The influence of diffuse idiopathic skeletal hyperostosis on bone mineral density measurements of the spine

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Introduction

In DISH, spinal and peripheral ligaments and entheses become ossified [1]. Most clinical symptoms of DISH are mild, although serious complications are being reported with increasing frequency including myopathy, unstable thoracolumbar fractures after minor trauma and complaints such as dysphagia and dyspnoea due to bony protrusions of the cervical spine [2–6]. Extraspinal manifestations consist of tendonitis and painful enthesophytes, which are often bilateral and symmetrical [7]. The aetiology of DISH is not known although several authors have proposed an association with increasing age, obesity and type 2 diabetes mellitus [8, 9]. Reported prevalences range from 2.9 in Korea to 25% in Caucasian men in the USA, and may well increase the coming decades because of the relation between DISH and modern lifestyle-related diseases like obesity and diabetes [10, 11]. Since DISH particularly affects the right side of the anterior longitudinal ligament (ALL), it has been hypothesized that pulsations of the aorta may prevent ossification on the left side [12]. This hypothesis is supported by the few cases of individuals with situs inversus and DISH, where ossifications of the ALL were found on the left side of the spine [13, 14].

The definition of DISH suggests a generalized state of hyperostosis and the exuberant ossifications of the thoracic spine displayed on chest radiographs could lead to an impression of skeletal robustness [15]. In accordance with this impression, BMD of patients with DISH has been described to be increased compared with unaffected individuals [15–17]. In these studies, BMD was established with the metacarpal index on conventional radiographs of the hand, DXA of the distal radius and DXA of the lumbar spine. An anteroposterior DXA scan of the lumbar spine may, however, not be a reliable method to establish BMD of vertebral bodies in DISH patients as the ossified ALL may well project in the field of view during DXA scanning, thereby possibly leading to an overestimation of BMD. This may lead to adverse clinical strategies; for instance, when osteoporosis goes undetected due to overestimation of the true vertebral BMD.

To the authors’ best knowledge, no studies have been published investigating the influence of DISH on BMD measurements of the spine. In the current study, we quantitatively investigated the contribution of the ossified ALL on calculated vertebral BMD in 10 human cadaveric spines with DISH and 10 control specimens without DISH and subsequently estimated the real vertebral BMD of spines affected by DISH.

Methods

Identification and preparation of specimens

From the Department of Anatomy, 20 formaldehyde fixed (4%) human thoracolumbar spines were obtained. The spines were obtained from individuals who donated their body for the benefit of science. We selected 10 specimens that showed definite features of DISH, according to the criteria defined by Resnick and Niwayama [18] at fluoroscopical examination (Omnidiagnost Eleva; Philips Medical Systems, Best, The Netherlands) and comprising flowing ligamentous ossification along the anterolateral aspect of at least four contiguous vertebral bodies with preservation of intervertebral disk height at the involved segment and absence of extensive degenerative changes. Another 10 age- and gender-matched specimens without signs of DISH were selected as controls. The spines were stripped from all soft tissues, except for the ligaments and intervertebral disks, and the ribs were subsequently removed. A regular off-the-shelf chipboard screw (6.0 × 120 mm) was drilled in each 12th thoracic vertebra to serve as reference during CT and DXA scanning. See Fig. 1 for a schematic representation of the workflow of the study.

CT

CT scanning with sagittal/coronal multi-planar reformatting was performed on a 64-slice scanner (Philips Brilliance;...
Philips Medical Systems), using 0.625-cm axial helical scans with high resolution (120 kV, 200 mAs, slice thickness 0.9 mm). The three most central and prominent bony bridges, spanning four vertebral bodies, were marked as ROI. For the control samples, ROIs identical to the DISH specimens were recorded. Controls with moderate osteophytes present at the ROI were not excluded, since the Resnick criteria also allow for the diagnosis DISH in the presence of 'localized pointed excrescences' [18].

The following parameters were assessed on transverse CT images for the two most central vertebral bodies of the ROI in the DISH specimens.

(i) AP axis, defined as the line through the middle of the anterior cortex of the vertebral body and the centre of the vertebral body (Fig. 2A; vertical yellow line).

(ii) Line from the outer left, to the outer right border of the ossified ALL (Fig. 2A; red line).

(iii) Angulation of the line through the midportion of the ossified ALL relative to anteroposterior (AP) axis (degrees). (iv) Transverse orientation of the previously inserted screw in the 12th thoracic vertebra relative to the AP axis, measured in degrees.

DXA scanning

From the above data, the experimental DXA scanning orientations were calculated for all DISH specimens individually and identical scanning orientations were used for the matched controls. A frame was designed to hold the specimen in the desired orientation while avoiding obstruction of the scanning field (Fig. 3). A ‘routine’ BMD was first established by AP DXA scanning to provide reference values for the four vertebral bodies in each ROI (Hologic QDR-4500 Discovery A, software version 12.3; Hologic, Bedford, MA, USA).
Subsequently, three experimental DXA scans were performed.

(i) Scan of the complete vertebrae in the direction perpendicular to the line that can be drawn from the outer left to the outer right border of the ossified ALL, named full exposure scan (FES; Fig. 2B, red square).

(ii) Scan of the complete vertebrae in the direction perpendicular to the orientation of technique (i), named parallel scan (PS; Fig. 2C, blue square).

(iii) Anteroposterior scan of the halves of the vertebrae, named half scan right (HSR) and half scan left (HSL) (Fig. 2D; yellow square).

In FES, the maximum amount of ossified ALL was projected in the field of view and should, theoretically, yield the highest BMD possible. In PS, the minimum amount of ossified ligament was projected in the field of view; this orientation should yield the lowest BMD possible. In the HSR scan, the largest part of the ossified ligament was inside the field of view in DISH specimens, in contrast to the HSL scan, where most of the ossified ligament was outside the scanning field. Differences in BMD between these latter two scanning orientations should be non-existent in controls due to the absence of any ossified ligament.

Data analysis and statistics

The contribution of the ossified ligament on the BMD measurements was determined by dividing the BMD of DISH specimens by the BMD of controls multiplied by 100 to get the percentage, followed by subtracting 100% [percentual difference = (BMD DISH/BMD controls) × 100–100]. For statistical analysis, SPSS software (version 16.0) was used. Differences between the DISH specimens and controls were calculated with a paired samples t-test (significance set at P < 0.05).

Results

The mean age at death for donors of the DISH spinal columns was 80.4 ± 8.2 years, whereas for the controls it was 81.0 ± 6.9 years; this difference was not significant (P = 0.382). Both groups consisted of five males and five females. The ROI most frequently used for this study were thoracic levels 6–9 and 7–10 (Table 1).

DISH specimens displayed a statistically significant higher mean BMD than their matched controls in all scanning orientations, except in HSL. In the routine AP view, BMD was 0.795 g/cm² in DISH specimens (range 0.510–1.028 g/cm²) compared with 0.643 g/cm² (range 0.540–0.759 g/cm²) in controls. A normal distribution was observed in these data and there were no outliers. The difference in BMD was the most prominent in the FES, where the maximum amount of ossified ALL was present in the field of view; BMD was 0.695 g/cm² in DISH specimens compared with 0.514 g/cm² in controls (+35.2%). In the PS orientation, where the minimum amount of ossified ligament was present in the scanning field, the difference was considerably smaller; 0.606 vs 0.469 g/cm² (+29.2%). See Table 2 for more details on the BMD measurements in different DXA scanning orientations.

The HSR scan displayed a 39% higher BMD in DISH specimens than in controls (0.898 vs 0.646 g/cm²). The HSL scans were not significantly different between the groups. The right-left difference was also statistically significant within DISH specimens (P = 0.001), but not in controls (P = 0.825). See Fig. 4 for a graphic representation of this finding.

Summarizing, all scans incorporating (part of) the ossified ALL in the scanning field yielded higher BMD than controls.

Discussion

In the present study, bone mineral density of 10 spinal columns affected by DISH was experimentally investigated and compared with 10 age- and gender-matched non-DISH specimens. It was found that the presence of ossified ligamentous structures in the field of view consistently yielded higher BMDs in DISH specimens, leading to a potential overestimation of BMD ranging from 23.6 to 39.0%. The vertebral BMD was not higher in DISH specimens, as demonstrated by comparable BMDs in the HSL scan for both the DISH cases and controls.

As was previously hypothesized, BMD measurements varied for the three experimental scanning orientations. In the DISH specimens, differences were most prominent in orientations where the maximum amount of ossified ALL was present in the field of view (FES) and less distinctive in orientations where the minimum amount of ossified ligament was present in the scanning field (PS). Differences were also present in controls, although less profound. It may have been possible that BMD measurements were influenced by the contribution of the posterior elements of the spine during the various scanning orientations, although the exact amount of this contribution is unknown. Because the orientations for the experimental DXA scans were calculated on the two central vertebrae within the ROI of four vertebrae, it may have been possible that ossification of the ALL extended more anteriorly and/or posteriorly at the adjacent levels making it difficult to fully exclude this structure in the PS scan. Overall, the accuracy of positioning the spinal column in the frame may have been higher in the anteroposterior and HSL/HSR

<table>
<thead>
<tr>
<th>ROI</th>
<th>No. of specimens</th>
</tr>
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<tbody>
<tr>
<td>T4–T7</td>
<td>1</td>
</tr>
<tr>
<td>T5–T8</td>
<td>2</td>
</tr>
<tr>
<td>T6–T9</td>
<td>3</td>
</tr>
<tr>
<td>T7–T10</td>
<td>3</td>
</tr>
<tr>
<td>T8–T11</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
</tr>
</tbody>
</table>

TABLE 2. Mean BMD of 10 DISH specimens vs 10 controls

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>DISH</th>
<th>Difference, %</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP</td>
<td>0.643 ± 0.027</td>
<td>0.795 ± 0.049</td>
<td>+23.6</td>
<td>0.004</td>
</tr>
<tr>
<td>FES</td>
<td>0.514 ± 0.020</td>
<td>0.695 ± 0.044</td>
<td>+35.2</td>
<td>0.002</td>
</tr>
<tr>
<td>PS</td>
<td>0.469 ± 0.020</td>
<td>0.606 ± 0.042</td>
<td>+29.2</td>
<td>0.001</td>
</tr>
<tr>
<td>HSR</td>
<td>0.646 ± 0.029</td>
<td>0.898 ± 0.059</td>
<td>+39.0</td>
<td>0.001</td>
</tr>
<tr>
<td>HSL</td>
<td>0.643 ± 0.024</td>
<td>0.676 ± 0.046</td>
<td>+5.1</td>
<td>0.446</td>
</tr>
</tbody>
</table>

Mean BMD is given in gram per square centimetres ± s.e.m.

Fig. 4. Mean BMD of HSs of 10 DISH specimens compared with 10 controls (*P = 0.001; †P = 0.825).
orientation compared with the other scanning orientations, possibly explaining the large right–left difference in DISH specimens compared with controls. Since all experimental orientations were calculated from the CT data beforehand, using the inserted screw as a reference during CT scanning and for final positioning in the frame before DXA scanning, the influence of this variability on BMD is, however, suggested to be low.

In the present study, BMD was measured in the thoracic spine (T4–T11), because these regions displayed features of DISH most prominently. Secondly, since the ossified ligament is most asymmetric in the thoracic spine it was feasible to include or exclude this structure during scanning. In clinical practice, BMD is usually measured in the lumbar spine (L2–L4) [19]. Although DISH is most commonly encountered in the thoracic spine and may therefore be substantially.

Other studies concerning BMD in patients with DISH have been published previously. Di Franco et al. [17] reported BMD to be increased in the distal radius of 42 DISH patients. Schwartz and Rackson [21] reported high BMD in a patient with exuberant bony changes of the lumbar spine as a result of DISH, whereas BMD of the forearm was decreased. The authors suggested that DISH caused artificially elevated lumbar BMD measured by DXA, but did not quantify the contribution of the ossified ligament to the BMD measurement. Sahin et al. [15] compared the BMD from a group of patients with type 2 diabetes mellitus and DISH with a group of type 2 diabetes without DISH and a group of healthy controls. Both the individuals with DISH and diabetes and the non-DISH diabetics reported a duration of diabetes of ~10 years. BMD of the lumbar spine was higher in individuals with DISH and diabetes than in diabetes without DISH and the controls. The reported differences in BMD were smaller for the femoral neck and hip. Retrospectively, it may not be unrealistic to suggest that the lumbar spine BMD measurements were artificially increased by the presence of the ossified ligament in the scanning field as demonstrated in the present study.

In conclusion, it was found that in DISH cases the presence of the ossified ALL in the scanning field of view consistently led to higher BMDs than in controls. The vertebral BMD was comparable in DISH specimens and controls. The results suggest that the presence of DISH may potentially lead to an overestimation of the true vertebral body BMD. Consequently, normal BMD values could imply osteopenia or osteoporosis in patients when features of DISH are present in the scanning field of view. Clinicians should be aware that routine AP spinal measurement of BMD may be unreliable in patients with DISH.

Rheumatology key messages
- Presence of DISH in DXA scanning field leads to overestimation of BMD.
- Vertebral body BMD is not increased in DISH.
- Anteroposterior DXA scanning may be unreliable in DISH patients.

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