Longitudinal changes in lumbar bone mineral density distribution may increase the risk of wedge fractures

Hugo Giambinia, Sundeep Khosla, Ahmad Nassr, Chunfeng Zhao, Kai-Nan An

Biomechanics Laboratory, Division of Orthopedic Research, Mayo Clinic, Rochester, MN, USA
Division of Endocrinology, Metabolism and Nutrition, Department of Internal Medicine College of Medicine, Mayo Clinic, Rochester, MN, USA
Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN, USA

A R T I C L E   I N F O
Article history:
Received 4 September 2012
Accepted 16 October 2012

Keywords:
Lumbar
Bone mineral density
Time
Risk of fracture
Vertebrae

A B S T R A C T

Background: Trabecular bone strength diminishes as a result of osteoporosis and altered biomechanical loading at the vertebral and spinal levels. The spine consists of the anterior, middle and posterior columns and the load supported by the anterior and middle columns will differ across different regions of the spine. Stress shielding of the anterior column can contribute to bone loss and increase the risk of wedge fracture. There is a lack of quantitative data related to regional spinal bone mineral density distribution over time. We hypothesize that there is an increase in the posterior-to-anterior vertebral body bone mineral density ratio and a decrease in whole-body bone mineral density over time.

Methods: Bone mineral density was measured in 33 subjects using quantitative computed tomography scans for L1–L3 vertebrae, region (anterior and posterior vertebral body), and time (baseline and 6 years after).

Findings: Lumbar bone mineral density decreased significantly (Δ: -15%) from baseline to the 6th year visit. Individual vertebra differences over time (L1: -14%, L2: -14%, L3: -17%) showed statistical significance. Anterior bone mineral density change was significantly greater than in the posterior vertebral body region (Δ anterior: -18%; Δ posterior: -13%). Posterior-to-anterior bone mineral density ratio was significantly greater in the 6th year compared to baseline values (mean (SD), 1.33 (0.2) vs. 1.23 (0.1)).

Interpretation: This study provides longitudinal quantitative measurement of bone mineral density in vertebrae as well as regional changes in the anterior and posterior regions. Understanding bone mineral density distribution over time may help to decrease the risk of wedge fractures if interventions can be developed to bring spine loading to its normal state.

© 2012 Elsevier Ltd. All rights reserved.

1. Introduction

Osteoporosis is characterized by low bone mass, decreased bone strength, architectural deterioration and a significant increase in fracture risk and bone fragility (Briggs et al., 2006; Homminga et al., 2004; Imai et al., 2009; Kayanja et al., 2004; Wang et al., 2012). Osteoporosis is a silent and asymptomatic disease usually not diagnosed until a person presents with an insufficiency fracture or after fractures have already occurred, thus delaying necessary treatment (Kayanja et al., 2004; McDonnell et al., 2007; Melton and Kallmes, 2006). Vertebral fractures often occur as a result of normal daily loads and may be clinically underdetected (Homminga et al., 2001, 2004; Imai et al., 2006; Kayanja et al., 2004). However these fractures can be associated with significant functional limitations (Nevitt et al., 1998).

Fracture risk is affected by loading changes at the regional and local levels. At the local vertebral level, it has been reported (Rockloff et al., 1969) that the cortical shell contributes about 45–75% of the vertebral strength, however Homminga et al. (2001, 2004) demonstrated that trabecular bone carries 50–70% of the total load. At the regional level, many factors affect spine loading including the sagittal alignment of the thoracic and lumbar spine (Kobayashi et al., 2008). Denis (1983) described the spine as three columns: “anterior (anterior half of the vertebral body), middle (posterior half of vertebral body), and posterior (pedicles, posterior elements and facets) columns”. The majority of the load is transmitted through the anterior and middle columns but differs across regions of the spine. Degenerative changes with time result in decreased load in the anterior column, and increased across the middle and posterior columns (Adams and Hutton, 1983; Pollintine et al., 2004). This shielding of the anterior column may contribute to bone loss and an increase in wedge fracture risk over time (Pollintine et al., 2004).

This posterior shift in loading that occurs with aging is not picked up by traditional bone mineral density (BMD) testing. Little has been published in current literature regarding these local changes in the vertebral BMD over time. Specifically does posterior vertebral BMD increase relative to anterior BMD over time? We hypothesize that with aging, there will be a total decrease in vertebral body BMD, but an increase in the posterior-to-anterior vertebral body BMD ratio over time. In order to investigate these changes we performed a longitudinal...
analysis of BMD changes in the L1–L3 vertebrae on a cohort of patients followed for a period of six years.

2. Methods

2.1. Study subjects

We utilized data previously collected as part of an ongoing study that has previously been described (Riggs et al., 2004). Twenty-one males with no history of fracture or bone spurs/endplate deformations and 12 males with at least one grade 2–3 thoracic vertebral fracture were included. Severe thoracic vertebral fractures (grade 2–3) were classified as a reduction of approximately 25% or greater in anterior/middle and/or posterior height, as previously described (Genant and Jergas, 2003; Melton et al., 2010). Subjects were selected so that they had approximately the same age and BMI (body mass index) (Table 1). All subjects had quantitative computed tomography (QCT) scans of the lumbar spine (L1, L2 and L3) obtained as part of the original study after they had provided written informed consent.

2.2. Bone density measurements

As previously described (Melton et al., 2010), QCT images of the lumbar region (L1, L2 and L3) were obtained by single-energy QCT using two different scanners over the course of the original study. Briefly, a 4-channel multidetector-row scanner (LightSpeed Qx/i) and a 64-channel system (Somatom Sensation 64) from Siemens Healthcare (Forchheim, Germany), with the same scanning parameters, were used for the image acquisition at both time points (Baseline and 6th years after). The baseline external calibration standard, Model 2 Liquid Phantom, was changed at the 6th year to a Model 3 Solid Phantom (Mindways Software, Inc., Austin, TX, USA).

The QCT-DICOM images were analyzed with Mimics image processing and editing software (Materialise US, Ann Arbor, MI USA). Segmentation was performed in vertebral body trabecular bone regions of L1, L2 and L3 at two time points, baseline and 6-years after. A standard Hounsfield unit (HU) window (HU>225) was applied to field units from all three regions (Fig. 1H and I). Trabecular Hounsfield units from all three segmentations (whole vertebral body, anterior and posterior region) for all vertebrae were exported in text-based format. Calibration phantoms (Models 2 and 3) containing reference material were used to obtain equivalent K2HPO4 densities of the unknown vertebrae regions using a custom linear regression program in MATLAB (Mathworks, Natick, MA). Equivalent K2HPO4 densities were obtained for each site (L1, L2 and L3), region (anterior and posterior), and time (baseline and 6 years after) for all 33 subjects.

2.3. Statistical analysis

Data analyses were completed using SAS (SAS Institute Inc., Cary, NC USA). A repeated measures analysis of variance model was run to test for overall differences between vertebrae sites (L1, L2, and L3), regions (posterior and anterior) and time (baseline and 6 years after); interactions between the different factors were also analyzed.

3. Results

There were no statistically significant differences in age or BMI between the 21 controls and the 12 males with grade 2–3 non-lumbar fractures (Table 1). Furthermore, there were no statistically significant differences in any of the measured values (whole body, anterior and posterior body BMDs, either at baseline or 6th year). For this reason, the subjects were combined into one pool of data comprising of 33 male subjects. Data presented corresponds to the pooled data. Fig. 2 describes the measured BMD per site and region for the 33 subjects. Lumbar (L1–L3) BMD decreased significantly (Δ: -15%) from 140.3 (37.9) mg/cm3 at baseline to 119 (38.8) mg/cm3 at the 6th year visit (P<0.0001) (Fig. 3). There was also a statistical difference (P=0.0136) between sites over time, with BMD decreasing ~14% in L1, ~14% in L2 and 17% in L3 (Fig. 4). Lumbar anterior vertebral body BMD decrease over time was significantly greater (P=0.0177) than in the posterior body region (anterior-baseline: 126 (32.9), anterior-6th year: 103.8 (33.9), Δ anterior: -18% and posterior-baseline: 154 (37.7), posterior-6th year: 134.2 (37.5) mg/cm3, Δ posterior: -13%) (Fig. 5). Posterior-to-anterior BMD ratio was significantly greater in the 6th year compared to baseline values (mean (SD), 1.33 (0.2) vs. 1.23 (0.1), P<0.0001) (Fig. 6).

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Gender</th>
<th>#</th>
<th>Time</th>
<th>Label</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Male</td>
<td>21</td>
<td>Baseline</td>
<td>Age (years)</td>
<td>62.28</td>
<td>11.03</td>
<td>62.27</td>
<td>43.59</td>
<td>85.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BMI (kg/m²)</td>
<td>29.10</td>
<td>4.95</td>
<td>27.49</td>
<td>22.17</td>
<td>40.95</td>
</tr>
<tr>
<td>Grade 2–3 non-lumbar</td>
<td>Male</td>
<td>12</td>
<td>Baseline</td>
<td>Age (years)</td>
<td>64.31</td>
<td>12.74</td>
<td>61.97</td>
<td>45.40</td>
<td>82.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BMI (kg/m²)</td>
<td>28.37</td>
<td>3.76</td>
<td>27.30</td>
<td>23.78</td>
<td>35.48</td>
</tr>
</tbody>
</table>

Table 1

Age and BMI at baseline and 6th year are presented as mean and SD. Median, minimum and maximum are also presented.
4. Discussion

In this study we were able to quantify the BMD of the lumbar region (L1–L3) in 33 male subjects based on QCT images at two different time points. We found the lumbar trabecular BMD to significantly decrease in a six year span and these differences varied significantly between vertebrae, with L3 having the highest change in BMD. The anterior vertebral region demonstrated a significant decrease compared to the posterior vertebral region. This resulted in a significant difference in the posterior-to-anterior ratio over time.

This study was motivated by the lack of quantitative data in the literature relating local lumbar trabecular changes in BMD over time. While many studies support a posterior shift in loading we are not aware of any studies that show that this translates into BMD changes in the posterior vertebral body. The results support our hypothesis that BMD decreases with time and that there is an increase in posterior-to-anterior BMD ratio in the lumbar region. These data also support previous literature reports stating stress shielding of the anterior column as a cause and contributor of bone loss (Pollintine et al., 2004).

Disc degeneration (Pollintine et al., 2004), age (Andresen et al., 1998; Melton et al., 2006) and changes in the sagittal alignment of
the spine (Kobayashi et al., 2008) have been associated with decreases in vertebral loading. With age, vertebral load is shifted to the facet joints thereby decreasing anterior BMD and the strength of the vertebral body, possibly increasing wedge fracture risk (Pollintine et al., 2004). Disc degeneration causes a shift in vertebral load and is associated to changes in trabecular and cortical BMD (Homminga et al., 2012; Wang et al., 2011). Spine curvature changes, including scoliosis, kyphotic and lordotic changes can also contribute to abnormal loading on the vertebrae, which may increase the risk of fracture (Li et al., 2008; Watanabe et al., 2007). These changes in spinal alignment have been linked with the development of osteoporosis (Routh et al., 2005; Sadat-Ali et al., 2008; Watanabe et al., 2007). Other studies have demonstrated that thoracic kyphosis is significantly and inversely correlated with lumbar BMD (Edmondston et al., 1994; Ettinger et al., 1994; Kobayashi et al., 2008; Thevenon et al., 1987 #18).

At the local vertebrae level, previous studies have shown the contribution of the cortical shell and trabecular bone in the load bearing capacity and fracture risk of the vertebra (Andresen et al., 1998; Cao et al., 2001; Cody et al., 1991; Eswaran et al., 2006; Homminga et al., 2001, 2004). However, these studies have not demonstrated BMD changes and distribution within and between vertebral bodies and their association with fracture risk.

A relative decrease in anterior-to-posterior BMD may predispose to wedge fractures in patients with osteoporosis. As previously described, flattening of the lumbar spine results in a forward shift and sagittal imbalance, multiple disc degeneration, and a higher load in the anterior portion of the vertebral body (Gelb et al., 1995; Hammerberg and Wood, 2003; Kobayashi et al., 2008). Understanding longitudinal curvature changes and BMD distribution within the vertebral body is of significant importance in preventive medicine. Specific interventions targeting this differential bone loss in the anterior body may decrease the risk of wedge fractures through bracing, therapy and other modalities aimed at normalizing spine loading. A better understanding of individual vertebrae, other than the lumbar (L1–L3) analyzed in this study will also contribute greatly to our understanding of these changes over time. Other factors associated with the development of osteoporotic vertebral fractures need to continue to be studied including: the role of muscle activity, micro-architecture and intrinsic material properties of bone.

This study has several limitations. First, the small subject number may have affected our results; however based on our observations, we believe that these findings would be similar in a larger study. Second, even though calibration phantoms were used for both (baseline and 6th year) scanning times, there might have been some variability in the image acquisition affecting the density measurements. Third, only the lumbar (L1–L3) region was acquired in the QCT scan, preventing us from drawing any conclusions at other spinal regions. Also, we were unable to measure spine curvature in the study population, preventing us from reaching conclusions between BMD distribution and spinal alignment. In addition to the small population number, spinal alignment and/or the degree of disc degeneration between the controls and the fractured population might have been an additional cause for not finding differences between the groups. Lastly, we were unable to measure the degree of disc degeneration thus preventing us from reaching concluding remarks between the longitudinal causes of BMD loss and the degenerative process.

5. Conclusions

In summary, BMD changes in the anterior, posterior and whole vertebral bodies (L1–L3) of 33 human subjects were quantified and measured from QCT images at two different time points. BMD in the lumbar region was shown to decrease and the posterior-to-anterior ratio to increase over time. These findings support previous hypotheses of a posterior load shift in the spine over time and lead to a better understanding between BMD changes and individual vertebral body measurements. This posterior shift in load bearing seen with aging and degenerative change in the spine may result in stress shielding of the anterior vertebral body that ultimately contributes the development of osteoporotic wedge fractures.
References


