Bone 52 (2013) 354–359

Contents lists available at SciVerse ScienceDirect

Bone

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

Original Full Length Article

Serum phosphate and hip bone mineral density as additional factors for high vascular calcification scores in a community-dwelling: The São Paulo Ageing & Health Study (SPAH)

Camille P. Figueiredo [a], Nalini M. Rajamannan [b], Jaqueline B. Lopes [a], Valeria F. Caparbo [a], Liliam Takayama [a], Márcia E. Kuroishi [c], Ilka S. Oliveira [c], Paulo R. Menezes [d], Marcia Scazufca [e], Eloisa Bonfá [a], Rosa M.R. Pereira [a,*]

[a] Bone Metabolism Laboratory, Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil
[b] Division of Cardiology, Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
[c] Radiology Division of Hospital Universitario, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil
[d] Department of Preventive Medicine, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil
[e] Departament of Psychiatry, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

ARTICLE INFO

Article history:
Received 27 April 2012
Revised 14 October 2012
Accepted 17 October 2012
Available online 23 October 2012

Edited by: Felicia Cosman

Keywords:
Serum phosphate
Bone mineral density
Vascular calcification

ABSTRACT

Objective: To analyze the association between abdominal aortic calcification scores (AACS) and bone metabolism parameters in a well-characterized general population of older adults.
Background: Several studies suggest a link between bone mineral metabolism disorders and vascular calcification; although only few of them analyze bone mineral density(BMD), laboratory bone markers and cardiovascular parameters at the same time and none were done in a miscegenated population.
Methods: This cross-sectional study included 815 subjects ≥65 years old. The risk factors for osteoporosis and cardiovascular disease as well as a wide array of demographic and lifestyle characteristics were collected using a standardized questionnaire. BMD was measured by DXA. Kauppila's method was used to quantify the AAC score (AACS) by spine X-rays. Laboratory analyses were also performed.
Results: AAC was observed in 63.2% of subjects with a median AACS of 2 (IQR: 0–7). AACS were categorized in quartiles and the highest quartile of AACS (>7) were compared with the three lower quartiles of AACS (≤7). Logistic regression analysis was performed using parameters with statistical significance in the univariate analysis. The best logistic regression model revealed that AACS>7 was negatively associated with femoral neck BMD and positively associated with phosphorus, adjusted by age, current smoking, LDL, and arterial hypertension in the elderly community-dwelling population.
Conclusions: We identified that higher serum phosphate levels and lower hip BMD are independent bone variables that are associated with elevated vascular calcification scores, supporting the search for effective prevention and treatment strategies that may simultaneously reduce these modifiable risk factors in older subjects.

Introduction

Osteoporosis and atherosclerosis are common age-related conditions that account for two major worldwide public health problems. As life expectancy continues to increase, the prevalence of these two processes will raise accordingly. A direct relationship between vascular calcification and the severity of atherosclerotic disease [1] and mortality [2] has been reported.

Studies in the last two decades demonstrated that vascular calcification is an active process of bio mineralization similar to ossification [3], and several epidemiological papers suggest a link between osteoporosis and vascular calcification [4–6]. In fact, Von der Recke et al. [4] showed that low bone mineral content at menopause was a risk factor for increased cardiovascular mortality in later life, and the Framingham Heart Study demonstrated an independent association between bone loss and the progression of aortic calcification [5].

Moreover, experimental evidence showed that some of the pathophysiological mechanisms underlying osteoporosis and vascular calcification seem to coincide in many biochemical pathways. Some mediators of

Abbreviations: OPG, osteoprotegerin; RANK, receptor activator of nuclear factor kappa B; RANKL, receptor activator of nuclear factor kappa B ligand; BMP, bone morphogenetic proteins; MGP, matrix Gla protein; Runx-2, runt-related transcription factor 2; BMD, bone mineral density; eGFR, estimated glomerular filtration rate; DXA, dual X-ray absorptiometry; 25OHD, 25-hydroxyvitamin D; iPTH, Intact parathyroid hormone; TSH, thyroid-stimulating hormone; free T4, free tetraiodothyronine.

* Corresponding author at: Faculdade de Medicina da Universidade de São Paulo, Disciplina de Reumatologia. Av. Dr. Arnaldo, 455, 3º andar, sala 3105. São Paulo, SP, 01246-903, Brazil. Fax: +55 11 30617490.
E-mail address: rosamariarp@yahoo.com (R.M.R. Pereira).

8756-3282/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.bone.2012.10.019

bone metabolism have also been associated with vascular calcification, including the OPG/RANK/RANKL axis, BMP, MGP and fetuin-A [7–11]. Clinical studies showed that MGP polymorphisms were associated with an increased risk of myocardial infarction and vascular calcification of femoral arteries [12].

Abdominal aortic calcification (AAC) detected on spinal X-rays has been associated with a higher risk of cardiovascular events and death [2,13]. Nevertheless, the association between AAC and bone mineral density (BMD) is still controversial since this inverse relationship did not persist after adjustments for age or other covariates in a few studies [14].

Importantly, most of the vascular calcification and bone metabolism studies have been conducted in patients of North American or European descent [5,6] and a clear association with ethnic background has been reported [15] precluding a definitive conclusions to be applied to miscegenated populations. Other possible confounding variables in previous studies are selection bias of referral for clinical testing [16,17] and not exclusion of patients with impaired renal function [6,13,18].

Therefore, the aim of this study was to evaluate AAC score and its possible association with BMD, clinical and laboratory data in a well-characterized Brazilian community-dwelling older population.

Methods

Subjects

This study was based on data from the São Paulo Ageing & Health Study (SPAH). Full details regarding the study population, assessments and procedures have been previously reported [19]. Briefly, 2266 older individuals were eligible and 2072 (91.4%) agreed to participate in the first phase of the study (2002–2003). In a second phase (2005 July to 2007 August), the participants were recruited again and 1368 agreed to undergo new assessments regarding bone metabolism and vascular calcification. In the present investigation, only well-functioning older participants were analyzed, thus 1020 participants were interviewed and examined in this second phase of the SPAH. Well-functioning older subjects, inclusion criteria, were defined as individuals able to perform basic activities of daily living, to come to our center without walking difficulties and with no life-threatening illness.

Of the 1020 participants, 205 (20%) were excluded for the following reasons: 50 were using drugs or supplements that affected bone metabolism (including bisphosphonates, vitamin D and calcium), 104 were using lipid-lowering drugs or supplements, 18 had a history of previous cancer (<5 years), 15 had primary hyperparathyroidism (serum calcium >10.5 mg/dL and PTH >65 pg/mL), 12 had kidney failure (eGFR <15 mL/min) and 6 had rheumatoid arthritis. Of the remaining 815 participants, 476 were women, and 339 were men.

This study was approved by the local ethics committee (#426/06), and all the participants provided written informed consent.

Data collection and assessments

Each subject was interviewed by a doctor and responded to a standardized questionnaire to obtain information on the putative risk factors for cardiovascular disease and osteoporosis/fractures; these risk factors included the following: the presence of diabetes mellitus (DM), arterial hypertension, or dyslipoproteinemia; a previous history or family history of cardiovascular disease; lifestyle; previous fragility fractures; a family history of hip fracture; a history of falls during the last year; levels of physical activity; current alcohol use and smoking habits; glucocorticoid use and daily calcium intake.

All study subjects were interviewed regarding previous personal history of cardiovascular disease, characterized by angina pectoris or unstable angina pectoris, myocardial infarction, transient ischemic attack or stroke and clinical arterial peripheral disease, and a family history of cardiovascular disease, that comprising all the above mentioned in addition of death caused by any of these events. Arterial hypertension and dyslipidemia were defined according to the literature [20,21].

Falls, physical activity, previous fragility fracture and race were described previously by our group [19].

Laboratory evaluation

Blood samples were collected under fasting conditions (between 8 and 10 a.m.) on the same day that the DXA and abdominal X-rays were obtained, and the samples were stored at −70 °C for later analysis. The laboratory analyses were determined using standard automated laboratory methods. The serum concentration of 25OHD was measured using a radioimmunoassay technique (DiaSorin, Stillwater, MN, USA), and iPTH by immunoradiometric assay (ELISA-PTH, CIS bio international, France).

Bone mineral density and vertebral fractures

BMD was measured by DXA (Hologic QDR 4500, Inc. Bedford, MA, USA) at the following sites: lumbar spine, femoral neck, and total femur and precision error was determined based on standard International Society for Clinical Densitometry (ISCD) protocols [22].

The identification of vertebral fractures was evaluated by T4-L4 vertebral image X-Ray, using a Genant semiquantitative (SQ) approach [23] and only grade 2 (moderate) or grade 3 (severe) vertebral deformities were classified as fractures [19].

Aortic calcification

The lateral lumbar spine radiographs were acquired to assess vertebral fractures as previously described [19], and to quantify aortic calcification. Briefly, the abdominal aortic calcium deposits index developed to grade the severity of the calcification in the aorta at the level of the first through the fourth lumbar vertebra was used. Calcific deposits were considered to be present if the densities were visible in an area that was parallel to the lumbar spine and anterior to the lower part of the spine. These calcific densities were graded on a 0 to 3 scale at each lumbar vertebrae segment: 0 denoted no aortic calcific deposits; 1 denoted small scattered calcific deposits that occupied less than one third of the longitudinal wall of the aorta; 2 indicated that one third or more but less than two thirds of the longitudinal wall of the aorta was calcified; and 3 indicated that two thirds or more of the longitudinal wall of the aorta was calcified.

A separate score was determined for the anterior and posterior aorta, and the values were summed across the 4 vertebrae resulting in an abdominal aortic calcium score (AACS) that ranged from 0 to 24 points [24].

Statistical analysis

Results were expressed as median and interquartile range (IQR), mean and standard deviation (SD) or percentages. The prevalence of AACS was estimated with a 95% CI. Since the variable abdominal aortic calcification scores (AACS) is not normally distributed, these scores were categorized in 0 score and any score of calcification, and also in quartiles. The threshold of 7 (highest quartile) of the distribution in all subjects were compared with AACS in the three lower quartiles (AACS ≤ 7). Logistic regression models were performed to verify which factors were independently associated with any abdominal aortic calcification, and also with scores higher than 7.

Only the variables that were significantly ($p<0.05$) associated with AACS in the univariate analysis were included in the final analysis. Because colinearity existed between BMD sites, the sites were sequentially added to the logistic regression analysis, and the best model was