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Cortical and trabecular bone in pediatric end-stage kidney disease

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Abstract

Background—Cortical bone represents nearly 80% of human bone mass and is the major determinant of bone strength; however, cortical bone parameters, and their relationship to trabecular bone in the pediatric CKD population have not been evaluated.

Methods—Biochemical values and cortical and trabecular bone parameters were assessed in 22 pediatric dialysis patients: 12 with high trabecular bone turnover and 10 with normal to low trabecular bone turnover.

Results—Trabecular bone turnover and osteoid volume correlated with PTH levels ($r=0.86$, $p<0.01$ and $r=0.93$, $p<0.01$, respectively). Internal cortical osteonal bone formation rate was directly related to alkaline phosphatase ($r=0.45$, $p<0.05$) and inversely related to IGF-1 values ($r=-0.55$, $p<0.01$) and internal cortical porosity was also related to serum alkaline phosphatase levels ($r=0.57$, $p<0.01$). A similar relationship was not found between external cortical bone formation rate and parameters of bone turnover and porosity, however. No relationship was found between trabecular and cortical bone formation rates.

Conclusions—Secondary hyperparathyroidism was associated with increased external cortical, relative to internal cortical, osteonal activity in pediatric dialysis patients. The clinical consequences of these changes and their response to therapy for secondary hyperparathyroidism remain to be defined.

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Keywords

cortical bone; histomorphometry; secondary hyperparathyroidism; adynamic bone; bone biopsies

Introduction

Cortical bone represents nearly 80% of human bone mass and is the major determinant of bone strength and cortical porosity due to elevated intracortical remodeling rates has been implicated in the high incidence of fractures in postmenopausal women (1). Renal osteodystrophy, the term used to describe the spectrum of bone lesions associated with chronic kidney disease (CKD), is associated with increased fracture rates, bone pain, deformities, and (in children), decreased linear growth (2, 3). While renal osteodystrophy has traditionally been classified according to bone turnover in trabecular bone, bone biopsy data has demonstrated that high rates of bone turnover in trabecular bone may also be associated with increased cortical porosity in adult dialysis patients (4).

Bone histology remains the gold standard for the diagnosis and treatment of renal osteodystrophy; however, cortical bone histomorphometry has not been evaluated in children with CKD. Imaging studies have suggested that lower cortical area, thickness, and density are associated with an increased risk of fracture (5, 6) and some quantitative computed tomography data suggest that childhood CKD and secondary hyperparathyroidism may be associated with reduced cortical area and bone mineral density (7). Significant cortical thinning may also be present post-renal transplantation (8) although some data suggest that cortical bone density may not differ in pre-dialysis CKD patients as compared to healthy controls (9, 10). Despite the importance of cortical bone for overall bone strength and despite suggestions from imaging studies that cortical bone structure and strength may be altered in CKD, no studies to date have assessed the relationship between histomorphometric parameters of cortical and trabecular bone in the pediatric CKD population. Thus, the current study was designed to characterize cortical bone by histomorphometry and to compare parameters of turnover, mineralization, and volume between cortical and trabecular bone in pediatric patients treated with maintenance dialysis.

Methods

Patients

Medically stable pediatric patients (age 2–21) treated with continuous cycling peritoneal dialysis (CCPD) were eligible for the study. Patients treated with immunosuppressant agents, those on growth hormone, and those who had undergone parathyroidectomy within the previous 12 months were excluded from the study. Vitamin D sterol therapy was withheld for at least 4 weeks prior to the bone biopsy. All subjects received calcium carbonate as a phosphate binder. The dialysate calcium concentration was 3.5 mEq/l (Dianeal; Baxter, Deerfield, IL, USA) and dextrose concentrations were determined according to ultrafiltration requirements. For purposes of analysis, subjects were divided into two groups; those with trabecular bone turnover above the normal range (“high trabecular bone turnover”) (n=12), as previously defined (11), and those with trabecular

bone turnover (“normal/low trabecular bone turnover”) within or below the normal range (n=10). The study was approved by the UCLA Human Subject Protection Committee. All patients included in the study had informed consent signed by their legal guardian.

Bone Histomorphometry

Patients were admitted to the UCLA Clinical Translational Research Center and full thickness bone biopsies were obtained from the anterior iliac crest (2 cm below the anterior superior iliac spine) using a modified Bordier trephine needle after double tetracycline-labeling, as has been previously described (12). Biopsy specimens were 0.5 cm in diameter by 1–2 cm in length. Specimens were dehydrated in alcohol, cleared with xylene, and embedded in methyl methacrylate. Static histomorphometric parameters were evaluated in un-decalcified 5 µm sections treated with modified Masson-Goldner trichrome stain; tetracycline labeling was assessed in unstained 10 µm sections. Primary bone histomorphometric parameters were assessed in trabecular and cortical bone under 200x magnification using the Osteometrics^R system (Osteometrics, Decatur, IL) by histomorphometrists (CC and RP) blinded to biochemical values. External and internal cortices were analyzed separately. Since soft tissue on both periosteal surfaces had been removed, criteria other than presence of muscle (13) were used to distinguish the two cortices. The cortex with the greater thickness of sub-periosteal primary intramembranous bone, characterized by fine collagen lamellae of low birefringence, running parallel to the periosteal surface and being traversed at angles of 45–60° by Sharpey’s fibres (14), was taken to be the external cortex. Mineralized bone was defined by light blue staining areas; orange seams at least 1.5 µm in width were included in measurements of osteoid. Derived indices were calculated by standard calculations (15, 16). Bone pathology in both trabecular and cortical bone was characterized using the Turnover, Mineralization and Volume (TMV) classification for renal osteodystrophy (2). Histomorphometric analysis of cortical bone turnover, mineralization and volume was also performed using OsteometricsTM software.

Biochemical Determinations

Serum calcium, phosphorus, parathyroid hormone (PTH), insulin-like growth factor (IGF), 25(OH)vitamin D, albumin, creatinine, and alkaline phosphatase values were obtained at the time of the biopsy. Serum calcium, phosphorus, creatinine, and alkaline phosphatase were measured using a Technicon Autoanalyzer II (SEAL Analytical Mequon, WI, USA). Values for calcium were adjusted based on serum albumin level by the formula: $\text{serum Ca} = \text{measured calcium} + (0.8 \times (4 - \text{serum albumin}))$. PTH concentrations were measured by the 1st generation immunometric assay (Nichols^R), (normal range: 10–65 pg/ml). Serum IGF1 values were measured by ELISA (Diagnostic Systems Laboratories, Webster, TX, USA). Serum 25(OH)vitamin D concentrations were measured by Diasorin Liaison (Heartland Assays, Ames, Iowa).

Statistical Analysis

Determinations of bone parameters and biochemical variables are reported as mean ± standard error (for normally distributed variables) or median (interquartile range) (for skewed values). The Student t-test, Wilcoxon rank sum, or Chi-square test was used to

evaluate differences between groups; paired t-tests were used to evaluate differences in parameters between internal and external cortices. Pearson correlation coefficients were used to express the relationship between bone histomorphometric variables and biochemical parameters and between trabecular and cortical bone variables; skewed values were log-transformed prior to correlation analysis. All statistical analyses were performed using SAS software (SAS Institute Inc., Cary, NC) and all tests were two-sided. A probability of type I error less than 5% was considered statistically significant and ordinary *p* values are reported.

Results

Patient Characteristics and Biochemical Parameters According to Trabecular Bone Turnover Rate

Twenty-two patients (12 females, 10 males) met entry criteria and were enrolled in the study. The average age of the subjects was 10.4 ± 0.7 years, with ages ranging from 2.0 to 15.8 years; all subjects were either pre-pubertal or pubertal. Twelve patients (54.5%) had high bone turnover on trabecular analysis (10 with osteitis fibrosa and 2 of with mild lesions of secondary hyperparathyroidism), 5 patients had low bone turnover (4 with adynamic bone disease and 1 with osteomalacia), and 5 had trabecular bone turnover within normal range. Although, by definition, bone formation rates were slightly higher in patients with normal bone turnover than in those with adynamic bone, the majority of the remainder of bone histomorphometric parameters (both cortical and trabecular) and biochemical parameters did not differ between these two groups (Supplemental Tables 1, 2 and 3); thus, for purposes of analysis, subjects with low and normal bone turnover were grouped together (normal/low bone turnover) and compared to those with high trabecular bone turnover.

Biochemical values are displayed in Table 1. Serum calcium levels were in the normal range in the majority of subjects; however, serum calcium levels were lower in patients with high trabecular bone turnover than in those with normal/low trabecular bone turnover ($p < 0.05$). Serum PTH concentrations were higher in patients with high trabecular bone turnover ($p < 0.05$) although serum alkaline phosphatase and phosphorus values did not differ between groups. 25(OH)vitamin D levels were lower than 30 ng/mL (17) in 73% of patients and values were below 20 ng/mL (18) in 59% of subjects. Levels did not differ between groups. Similarly, IGF1 levels did not differ between groups.

Bone Variables According to Trabecular Bone Turnover Rate

Table 2 displays the trabecular and Table 3 displays the cortical bone parameters in patients with adynamic/normal trabecular bone turnover as compared to those with high trabecular bone turnover. By definition, trabecular bone formation rate and osteoid accumulation were higher in patients with high trabecular bone turnover than in those with normal/low trabecular bone turnover; however, parameters of trabecular bone volume did not differ between groups. External cortical eroded surface was higher in patients with high trabecular bone turnover than in patients with low trabecular bone turnover, although no other parameters of cortical bone differed between groups. Interestingly, osteonal osteoid surface (OS/BS) and cortical porosity were greater in the external cortex than in the internal cortex

in patients with high trabecular bone turnover ($p<0.05$), although no such difference was observed between the cortices in patients with normal/low trabecular bone turnover.

Relationship between Biochemical and Bone Parameters

Consistent with previous data (19), trabecular bone turnover was significantly correlated with both alkaline phosphatase and PTH levels ($r=0.67$, $p<0.01$ and $r=0.86$, $p<0.01$, respectively) but inversely related to serum calcium concentrations ($r=-0.55$, $p<0.01$). Static parameters of trabecular mineralization, as measured by osteoid volume (OV/BV), osteoid surface (OS/BS), and osteoid thickness (O.Th) were similarly correlated with alkaline phosphatase ($r=0.62$, $p<0.01$; $r=0.53$, $p<0.01$; and $r=0.70$, $p<0.01$, respectively) and PTH ($r=0.93$, $p<0.01$; $r=0.83$, $p<0.01$, and $r=0.85$, $p<0.01$, respectively) and inversely related to serum calcium concentration ($r=-0.67$, $p<0.01$; $r=-0.65$, $p<0.01$; and $r=-0.56$, $p<0.01$, respectively). By contrast, trabecular mineralization lag time was inversely related to both alkaline phosphatase and PTH concentrations ($r=-0.66$, $p<0.01$ and $r=-0.70$, $p<0.01$, respectively) while trabecular osteoid maturation time was not related to any biochemical variables.

In contrast to the strong traditional associations between trabecular bone and serum biochemical values, cortical bone parameters correlated less strongly with biochemical markers. Internal cortical osteonal bone formation rate was directly related to alkaline phosphatase ($r=0.45$, $p<0.05$) and inversely related to IGF-1 values ($r=-0.55$, $p<0.01$) and internal cortical porosity was also related to serum alkaline phosphatase levels ($r=0.57$, $p<0.01$). A similar relationship was not found between external cortical bone formation rate and parameters of bone turnover and porosity; however, both external and internal cortical osteoid accumulation were directly related to alkaline phosphatase and PTH levels (external cortical osteoid surface with alkaline phosphatase: $r=0.60$, $P<0.01$ and with PTH: $r=0.63$, $p<0.01$; and internal cortical osteoid volume with alkaline phosphatase: $r=0.49$, $p<0.05$ and with PTH: $r=0.49$, $p<0.05$).

Relationship between Cortical and Trabecular Bone Parameters

Parameters of both external and internal cortical osteonal osteoid accumulation correlated with trabecular osteoid accumulation (Figures 1 and 2). The correlation coefficients for external cortical osteoid surface with trabecular OV/BV, OS/BS, and O.Th were $r=0.56$, $p<0.01$; $r=0.44$, $p<0.05$; and $r=0.49$, $p<0.05$ respectively and those for internal cortical osteoid volume with trabecular OV/BV, OS/BS, and O.Th were $r=0.50$, $p<0.05$; $r=0.52$, $p<0.05$; and $r=0.49$, $p<0.05$ respectively. These correlations were not driven by the one patient with a diagnosis of osteomalacia since the relationship between trabecular and cortical parameters did not change upon removal of this patient from the analysis. No relationship was found between trabecular and cortical bone formation rates; however, external (although not internal) cortical thickness was related to trabecular bone thickness ($r=0.44$, $p<0.05$).

Discussion

The current study is the first to evaluate cortical bone through histomorphometric analysis in a pediatric CKD population. In this group of dialysis patients, internal cortical osteonal bone formation rate and porosity were related to circulating alkaline phosphatase values and both external and internal cortical osteoid accumulation were directly related to trabecular bone osteoid accumulation, alkaline phosphatase and PTH levels. Stronger relationships were observed between biochemical variables and trabecular parameters of both osteoid accumulation and bone turnover. Differences in cortical bone porosity and osteoid surface were observed between the internal and external cortices in patients with high trabecular bone turnover, although not in those with low trabecular bone turnover.

As cortical bone is the major determinant of bone strength, architectural changes in this skeletal compartment could account for the greatly increased fracture risk in the CKD population. In post-menopausal women with normal kidney function, an increased risk of bone fragility and fractures has been correlated with cortical porosity and thinning (20, 21). Cortical bone biopsy analysis in CKD patients is scarce; however, data by Malluche et al. have suggested that high trabecular bone turnover in patients treated with chronic dialysis is associated with increased cortical porosity and greater degree of cortical erosion (4), features similar to those found in individuals with primary hyperparathyroidism (22, 23). The current study confirmed a greater degree of erosion present in cortical bone in children with secondary hyperparathyroidism than in those with normal or low trabecular bone turnover. Interestingly, however, this difference was apparent primarily in external, and not internal, cortical bone. Similarly, differences in osteoid accumulation were apparent between the external and internal compartments in patients with high trabecular bone turnover, with greater osteoid accumulation consistently apparent in the external cortex. These findings suggest that one cortex—namely, the external cortex—may be more metabolically active and/or sensitive to PTH than the other, a finding which is supported by the stronger relationship between biochemical and trabecular bone parameters than between biochemical and cortical bone and the lack of correlation between cortical and trabecular bone formation rate.

Rauch et al. have previously described that osteon number may be greater in the external than in the internal cortex, and that bone formation rate and relative percentage of active osteons may be greater in the internal than external cortex (13). These findings are consistent with the current study demonstrating differences in bone turnover between the two cortices. However, the current finding that the external cortex appears more active than the internal cortex in patients with secondary hyperparathyroidism appears to differ than normal development and suggests a potential cause of bone fragility in these patients. The cortical bone evaluated in the current study was obtained from iliac crest rather than from long bone, complicating the interpretation of any comparison with pathology affecting the appendicular skeleton; however, it is important to note that both iliac crest and the long bones are derived from endochondral bone formation; thus, the processes by which both are formed are similar. Since the subjects included in the study were all either pre-pubertal or pubertal, differences between internal and external cortices may be unique to growing children and may reflect the asymmetric process of modeling in the pediatric population.

Furthermore, although weight-bearing biomechanics play a large role in the asymmetric development of deformities in patients with high turnover renal osteodystrophy, differences in porosity and bone turnover between internal and external characteristics may play an additional role. How current therapies, including phosphate binders, active vitamin D sterols, and growth hormone affect these cortical parameters remains unknown but could have implications for bone growth and strength in the pediatric population.

In conclusion, the current study demonstrates that secondary hyperparathyroidism is associated with increased external cortical, relative to internal cortical, osteonal activity in pediatric dialysis patients. Although its clinical consequences are incompletely defined, further studies of the prevalence of cortical bone abnormalities, their response to therapy, and their correlation with clinical outcomes are warranted given the high rates of fractures, bone deformities, and disability rates of young people affected with CKD (3).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Seeman E. The structural and biomechanical basis of the gain and loss of bone strength in women and men. *Endocrinol Metab Clin North Am.* 2003; 32:25–38. [PubMed: 12699291]
2. Moe S, Drueke T, Cunningham J, Goodman W, Martin K, Olgaard K, Ot S, Sprague S, Lameire N, Eknoyan G. Definition, evaluation, and classification of renal osteodystrophy: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int.* 2006; 69:1945–1953. [PubMed: 16641930]
3. Groothoff JW, Offringa M, Van Eck-Smi BL, Gruppen MP, Van De Kar NJ, Wolff ED, Lilien MR, Davin JC, Heymans HS, Dekker FW. Severe bone disease and low bone mineral density after juvenile renal failure. *Kidney Int.* 2003; 63:266–275. [PubMed: 12472792]
4. Malluche HH, Mawad HW, Monier-Faugere MC. Renal osteodystrophy in the first decade of the new millennium: analysis of 630 bone biopsies in black and white patients. *J Bone Miner Res.* 2011; 26:1368–1376. [PubMed: 21611975]
5. Jamal SA, Gilbert J, Gordon C, Baue DC. Cortical pQCT measures are associated with fractures in dialysis patients. *J Bone Miner Res.* 2006; 21:543–548. [PubMed: 16598374]
6. Nickolas TL, Stein E, Cohen A, Thomas V, Staron RB, McMahon DJ, Leonard MB, Shane E. Bone mass and microarchitecture in CKD patients with fracture. *J Am Soc Nephrol.* 2010; 21:1371–1380. [PubMed: 20395370]
7. Wetzsteon RJ, Kalkwarf HJ, Shults J, Zemel BS, Foster BJ, Griffin L, Strife CF, Foerster DL, Jean-Pierre DK, Leonard MB. Volumetric bone mineral density and bone structure in childhood chronic kidney disease. *J Bone Miner Res.* 2011; 26:2235–2244. [PubMed: 21590737]
8. Ruth EM, Weber LT, Schoenau E, Wunsch R, Seibel MJ, Feneberg R, Mehls O, Tonshoff B. Analysis of the functional muscle-bone unit of the forearm in pediatric renal transplant recipients. *Kidney Int.* 2004; 66:1694–1706. [PubMed: 15458468]

9. Bacchetta J, Boutroy S, Juillard L, Vilayphiou N, Guebre-Egziabher F, Pelletier S, Delmas PD, Fouque D. Bone imaging and chronic kidney disease: will high-resolution peripheral tomography improve bone evaluation and therapeutic management? *J Ren Nut.* 2009; 19:44–49.
10. Bacchetta J, Boutroy S, Vilayphiou N, Ranchin B, Fouque-Aubert A, Basmaison O, Cochat P. Bone assessment in children with chronic kidney disease: data from two new bone imaging techniques in a single-center pilot study. *Pediatr Nephrol.* 2011; 26:587–595. [PubMed: 21246220]
11. Wesseling-Perry K, Pereira RC, Sahney S, Gales B, Wang HJ, Elashoff R, Juppner H, Salusky IB. Calcitriol and doxercalciferol are equivalent in controlling bone turnover, suppressing parathyroid hormone, and increasing fibroblast growth factor-23 in secondary hyperparathyroidism. *Kidney Int.* 2011; 79:112–119. [PubMed: 20861820]
12. Hernandez JD, Wesseling K, Pereira R, Gale B, Harrison R, Salusky IB. Technical approach to iliac crest biopsy. *Clin J Am Soc Nephrol.* 2008; 3(Suppl 3):S164–169. [PubMed: 18988702]
13. Rauch F, Travers R, Glorieux FH. Intracortical remodeling during human bone development--a histomorphometric study. *Bone.* 2007; 40:274–280. [PubMed: 17049943]
14. Schnitzler CM, Mesquita JM, Pettifor JM. Cortical bone development in black and white South African children: iliac crest histomorphometry. *Bone.* 2009; 44:603–611. [PubMed: 19136082]
15. Parfitt AM, Drezner MK, Glorieux FH, Kanis JA, Malluche H, Meunier PJ, Ott SM, Recker RR. Bone histomorphometry: standardization of nomenclature, symbols, and units. Report of the ASBMR Histomorphometry Nomenclature Committee. *J Bone Miner Res.* 1987; 2:595–610. [PubMed: 3455637]
16. Dempster DW, Compston JE, Drezner MK, Glorieux FH, Kanis JA, Malluche H, Meunier PJ, Ott SM, Recker RR, Parfitt AM. Standardized nomenclature, symbols, and units for bone histomorphometry: a 2012 update of the report of the ASBMR Histomorphometry Nomenclature Committee. *J Bone Miner Res.* 2013; 28:2–17. [PubMed: 23197339]
17. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis.* 2003; 42:S1–201. [PubMed: 14520607]
18. Dietary reference intakes for calcium and vitamin D. 2011. <http://www.iom.edu/Reports/2010/Dietary-Reference-Intakes-for-calcium-and-vitamin-D.aspx>
19. Bakkaloglu SA, Wesseling-Perry K, Pereira RC, Gales B, Wang HJ, Elashoff RM, Salusky IB. Value of the new bone classification system in pediatric renal osteodystrophy. *Clin J Am Soc Nephrol.* 2010; 5:1860–1866. [PubMed: 20634327]
20. Zebaze RM, Ghasem-Zadeh A, Bohte A, Iuliano-Burns S, Mirams M, Price RI, Mackie EJ, Seeman E. Intracortical remodelling and porosity in the distal radius and post-mortem femurs of women: a cross-sectional study. *Lancet.* 2010; 375:1729–1736. [PubMed: 20472174]
21. Sornay-Rendu E, Boutroy S, Munoz F, Bouxsein ML. Cortical and trabecular architecture are altered in postmenopausal women with fractures. *Osteoporos Int.* 2009; 20:1291–1297. [PubMed: 19590838]
22. Vu TD, Wang XF, Wang Q, Cusano NE, Irani D, Silva BC, Ghasem-Zadeh A, Udesky J, Romano ME, Zebaze R, Jerums G, Boutroy S, Bilezikian JP, Seeman E. New insights into the effects of primary hyperparathyroidism on the cortical and trabecular compartments of bone. *Bone.* 2013; 55:57–63. [PubMed: 23541782]
23. Stein EM, Silva BC, Boutroy S, Zhou B, Wang J, Udesky J, Zhang C, McMahon DJ, Romano M, Dworakowski E, Costa AG, Cusano N, Irani D, Cremers S, Shane E, Guo XE, Bilezikian JP. Primary hyperparathyroidism is associated with abnormal cortical and trabecular microstructure and reduced bone stiffness in postmenopausal women. *J Bone Miner Res.* 2013; 28:1029–1040. [PubMed: 23225022]

Figure 1.

Relationship between trabecular osteoid volume and external cortical (EC) osteonal osteoid volume. The Pearson correlation coefficient and p value are displayed.

Figure 2.

Relationship between trabecular osteoid volume and internal cortical (IC) osteonal osteoid volume. The Pearson correlation coefficient and p value are displayed.

Table 1

Demographic data and biochemical parameters in patients with high versus low trabecular bone turnover

	Low Turnover (n=10)	High Turnover (n=12)
Demographics		
Age	8.8 ± 1.3	11.9 ± 1.5
Gender (M/F)	7/3	3/9 *
Tanner Stage (n(%))		
0		1 (8%)
1	6 (60%)	5 (42%)
2	3 (30%)	1 (8%)
3	1 (10%)	4 (33%)
4		1 (8%)
Ethnicity n (%)		
White	4 (40%)	2 (17%)
Black		1 (8%)
Asian	1 (10%)	
Hispanic	5 (50%)	9 (75%)
Height Z Score (SDS)	-2.29 ± 0.38	-1.95 ± 0.33
Weight Z Score (SDS)	-1.52 ± 0.31	-1.55 ± 0.27
Calcium (mg/dl)	10.0 ± 0.2	9.0 ± 0.3 *
Phosphorus (mg/dl)	5.4 ± 0.6	5.2 ± 0.3
Alkaline Phosphatase (IU/dl)	271 ± 56	469 ± 80
PTH (pg/ml)	122 (87, 158)	554 (433, 937) *
25(OH)vitamin D (ng/ml)	12.1 ± 10.2	28.3 ± 10.6
IGF1	226 ± 37	334 ± 65

*
p<0.05 between patients with high and low bone turnover

Table 2

Trabecular bone parameters in patients with high versus low bone turnover

	Low Turnover (n=10)	High Turnover (n=12)	Normal Range
BV/TV (%)	23.3 ± 1.4	25.1 ± 1.7	8.9 – 34.4
Tb.Th (µm)	137 ± 9	149 ± 8	91 – 175
Tb.Sp (µm)	440 ± 23	514 ± 73	351 – 737
Tb.N (#/mm ²)	1.69 ± 0.09	1.71 ± 0.11	1.1 – 2.2
OV/BV (%)	6.2 ± 1.7	12.9 ± 1.8 *	0.2 – 5.8
OS/BS (%)	34.7 ± 4.8	57.3 ± 3.8 *	4.3 – 37.0
O.Th (µm)	10.9 ± 1.1	15.9 ± 1.3 *	2.0 – 13.2
OMT (d) [#]	10.0 (9.0, 14.0)	11.0 (10.0, 12.0)	1.2 – 11.5
MLT (d) [#]	99 (69, 112)	31 (24, 44) *	2.3 – 63.8
BFR/BS (µm ³ /mm ² /yr) [#]	15.0 (9.2, 16.8)	98.9 (67.3, 175.8) *	8.0 – 73.4
ES/BS (%) [#]	0.7 (0.6, 1.3)	1.0 (0.6, 2.0)	0.5 – 4.3

* p<0.05 between patients with high and low bone turnover

[#] median (IQ range) displayed due to skewed distribution

Table 3

External and internal cortical bone parameters in patients with high versus low bone turnover

	External Cortex	Internal Cortex
Low trabecular bone turnover (n=10)		
Channel Width (μm) **	56.3 $\pm$ 8.1	70.1 $\pm$ 9.8
Cortical Thickness (μm)	338 $\pm$ 31	335 $\pm$ 39
Porosity (%)	7.6 $\pm$ 1.5	7.8 $\pm$ 2.0
Osteonal OV/TV (%)	1.14 $\pm$ 0.35	0.67 $\pm$ 0.19
Osteonal OS/BS (%)	39.6 $\pm$ 6.6	30.0 $\pm$ 5.7
Osteonal BFR/BS ($\mu\text{m}^3/\text{mm}^2/\text{yr}$) #	70.0 (5.8, 103.6)	45.6 (20.5, 81.3)
Osteonal ES/BS (%) #	1.4 (0, 9.9)	6.9 (2.5, 20.1)
High trabecular bone turnover (n=12)		
Channel Width (μm)	66.6 $\pm$ 9.8	53.9 $\pm$ 8.2
Cortical Thickness (μm)	378 $\pm$ 51	344 $\pm$ 46
Porosity (%)	11.0 $\pm$ 1.6	7.8 $\pm$ 1.7
Osteonal OV/TV (%)	1.77 $\pm$ 0.42	2.54 $\pm$ 1.17
Osteonal OS/BS (%)	47.5 $\pm$ 3.1	43.0 $\pm$ 6.0
Osteonal BFR/BS ($\mu\text{m}^3/\text{mm}^2/\text{yr}$) #	53.5 (18.4, 132.1)	54.2 (0, 85.7)
Osteonal ES/BS (%) #	6.7 (4.5, 17.6) *	11.0 (2.8, 15.0)

median (IQ range) displayed due to skewed distribution

* p<0.05 between patients with high and low bone turnover

p<0.05 between external and internal cortical bone parameters

** refers to osteonal channel diameter