 – 72.5)	144.5 (97.0 – 173.7)	0.01
OC (ng/ml)	125.8 (30.8 – 161.7)	24.3 (20.3 – 38.1)	0.01
β-CTx (ng/ml)	1.08 (0.81 – 2.3)	0.69 (0.41 – 1.24)	0.02
P1NP (µg/L)	134.2 (43.0 – 269.2)	66.0 (42.8 – 117.0)	0.20

Abbreviations: eGFR, estimated glomerular filtration rate; iPTH, intact parathyroid hormone; ALP, alkaline phosphatase; 25[OH]D, 25-hydroxyvitamin D; 1,25[OH]₂D, serum 1,25-dihydroxyvitamin D; OC, osteocalcin; β-CTx, beta-cross linked telopeptides; P1NP, procollagen type 1 N-terminal propeptide

*Values at baseline for pre-dialysis patients receiving pre-emptive transplants only (n=4)

Table 4. Bone microarchitecture parameters measured by magnetic resonance imaging (MRI), bone mineral density (BMD) determined by dual energy x-ray absorptiometry (DXA) and peripheral quantitative computed tomography (pQCT) and Trabecular Bone Score (TBS) at the time of transplantation and at 12 months follow up

Modality	Parameter	Baseline	12 months	P value
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	S/C	5.5 ± 1.50	4.6 ± 1.66	0.03
	EI	0.9 ± 0.29	1.11 ± 0.34	0.01
	BV/TV (%)	10.0 ± 2.1	9.9 ± 2.4	0.76
	TbTh (µm)	125.0 ± 5.3	125.7 ± 5.0	0.33
MRI (tibia)	TbN	0.80 ± 0.14	0.77 ± 0.14	0.54
	TbS (µm)	1161.6 ± 246.3	1187.1 ± 241.1	0.72
	CtTh (mm)	2.68 ± 0.55	2.89 ± 0.64	0.06
	Total area (mm ²)	9788.8 ± 1996.3	9931.0 ± 2712.6	0.59
	Trabecular area (mm ²)	6692.2 ± 1742.4	6443.0 ± 2552.3	0.65
	Cortical area (mm ²)	3107.8 ± 692.5	3428.5 ± 811.5	0.04
	LS BMD (g/cm ²)	1.02 ± 0.09	0.99 ± 0.10	0.20
	LS T-score	-0.85 (-1.2 – 0.37)	-0.9 (-1.5 – 0.15)	0.17
DXA	FN BMD (g/cm ²)	0.70 ± 0.14	0.69 ± 0.12	0.50
	FN T-score	-1.5 (-2.4 - -0.6)	-1.6 (-2.5 - -0.9)	0.47
	TH BMD (g/cm ²)	0.86 ± 0.14	0.86 ± 0.11	0.50
	TH T-score	-0.9 (-1.7 - -0.25)	-0.6 (-1.6 - -0.25)	0.30
TBS	TBS	1.27 ± 0.11	1.21 ± 0.12	0.02
	Tb vBMD (g/cm ³)	186.8 ± 48.7	174 ± 43.5	0.07
	Ct vBMD (g/cm ³)	1164.2 ± 50.9	1161.4 ± 39.7	0.65
pQCT (radius)	Total vBMD (g/cm ³)	319.6 ± 76.4	302 ± 69.2	0.20
	CtTh (mm)	2.62 ± 0.50	2.72 ± 0.45	0.20
	Trabecular area (mm ²)	176.6 ± 29.8	175.6 ± 34.02	0.81
	Cortical area (mm ²)	92.0 ± 19.8	92.1 ± 21.3	0.72

Abbreviations: S/C, Surface to curve ratio; EI, Erosion index; BV/TV, trabecular bone volume; TbTh, trabecular thickness; TbN, trabecular number; TbS, Trabecular separation; CtTh, cortical thickness; LS, Lumbar spine; FN, femoral neck; TH, total hip; vBMD, trabecular and cortical volumetric bone mineral density (Tb vBMD and Ct vBMD)

Figures

Figure 1. Longitudinal changes in levels (mean $\pm$ SD) of parathyroid hormone (PTH) and bone turnover markers after transplantation.

*Comparison between values at baseline (0 months) and 12 months.

There were no statistically significant changes in 6-month and 12-month levels of bone turnover markers.

^ Comparison of PTH values between 3 months and 12 months.

Abbreviations: PTH, intact parathyroid hormone; β -CTx, beta-cross linked telopeptides; P1NP, procollagen type 1 N-terminal propeptide

Figure 2. Longitudinal changes in MRI-derived parameters of bone microarchitecture

Figure 3. Relationship between parathyroid hormone (PTH) levels and parameters of trabecular connectivity derived by MRI at 12 months post kidney transplantation

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