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Lumbar trabecular bone mineral density distribution in patients with and without vertebral fractures: a case–control study

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Abstract

Purpose—The proportion of load transmitted through the lumbar neural arch increases with aging, spinal degeneration, and lordosis, effectively shielding the lumbar vertebral bodies from load. This stress shielding may contribute to bone loss in the vertebral body, leading to increased fracture risk. To test his hypothesis, we performed a study to determine if vertebral body fractures were associated with a higher neural arch/vertebral body volumetric bone mineral density (vBMD) ratio.

Methods—Trabecular vBMD was calculated by quantitative CT in the L3 vertebral body and neural arch (pars interarticularis) of 36 women with vertebral compression fractures and 39 controls. Neural arch/vertebral body vBMD ratio was calculated, and its relationship to fracture status was determined using linear regression models adjusted for age and body mass index.

Results—Vertebral body trabecular vBMD was lower in fracture cases as compared to controls (mean $\pm$ SD, 49.0 ± 36.0 vs. 87.5 ± 36.8 mg/cm³, respectively; $P < 0.001$), whereas trabecular vBMD of the neural arch was similar (96.1 ± 57.6 in cases vs. 118.2 ± 57.4 mg/cm³ in controls; $P = 0.182$). The neural arch/vertebral body vBMD ratio was significantly greater in the fracture group than in controls (2.31 ± 1.07 vs. 1.44 ± 0.57 , respectively; $P < 0.001$).

Conclusion—These results support the hypothesis that stress shielding is a contributor to vertebral body bone loss and may increase fracture risk. Although further studies are needed, there may be a role for interventions that can shift vertebral loading in the spine to help prevent fracture.

Keywords

Bone mineral density; Osteoporosis; Spinal fractures; Risk; Quantitative computed tomography

Introduction

Osteoporosis causes loss of bone mineral and alterations of trabecular architecture, which lead to an increased risk of vertebral fractures. Although age-related bone loss is generally attributed to sex steroid deficiency [1], bone is also very sensitive to mechanical loading [2]. Indeed, normal loading produces internal stresses that stimulate increased bone density and changes in trabecular structure that favor bone strength. Conversely, reductions in everyday loading lead to rapid bone loss, and disuse alone may result in osteoporosis [3].

Fractures occur when skeletal loads exceed the breaking strength of bone, and fracture risk can be estimated by bone mineral density (BMD) measurements [4]. Whereas most appendicular osteoporotic fractures are precipitated by falling [5], vertebral fractures often occur in the course of normal activities of daily living [6]. Normal loads may lead to fracture when internal stress exceeds the fracture threshold [7], and most vertebral body fractures in the setting of osteoporosis are considered insufficiency fractures as opposed to either traumatic fractures (due to high energy loading) or stress fractures (due to repetitive loading).

The ability of bone to carry load depends on several factors including the mechanical properties of the bone, its geometry and architecture, as well as the loading conditions. The distribution of compressive load between the cortical shell and the trabecular core of lumbar vertebral bodies is debated and appears to be dependent on the conditions of loading and the degree of mineralization [8, 9]. Regardless of the load distribution, trabecular bone in osteoporotic spines is at higher risk of fracture [10, 11], and a strong correlation exists between lumbar vertebral failure load and regional volumetric bone mineral density (vBMD) values derived from quantitative computed tomography (QCT) [12].

The total axial load on the lumbar spine is shared by the vertebral body and the neural arch (via the facet joints). King et al. [13] found that, under normal circumstances, the share of

compressive load borne by the facet joints may vary from 0 to 33 % depending on spine posture. Facet load share of 50 % or greater is associated with degenerative changes in cartilage and bone in cadaveric studies [14]. The load share of the vertebral bodies in the lumbar spine decreases with aging, degenerative change, and lumbar lordosis [15]. As the vertebral body load decreases, the proportion of load transmitted through the neural arch and facet joints increases [16]. This posterior shift in load bearing is most likely to occur in the lumbar and lower thoracic regions, where the posture is usually lordotic or neutral.

Posterior load shifting may result in stress shielding of the vertebral body, which has been hypothesized to be a contributing factor in vertebral body bone loss and increased vertebral fracture risk [17]. If true, greater load on the neural arch and facet joints over time would lower vertebral body load, thus reducing vBMD of the vertebral body, while maintaining or increasing vBMD in the neural arch. This would increase the neural arch/vertebral body vBMD ratio. We found no studies that reported trabecular vBMD in the neural arch. Anatomically, the pars interarticularis (neural arch) is the only posterior structure with substantial trabecular bone. We hypothesized that a higher ratio of neural arch to vertebral body trabecular vBMD in the L3 vertebra (which is typically at or near the apex of the lumbar lordosis) would be associated with an increased likelihood of fracture in the thoracic and/or lumbar spine. We carried out a prospective analysis of previously acquired scans to test this hypothesis.

Materials and methods

Subjects

We utilized data previously collected on women 50 years of age with clinically diagnosed vertebral fractures (confirmed by lateral QCT scout images) within the past 5 years who were recruited from the community [18]. All subjects had QCT scans of the lumbar spine. Those with vertebral fractures due to severe trauma (by convention, more than a fall from standing height) or non-osteoporotic pathology (e.g., metastatic malignancy) had been excluded, as well as women who had undergone vertebroplasty or intermittent parathyroid hormone therapy. Patients who had been treated with antiresorptive drugs (bisphosphonates, hormone therapy or selective estrogen receptor modulators) were included, as those agents do not promote bone deposition or greatly alter bone structure like anabolic agents do [19]. Those taking anabolic agents such as teriparatide were excluded because their vBMD may not reflect typical bone mineralization. Of the cases with at least one grade 2 or 3 fracture, by the semi-quantitative method [20], those with fracture involving the L3 vertebra were excluded. From the remaining subjects, 40 were randomly chosen by the data librarian for evaluation. They were compared to 40 control subjects from a pool of 90 available [18] that had no fracture or vertebral deformity. Cases and controls were frequency matched on age. No additional risk was posed to subjects by the present analysis, which used only de-identified data. The study was approved by the Mayo Clinic Institutional Review Board.

Data collection

QCT images of the lumbar spine were obtained by single-energy CT scanning, as previously described [18]. DICOM images of the L3 vertebrae were uploaded and analyzed with

Mimics image processing and editing software (Materialise US, Ann Arbor, MI USA). Segmentation was performed in two slices (mean $\pm$ SD, 0.75 mm $\pm$ 0.03 in height) containing the vertebral body and neural arch trabecular bone, based on the spine sagittal view. A slice midway between the superior and inferior endplates and the slice superior to it were analyzed (Fig. 1a). The anterior vertebral body boundary was defined by a line tangential to the neural arch and aligned with the coronal plane. The posterior neural arch boundary was defined by a line passing through the most narrowest point of the pedicle channel. The images were evaluated first by applying a Hounsfield unit (HU) bone window to define the cortical bone mask in each scan (cortical bone HU threshold >225) (Fig. 1b). Pixels from the vertebral trabecular region that had similar density as cortex, but were not part of the cortex, were removed from the region of interest (ROI) leaving only the cortex mask; these pixels appeared as islets which had no contact with peripheral cortical bone. Region growing operations allowed the vertebral body cortex to be separated and segmented from the cortex of the neural arch, permitting each part to be analyzed separately (Fig. 1c). An additional HU window was applied to generate a mask including the entire DICOM image from which, by applying a subtractive Boolean operation between masks, trabecular bone could then be segmented. Individual masks containing the entire vertebral body (anterior and middle vertebral columns) and neural arch (posterior vertebral column) cross-sections were thus obtained without cortical bone (Fig. 1d). Vertebral and neural arch trabecular HU data were exported from Mimics in text-based format. A Mindways CT calibration phantom (Mindways Software Inc., San Francisco, CA) containing reference material and included in each subject's scan was used to calculate equivalent K_2HPO_4 densities (i.e., vBMD, mg/cm³) from HU data using a linear regression model aided by a custom MATLAB (Mathworks, Natick, MA) program. The average vertebral and neural arch trabecular vBMD from both slices was measured.

Statistical methods

Two sample *t* tests were used to compare age and body mass index (BMI) between the fracture cases and controls. Linear regression was used to compare vBMD by case status after adjusting for age and BMI. All analyses were performed using SAS version 9 (SAS Institute, Cary, NC USA) and S-plus (TIBCO Corporation, Palo Alto, CA USA).

Results

Of the 40 cases with a grade 2–3 vertebral fracture, three had QCT data that did not produce reliable results with the described methods and were, therefore, omitted. Two others were found to have identical data (the same subject was analyzed twice due to a clerical error), and therefore one was omitted. In addition, one control subject was omitted, also because the QCT data did not produce reliable results with the methods described. Thus, 36 cases with at least one vertebral fracture (46 grade 2–3 fractures altogether) and 39 controls without fracture were analyzed. The investigators analyzing the images were able to view the QCT data of L1, L2 and L3 only. Consequently, they would have known the group status (fracture or control) of 7 cases with fractures at those levels (6 at L1 and 1 at L2). The group status of the other 68 subjects was not known to the persons analyzing the QCT data.

The mean $\pm$ SD age of cases (74.5 ± 10.4 years) and controls (70.9 ± 8.3 years) was comparable, as well as BMI of the two groups (28.1 ± 5.9 vs. 28.2 ± 5.1 , respectively). Except for one Hispanic woman, all subjects were white by self-report, reflecting the racial composition of the community (96 % white in 2000). The distribution of vertebral fractures for the 36 cases is shown in Fig. 2. Some subjects had more than one fracture.

Trabecular vBMD values are shown in Fig. 3. The mean neural arch trabecular vBMD of the controls was 118.2 ± 57.4 mg/cm³, which was more than the 96.1 ± 57.6 mg/cm³ mean in the fracture cases, but not statistically different after adjusting for age and BMI ($P = 0.182$). By contrast, the mean vertebral body trabecular vBMD was significantly greater in the controls than in the fracture group (87.5 ± 36.8 vs. 49.0 ± 36.0 mg/cm³; $P < 0.001$). Consequently, the neural arch/vertebral body trabecular vBMD ratio was significantly greater in the fracture group as compared to the control group (2.31 ± 1.07 vs. 1.44 ± 0.57 , respectively), after adjustment for age and BMI ($P < 0.001$). A scatter plot of the neural arch/vertebral body trabecular vBMD ratio by age and fracture status is shown in Fig. 4.

Of the selected subjects, two controls (5 %) and 14 cases (37 %) were under bisphosphonate treatment. After exclusion of these subjects from the analysis, similar differences between the groups were seen after adjusting for age and BMI in regard to vertebral body vBMD (controls: 86.9 ± 36.8 vs. cases: 57.6 ± 39.3 ; $P = 0.006$), while mean neural arch trabecular vBMD again did not differ (controls: 119.9 ± 58.1 vs. cases: 104.9 ± 59.1 ; $P = 0.366$). Thus, the mean neural arch/vertebral body trabecular vBMD ratio in this subset of case and control subjects remained significantly different (controls: 1.47 ± 0.57 vs. cases: 2.10 ± 0.92 ; $P = 0.003$). In spite of the treated control and case subjects (2 controls, 14 cases) showing similar trends in regard to vertebral body vBMD and neural arch trabecular vBMD, there is no statistical power to reach any conclusions relating vBMD distribution from those two isolated groups (data not shown). Table 1 summarizes the data obtained.

Discussion

A previous publication using this cohort [18] reported that lumbar spine (L1–L3) trabecular vBMD was significantly less in women with a vertebral fracture compared to unfractured control women (115 ± 21 vs. 146 ± 32 mg/cm³, respectively). In this analysis of a subset of those subjects, we found the ratio of trabecular vBMD in the neural arch to that in the vertebral body to be significantly greater in subjects with vertebral fractures as compared to a control group without fractures. The difference in vertebral body trabecular bone density was highly significant, a result which was not unexpected. At the same time, the mean trabecular vBMD observed in the neural arch was not statistically different, consistent with our hypothesis. Bone density in the neural arch was likely maintained as a result of increased posterior load bearing [17]. These results support the hypothesis that stress shielding likely contributes to vertebral body bone loss and a subsequent increase in fracture risk.

Adult bone mass is influenced by many factors, including genetics [20], bone mass acquisition during adolescence [21] and physical activity [22, 23]. Weight bearing also plays a significant role in bone remodeling and the maintenance of bone mass [24–26]. This can

be observed in paraplegic patients who, similar to controls and contrary to paraplegic subjects, show normal BMD results in the lumbar spine [27, 28]. Furthermore, paraplegic patients undergoing weight bearing standing exercises seem to conserve BMD at the femoral shaft compared to patients not performing standing movements [27]. Thus, the bone density in a specific area of the vertebra should reflect the load history in that region. Spinal aging, especially degenerative change, alters the pattern of load bearing and shifts load to posterior structures [16]. To the extent that such a shift results in stress shielding, it follows that vBMD and strength in the vertebral body may be reduced and fracture risk increased. Understanding the load distribution between the vertebral body and neural arch may lead to preventative therapies such as exercise that can potentially reduce posterior vertebral loading and help to prevent insufficiency fractures.

This study has several limitations. First, cases and controls were not individually matched. The controls were, however, obtained from an age-stratified cohort of community residents, and the results were adjusted for age and BMI. Second, as described elsewhere [18], CT scanners changed during the time that the QCT studies in this cohort were collected. This may have resulted in increased variability of the data; however, 37 of 39 controls and 34 of 36 cases were scanned in the same scanner. In addition, any such effect was minimized by the use of a common spine phantom. Third, the quantification of vertebral compression fractures is controversial [6]. This study graded deformities in the customary semi-quantitative manner [29] as mild (grade 1), moderate (grade 2) or severe (grade 3). We did not include subjects with minimal vertebral body height loss (grade 1) in our analysis as it is unclear the extent to which they represent actual vertebral fractures [6]. This may have biased our results. Fourth, subjects differ in their spine architecture so each section examined may not represent identical mid-regions of the L3 vertebral body. The measurement used (vBMD) quantifies changes in trabecular bone density, which may impact bone strength, but does not directly reflect bone architecture which also impacts strength. Similarly, changes in the degree of mineralization and collagen quality with age affect physical properties of bone and the compressive strength of vertebrae [30–32]. However, we are unaware of a method that can measure these properties in vivo as has been done in animal studies [33]. In addition, spine curvature was not measured in the study population, preventing us from reaching conclusions regarding the influence of spinal alignment on neural arch and vertebral body trabecular bone distribution. Finally, cortical vBMD was not measured due to CT resolutions which could not differentiate between trabecular bone and the cortical shell of the vertebral body. A cortical pixel might include not only cortical bone, but also trabecular bone, lowering the real value of the cortical BMD. However, we believe that increased neural arch loading would likely have influenced and increased cortical bone as well.

Conclusions

Persons with vertebral fractures had lower vBMD than those without fracture, but this difference was statistically different only in the vertebral body and not in the neural arch. These results suggest that the posterior shift in load bearing, which has been noted to occur with age and degenerative change, results in stress shielding of the vertebral body and contributes to trabecular loss while maintaining bone density in the neural arch. Such bone

loss would eventually increase fracture risk in women with osteoporosis. However, proof of this dynamic concept still needs to be evaluated. We used a previously established technique to quantify volumetric BMD with QCT in both the vertebral body and the neural arch. We are unaware of other studies using this technique in the neural arch (in this case the pars interarticularis). Although the methodology is validated in the vertebral body, we welcome external validation of the technique in the neural arch. Future studies should analyze vBMD in spinal regions and examine its relationship to spine posture and bone architecture. They should also consider other areas, such as the facets, and study the effect of contact and loading. Such findings suggest a need to develop new therapies or interventions that can shift vertebral loading anteriorly to help maintain bone integrity and possibly decrease fracture risk in women with reduced bone density.

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Fig. 1.

a Sagittal view of the lumbar spine showing the region of interest (ROI). Two slices (*Slices 1 and 2*) were analyzed containing vertebral body and neural arch trabecular bone. *Slice 1* represents the mid-slice between the endplates distance (L) at $L/2$. **b** A Hounsfield unit window was used to define cortical bone of the spine. **c** Using image editing and the tangent lines defining the vertebral body and neural arch as boundaries, vertebral body and neural arch cortical regions were separated for analysis. **d** Boolean operations and additional image editing allowed for vertebral body and neural arch (pars interarticularis) trabecular bone to be segmented separately

Fig. 2.
Distribution of vertebral body fractures by location in the spine

Fig. 3.

Vertebral volumetric bone mineral density (vBMD, mean $\pm$ SD) of the neural arch and vertebral body, and the neural arch/vertebral body ratio (adjusted for age at scan and BMI), among women with moderate or severe vertebral fractures (cases) compared to controls. (* $P = 0.182$; ** $P < 0.001$)

Fig. 4. Ratio of neural arch/vertebral body vBMD by age and fracture status (grade 2 or 3 vertebral fracture cases vs. controls with no vertebral fracture). Regression lines are shown representing fracture cases (*dashed line*) and controls (*solid line*)

Table 1

Vertebral Body and Neural Arch trabecular vBMD measurements

Patient no.	Control		Cases		Ratio
	vBMD (mg/cm ³)		vBMD (mg/cm ³)		
	Vertebral body	Neural arch	Vertebral body	Neural Arch	
1	86.7	71.8	79.6	192.5	2.42
2	54.8	135.3	53.6	76.0	1.42
3	90.6	226.7	58.8	54.7	0.93
4	54.9	104.7	45.3	125.3	2.77
5	161.7	240.0	48.5	84.4	1.74
6	44.8	68.1	72.1	181.3	2.51
7	123.9	122.8	54.5	118.1	2.17
8	123.1	124.4	51.8	117.2	2.26
9	113.7	48.1	74.5	83.4	1.12
10	77.5	69.0	32.8	45.9	1.40
11	115.8	114.6	62.6	62.5	1.00
12	28.2	40.5	45.9	120.6	2.63
13	112.2	182.2	201.7	265.0	1.31
14	34.9	55.2	19.2	66.2	3.45
15	82.7	117.7	35.9	27.3	0.76
16	38.3	82.1	95.2	138.7	1.46
17	88.4	78.4	17.0	71.6	4.21
18	48.3	78.1	90.8	138.8	1.53
19	90.9	166.6	57.6	107.6	1.87
20	102.8	102.9	72.7	187.8	2.58
21	120.8	146.0	27.5	59.8	2.17
22	101.2	98.4	14.1	41.3	2.93
23	82.7	132.8	12.6	46.2	3.67
24	89.6	158.1	21.8	47.4	2.17
25	139.8	161.3	38.6	99.7	2.58
26	18.2	59.3	32.4	111.6	3.44

Patient no.	Control		Cases		
	vBMD (mg/cm ³)		Ratio		Ratio
	Vertebral body	Neural arch	Vertebral body	Neural Arch	
27	48.6	49.0	87.9	213.0	2.42
28	36.8	64.9	23.2	113.2	4.88
29	104.9	204.6	46.6	98.8	2.12
30	178.7	252.0	32.6	62.0	1.90
31	91.8	157.8	8.1	15.2	1.88
32	100.0	103.1	28.0	31.9	1.14
33	47.1	66.8	39.0	108.9	2.79
34	80.8	82.4	3.6	11.7	3.25
35	104.9	230.3	66.6	74.4	1.12
36	97.0	150.8	11.7	60.7	5.19
37	98.7	91.1	–	–	–
38	64.2	58.2	–	–	–
39	134.1	113.6	–	–	–
Total average	87.5 ± 36.8*	118.2 ± 57.4	49.0 ± 36.0*	96.1 ± 57.6	2.31 ± 1.07**
Non-treated average	86.9 ± 36.8 ^β	119.9 ± 58.1	47.6 ± 39.3 ^β	104.9 ± 59.1	2.10 ± 0.92 ^ε

– Dashed line separates treated versus untreated subjects

*** $P < 0.001$,
 $\beta_P = 0.006$,
 $\epsilon_P = 0.003$