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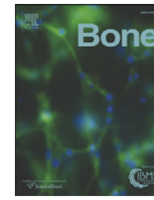

Original Full Length Article

Regional variations in trabecular architecture of the lumbar vertebra: Associations with age, disc degeneration and disc space narrowing

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ABSTRACT

Previous studies suggest that age and disc degeneration are associated with variations in vertebral trabecular architecture. In particular, disc space narrowing, a severe form of disc degeneration, may predispose the anterior portion of a vertebra to fracture. We studied 150 lumbar vertebrae and 209 intervertebral discs from 48 cadaveric lumbar spines of middle-aged men to investigate regional trabecular differences in relation to age, disc degeneration and disc narrowing. The degrees of disc degeneration and narrowing were evaluated using radiography and discography. The vertebrae were dried and scanned on a μCT system. The μCT images of each vertebral body were processed to include only vertebral trabeculae, which were first divided into superior and inferior regions, and further into central and peripheral regions, and then anterior and posterior regions. Structural analyses were performed to obtain trabecular microarchitecture measurements for each vertebral region. On average, the peripheral region had 12–15% greater trabecular bone volume fraction and trabecular thickness than the central region ($p < 0.01$). Greater age was associated with better trabecular structure in the peripheral region relative to the central region. Moderate and severe disc degeneration were associated with higher trabecular thickness in the peripheral region of the vertebral trabeculae ($p < 0.05$). The anterior region was of lower bone quality than the posterior region, which was not associated with age. Slight to moderate narrowing was associated with greater trabecular bone volume fraction in the anterior region of the inferior vertebra ($p < 0.05$). Similarly, greater disc narrowing was associated with higher trabecular thickness in the anterior region ($p < 0.05$). Better architecture of peripheral trabeculae relative to central trabeculae was associated with both age and disc degeneration. In contrast to the previous view that disc narrowing stress-shields the anterior vertebra, disc narrowing tended to associate with better trabecular architecture in the anterior region, as opposed to the posterior region.

Introduction

Osteoporosis and disc degeneration are two common conditions affecting the lumbar spines of older adults and are important contributors to back pain [1]. While the vertebral bones and intervertebral discs are typically studied separately, a growing body of evidence suggests that they are closely related. For example, higher bone mineral density (BMD) of the vertebra [2] and vertebral body [3], as measured using either dual-energy X-ray absorptiometry (DXA) or micro-computed tomography (μCT), was found to be associated with more severe disc degeneration. Better trabecular microarchitecture in the vertebra, such as greater bone volume [4,5] and greater trabecular number and thickness [5], was also found to be associated with more degeneration in the adjacent disc. The vertebral bone may contribute to disc degeneration [5] and vertebral trabeculae may undergo rapid and profound remodeling in response to annular tears in the disc [6], suggesting an interplay of the two structures.

The vertebra–disc interaction can be explained as a remodeling process in the spinal segment's attempts to adapt to an altered biomechanical environment. In the discs of a young individual, the compressive stress is typically focused on the elastic nucleus pulposus [7], leading to better trabecular bone architecture under the nucleus than under the annulus [8]. The load distribution pattern in the vertebra–disc segment, however, is subject to change. Gradually, more loads are transmitted through the vertebral periphery underneath the annulus [9,10], resulting in better trabecular microarchitecture in the periphery of the vertebra than in the central region [11]. The mechanism underlying the load redistribution remains unclear, and was reported to be associated with age [12], disc degeneration [13], or both [11].

In the presence of severe disc degeneration, particularly a severely narrowed disc, the stress distribution in a vertebra–disc segment may further change [14]. With significant disc narrowing, more load is transferred through the neural arches to the posterior facet joints in

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upright posture, resulting in relatively less load transmission through the anterior portion of the vertebra (stress-shielding) [15]. When the spine is flexed, however, load was found to concentrate on the anterior vertebral body. As such, the anterior region of the vertebra is predisposed to fracture when the spine bends anteriorly [14,15]. Although this theory helps to explain why osteoporotic fracture is more common in the anterior region [16], related studies are based on histological measures of disc degeneration, and not specifically disc narrowing [15–17]. While disc narrowing is associated with a greater risk of vertebral fracture in postmenopausal women [18], disc degeneration, as measured using either histology or magnetic resonance imaging, was found to be associated with less likelihood of vertebral fracture [19,20]. As disc degeneration and disc narrowing may represent two different phenomena of age-related disc changes [21], it may not be appropriate to use disc degeneration as a synonym for disc narrowing.

Related studies are also limited by proxy trabecular measurements, which were typically measured by sampling a thin slice and quantified with a 2D histological approach [5,16]. Due to the heterogeneity of vertebral trabeculae [4,5], bone samples of small volume may not be representative of vertebral regions of interest [22,23]. Using μCT, the objectives of the current study were to determine the magnitude of regional trabecular variations and to clarify their relation to age, disc degeneration and disc narrowing. Better trabecular architecture, as we define it, is characterized by higher bone volume fraction, higher trabecular thickness and lower trabecular separation. We hypothesized that: 1) better trabecular architecture in the peripheral vertebra relative to the central vertebra is associated with greater age and disc degeneration; and 2) disc narrowing is associated with inferior trabecular architecture in the anterior vertebra.

Materials and methods

Samples

This study used a cadaveric spine archive, which consists of 149 cadavers of Caucasian men [24]. The criteria for inclusion of subjects in the archive have previously been described in detail [3]. In brief, only employed men below the age of 65 years who passed away with a short history of illness were included. Some of the archived vertebrae and disc degeneration data were lost. As the local interaction between the vertebrae and adjacent discs was of particular interest, we selected samples based on the availability of vertebrae and adjacent disc degeneration data. As a result, 150 cadaveric lumbar vertebrae (13 L1, 24 L2, 19 L3, 47 L4 and 47 L5) and 209 adjacent lumbar intervertebral discs from 48 spines of men with a mean age 50 years (range 21 to 64 years) were investigated. The study was approved by the Health Research Ethics Board at the University of Alberta.

Measurements of disc degeneration and disc space narrowing

After a routine autopsy examination of the lumbar spines, anterior–posterior and lateral plain radiographs were taken. Then, discography was performed by injecting 2–5 ml of barium sulfate ($BaSO_4$) anteriorly into the center of L1/2 to L5/S1 intervertebral discs using maximal finger pressure. The lumbar spines were then radiographed again [24]. After discography, the soft tissues around the vertebra were removed. Vertebrae were dried under room temperature and then archived, together with the plain and discography films.

According to the spread of $BaSO_4$ in the discogram, a 4-grade ordinal scale was used to evaluate the degree of disc degeneration as evidenced by annular disruption. Disc degeneration was rated as *none* if the dye remained in the center of the disc; *slight* if the dye spread into the inner annulus; *moderate* if the dye spread from the inner to the middle region of the annulus; and *severe* if the dye spread to the outer portion of the annulus [25]. For intra-observer agreement, a weighted kappa of 0.81 was obtained for the discography measurements [24].

Disc space narrowing was evaluated from plain lateral radiographs. Typically, disc narrowing is evaluated using a 4-point scale [26]. While it can be difficult to differentiate slight narrowing from moderate narrowing, our main interest was “severe” disc narrowing [14]. Thus, to minimize measurement error, we modified Lane's protocol into a three-point scale (*none*, *slight to moderate* and *severe*) and defined severe disc narrowing as a loss of disc height of 50% or more relative to the above normal disc. A random sample of 20 other lumbar radiographs from the archive was used for training, and evaluated by two of the authors (YW and TV) together. After agreement was reached between the two raters, the lumbar radiographs of the study subjects were assessed independently. A weighted kappa of 0.71 was obtained for the inter-observer agreement. If ratings of a disc space differed, the disc was discussed to obtain a final score.

Measurements of trabecular microarchitecture

A total of 150 lumbar vertebrae were scanned using μCT (XtremeCT, Scanco Medical, Brüttisellen, Switzerland) and the following scanning parameters: 60 kVp, 1000 μA, 200 ms integration time, and 750 projections. Vertebrae first were scanned in air at a nominal isotropic resolution of 82 μm (field of view 125 mm, 1536 × 1536 pixels). Regions of interest were identified for the vertebral body in each μCT image, which was contoured using a semi-automated contouring method [27]. The contour included only the trabecular region of the vertebral body, such that the posterior elements of the vertebra and the cortex of the vertebral body were excluded from the data analyses. By volume, the vertebra was divided equally into superior and inferior regions (Fig. 1A).

Both the superior and inferior regions were further divided into a cylindrical central region and a concentric peripheral ring to simulate the shape and size of the nucleus and the annulus, respectively. By manually centering the midpoint of a vertebra, a cylinder with approximately one fifth of the total volume of the vertebra was extracted. The diameter of this central cylinder ranged from 6 to 12 mm, depending on the size of the vertebra. The peripheral ring was symmetrically partitioned into left and right portions, which were further divided into anterior and posterior sections using the mid-transverse axis of the vertebra (Fig. 1B). In summary, each superior and inferior region of the vertebra was divided into five sub-regions.

Structural and densitometric analyses were performed (Image Processing Language, v5.15, Scanco Medical AG, Brüttisellen, Switzerland) to obtain volume, BMD (mg HA/cm^3), trabecular number (Tb.N; 1/mm) and connectivity density (Conn.D; 1/mm^3) measurements for each section, including the central cylinder, the whole peripheral ring, two anterior sections and two posterior sections. Trabecular bone volume fraction (BV/TV; %) was calculated based on the BMD measurements, with the assumption that fully mineralized bone has a density of 1200 mg HA/cm^3 [28]. Trabecular thickness (Tb.Th; mm) and trabecular separation (Tb.Sp; mm) were determined by semi-derived methods [28]. The reliability, validity and precision of μCT for the measurement of trabecular microstructures are well established [29,30].

Statistical analysis

Since there is a considerable vertical inhomogeneity in vertebral trabecular architecture [22,31], the superior and inferior vertebral regions were analyzed separately. Paired t-tests were used to compare the differences of trabecular architecture between central and peripheral regions, and between anterior and posterior regions. The differences of regional architectural parameters were expressed as the percentage increase relative to the central region and anterior region, respectively. Multiple variable regressions were used to examine the associations between regional trabecular variations and age, disc degeneration and disc space narrowing. Because the local mechanical vertebra–disc