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ORIGINAL ARTICLE

Age-related vessel calcification at distal extremities is a risk factor of osteoporosis

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Summary We conducted a cohort study to investigate if the vessel calcifications (VCs) found in the distal extremities are an index of low bone mass at multiskeletal sites. A total of 332 healthy women aged 41—80 years were recruited for bone mineral content (BMC) and bone mineral density measurement using peripheral quantitative computed tomography (pQCT) and dual-energy X-ray absorptiometry (DXA). Seven percent of the women showed VC at both upper and lower distal extremities based on pQCT images. Women who had VC were then compared with their age-matched non-VC counterparts. Results showed that peripheral VC was mainly formed at distal lower extremities, and the prevalence of VC increased with advancing age, with 0%, 5.6%, 9.3%, and up to 34.5% in the age groups of 41—50 years, 51—60 years, 61—70 years, and 71—80 years, respectively. Compared with the control group, the VC group showed a significantly higher body mass index (25.2 vs. 23.2, $p < 0.01$), lower BMC at the spine (27.4 g vs. 31.3 g, $p < 0.05$), and lower BMC (1.8 g vs. 2.0 g, $p < 0.05$) and bone mineral density (0.57 g/cm^2 vs. 0.66 g/cm^2, $p < 0.05$) at the hip as measured by DXA. The diagnosis of VC in the distal extremities by pQCT increased the diagnosis sensitivity of osteoporosis by 50%. The significance of our findings imply that in clinical settings using pQCT for bone assessment and identification of patients with VC in the distal extremities, patients should also be referred for central DXA measurement at

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Introduction

The link between ageing and osteoporosis is a challenging healthcare issue that has a profound impact in the orthopaedic community in terms of the significant increase in osteoporosis-associated fragility fractures [1—4]. Identifying the risk factors associated with osteoporosis is highly desirable for a better prediction of osteoporosis and associated fractures. Among the many risk factors, cardiovascular disorders are well recognised as they are commonly found in osteoporotic patients [1,3,5—7].

It is known that bone mineral density and content (BMD and BMC) at the lumbar spine measured by dual-energy X-ray absorptiometry (DXA) may be confounded by the calcification of soft tissues located within the beam path of the X-ray projected through the abdominal wall, a prominent and early site of spinal ligament and abdominal vascular (aorta) calcification with advancing age [6—8]. In other words, such changes may result in false negative diagnosis on the severity of osteoporosis especially in people older than 65 years.

In previous studies with healthy peri- and postmenopausal women for identification of high-risk patients with low BMD and fast bone loss and for evaluating habitual or programmed exercises for prevention and treatment of postmenopausal osteoporosis [2,9—14], the authors identified women with vessel calcification (VC) at the lower limb based on the three-dimensional images of peripheral quantitative computed tomography (pQCT), a popular device for BMD measurement in orthopaedic clinics in Western countries [15,16] and Hong Kong for the past 15 years [2,9—14,17]. The aim of this study was to investigate if women with peripheral VC were at risk of osteoporosis by evaluating the relationship between VC and bone mineral status measured with both pQCT and DXA at the peripheral and axial skeletal sites, respectively.

Materials and methods

Participants

A total of 332 healthy Hong Kong Chinese women aged 44—80 years were recruited from various communities in Hong Kong via telephone contact and poster distribution as described previously [11,12]. These women were in postmenopause for at least 1 year or had an irregular menstruation cycle in the past 9 months (perimenopausal). Exclusion criteria were women under hormonal replacement therapy or drug treatments known to affect bone metabolism, with conditions such as hypo- or hyperparathyroidism and hypo- or hyperthyroidism, renal or liver disease, diabetes, fracture history, and calcium/vitamin D deficiency/supplementation. The study was conducted in compliance with the ethical principles of the Declaration of Helsinki and the Clinical Research Ethics Committee of the Chinese University of Hong Kong approved the study protocol (Ref. No. CRE-660).

Anthropometric measurements

Body height and body weight were measured. Body mass index (BMI) in kg/m^2 was also calculated [7,11,12].

BMD measurement

pQCT measurements

Volumetric BMD (g/cm^3) of the nondominant distal radius and tibia was measured using a multilayer QCT (Densiscan, Scanco Medical, Zurich, Switzerland). A standard 16 tomographs screening programme was used, with the first 10 consecutive layers for measuring the ultradistal radius and ultradistal tibia, and six consecutive layers for measuring distal radius and tibia diaphysis. The thickness of each layer was 1 mm, with a 1.5-mm interval between each layer. The trabecular BMD in core volume (central 50% area of the total bone area) and the integral BMD of both cortical and trabecular bones within the total bone area of ultradistal radius were obtained from the first 10 distal layers. The cortical BMD was obtained from the cross-sectional area of the cortical compartment of distal diaphysis from the six proximal layers [2,11,12]. Sixteen layers of pQCT tomographs from both distal radius and tibia were examined to identify the individuals with VC—i.e., a sign of calcium plaque visualised as a bright spot in the pQCT images (Fig. 1) and confirmed with low-power real-time X-ray fluoroscopy system (XiScan; XiTec Holdings LLC, East Windsor, CT, USA) (Fig. 2). Participants who had at least one visualised calcium plaque found in either the distal radius or the tibia comprised the VC group, and those who had none served as the control group.

DXA measurements

BMC and areal BMD (g/cm^2) of spine (L2—L4), femoral neck, and the intertrochanteric region of the nondominant hip were measured using DXA (Norland XR-36; Coopersurgical Inc., Connecticut, USA) [2,12,18].

Statistical analysis

Independent Student t test (two-tailed) was used to detect the differences in age, anthropometric variables, and bone density measurement between the VC group and the control group. Chi-square analysis was used for testing the differences in the incidence of osteoporosis based on the DXA T score ≤ -2.5 SD. The statistical significance level was set at $p < 0.05$. IBM SPSS statistics 13.0 (IBM, New York, USA) was used for data evaluation.

Results

Prevalence of VC

Based on the multilayer pQCT images, a total of 23 women were identified to have VC at the distal tibia. All of them