**Bone microarchitecture, volumetric or areal bone mineral density for discrimination of vertebral deformity in adults: a cross-sectional study**

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**Conflict of Interest:** All authors declare that they have no conflicts of interest.

**Abstract**

*Introduction/Background:* Both areal bone mineral density (aBMD) and bone microarchitecture have been associated with vertebral deformity (VD), but there are limited data on the utility of bone microarchitecture measures in combination with aBMD in discriminating VD. This study aimed to describe whether radial bone microarchitecture measures alone or in combinations with radial volumetric bone mineral density (vBMD) or spine aBMD can improve discrimination of VD in adults. *Methods:* Data on 196 subjects (mean age (standard deviation, SD) =72 (7) years, female 46%) were utilized. VD of T4-L4 and spine aBMD were measured using dual-energy X-ray absorptiometry. VD was defined if anterior to posterior height ratio (Ha/Hp) was more than 3-SD, 4-SD below, or >25% decrease compared with the sex-matched normal means. Bone microarchitecture parameters at distal radius were collected using high-resolution peripheral computed tomography (HRpQCT) and analyzed using StrAx. *Results:* The strongest associations were seen for the cortical thickness (odds ratios (ORs): 2.63/SD decrease for 25% and 2.38/SD decrease for 3-SD criterion) and compact cortical area (OR: 3.33/SD decrease for 4-SD criterion). The area under the receiver operating characteristic curve (AUC) for spine aBMD for VD was 0.594, 0.597 and 0.634 for 25%, 3-SD and 4-SD criteria, respectively (all P<0.05). Compact cortical area, cortical thickness and compact cortical thickness alone had the largest AUCs for VD (0.680-0.685 for 25% criterion, 0.659-0.674 for 3-SD criterion and 0.699-0.707 for 4-SD criterion). Adding spine aBMD or radial volumetric bone mineral density (vBMD) to each cortical measure did not improve VD discrimination (∆ AUC 0.8% to 2.1%). *Conclusions:* Cortical measures had the best utility for discriminating VD when used alone. Adding either spine aBMD or radial vBMD did not improve the utility of cortical measures.

**Keywords:** Dual-energy X-ray absorptiometry; High-resolution peripheral quantitative computed tomography; Vertebral deformity; Discrimination;

**Introduction**

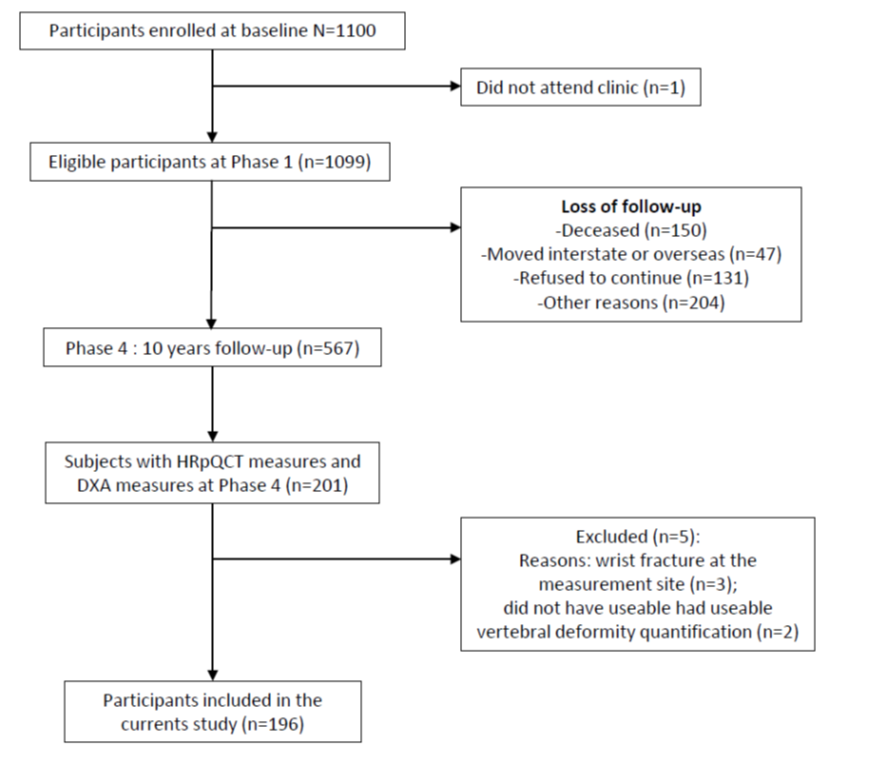
Osteoporotic fractures are a major public health problem (1). The vertebral deformity (VD) is mainly attributable to osteoporosis (2). The spine is the most frequent site for fracture even though a large proportion of spine fractures are asymptomatic (3, 4). Vertebral fractures are under-diagnosed both clinically and radiologically (4, 5), as the diagnosis must be confirmed with a spinal imaging study irrespective of medical history and symptoms (3). VD have a prevalence of 30-50% in those aged over 80 years, and lead to an increased risk of subsequent fractures (6). There is no consensus “gold standard” for diagnosing VD. The most widely used Genant semiquantitative assessment (7), requires a highly experienced radiologist and has a poor test retest reliability (4). Some other methods include 3-standard deviation (SD) and 4-SD reduction criteria the latter of which correlates best with clinically diagnosed spine fractures, significant back pain, disability and adverse outcomes (8, 9).

Areal bone mineral density (aBMD) derived from dual-energy X-ray absorptiometry (DXA) is widely used to predict osteoporotic fractures, but a weak correlation with VD is seen (10). This could be attributed to the presence of spinal degenerative disease, spinal osteophytosis and calcification which may falsely elevate spinal aBMD and thus lessen the association between aBMD and VD (11, 12). Of note, vertebral bone strength is determined by both bone mass, bone microarchitecture, and bone matrix properties (13). High-resolution peripheral quantitative computed tomography (HRpQCT) can provide more information about bone strength including cortical and trabecular bone microarchitecture and volumetric bone mineral density (vBMD), which have been shown to be associated with VD (14). Previous cross-sectional study has suggested that cortical and trabecular microarchitecture are associated with VD in postmenopausal women (15). A large international cohort study indicated that bone microarchitecture could improve the prediction of major osteoporotic fractures independent of aBMD (16), but did not have data for spine fractures. In addition, it is unclear whether vBMD is comparable or superior to aBMD in discriminating vertebrae with and without VD, or whether their combination adds more information as has been reported for DXA and heel ultrasound (17).

Therefore, we used data from Tasmania Older Adult Cohort Study (TasOAC) to describe whether bone microarchitecture measures alone or in combination with aBMD improves the discrimination of VD in adults.

**Material and Methods**

**Participants**

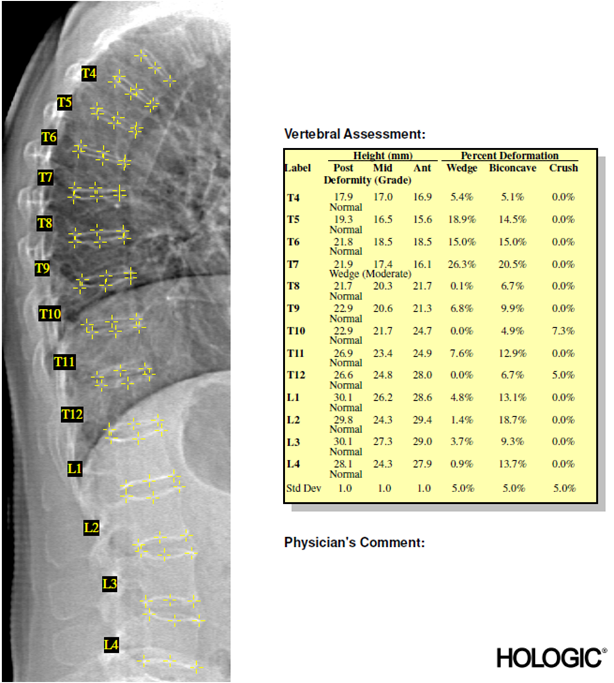
The TasOAC study is a prospective, population-based cohort study, for which adults aged between 50 and 79 years in 2002 were selected from the electoral roll in Southern Tasmania (population 229,000) using sex-stratified random sampling (18). The study population was 98% white or of Caucasian ancestry. A flow-chart of study participants is given in Figure 1. The overall response rate was 57%. Participants were excluded if they were institutionalized or had contraindications to magnetic resonance imaging (MRI). Baseline data (phase 1) were collected between February 2002 and September 2004 in 1099 participants. The latest follow-up was conducted among 567 participants between 2013 and 2014 (phase 4). The current study consisted of a convenience consecutive sample of 196 participants who had useable VD quantification, aBMD measurements and bone microarchitecture parameters measured at phase 4. The study conducted in this manuscript is in compliance with the Helsinki Declaration and was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee, and written informed consent was obtained from all participants.

**Figure 1**. Flow-chart of study participants

**Vertebral deformity quantification and areal bone mineral density (aBMD)**

Lateral views of the thoracic (T) and lumbar spine (L) were taken from DXA (Discovery W, Hologic, Bedford MA, USA). Two readers assessed the vertebral DXA scans. The reader assessed all vertebral scan readings independently and was blinded to participants’ data. Each vertebral scan was assessed by only one reader, who has a good reassessment accuracy. Quantitative vertebral morphometry was performed using the Hologic APEX software version 4.0.2. This was done by placing markers on all four corners of the vertebrae and two in the middle of each vertebral endplate (Figure 2). These markers were stored as co-ordinates which were used to obtain as anterior (Ha), middle (Hm), and posterior (Hp) height for each vertebral body from T4-L4. We assessed anterior wedging (Ha/Hp), which is the most common type of VD. We defined deformity in three ways: either a 3-SD or 4-SD reduction of anterior to posterior height (Ha/Hp) ratio in comparison with sex-matched normal values, or a decrease of more than 25% in the Ha/Hp. AS performed baseline data evaluation of samples. Normal values were derived as mean (SD) of TasOAC baseline data from 328 women (mean age 61.3 years) and 245 men (mean age 62.3 years), who were considered free of deformity (Ha/Hp > 0.8).

The same DXA scanner was used for all participants to measure aBMD at the lumbar spine and total hip during 2013-2014. DXA scans were performed by a radiographer (KS). The longitudinal coefficient of variations for our machine using daily measurements of a spine phantom were 0.48% for the whole duration of this study, which has been reported previously (19, 20). Detailed descriptions of protocol for the phantom scan and calibration are shown in Supplementary 1.



**Figure 2:** Example spine scan of a lateral view showing placement of markers in all four corners with wedge vertebral deformity at T7.

**Bone microarchitecture at the distal radius**

HRpQCT (Xtreme CT, Scanco Medical, Bruttisellen, Switzerland) was used to scan the dominant distal radius. HRpQCT scans were performed by a radiographer (KS). The region of interest of 9.02mm (110 CT slices) was at the standardized distance of 9.5 mm from the manually positioned reference line at the end plate of the distal radius. Acquired images were analyzed using StrAx1.0 (StraxCorp, Melbourne, Australia). StrAx1.0 analysis is limited to the proximal 49 slices where cortices at the thickest allowing a more robust quantification of porosity (21). The compact‐appearing cortical areas, outer and inner transitional zones, and trabecular compartments were segmented. Total, cortical, and trabecular cross-sectional area of selected slices, vBMD, porosity within the total cortex and its compartments, cortical thickness (Ct.Th), trabecular bone volume fraction (Tb.BV/TV), number (Tb.N), thickness (Tb.Th) and separation (Tb.Sp), and matrix mineral density were quantified. The reproducibility errors for segmentations and quantification of porosity expressed as root mean square coefficients of variation ranged from 0.54% to 3.98% and were <1.5% for vBMD (22). Detailed descriptions of HRpQCT protocol and segmentation algorithm are described in Supplementary 1.

**Anthropometry and other factors**

Age, sex, former and current smoking status, anti-osteoporotic medication (including calcium, vitamin D and bisphosphonates) and previous fractures were recorded in a questionnaire during an interview. Osteoporosis is defined by T-scores ≤ -2.5 at the hip or lumbar spine, according to the World Health Organization criteria (23). Standing height was measured to the nearest 0.1cm (bare feet) using a stadiometer. Body weight was measured to the nearest 0.1 kg using calibrated electric scales (without shoes, socks, and bulky clothing). Body mass index (BMI) was calculated as weight/height2 (kg/m2).

**Statistical analysis**

The Shapiro-Wilk test and Q-Q plot were used to assess the normality of data distribution. The normally distributed data were presented as means with SD, otherwise were presented as median with interquartile range (IQR). Participants’ general characteristics, DXA and HRpQCT bone parameters are presented as mean (SD) or number (%). Students’ t-tests and chi-square tests were used to compare differences in means and proportions between participants with and without VD. Odds ratio (OR) for associations between bone measures and prevalence of VD (expressed as OR per SD decrease of each bone measures) were computed using logistic regressions with adjustment for age, sex, and weight. Receiver operating characteristic curves were used to estimate and compare the utility of bone microarchitecture for discriminating VD (using spine aBMD as the referent). An area under the receiver operating characteristic curve (AUC) of 0.50 indicates a discriminative utility no better than chance, and an AUC < 0.6 indicates poor, 0.6 to 0.8 moderate, and > 0.8 excellent discriminative utility, respectively (24). Additionally, we compared the discriminative utility of models including the HRpQCT measures with the largest AUC plus radial vBMD (total vBMD, cortical vBMD and compact cortical vBMD) or spine aBMD with models that included the best HRpQCT measure. A two-tailed p value <0.05 was considered as statistically significant. All analyses were performed using Stata V.15.0 (StataCorp LP).

**Results**

Of 201 participants studied at phase 4, three had a wrist fracture at the measurement site and another 2 did not have vertebral DXA scans. Therefore, this analysis included 196 adults (91 women and 105 men) with a mean age of 72 (6) years (age range 62 to 89). Table 1 shows characteristics of study participants with and without VD by the 25% criterion. Participants with at least one VD had lower spine and hip aBMD and radial vBMD, smaller and thinner cortical bone and a higher proportion with cortical porosity. The prevalence of VD was 35% (69/196) by the 25% criterion, 38% (74/196) by the 3-SD criterion and 21% (42/196) by the 4-SD criterion. The proportion of participants who had more than one VD was 12% (23/196) by 25% criterion, 15% (30/196) by 3-SD criterion, and 6% (11/196) by 4-SD criterion. The proportion of participants who had compression and biconcave deformity were 1% (2/196) and 3% (6/196) by 25% criterion, respectively.

Table 2 provides odds ratio (OR) for the prevalence of VD per 1 SD decrease in spine aBMD and bone microarchitecture measures, adjusting for age, sex and weight. Lower cortical geometry, cortical vBMD and cortical porosity were significantly associated with higher prevalence of VD by all criteria. The strongest associations were seen for cortical thickness (25% and 3-SD criteria) and compact cortical area (4-SD criterion). These three strongest associations remained significant after additional adjustment for spine aBMD. Additionally, radial total vBMD and cortical vBMD had similar associations to spine aBMD with the prevalence of VD (25% and 3-SD criteria), but these associations were no longer significant after further adjustment for spine aBMD.

Table 3 shows the overall AUCs for spine aBMD and each HRpQCT measures alone in discriminating VD. Compact cortical area, cortical thickness and compact cortical thickness had the numerically largest AUC by all criteria, and the difference in AUC for these variables and for spine aBMD alone approached but did not reach statistical significance (Table 3). Additionally, AUCs for the radial vBMD (total vBMD, cortical vBMD and compact cortical vBMD) were similar to those for spine aBMD for all criteria (Table 3). Analyses stratified by sex are shown in Table 5 and 6 (Supplementary 3 and 4).

After combining spine aBMD with HRpQCT measures, AUCs for the compact cortical area, cortical thickness and compact cortical thickness in discriminating VD were still the largest among combination models, and significantly larger than those for spine aBMD alone. However, AUCs for the combination of spine aBMD and each HRpQCT measures in discriminating VD showed little improvement compared to those for each HRpQCT measure alone (Table 3, and Table 4 in Supplementary 2) for HRpQCT measures alone and for each HRpQCT measure combined with spine aBMD respectively).

Lastly, we compared the discriminative utility of models including each cortical measure (compact cortical area, cortical thickness and compact cortical thickness) plus radial vBMD (total vBMD, cortical vBMD and compact cortical vBMD) or spine aBMD with models that included the cortical measures alone. There were no significant differences in AUCs for the combination of cortical measures with radial vBMD (total vBMD, cortical vBMD and compact cortical vBMD) and for the combination of cortical measures with spine aBMD in discriminating VD by all criteria (Figure 3-5 in Supplementary 5). Adding either radial vBMD (total vBMD, cortical vBMD and compact cortical vBMD) or spine aBMD to cortical measures did not improve AUCs for cortical measures by all VD criteria, compared with AUCs for cortical measures alone (Figure 3-5 in Supplementary 5).

**Discussion**

Overall, this study found that, out of HRpQCT and DXA measures, cortical bone geometry measures had the best (albeit moderate) utility for the discrimination of VD. Radial vBMD and spine aBMD alone had similar but weaker utility for discriminating VD. Importantly, adding either radial vBMD or spine aBMD to the cortical measures did not further improve discrimination of VD. These findings suggest that assessing HRpQCT alone might be more beneficial for discriminating VD than DXA measures and/or their combination.

Previous studies have reported that aBMD had reasonable predictive utility for vertebral fractures and vBMD had been considered a better parameter for quantifying bone loss (25, 26). Thus, we expected that radial vBMD might have a numerical advantage in discriminating VD than aBMD even given it was measuring bone mass at a peripheral site. However, this was not the case in our study in which radial vBMD and spine aBMD alone had similar utility for the discrimination of VD. This is consistent with a previous cross-sectional study among postmenopausal women, particularly for mild VD (AUCs for radial vBMD and spine aBMD were both 0.55 in VD) (15). The limitations of DXA could lead to artefactual changes in aBMD which disguise true bone density change and may lead to underestimation of fracture risk in older age (27, 28), especially at sites with significant bone area change. Therefore, spine aBMD is directly affected by the presence of spinal degenerative disease, spinal osteophytosis and calcification (11). vBMD is less likely confounded by bone area change than aBMD (29). However, spine vBMD can be measured by quantitative computed tomography (QCT) rather than HRpQCT. Additionally, radial vBMD measured by using HRpQCT could be used to evaluate the general bone loss, but less value for spine (30, 31).

Among HRpQCT and DXA measures, compact cortical area, cortical thickness and compact cortical thickness had the strongest associations with the prevalence of VD and the best utility in discriminating VD. Similar findings were also seen in postmenopausal women (15), suggesting that measurement of cortical thickness may enhance the prediction of vertebral fragility (32). These findings might be explained by the observation that the relative contribution of cortical bone to vertebral bone strength increases with age (32, 33).

It has been suggested that combining BMD with bone microarchitecture may improve the prediction of fracture (33, 34). To our knowledge, this is first study using cortical measures plus bone density variables to discriminate VD in adults. The combination of cortical measures and spine aBMD had better discrimination of VD compared to spine aBMD alone. Surprisingly, we did not find evidence to support that adding either radial vBMD or spine aBMD to cortical bone measures improved the utility in discriminating VD compared with the cortical measures alone.

This study has some limitations. First, our study design was cross-sectional thus we cannot comment about causal pathways. Secondly, our study only has HRpQCT parameters at the distal radius but not tibia. However, there is a significant correlation in bone microarchitecture between these two peripheral sites (35). Thirdly, relatively rare types of deformity such as biconcave deformities were not taken into account in this study. However, the proportion of participants who had compression and biconcave deformity were very low in our study (1% and 3%, respectively), suggesting that our results may not have been affected. Lastly, the response rate at baseline was 57%, which may bias the generalizability of results. However, there were no differences between those included in this study and the rest of the cohort, suggesting our results are likely to be generalizable to the original cohort.

In conclusion, cortical measures had the best utility in discriminating VD when used alone. Adding either spine aBMD or radial vBMD did not improve the utility of cortical measures.

**Disclosure**

The authors state that they have no conflicts of interest.

**Acknowledgement**

We would like to thank all participants and staff involved in this study. This work was supported by National Health and Medical Research Council (APP1045408) and NHMRC Early Career Fellowship (1070586).

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**Table 1.** Characteristics of participants with and without vertebral deformity defined by ≥25% anterior wedging

|  |  |  |  |
| --- | --- | --- | --- |
|  | Vertebral deformity present  (n= 69) | No vertebral deformity  (n= 127) | P-value |
| **Participants demographics** |  |  |  |
| Age (years) | 73 (7) | 72 (6) | 0.37 |
| Female, n (%) | 34 (49) | 57 (45) | 0.52 |
| Height (cm) | 165.5 (9.7) | 167.8 (8.7) | 0.09 |
| Weight (kg) | 76.5 (16.6) | 77.8 (13.3) | 0.51 |
| BMI (kg/m2) | 27.8 (4.7) | 27.6 (4.1) | 0.88 |
| Former smoking status, n (%) | 29 (42) | 40 (36) | 0.42 |
| Current smoking status, n (%) | 2 (3) | 8 (6) | 0.30 |
| Previous fractures, n (%) | 35 (51) | 70 (55) | 0.56 |
| Osteoporosis, n (%) | 4 (6) | 8 (6) | 0.89 |
| anti-osteoporotic medication, n (%) | 4 (6) | 6 (5) | 0.76 |
| **DXA** |  |  |  |
| Spine aBMD (g/cm2) | **0.99 (0.18)** | **1.05 (0.19)** | **<0.05** |
| Total hip aBMD (g/cm2) | **0.92 (0.15)** | **0.97 (0.14)** | **<0.05** |
| Spine T-scores | **-0.70 (1.6)** | **-0.08 (1.7)** | **<0.05** |
| Total hip T-scores | **-0.58 (0.94)** | **-0.22 (0.97)** | **<0.05** |
| **HRpQCT** |  |  |  |
| **Distal radius** |  |  |  |
| Tt.Ar (mm2) | 284.91 (69.77) | 288.53 (73.87) | 0.73 |
| Ct.Ar (mm2) | **102.12 (22.11)** | **109.74 (24.35)** | **<0.05** |
| CCt.Ar (mm2) | **35.98 (12.87)** | **41.61 (11.93)** | **<0.01** |
| OTZ.Ar (mm2) | 29.92 (6.41) | 31.64 (7.03) | 0.09 |
| ITZ.Ar (mm2) | 36.22 (8.28) | 36.48 (9.20) | 0.82 |
| Tb.Ar (mm2) | 182.79 (53.57) | 178.78 (53.81) | 0.62 |
| Ct.Th (mm) | **1.85 (0.29)** | **2.02 (0.30)** | **<0.001** |
| CCt.Th (mm) | **0.61 (0.21)** | **0.72 (0.18)** | **<0.001** |
| OTZ.Th (mm) | **0.54 (0.09)** | **0.59 (0.10)** | **<0.01** |
| ITZ.Th (mm) | 0.70 (0.09) | 0.71 (0.11) | 0.31 |
| **vBMD** |  |  |  |
| Tt.vBMD (mg HA/cm3) | **351.60 (84.14)** | **380.76 (76.75)** | **<0.05** |
| Ct.vBMD (mg HA/cm3) | **712.29 (98.71)** | **745.42 (79.42)** | **<0.05** |
| CCt.vBMD (mg HA/cm3) | 914.31 (94.08) | 934.87 (77.60) | 0.10 |
| OTZ.vBMD (mg HA/cm3) | **882.40 (80.89)** | **907.24 (65.21)** | **<0.05** |
| ITZ.vBMD (mg HA/cm3) | 376.31 (59.54) | 391.33 (57.66) | 0.07 |
| Tb.vBMD (mg HA/cm3) | 140.80 (58.31) | 149.08 (56.72) | 0.30 |
| **Microarchitecture** |  |  |  |
| Ct.Po (%) | **56.14 (7.70)** | **53.61 (6.21)** | **<0.05** |
| CCt.Po (%) | 40.49 (7.78) | 38.79 (6.41) | 0.10 |
| OTZ.Po (%) | **43.08 (6.61)** | **41.07 (5.34)** | **<0.05** |
| ITZ.Po (%) | 82.19 (3.99) | 81.27 (3.91) | 0.10 |
| Tb.N (mm-1) | 3.18 (0.61) | 3.33 (0.56) | 0.07 |
| Tb.Th (mm) | 0.19 (0.01) | 0.19 (0.01) | 0.86 |
| Tb.Conn (mm-3) | 0.79 (0.24) | 0.80 (0.25) | 0.66 |
| Tb.Sp (mm) | 1.13 (0.29) | 1.10 (0.26) | 0.41 |
| Tb.BVTV (%) | 5.03 (2.45) | 5.26 (2.69) | 0.52 |
| Matrix mineral density (%) | 67.65 (0.96) | 67.84 (0.83) | 0.16 |

All values are mean (standard deviation) unless otherwise stated. Bold values denote statistically significant difference between the two groups.

Abbreviations: aBMD: areal bone mineral density. Tt.Ar: total cross-sectional area; Ct.Ar: total cortical area; CCt.Ar: compact cortical area; OTZ.Ar: outer transitional zone bone area; ITZ.Ar: inner transitional zone bone area; Tb.Ar: trabecular area; Ct.Th: total cortical thickness; CCt.Th: compact cortical thickness; OTZ.Th: outer transitional zone bone thickness; ITZ.Th: inner transitional zone bone thickness; Tt.vBMD: total volumetric bone density; Ct.vBMD: total cortical volumetric bone density; CCt.vBMD: compact cortical volumetric bone density; OTZ.vBMD: outer transitional zone volumetric bone density; ITZ.vBMD: inner transitional zone volumetric bone density; Tb.vBMD: trabecular volumetric bone density; Ct.Po: cortical porosity; CCt.Po: compact cortical porosity; OTZ.Po: outer transitional zone bone porosity; ITZ.Po: inner transitional zone bone porosity; Tb.N: trabecular number; Tb.Th: trabecular thickness; Tb.Conn: trabecular connectivity; Tb.Sp: trabecular separation; Tb.BV/TV: trabecular bone volume fraction; HA: hydroxyapatite.

**Table 2****.** Associations between standardized bone measures and the prevalence of vertebral deformity

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 25% criterion | |  | 3-SD criterion | |  | 4-SD criterion | |
| OR (95% CI)a  n=196 | OR (95% CI)b  n=196 | | OR (95% CI)a  n=196 | OR (95% CI)b n=196 |  | OR (95% CI)a  n=196 | OR (95% CI)b  n=196 |
| Spine aBMD | **1.45 (1.01, 2.04)** | NA | | **1.47 (1.03, 2.08)** | NA | | **1.79 (1.15, 2.78)** | NA |
|  |  |  | |  |  | |  |  |
| **HRpQCT** |  |  | |  |  | |  |  |
| Tt.Ar | 0.94 (0.58, 1.51) | 0.90 (0.56, 1.47) | | 0.81 (0.50, 1.30) | 0.76 (0.47, 1.23) | | 1.14 (0.65, 1.96) | 1.06 (0.61, 1.89) |
| Ct.Ar | **2.38 (1.28, 4.35)** | **2.08 (1.10, 4.00)** | | **1.92 (1.08, 3.45)** | 1.64 (0.89, 3.03) | | **3.03 (1.43, 6.25)** | **2.38 (1.10, 5.26)** |
| CCt.Ar | **2.44 (1.47, 4.00)** | **2.27 (1.32, 3.85)** | | **2.22 (1.35, 3.57)** | **2.00 (1.19, 3.33)** | | **3.33 (1.79, 6.25)** | **2.86 (1.49, 5.56)** |
| OTZ.Ar | 1.67 (0.98, 2.86) | 1.56 (0.91, 2.70) | | 1.56 (0.93, 2.63) | 1.45 (0.85, 2.44) | | 1.79 (0.96, 3.33) | 1.61 (0.85, 3.03) |
| ITZ.Ar | 0.97 (0.67, 1.41) | 0.94 (0.65, 1.39) | | 0.88 (0.61, 1.27) | 0.85 (0.58, 1.23) | | 0.94 (0.61, 1.45) | 0.90 (0.58, 1.41) |
| Tb.Ar | 0.78 (0.51, 1.16) | 0.78 (0.51, 1.18) | | 0.69 (0.46, 1.04) | 0.69 (0.45, 1.04) | | 0.89 (0.56, 1.43) | 0.89 (0.56, 1.45) |
| Ct.Th | **2.63 (1.61, 4.17)** | **2.44 (1.49, 4.00)** | | **2.38 (1.49, 3.70)** | **2.17 (1.37, 3.57)** | | **2.38 (1.39, 4.00)** | **2.04 (1.19, 3.57)** |
| CCt.Th | **2.08 (1.39, 3.13)** | **1.96 (1.28, 3.03)** | | **2.04 (1.35, 3.03)** | **1.89 (1.25, 2.86)** | | **2.38 (1.45, 4.00)** | **2.08 (1.25, 3.57)** |
| OTZ.Th | **1.96 (1.28, 2.94)** | **1.89 (1.25, 2.86)** | | **1.92 (1.28, 2.94)** | **1.89 (1.25, 2.86)** | | **1.69 (1.06, 2.70)** | **1.59 (1.02, 2.50)** |
| ITZ.Th | 1.16 (0.84, 1.61) | 1.19 (0.85, 1.64) | | 1.05 (0.76, 1.45) | 1.06 (0.77, 1.47) | | 0.98 (0.68, 1.43) | 1.00 (0.68, 1.45) |
| **vBMD** |  |  | |  |  | |  |  |
| Tt.vBMD | **1.45 (1.04, 2.00)** | 1.32 (0.92, 1.89) | | **1.56 (1.12, 2.17)** | 1.43 (1.00, 2.04) | | **1.54 (1.04, 2.27)** | 1.28 (0.84, 1.96) |
| Ct.vBMD | **1.45 (1.04, 2.00)** | 1.33 (0.93, 1.89) | | **1.47 (1.06, 2.04)** | 1.33 (0.95, 1.89) | | **1.54 (1.04, 2.22)** | 1.32 (0.87, 1.96) |
| CCt.vBMD | 1.25 (0.91, 1.72) | 1.14 (0.81, 1.59) | | 1.20 (0.88, 1.67) | 1.09 (0.78, 1.52) | | 1.23 (0.86, 1.79) | 1.06 (0.72, 1.59) |
| OTZ.vBMD | **1.39 (1.01, 1.92)** | 1.27 (0.89, 1.82) | | 1.35 (0.98, 1.89) | 1.22 (0.86, 1.72) | | 1.41 (0.97, 2.04) | 1.20 (0.80, 1.82) |
| ITZ.vBMD | 1.32 (0.94, 1.82) | 1.15 (0.79, 1.64) | | **1.45 (1.04, 2.00)** | 1.28 (0.89, 1.85) | | 1.37 (0.93, 2.00) | 1.09 (0.71, 1.67) |
| Tb.vBMD | 1.15 (0.83, 1.59) | 0.96 (0.66, 1.39) | | 1.23 (0.89, 1.72) | 1.08 (0.74, 1.54) | | 1.32 (0.88, 1.96) | 1.02 (0.65, 1.59) |
| **Microarchitecture** |  |  | |  |  | |  |  |
| Ct.Po | **0.69 (0.50, 0.96)** | 0.76 (0.53, 1.09) | | **0.69 (0.50, 0.95)** | 0.76 (0.54, 1.08) | | **0.66 (0.45, 0.97)** | 0.77 (0.51, 1.16) |
| CCt.Po | 0.80 (0.58, 1.10) | 0.88 (0.63, 1.23) | | 0.83 (0.60, 1.12) | 0.92 (0.66, 1.28) | | 0.81 (0.56, 1.16) | 0.93 (0.63, 1.39) |
| OTZ.Po | 0.72 (0.52, 1.00) | 0.79 (0.56, 1.16) | | 0.74 (0.54, 1.02) | 0.83 (0.58, 1.16) | | 0.71 (0.49, 1.03) | 0.83 (0.56, 1.25) |
| ITZ.Po | 0.78 (0.56, 1.09) | 0.89 (0.62, 1.28) | | **0.71 (0.52, 0.99)** | 0.81 (0.56, 1.16) | | 0.75 (0.51, 1.10) | 0.94 (0.61, 1.45) |
| Tb.N | 1.30 (0.93, 1.82) | 1.14 (0.78, 1.64) | | **1.52 (1.09, 2.13)** | 1.37 (0.93, 2.00) | | **1.54 (1.06, 2.27)** | 1.27 (0.83, 1.96) |
| Tb.Th | 1.03 (0.74, 1.43) | 0.97 (0.69, 1.37) | | 1.11 (0.80, 1.54) | 1.05 (0.75, 1.47) | | 0.99 (0.68, 1.45) | 0.91 (0.62, 1.35) |
| Tb.Conn | 1.05 (0.75, 1.47) | 0.87 (0.60, 1.27) | | 1.20 (0.87, 1.69) | 1.03 (0.71, 1.49) | | 1.30 (0.87, 1.92) | 1.02 (0.65, 1.59) |
| Tb.Sp | 0.90 (0.66, 1.23) | 1.05 (0.74, 1.49) | | 0.78 (0.57, 1.06) | 0.88 (0.63, 1.23) | | 0.76 (0.53, 1.09) | 0.92 (0.62, 1.35) |
| Tb.BVTV | 1.09 (0.78, 1.52) | 0.91 (0.62, 1.32) | | 1.20 (0.86, 1.69) | 1.02 (0.70, 1.49) | | 1.27 (0.84, 1.89) | 0.97 (0.62, 1.54) |
| Matrix.MD | 1.25 (0.93, 1.69) | 1.20 (0.88, 1.61) | | 1.19 (0.89, 1.61) | 1.14 (0.85, 1.54) | | 1.39 (0.98, 1.96) | 1.30 (0.92, 1.85) |

Odds ratio (OR) is shown for 1 standard deviation decrease in each bone measures; HRpQCT measures were from the distal radius.

a Adjusted for age, sex and weight;

b Adjusted for age, sex, weight and spine aBMD.

Bold denotes statistical significance, p < 0.05.

Abbreviations: SD: standard deviation. aBMD: areal bone mineral density. Tt.Ar: total cross-sectional area; Ct.Ar: total cortical area; CCt.Ar: compact cortical area; OTZ.Ar: outer transitional zone bone area; ITZ.Ar: inner transitional zone bone area; Tb.Ar: trabecular area; Ct.Th: total cortical thickness; CCt.Th: compact cortical thickness; OTZ.Th: outer transitional zone bone thickness; ITZ.Th: inner transitional zone bone thickness; Tt.vBMD: total volumetric bone density; Ct.vBMD: total cortical volumetric bone density; CCt.vBMD: compact cortical volumetric bone density; OTZ.vBMD: outer transitional zone volumetric bone density; ITZ.vBMD: inner transitional zone volumetric bone density; Tb.vBMD: trabecular volumetric bone density; Ct.Po: cortical porosity; CCt.Po: compact cortical porosity; OTZ.Po: outer transitional zone bone porosity; ITZ.Po: inner transitional zone bone porosity; Tb.N: trabecular number; Tb.Th: trabecular thickness; Tb.Conn: trabecular connectivity; Tb.Sp: trabecular separation; Tb.BV/TV: trabecular bone volume fraction; HA: hydroxyapatite.

**Table 3.** Area under the receiver operating characteristic curve (AUC) for HRpQCT compared with spine aBMD alone in discriminating vertebral deformity by different criterion in adults

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 25% criterion | | | 3-SD criterion | |  | 4-SD criterion | | |
| AUC (95% CI)a  n= 196 | P-value |  | AUC (95% CI)a  n= 196 | P-value | | | AUC (95% CI)a  n= 196 | P-value |
| Spine aBMD | 0.594 (0.509, 0.679) | Reference | | 0.597 (0.512, 0.681) | Reference | | | 0.634 (0.536, 0.733) | Reference |
| **HRpQCT** |  |  | |  |  | | |  |  |
| Tt.Ar | 0.534 (0.509, 0.679) | 0.21 | | 0.576 (0.489, 0.663) | 0.70 | | | 0.553 (0.454, 0.651) | 0.18 |
| Ct.Ar | 0.625 (0.544, 0.706) | 0.50 | | 0.595 (0.513, 0.677) | 0.97 | | | 0.655 (0.566, 0.743) | 0.74 |
| Compact Cortical Ar | 0.680 (0.599, 0.761) | 0.06 | | 0.662 (0.598, 0.759) | 0.16 | | | 0.707 (0.618, 0.797) | 0.21 |
| Outer TZ Ar | 0.577 (0.494, 0.660) | 0.72 | | 0.568 (0.485, 0.650) | 0.55 | | | 0.592 (0.494, 0.690) | 0.50 |
| Inner TZ Ar | 0.532 (0.439, 0.625) | 0.18 | | 0.567 (0.480, 0.653) | 0.54 | | | 0.528 (0.419, 0.636) | 0.09 |
| Tb.Ar | 0.575 (0.486, 0.663) | 0.69 | | 0.600 (0.514, 0.685) | 0.95 | | | 0.533 (0.424, 0.641) | 0.11 |
| Ct.Th | 0.682 (0.604, 0.759) | 0.06 | | 0.659 (0.582, 0.737) | 0.18 | | | 0.673 (0.583, 0.763) | 0.50 |
| Compact Ct.Th | 0.685 (0.603, 0.767) | 0.05 | | 0.674 (0.594, 0.754) | 0.09 | | | 0.699 (0.604, 0.795) | 0.27 |
| Outer TZ Thickness | 0.626 (0.545, 0.706) | 0.55 | | 0.623 (0.542, 0.704) | 0.61 | | | 0.604 (0.505, 0.702) | 0.62 |
| Inner TZ Thickness | 0.558 (0.472, 0.644) | 0.46 | | 0.534 (0.445, 0.623) | 0.20 | | | 0.521 (0.415, 0.628) | 0.07 |
| **vBMD** |  |  | |  |  | | |  |  |
| Tt.vBMD | 0.602 (0.514, 0.689) | 0.86 | | 0.617 (0.533, 0.701) | 0.64 | | | 0.608 (0.507, 0.710) | 0.62 |
| Ct.vBMD | 0.600 (0.512, 0.687) | 0.90 | | 0.599 (0.515, 0.683) | 0.96 | | | 0.593 (0.492, 0.694) | 0.47 |
| CCt.vBMD | 0.556 (0.468, 0.644) | 0.40 | | 0.556 (0.473, 0.640) | 0.36 | | | 0.546 (0.445, 0.646) | 0.14 |
| OTZ.vBMD | 0.593 (0.507, 0.679) | 0.98 | | 0.584 (0.501, 0.667) | 0.77 | | | 0.573 (0.478, 0.669) | 0.29 |
| ITZ.vBMD | 0.562 (0.474, 0.651) | 0.42 | | 0.598 (0.513, 0.684) | 0.97 | | | 0.578 (0.473, 0.684) | 0.26 |
| Tb.vBMD | 0.534 (0.443, 0.626) | 0.12 | | 0.558 (0.471, 0.645) | 0.39 | | | 0.572 (0.467, 0.676) | 0.18 |
| **Microarchitecture** |  |  | |  |  | | |  |  |
| Cortical porosity | 0.598 (0.509, 0.679) | 0.94 | | 0.598 (0.514, 0.681) | 0.98 | | | 0.590 (0.489, 0.691) | 0.45 |
| Compact cortical porosity | 0.557 (0.469, 0.644) | 0.40 | | 0.556 (0.473, 0.640) | 0.36 | | | 0.544 (0.444, 0.645) | 0.14 |
| Outer TZ porosity | 0.592 (0.507, 0.678) | 0.96 | | 0.583 (0.501, 0.666) | 0.76 | | | 0.571 (0.475, 0.667) | 0.26 |
| Inner TZ porosity | 0.559 (0.470, 0.648) | 0.39 | | 0.594 (0.508, 0.680) | 0.95 | | | 0.574 (0.468, 0.679) | 0.22 |
| Tb.N | 0.563 (0.475, 0.651) | 0.40 | | 0.602 (0.518, 0.685) | 0.89 | | | 0.604 (0.504, 0.704) | 0.54 |
| Tb.Th | 0.528 (0.435, 0.621) | 0.15 | | 0.542 (0.454, 0.631) | 0.25 | | | 0.521 (0.415, 0.626) | 0.07 |
| Tb. Connectivity | 0.528 (0.435, 0.621) | 0.13 | | 0.561 (0.475, 0.647) | 0.36 | | | 0.567 (0.464, 0.671) | 0.16 |
| Tb. Separation | 0.526 (0.434, 0.619) | 0.10 | | 0.574 (0.489, 0.659) | 0.56 | | | 0.571 (0.470, 0.672) | 0.18 |
| Tb.BV/TV | 0.526 (0.433, 0.619) | 0.11 | | 0.563 (0.476, 0.649) | 0.40 | | | 0.567 (0.464, 0.669) | 0.18 |
| Matrix mineral density | 0.578 (0.489, 0.666) | 0.73 | | 0.568 (0.482 0.654) | 0.55 | | | 0.604 (0.498, 0.710) | 0.65 |

a All models included age, sex and weight.

P-values were for the difference in AUC of each HRpQCT compared with spine aBMD alone (by 25%, 3-SD and 4-SD criterion).

Abbreviations: SD: standard deviation; aBMD: areal bone mineral density; Tt.Ar: total cross-sectional area; Ct.Ar: total cortical area; TZ Ar: transitional zone bone area; Tb.Ar: trabecular area; Ct.Th: cortical thickness; TZ: transitional zone bone; Tt.vBMD: total volumetric bone density; Ct.vBMD: total cortical volumetric bone density; CCt.vBMD: compact cortical volumetric bone density; OTZ.vBMD: outer transitional zone bone volumetric bone density; ITZ.vBMD: inner transitional zone bone volumetric bone density; Tb.vBMD: trabecular volumetric bone density; Tb.N: trabecular number; Tb.Th: trabecular thickness; Tb.BV/TV: trabecular bone volume fraction; HA: hydroxyapatite.

**Table 4.** Area under the receiver operating characteristic curve (AUC) for the combination of each HRpQCT measures and aBMD compared with spine aBMD alone in discriminating vertebral deformity by different criteria

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 25% criterion | | | 3-SD criterion | | |  | 4-SD criterion | |
| AUC (95% CI)b  n= 196 | P-valuec |  | | AUC (95% CI)b  n= 196 | P-valuec | | AUC (95% CI)b  n= 196 | P-valuec |
| Spine aBMD | 0.594 (0.509, 0.679) | Reference | | 0.597 (0.512, 0.681) | | Reference | | 0.634 (0.536, 0.733) | Reference |
| **HRpQCT** |  |  | |  | |  | |  |  |
| Tt.Ar | 0.599 (0.514, 0.684) | 0.54 | | 0.612 (0.528, 0.696) | | 0.40 | | 0.634 (0.537, 0.732) | 1.00 |
| Ct.Ar | 0.642 (0.562, 0.722) | 0.14 | | 0.620 (0.539, 0.702) | | 0.33 | | 0.684 (0.602, 0.765) | 0.17 |
| Compact Cortical Ar | **0.680 (0.599, 0.760)** | **0.03** | | 0.665 (0.584, 0.745) | | 0.06 | | 0.719 (0.634, 0.804) | 0.06 |
| Outer TZ Ar | 0.618 (0.536, 0.700) | 0.35 | | 0.610 (0.528, 0.692) | | 0.55 | | 0.650 (0.556, 0.743) | 0.54 |
| Inner TZ Ar | 0.594 (0.509, 0.679) | 0.89 | | 0.606 (0.522, 0.690) | | 0.52 | | 0.636 (0.536, 0.736) | 0.83 |
| Tb.Ar | 0.602 (0.517, 0.687) | 0.71 | | 0.623 (0.539, 0.706) | | 0.34 | | 0.633 (0.533, 0.732) | 0.85 |
| Ct.Th | **0.690 (0.613, 0.767)** | **0.02** | | **0.670 (0.692, 0.748)** | | **0.049** | | 0.694 (0.603, 0.784) | 0.10 |
| Compact Ct.Th | **0.691 (0.610, 0.771)** | **0.01** | | **0.679 (0.599, 0.758)** | | **0.02** | | 0.709 (0.619, 0.800) | 0.05 |
| Outer TZ Thickness | 0.659 (0.579, 0.739) | 0.07 | | 0.653 (0.573, 0.732) | | 0.13 | | 0.661 (0.564, 0.758) | 0.35 |
| Inner TZ Thickness | 0.599 (0.515, 0.684) | 0.77 | | 0.596 (0.512, 0.680) | | 0.95 | | 0.635 (0.536, 0.733) | 0.64 |
| **vBMD** |  |  | |  | |  | |  |  |
| Tt.vBMD | 0.610 (0.525, 0.695) | 0.53 | | 0.629 (0.546, 0.711) | | 0.28 | | 0.650 (0.549, 0.743) | 0.57 |
| Ct.vBMD | 0.615 (0.530, 0.700) | 0.44 | | 0.617 (0.534, 0.699) | | 0.45 | | 0.646 (0.550, 0.742) | 0.60 |
| CCt.vBMD | 0.600 (0.516, 0.684) | 0.70 | | 0.598 (0.514, 0.681) | | 0.89 | | 0.633 (0.535, 0.731) | 0.81 |
| OTZ.vBMD | 0.612 (0.528, 0.695) | 0.47 | | 0.604 (0.522, 0.687) | | 0.68 | | 0.641 (0.546, 0.736) | 0.70 |
| ITZ.vBMD | 0.591 (0.506, 0.677) | 0.82 | | 0.612 (0.528, 0.696) | | 0.50 | | 0.633 (0.534, 0.732) | 0.85 |
| Tb.vBMD | 0.602 (0.517, 0.686) | 0.38 | | 0.594 (0.509, 0.679) | | 0.80 | | 0.637 (0.538, 0.735) | 0.75 |
| **Microarchitecture** |  |  | |  | |  | |  |  |
| Cortical porosity | 0.616 (0.531, 0.700) | 0.43 | | 0.613 (0.531, 0.695) | | 0.51 | | 0.645 (0.549, 0.740) | 0.64 |
| Compact cortical porosity | 0.600 (0.516, 0.684) | 0.68 | | 0.598 (0.514, 0.682) | | 0.88 | | 0.633 (0.535, 0.731) | 0.87 |
| Outer TZ porosity | 0.612 (0.529, 0.695) | 0.45 | | 0.604 (0.521, 0.687) | | 0.69 | | 0.641 (0.546, 0.736) | 0.67 |
| Inner TZ porosity | 0.592 (0.507, 0.677) | 0.83 | | 0.611 (0.527, 0.695) | | 0.46 | | 0.632 (0.533, 0.731) | 0.71 |
| Tb.N | 0.594 (0.510, 0.679) | 0.99 | | 0.609 (0.526, 0.692) | | 0.60 | | 0.646 (0.549, 0.742) | 0.54 |
| Tb.Th | 0.600 (0.516, 0.684) | 0.16 | | 0.599 (0.514, 0.683) | | 0.74 | | 0.638 (0.540, 0.736) | 0.74 |
| Tb. Connectivity | 0.610 (0.526, 0.694) | 0.26 | | 0.597 (0.513, 0.681) | | 0.90 | | 0.634 (0.536, 0.733) | 1.00 |
| Tb. Separation | 0.599 (0.514, 0.683) | 0.44 | | 0.604 (0.521, 0.688) | | 0.56 | | 0.636 (0.538, 0.735) | 0.81 |
| Tb.BV/TV | 0.605 (0.521, 0.690) | 0.28 | | 0.597 (0.513, 0.681) | | 0.83 | | 0.634 (0.536, 0.732) | 0.93 |
| Matrix mineral density | 0.602 (0.517, 0.687) | 0.72 | | 0.600 (0.515, 0.684) | | 0.84 | | 0.646 (0.549, 0.743) | 0.64 |

b All models included age, sex, weight and spine aBMD.

c P-values were for the difference in AUC of the combination of each HRpQCT and spine aBMD comparison with spine aBMD alone (by 25%, 3-SD and 4-SD criterion).

Bold denotes statistical significance, p<0.05.

Abbreviations: SD: standard deviation. aBMD: areal bone mineral density. Tt.Ar: total cross-sectional area; Ct.Ar: total cortical area; CCt.Ar: compact cortical area; OTZ.Ar: outer transitional zone bone area; ITZ.Ar: inner transitional zone bone area; Tb.Ar: trabecular area; Ct.Th: total cortical thickness; CCt.Th: compact cortical thickness; OTZ.Th: outer transitional zone bone thickness; ITZ.Th: inner transitional zone bone thickness; Tt.vBMD: total volumetric bone density; Ct.vBMD: total cortical volumetric bone density; CCt.vBMD: compact cortical volumetric bone density; OTZ.vBMD: outer transitional zone volumetric bone density; ITZ.vBMD: inner transitional zone volumetric bone density; Tb.vBMD: trabecular volumetric bone density; Ct.Po: cortical porosity; CCt.Po: compact cortical porosity; OTZ.Po: outer transitional zone bone porosity; ITZ.Po: inner transitional zone bone porosity; Tb.N: trabecular number; Tb.Th: trabecular thickness; Tb.Conn: trabecular connectivity; Tb.Sp: trabecular separation; Tb.BV/TV: trabecular bone volume fraction; HA: hydroxyapatite.

**Table 5**. Associations between standardized bone measures and the prevalence of vertebral deformity defined by ≥25% anterior wedging in males and females

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Males | |  | Females | |
|  | OR (95% CI)d | OR (95% CI)e |  | OR (95% CI)d | OR (95% CI)e |
|  | n=105 | n=105 |  | n=91 | n=91 |
| Spine aBMD | **1.72 (1.02, 2.94)** | NA |  | 1.06 (0.63, 1.75) | NA |
|  |  |  |  |  |  |
| **HRpQCT** |  |  |  |  |  |
| Tt.Ar | 1.23 (0.70, 2.22) | 1.20 (0.69, 2.13) |  | 0.58 (0.21, 1.61) | 0.56 (0.20, 1.59) |
| Ct.Ar | **3.23 (1.41, 7.69)** | **2.78 (1.20, 6.67)** |  | 1.67 (0.57, 5.00) | 1.79 (0.54, 5.88) |
| CCt.Ar | **2.94 (1.52, 5.88)** | **2.63 (1.30, 5.26)** |  | 1.92 (0.84, 4.35) | 2.08 (0.84, 5.00) |
| OTZ.Ar | **2.22 (1.10, 4.55)** | **2.13 (1.05, 4.35)** |  | 1.25 (0.47, 3.33) | 1.23 (0.44, 3.45) |
| ITZ.Ar | 1.08 (0.66, 1.72) | 1.06 (0.65, 1.72) |  | 0.83 (0.43, 1.56) | 0.81 (0.42, 1.56) |
| Tb.Ar | 0.98 (0.61, 1.59) | 0.98 (0.60, 1.61) |  | 0.50 (0.20, 1.22) | 0.50 (0.20, 1.22) |
| Ct.Th | **2.86 (1.47, 5.56)** | **2.63 (1.32, 5.26)** |  | **2.13 (1.04, 4.35)** | **2.27 (1.06, 4.76)** |
| CCt.Th | **2.22 (1.25, 3.85)** | **1.96 (1.10, 3.57)** |  | 1.85 (0.99, 3.45) | 1.92 (0.99, 3.70) |
| OTZ.Th | **2.13 (1.19, 3.85)** | **2.13 (1.18, 3.85)** |  | 1.67 (0.90, 3.13) | 1.69 (0.89, 3.23) |
| ITZ.Th | 1.20 (0.75, 1.92) | 1.28 (0.79, 2.08) |  | 1.01 (0.60, 1.69) | 1.00 (0.59, 1.45) |
| **vBMD** |  |  |  |  |  |
| Tt.vBMD | 1.43 (0.88, 2.27) | 1.18 (0.68, 2.00) |  | 1.32 (0.82, 2.13) | 1.35 (0.81, 2.22) |
| Ct.vBMD | 1.61 (0.96, 2.70) | 1.39 (0.79, 2.44) |  | 1.22 (0.78, 1.92) | 1.23 (0.76, 2.00) |
| CCt.vBMD | 1.39 (0.82, 2.33) | 1.22 (0.70, 2.08) |  | 1.03 (0.67, 1.59) | 1.01 (0.64, 1.61) |
| OTZ.vBMD | 1.52 (0.90, 2.56) | 1.28 (0.74, 2.27) |  | 1.15 (0.73, 1.82) | 1.15 (0.70, 1.89) |
| ITZ.vBMD | 1.37 (0.88, 2.17) | 1.10 (0.65, 1.89) |  | 1.10 (0.67, 1.82) | 1.10 (0.64, 1.89) |
| Tb.vBMD | 1.15 (0.74, 1.79) | 0.82 (0.47, 1.43) |  | 1.05 (0.63, 1.79) | 1.04 (0.60, 1.79) |
| **Microarchitecture** |  |  |  |  |  |
| Ct.Po | 0.63 (0.37, 1.05) | 0.74 (0.42, 1.28) |  | 0.82 (0.52, 1.28) | 0.81 (0.51, 1.32) |
| CCt.Po | 0.73 (0.43, 1.22) | 0.83 (0.48, 1.43) |  | 0.97 (0.63, 1.49) | 0.98 (0.62, 1.56) |
| OTZ.Po | 0.67 (0.40, 1.12) | 0.78 (0.45, 1.37) |  | 0.87 (0.55, 1.37) | 0.66 (0.53, 1.43) |
| ITZ.Po | 0.74 (0.47, 1.15) | 0.93 (0.55, 1.56) |  | 0.94 (0.57, 1.59) | 0.96 (0.56, 1.64) |
| Tb.N | 1.52 (0.86, 2.70) | 1.11 (0.55, 2.22) |  | 1.12 (0.71, 1.75) | 1.12 (0.68, 1.82) |
| Tb.Th | 1.09 (0.69, 1.72) | 0.95 (0.59, 1.54) |  | 0.97 (0.59, 1.59) | 0.97 (0.59, 1.59) |
| Tb.Conn | 1.12 (0.70, 1.79) | 0.79 (0.45, 1.39) |  | 0.91 (0.55, 1.52) | 0.88 (0.52, 1.52) |
| Tb.Sp | 0.84 (0.49, 1.45) | 1.27 (0.65, 2.50) |  | 1.01 (0.66, 1.54) | 1.02 (0.66, 1.59) |
| Tb.BVTV | 1.15 (0.75, 1.75) | 0.84 (0.50, 1.41) |  | 0.90 (0.51, 1.61) | 0.88 (0.49, 1.59) |
| Matrix.MD | 1.37 (0.88, 2.13) | 1.33 (0.85, 2.08) |  | 0.96 (0.62, 1.49) | 0.95 (0.61, 1.49) |

Odds ratio (OR) is shown for 1 standard deviation decrease in each bone measures; HRpQCT measures were from the distal radius.

d Adjusted for age and weight.

e Adjusted for age, weight and spine aBMD.

Bold denotes statistical significance, p<0.05.

Abbreviations: SD: standard deviation. aBMD: areal bone mineral density. Tt.Ar: total cross-sectional area; Ct.Ar: total cortical area; CCt.Ar: compact cortical area; OTZ.Ar: outer transitional zone bone area; ITZ.Ar: inner transitional zone bone area; Tb.Ar: trabecular area; Ct.Th: total cortical thickness; CCt.Th: compact cortical thickness; OTZ.Th: outer transitional zone bone thickness; ITZ.Th: inner transitional zone bone thickness; Tt.vBMD: total volumetric bone density; Ct.vBMD: total cortical volumetric bone density; CCt.vBMD: compact cortical volumetric bone density; OTZ.vBMD: outer transitional zone volumetric bone density; ITZ.vBMD: inner transitional zone volumetric bone density; Tb.vBMD: trabecular volumetric bone density; Ct.Po: cortical porosity; CCt.Po: compact cortical porosity; OTZ.Po: outer transitional zone bone porosity; ITZ.Po: inner transitional zone bone porosity; Tb.N: trabecular number; Tb.Th: trabecular thickness; Tb.Conn: trabecular connectivity; Tb.Sp: trabecular separation; Tb.BV/TV: trabecular bone volume fraction; HA: hydroxyapatite.

**Table 6**. Area under the receiver operating characteristic curve (AUC) for HRpQCT compared with spine aBMD alone in discriminating vertebral deformity defined by ≥25% anterior in males and females

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Males | |  | Females | |
|  | AUC (95% CI)d  n=105 | P-value |  | OR (95% CI)d n=91 | P-value |
| Spine aBMD | 0.643 (0.531, 0.754) | Reference |  | 0.681 (0.562, 0.799) | Reference |
|  |  |  |  |  |  |
| **HRpQCT** |  |  |  |  |  |
| Tt.Ar | 0.613 (0.531, 0.755) | 0.60 |  | 0.694 (0.580, 0.808) | 0.55 |
| Ct.Ar | 0.680 (0.575, 0.786) | 0.54 |  | 0.675 (0.554, 0.796) | 0.73 |
| CCt.Ar | 0.722 (0.615, 0.830) | 0.19 |  | 0.713 (0.600, 0.825) | 0.24 |
| OTZ.Ar | 0.658 (0.544, 0.770) | 0.82 |  | 0.672 (0.551, 0.792) | 0.40 |
| ITZ.Ar | 0.610 (0.489, 0.732) | 0.56 |  | 0.684 (0.566, 0.802) | 0.77 |
| Tb.Ar | 0.613 (0.493, 0.732) | 0.58 |  | 0.700 (0.585, 0.814) | 0.50 |
| Ct.Th | 0.710 (0.606, 0.815) | 0.26 |  | 0.718 (0.606, 0.829) | 0.31 |
| CCt.Th | 0.694 (0.581, 0.807) | 0.40 |  | 0.715 (0.602, 0.829) | 0.30 |
| OTZ.Th | 0.662 (0.551, 0.774) | 0.77 |  | 0.686 (0.569, 0.803) | 0.86 |
| ITZ.Th | 0.610 (0.490, 0.730) | 0.57 |  | 0.681 (0.562, 0.799) | 1.00 |
| **vBMD** |  |  |  |  |  |
| Tt.vBMD | 0.616 (0.503, 0.730) | 0.57 |  | 0.689 (0.570, 0.808) | 0.71 |
| Ct.vBMD | 0.637 (0.524, 0.750) | 0.91 |  | 0.681 (0.560, 0.802) | 1.00 |
| CCt.vBMD | 0.626 (0.512, 0.740) | 0.75 |  | 0.677 (0.558, 0.796) | 0.59 |
| OTZ.vBMD | 0.638 (0.527, 0.749) | 0.92 |  | 0.678 (0.559, 0.797) | 0.83 |
| ITZ.vBMD | 0.614 (0.500, 0.728) | 0.50 |  | 0.679 (0.560, 0.799) | 0.87 |
| Tb.vBMD | 0.590 (0.471, 0.709) | 0.25 |  | 0.674 (0.555, 0.794) | 0.84 |
| **Microarchitecture** |  |  |  |  |  |
| Ct.Po | 0.637 (0.524, 0.750) | 0.91 |  | 0.680 (0.559, 0.801) | 0.98 |
| CCt.Po | 0.625 (0.511, 0.740) | 0.74 |  | 0.677 (0.558, 0.796) | 0.59 |
| OTZ.Po | 0.638 (0.527, 0.749) | 0.92 |  | 0.678 (0.558, 0.797) | 0.80 |
| ITZ.Po | 0.606 (0.491, 0.720) | 0.40 |  | 0.682 (0.564, 0.801) | 0.84 |
| Tb.N | 0.615 (0.500, 0.731) | 0.52 |  | 0.679 (0.559, 0.798) | 0.84 |
| Tb.Th | 0.607 (0.489, 0.725) | 0.49 |  | 0.677 (0.558, 0.795) | 0.60 |
| Tb.Conn | 0.591 (0.470, 0.711) | 0.28 |  | 0.677 (0.559, 0.794) | 0.73 |
| Tb.Sp | 0.589 (0.469, 0.708) | 0.24 |  | 0.678 (0.561, 0.798) | 0.89 |
| Tb.BVTV | 0.592 (0.473, 0.711) | 0.28 |  | 0.678 (0.561, 0.795) | 0.83 |
| Matrix.MD | 0.616 (0.500, 0.731) | 0.66 |  | 0. 678 (0.560, 0.796) | 0.75 |

d All models included age and weight.

P-values were for the difference in AUC of each HRpQCT compared with spine aBMD alone.

Abbreviations: SD: standard deviation; aBMD: areal bone mineral density; Tt.Ar: total cross-sectional area; Ct.Ar: total cortical area; TZ Ar: transitional zone bone area; Tb.Ar: trabecular area; Ct.Th: cortical thickness; TZ: transitional zone bone; Tt.vBMD: total volumetric bone density; Ct.vBMD: total cortical volumetric bone density; CCt.vBMD: compact cortical volumetric bone density; OTZ.vBMD: outer transitional zone bone volumetric bone density; ITZ.vBMD: inner transitional zone bone volumetric bone density; Tb.vBMD: trabecular volumetric bone density; Tb.N: trabecular number; Tb.Th: trabecular thickness; Tb.BV/TV: trabecular bone volume fraction; HA: hydroxyapatite.

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**Figure legends:** Receiver-operating characteristic (ROC) curves and area under the ROC curve (AUC) statistics for the discrimination of vertebral deformity by three criteria in adults.

**Figure 3A-C.** AUCs comparisons of compact cortical area + spine aBMD and compact cortical area + radial vBMD with compact cortical area alone by the 25% (A), 3-SD (B) and 4-SD (C) criterion. SD: standard deviation. CCt.Ar: compact cortical area; aBMD: areal bone mineral density; Tt.vBMD: total volumetric bone mineral density; Ct.vBMD: cortical volumetric bone mineral density; CCt.vBMD: compact cortical bone volumetric bone mineral density.

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**Figure legends:** Receiver-operating characteristic (ROC) curves and area under the ROC curve (AUC) statistics for the discrimination of vertebral deformity by three criteria in adults.

**Figure 4A-C.** AUCs comparisons of cortical thickness + spine aBMD and cortical thickness + radial vBMD with cortical thickness alone by the 25% (A), 3-SD (B) and 4-SD (C) criterion. SD: standard deviation. CCt.Ar: compact cortical area; aBMD: areal bone mineral density; Tt.vBMD: total volumetric bone mineral density; Ct.vBMD: cortical volumetric bone mineral density; CCt.vBMD: compact cortical bone volumetric bone mineral density.

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**Figure legends:** Receiver-operating characteristic (ROC) curves and area under the ROC curve (AUC) statistics for the discrimination of vertebral deformity by three criteria in adults.

**Figure 5A-C.** AUCs comparisons of compact cortical thickness + spine aBMD and compact cortical thickness + radial vBMD with compact cortical thickness alone by 25%, 3-SD and 4-SD criterion. SD: standard deviation. CCt.Ar: compact cortical area; aBMD: areal bone mineral density; Tt.vBMD: total volumetric bone mineral density; Ct.vBMD: cortical volumetric bone mineral density; CCt.vBMD: compact cortical bone volumetric bone mineral density.