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Vertebral fractures and abdominal aortic calcification in postmenopausal women. A cohort study

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ABSTRACT

Introduction: Vertebral fracture assessment (VFA) imaging with a bone densitometer can simultaneously detect prevalent vertebral fractures (VFs) and abdominal aortic calcification (AAC).
Objective: To study the relation between the prevalence of VFs using VFA in asymptomatic women and the prevalence and severity of AAC.
Design: This is a cross-sectional study.
Settings: Subjects were recruited in a third care center from asymptomatic women selected from the general population.
Participants: We enrolled 908 post-menopausal women with a mean age of 60.9 years ± 7.7 (50 to 91) with no prior known diagnosis of osteoporosis or taking medication interfering with bone metabolism.
Primary and secondary outcome measures: Lateral VFA images and scans of the lumbar spine and proximal femur were obtained using a GE Healthcare Lunar Prodigy densitometer. VFs were defined using a combination of Genant semiquantitative (SQ) approach and morphometry. VFA images were scored for AAC using a validated 24 point scale.
Results: VFA images showed that 179 of the participants (19.7%) had at least one grade 2/3 VF, 81% did not have any detectable AAC whereas the prevalence of significant atherosclerotic burden, defined as AAC score of 5 or higher, was 12%. The group of women with 2/3 VFs had a statistically significant higher AAC score and higher proportion of subjects with extended AAC, and lower weight, height, and lumbar spine and hip BMD and T-scores than those without VFA-identified VFs. Multiple regression analysis showed that the presence of grade 2/3 VFs was significantly associated with age, BMI, history of peripheral fracture, AAC score ≥ 5 and densitometric osteoporosis.
Conclusion: In post-menopausal women, extended AAC is independently associated with prevalent VFs regardless of age, BMI, history of fractures, and BMD.

Introduction

Vascular calcifications and osteoporotic fractures prevalence increase with age and both are commonly observed in the elderly [1]. Although multiple reports have suggested a link between atherosclerosis and osteoporosis, making an unequivocal connection between these two age-dependent conditions has been difficult [2]. Moreover, due to the great increase in life expectancy, a marked rise in the prevalence of both of these disorders is expected.

Cardiovascular disease remains the leading cause of mortality among elderly women. Abdominal aortic calcification (AAC) is easily detected on routine lateral lumbar spine radiographs and has been shown to be significantly predictive of overall cardiovascular disease incidence and mortality, coronary heart disease, stroke, congestive heart failure, and peripheral vascular disease, independently of classic risk factors such as high blood pressure, high total and LDL cholesterol levels, smoking, obesity, and the presence of diabetes mellitus [3,4].

Bone densitometry is now widely recommended for all women age 65 and older [5]. Simultaneous lateral spine imaging also called vertebral fracture assessment (VFA) is now also recommended for a sizable subset of the elderly female population to detect prevalent vertebral fractures (VFs) and has been shown to be cost-effective for that subset [6,7]. It has been shown in many populations that this technique can simultaneously identify AAC (Fig. 1) and then improve the utility of this technology for this population even further [8,9].

Although the associations of age and bone mineral density (BMD) with AAC have been well examined [10–13], whether osteoporotic vertebral fractures (VFs) and AAC are related to each other or are independent, age-related processes remain uncertain. Identifying women at risk for both cardiovascular events and osteoporotic fracture may help reduce morbidity and mortality associated with these highly common conditions. The purpose of the present study was to test the hypotheses

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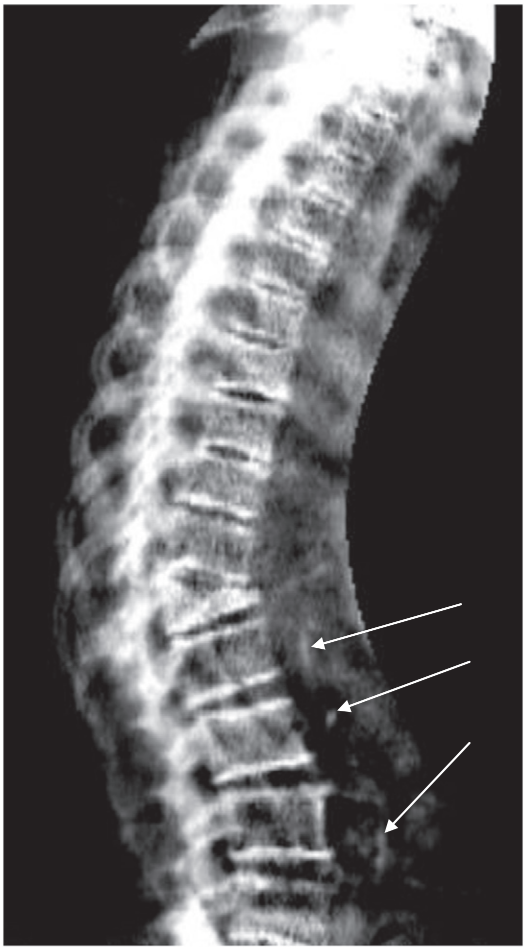

Fig. 1. A VFA image showing multiple vertebral fractures (T12 grade 3, T9 and T8 grade 1) and abdominal aortic calcifications (arrows) scored 3.

that there is a significant age-independent relation between AAC and osteoporosis and VFs.

Material and methods

Subjects

A total of 973 Caucasian postmenopausal women (age range: 50—91 yr) living in the Rabat area participated in the present study. Inclusion and exclusion criteria were described elsewhere [14]. Briefly, women were recruited through advertisements and "word of mouth" from June 2010 to March 2012. Original inclusion criteria were age >50, menopause >1 year and no previous osteoporotic fracture or known diagnosis of osteoporosis. Women with liver or renal disease, endocrine or metabolic abnormalities, and receiving medicine known to influence bone mineralization, such as corticosteroids, heparin, anticonvulsants, vitamin D, and bisphosphonates, were excluded. Our institutional review board (Faculty of Medicine of Rabat) approved this study. The procedures of the study were in accordance with the Declaration of Helsinki, and local ethics committee approval was obtained for the study. All the participants gave an informed and written consent. Medical histories, obtained by the DXA technologists prior to scanning, included current medication use, history of peripheral traumatic fractures, and current use of tobacco and alcohol. Height and weight were measured in light indoor clothes without shoes. Body mass index (BMI)] was calculated by dividing weight in kilograms by height in meters squared. Although this is not a population-based cohort, care was taken to ensure representativeness of the general population with a particular regard to the inclusion of a wide range of body sizes and activities. We did not exclude individuals using inhalation steroids or with certain lifestyle habits such as heavy smoking, being sedentary, being athletic, or having a high or low calcium intake, which are examples of voluntary factors that may have some impact on bone metabolism.

BMD measurement

Bone mineral density was determined by a Lunar Prodigy Vision DXA system (Lunar Corp., Madison, WI). The DXA scans were obtained by standard procedures supplied by the manufacturer for scanning and analysis. All BMD measurements were carried out by 2 experienced technicians. Daily quality control was carried out by measurement of a Lunar phantom. At the time of the study, phantom measurements showed stable results. The phantom precision expressed as the coefficient of variation was 0.08%. Moreover, reproducibility has been assessed in clinical practice and showed a smallest detectable difference of 0.04 g/cm [2] (spine) and 0.02 (hips) [15,16]. Patient BMD was measured at the lumbar spine (anteroposterior projection at L1–L4) and at the femurs (i.e., femoral neck, trochanter, and total hip). Using the Moroccan female normative data [17], the World Health Organization (WHO) classification system was applied, defining osteoporosis as T-score ≤ -2.5 and osteopenia as $-2.5 <$ T-score < -1. Study participants were categorized by the lowest T-score of the L1–4 lumbar spine, femur neck, or total femur.

Vertebral fracture assessment

VFs was classified using a combination of Genant [18] semiquantitative (SQ) approach and morphometry in the following manner: each VFA image was inspected visually by one trained clinician (IG) to decide whether it contained a fracture in any of the visualized vertebrae and assigned a grade based on Genant SQ scale, where grade 1 (mild) fracture is a reduction in vertebral height of 20–25%, grade 2 (moderate) a reduction of 26–40%, and grade 3 (severe) a reduction of over 40%. In case of doubt regarding fracture grade, the vertebrae in question was measured using built-in morphometry. Automatic vertebral recognition by the software was used. Positioning of the six morphometry points was modified by an experienced clinician (IG) only when the software failed to correctly recognize vertebral heights. The intra-rater reproducibility was evaluated using the kappa score to 0.90 ($p < 0.0001$). Subjects with no fractures were included in the non-fracture group, whereas those with grade 1 or higher fractures were included in the fracture group. However, as many studies rarely report mild deformities as "fractures", and to realize comparisons with the literature, we performed a double analysis including and excluding grade 1 fractures from the fracture group. The spinal deformity index (SDI), as described by Kerkeni et al. [19], was then calculated by summing in each patient the grade of each vertebra from T4 to L4. In theory, the SDI value can vary between 0 (no fracture) and 39 (all the assessed vertebrae are grade 3).

Assessment of aortic calcifications

All VFA scans were studied on a separate occasion by the same reader (IG) to assess the presence of AAC. To score the AAC extension, we used the score described by Kauppila et al. [20]. The anterior and posterior aortic walls were divided into four segments, corresponding to the areas in front of the lumbar vertebrae L1–L4. Within each of these 8 segments, aortic calcification was recognized visually as either a diffuse white stippling of the aorta extending out to the anterior and/or posterior aortic walls, or as white linear calcification of the anterior and/or posterior walls. Aortic calcification scored as 0 if there was no calcification, as 1 if one-third or less of the length of the aortic wall in that segment was calcified, as 2 if more than one-third but