Bone 50 (2012) 1416–1425

Contents lists available at SciVerse ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Original Full Length Article

Failure strength of human vertebrae: Prediction using bone mineral density measured by DXA and bone volume by micro-CT

Egon Perilli [a,b,*], Andrew M. Briggs [c,d], Susan Kantor [d], John Codrington [a,e], John D. Wark [d], Ian H. Parkinson [a,b], Nicola L. Fazzalari [a,b]

[a] Bone and Joint Research Laboratory, SA Pathology and Hanson Institute, Adelaide, South Australia, Australia
[b] Discipline of Anatomy and Pathology, The University of Adelaide, Adelaide, South Australia, Australia
[c] Curtin Health Innovation Research Institute, Curtin University, Perth, Western Australia, Australia
[d] Department of Medicine, University of Melbourne, and Bone and Mineral Service, Royal Melbourne Hospital, Melbourne, Victoria, Australia
[e] School of Mechanical Engineering, The University of Adelaide, Adelaide, South Australia, Australia

ARTICLE INFO

Article history:
Received 22 September 2011
Revised 16 February 2012
Accepted 1 March 2012
Available online 10 March 2012

Edited by: Harry Genant

Keywords:
Vertebra
Osteoporosis
Densitometry
DXA
Micro-CT
Mechanical strength

ABSTRACT

Significant relationships exist between areal bone mineral density (BMD) derived from dual energy X-ray absorptiometry (DXA) and bone strength. However, the predictive validity of BMD for osteoporotic vertebral fractures remains suboptimal. The diagnostic sensitivity of DXA in the lumbar spine may be improved by assessing BMD from lateral-projection scans, as these might better approximate the objective of measuring the trabecular-rich bone in the vertebral body, compared to the commonly-used posterior–anterior (PA) projections. Nowadays, X-ray micro-computed tomography (μCT) allows non-destructive three-dimensional structural characterization of entire bone segments at high resolution. In this study, human lumbar cadaver spines were examined *ex situ* by DXA in lateral and PA projections, as well as by μCT, with the aims (1) to investigate the ability of bone quantity measurements obtained by DXA in the lateral projection and in the PA projection, to predict variations in bone quantity measurements obtained by μCT, and (2) to assess their respective capabilities to predict whole vertebral body strength, determined experimentally.

Human cadaver spines were scanned by DXA in PA projections and lateral projections. Bone mineral content (BMC) and BMD for L2 and L3 vertebrae were determined. The L2 and L3 vertebrae were then dissected and entirely scanned by μCT. Total bone volume (BV_{tot} = cortical + trabecular), trabecular bone volume (BV), and trabecular bone volume fraction (BV/TV) were calculated over the entire vertebrae. The vertebral bodies were then mechanically tested to failure in compression, to determine ultimate load.

The variables BV_{tot}, BV, and BV/TV measured by μCT were better predicted by BMC and BMD measured by lateral-projection DXA, with higher R^2 values and smaller standard errors of the estimate ($R^2 = 0.65$–0.90, SEE = 11%–18%), compared to PA-projection DXA ($R^2 = 0.33$–0.53, SEE = 22%–34%). The best predictors of ultimate load were BV_{tot} and BV assessed by μCT ($R^2 = 0.88$ and $R^2 = 0.81$, respectively), and BMC and BMD from lateral-projection DXA ($R^2 = 0.82$ and $R^2 = 0.70$, respectively). Conversely, BMC and BMD from PA-projection DXA were lower predictors of ultimate load ($R^2 = 0.49$ and $R^2 = 0.37$, respectively).

This *ex vivo* study highlights greater capabilities of lateral-projection DXA to predict variations in vertebral body bone quantity as measured by μCT, and to predict vertebral strength as assessed experimentally, compared to PA-projection DXA. This provides basis for further exploring the clinical application of lateral-projection DXA analysis.

Introduction

Dual energy X-ray absorptiometry (DXA) is currently the clinical tool of first choice for measuring areal bone mineral density (BMD) and for making clinical decisions concerning vertebral fragility and response to therapies. This is mainly due to its high precision, accuracy, efficiency, low radiation dose, accessible measurement sites, and low cost relative to other densitometry techniques [1–3]. However, marked differences in the prevalence of vertebral fractures for a comparable BMD, as measured by DXA, are reported [4–11]. Possible explanations for these discrepancies include the inability to measure three-dimensional (3D) bone microstructure and bone quality, confounding factors such as degeneration and sclerosis, extra-skeletal calcium, inadequate measurement specificity, the generally stochastic nature of vertebral

* Corresponding author at: Bone and Joint Research Laboratory, SA Pathology and Hanson Institute, Frome Rd 5000 SA, Adelaide, South Australia, Australia. Fax: +61 8 82223293.
E-mail address: egon.perilli@adelaide.edu.au (E. Perilli).

8756-3282/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.bone.2012.03.002

fractures and the influence of clinical risk factors for fracture other than BMD [11].

For the clinical measurement of vertebral BMD, routinely posterior–anterior (PA) projections are taken of the spine with the patient lying supine on the scanner bed. However, in this scanning modality, the projection data also include the posterior vertebral elements, and they also potentially include aortic calcifications and degenerative spinal conditions in some patients. This can influence, particularly overestimate, the measured bone mineral content (BMC) and BMD data to an unknown extent, constituting an unwanted bias [12,13]. However, these bias elements can be excluded or minimized with a lateral-projection scanning approach [7,14]. In a number of studies, BMD estimated by lateral-projection DXA has shown stronger relationships with vertebral fractures and age, compared to BMD using PA-projection DXA [14–16]. Moreover, the treatment effects of a pharmacologic intervention were greater when evaluated by lateral-BMD data, in contrast to PA-derived data [17,18].

The ability of bone as an organ to withstand an applied load is also linked to its internal microarchitecture. BMD measurements made using DXA are derived from planar projections, from which no distinction between cortical and trabecular bone can be made. Vertebral bodies have trabecular bone structures with thicknesses as small as 100 μm [19,20], hence, 3D imaging methods with high resolution are essential for their accurate description. The development of high-resolution 3D imaging techniques, such as micro-computed tomography (μCT) has made it possible to assess trabecular bone structure in 3D non-destructively [21]. The first studies characterizing vertebral microarchitecture with μCT were based on excised bone cores [19,22]. In order to then study mechanical properties, the cores were subjected to mechanical testing [22–24]. It is now possible to scan the whole vertebral body, rather than an excised core [25–29]. This provides high-resolution structural data of the whole vertebra in 3D, which can be used in combination with finite element models [26], or with mechanical test data of the whole vertebral body [20,30,31], to examine the resistance to fracture of the vertebra from which vertebral fragility can be inferred.

Accurate assessment of vertebral strength is of clinical importance for the management of bone fragility, and DXA is currently the clinical tool most widely used to inform clinical decisions regarding fracture risk. *In vitro* studies, examining BMC and BMD measurements on lumbar vertebrae from lateral-projection DXA compared to PA-projection DXA, suggested a more accurate prediction of lumbar vertebral failure load for lateral-projection DXA, with higher coefficients of determination and lower standard errors of the estimate in regression models [32,33]. Lateral-projection DXA might have some potential advantages for assessing vertebral bone status compared to PA-projection DXA, in particular as lateral scans might better approximate the objective of measuring the trabecular-rich bone in the vertebral body [14,17]. As such, it is valuable to investigate the capability of lateral-projection DXA, compared to PA-projection DXA, in predicting variations of bone quantity in human vertebrae as assessed by a high-resolution 3D imaging modality such as μCT.

The aims of this study on excised human spines were (1) to investigate the ability of bone quantity measurements (BMC and BMD) obtained by DXA in the lateral projection and in the PA projection, to predict variations in bone quantity measurements (bone volume and bone volume fraction) obtained by μCT, and (2) to assess the capability of the bone quantity measurements obtained by DXA in both the lateral and the PA projections, and of the bone quantity measurements obtained by μCT, to predict vertebral body failure strength determined experimentally. In particular this study will investigate (1) whether vertebral bone quantity assessed by lateral-projection DXA, compared to PA-projection DXA, will better predict variations in bone quantity as determined by μCT, and (2) whether vertebral bone quantity assessed from lateral-projection DXA, compared to PA-projection DXA, will better predict vertebral failure load.

Materials and methods

Study design

This multi-centre project is currently run through three Australian centres [25,34]: Curtin University, Western Australia; SA Pathology, South Australia; and University of Melbourne (Royal Melbourne Hospital), Victoria. Initially, DXA scanning was performed in Melbourne, followed by μCT scanning and biomechanical testing in Adelaide. Finally data were analysed at both these sites and in Perth.

Specimens

Lumbar spine specimens (L2, L3) from eight embalmed cadavers (5 male, 3 female) of mean (SD) age at death 77.5 (10.4) years were used in this investigation. The intact cadavers were embalmed with 20–40 L of embalming fluid (55% ethanol, 5% formaldehyde, 5% phenol, 20% propylene glycol and 15% water) and stored at 4 °C for 3 months prior to harvesting of the spine. Previous investigators have found no effect of formalin fixation on BMD estimations by DXA on cadaver spines compared to fresh specimens, over this timescale [35,36]. The ribs and ilia were removed, leaving intact spine segments with vertebrae, discs and posterior vertebral elements in place, from T12–L5. The spines were sealed in a water-tight shrink-wrap thermoplastic. An experienced medical scientist examined the spines to identify vertebral levels *ex situ*. Prior to any scanning, lateral radiographs were acquired from each specimen to screen for vertebral fractures and any other obvious pathology and to verify vertebral levels in conjunction with the PA-DXA image. One L2 vertebra showed a fracture and thus was excluded from the analyses, whereas the L3 vertebra of the same spine was maintained. All samples were free of any serological conditions. Approval to use the specimens for research purposes was granted by the Human Research Ethics Committee at the Royal Adelaide Hospital, South Australia, and Curtin University, Western Australia, in accordance with the Declaration of Helsinki, 1975. The resulting 15 L2 and L3 vertebrae ($n=7$ and $n=8$, respectively) were used for both quantitative bone imaging modalities. The scanning and analysis procedures have been described in detail elsewhere using a protocol developed by our group [25,34,37,38], and are outlined below.

Dual energy X-ray absorptiometry (DXA)

All scanning was performed using a Hologic (Hologic Inc., Bedford, MA; USA) QDR4500A fan beam densitometer, with rotating C-arm functionality, running operating software version 9.10D. The 12 month precision of the densitometer for the Hologic spine phantom was 0.39% for BMD and 0.58% for BMC. Spine samples were placed supine in a water bath ($270\times180\times150$ mm) of tap water to a depth of 18 cm to simulate soft tissue composition. Specimens were wrapped in water-tight plastic wrap free of air and were secured to the base of the water bath with Velcro straps to prevent motion and rotation artefact during scanning. This procedure has been used in previous studies with validity and reliability established for both lumbar and thoracic vertebrae [33,37,39–41]. A matched PA-supine lateral scan was performed on each specimen using the array scanning mode. Analysis of the PA scan was performed according to the standard lumbar spine protocol described by Hologic (Fig. 1a) [42]. At the completion of the lateral scan, standard analysis was performed. To ensure standardisation, the global region of interest width remained constant throughout the analysis, set at its maximum (141×152 pixels) (pixel size = 1.0 mm). Areal BMD was calculated for the whole vertebral body area (defined as region of interest, ROI) (Fig. 1b). The whole vertebral area (ROI) was defined by the four corners of the vertebra of interest from the lateral-DXA image, including the vertebral endplates and excluding the posterior elements, as described previously [25,34,38]. Overt osteophytes were