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# Original article

# Relationship between diffuse idiopathic skeletal hyperostosis, abdominal aortic calcification and associated metabolic disorders: Data from the Camargo Cohort<sup>†</sup>



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#### ABSTRACT

*Background and objective:* Diffuse idiopathic skeletal hyperostosis (DISH) and abdominal aortic calcification (AAC) are related to an increased cardiovascular risk. The aim of this study was to analyze a possible relationship between both entities and also the association between metabolic disorders and DISH. *Patients and method:* Analytic cross-sectional study in a population-based cohort. DISH (with Resnick-Niwayama criteria) and AAC (with AAC-24 scale) were assessed on plain X-ray images. Interaction terms between DISH and forty clinical covariates were also investigated, through correlation analysis and multivariate regression.

*Results*: Nine hundred eighty-seven males aged  $\geq$ 50 years, with a mean age = 65.5  $\pm$ 9 years, were evaluated. Prevalence rates of DISH and AAC were 21.6% and 58.7%, respectively. DISH+ subjects were older (68.1  $\pm$ 9 vs. 63.8  $\pm$ 9 years; *p* = 0.0001) and more likely to be affected by metabolic syndrome (MS) (55.6% vs. 36.6%; *p* = 0.0001). In DISH+ subjects, the AAC was 3.7  $\pm$ 5 points, whereas in DISH– subjects it was 3.3  $\pm$ 5 (*p* = 0.25). AAC was associated with an increased risk of prevalent DISH (unadjusted OR = 1.4 [95% CI: 1.01–1.9]; *p* = 0.04), that disappeared when it was adjusted for age (adjusted OR = 1.1 [95% CI: 0.8–1.5]; *p* = 0.47). No association was found between DISH and hypertension, diabetes or dyslipidemia; however, age (OR = 2.2 [95% CI: 1.6–3]; *p* = 0.0001), BMI (OR = 1.5 [95% CI: 1.1–2.2]; *p* = 0.007), waist circumference (OR = 1.5 [95% CI: 1.04–2.3]; *p* = 0.03) and MS (OR = 1.7 [95% CI: 1.1–2.4]; *p* = 0.005) showed a significant relationship with DISH after adjusting for confounders.

*Conclusions:* The study was not able to demonstrate a consistent association between DISH and AAC, proving only a weak and age-dependent relationship between them. DISH proved to be significantly associated with age, BMI, waist circumference and MS.

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# Relación entre hiperostosis esquelética idiopática difusa, calcificación de la aorta abdominal y las alteraciones metabólicas asociadas: datos de la Cohorte Camargo

RESUMEN

Antecedentes y objetivo: La hiperostosis esquelética idiopática difusa (DISH, del inglés *diffuse idiopathic skeletal hyperostosis*) y la calcificación aórtica abdominal (CAA) se asocian a un incremento del riesgo cardiovascular. El objetivo fue analizar una posible relación entre ambas, así como las alteraciones metabólicas asociadas a la DISH.

*Pacientes y método:* Estudio transversal-analítico, incluido en una cohorte poblacional. La DISH (criterios de Resnick-Niwayama) y la CAA (mediante la escala AAC-24) fueron evaluadas sobre imágenes de radiología simple. Se evaluaron asimismo otras 40 variables clínicas mediante correlaciones y regresión multivariante.

*Resultados*: Fueron analizados 987 varones  $\geq$  50 años, con una edad media = 65,5 ± 9 años. Las prevalencias de DISH y CAA fueron del 21,6% y del 58,7%, respectivamente. El sujeto con DISH tenía mayor edad (68,1 ± 9 vs. 63,8 ± 9 años; p = 0,0001) y con mayor frecuencia presentaba síndrome metabólico (SM) (55,6 vs. 36,6%; p = 0,0001). La CAA fue de 3,7 ± 5 puntos en sujetos con DISH frente a 3,3 ± 5 en sujetos sin DISH (p=0,25), y se asoció a un riesgo incrementado de DISH prevalente (OR cruda = 1,4 [IC95%: 1,01-1,9]; p=0,04), que desapareció al ajustar por edad (OR ajustada = 1,1 [IC95%: 0,8-1,5]; p=0,47). No se observó asociación de la DISH con la hipertensión arterial, diabetes mellitus o dislipidemia, pero mantuvieron una relación significativa tras ajustar por confusores la edad (OR = 2,2 [IC95%: 1,6-3]; p=0,0001), el IMC (OR = 1,5 [IC95%: 1,1-2]; p=0,007), el perímetro abdominal (OR = 1,5 [IC95%: 1,04-2,3]; p=0,03) y el SM (OR = 1,7 [IC95%: 1,1-2,4]; p=0,005).

*Conclusiones:* No se ha podido demostrar una asociación consistente entre la DISH y la CAA, presentando ambas una débil relación dependiente de la edad. La DISH ha mostrado unas asociaciones significativas con la edad, el IMC, el perímetro abdominal y el SM.

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## Introduction

Diffuse idiopathic skeletal hyperostosis (DISH) is a rheumatic disease characterized by ossification of ligaments, tendons and joint capsules, and was first described by Forestier and Rotés-Querol in 1950.<sup>1</sup> It can involve many locations, but it shows a special preference for the axial skeleton, especially the anterior longitudinal ligament of the spine, the most characteristic manifestation of the disease.<sup>1,2</sup>

It is observed more frequently in men and in advanced ages,<sup>2</sup> and today it is considered as a clinical entity different from spondylarthrosis, with which it can coexist.<sup>3</sup> It is usually asymptomatic, but some patients may report pain and limited axial mobility, as well as increased susceptibility to vertebral fractures.<sup>2</sup> Its etiology is unknown, and the factors involved are: genetic factors – such as certain polymorphisms of the COL6A1 gene encoding the collagen chainα type VI<sup>4</sup> – drugs – such as isotretinoin and other derivatives of vitamin A<sup>2</sup> – and metabolic factors, including obesity, a high abdominal girth, hypertension (HT), hyperinsulinemia, diabetes mellitus (DM), hyperuricemia and dyslipidemia.<sup>2,5</sup> Although some of these associations have been questioned,<sup>5–7</sup> it has been observed that subjects with DISH have a higher frequency of metabolic syndrome (MS) and an increased risk of cardiovascular morbidity.<sup>8</sup>

On the other hand, abdominal aortic calcification (AAC) is considered an indicator of atherosclerotic load and cardiovascular risk (CVR), especially in advanced stages.<sup>9</sup> It is consistently and independently associated with other CVR factors, to an increased risk of myocardial infarction, heart failure, peripheral arterial disease, and stroke.<sup>10</sup> AAC is more prevalent in males and elderly,<sup>11</sup> and has also been related to the presence of MS or its various components.<sup>12</sup>

Based on these observations, DISH and AAC present certain similarities: they are characterized by heterotopic calcification/ossification, are more prevalent in men and in advanced ages, are closely related to MS and associate an increase in CVR. It is therefore likely that the 2 processes are related. However, to our knowledge, there are no published papers specifically investigating this association and there are very few studies offering an approach to this hypothesis.<sup>13,14</sup>

For this reason, we have considered whether there is a relationship between DISH and AAC. On the other hand, and given the absence of a generalized consensus, a second aim has been to contribute with our results to the debate on the metabolic changes associated to DISH.

### Patients and methodology

#### Population and sample

The general design corresponds to an analytical cross-sectional study, within a cohort. The study population consisted of all males  $\geq$ 50 years old included in a population-based prospective cohort, Cohorte Camargo, whose details have been previously published.<sup>15</sup> The Camargo Cohort was initiated in 2006 with the purpose of knowing the incidence and prevalence of metabolic bone diseases in the general population. Its participants are postmenopausal women and men  $\geq$ 50 years old, attended at the 2 Health Centers of the Camargo Valley, in Cantabria. In the initial study, all patients were provided with a questionnaire on bone metabolism and general diseases, current or past consumption of medication, and risk factors for osteoporosis and fractures. They underwent an analytical study (general and specific for bone metabolism as well as genetic studies), a simple spine X-ray study, a bone densitometry study (DXA) and an ultrasonographic study of the calcaneus. After being informed of the purpose of the cohort study, subjects were invited to participate, and all participants provided written informed consent. The Camargo Cohort study was approved by the Committee of Ethics in Clinical Research of Cantabria. In February 2013, all males enrolled in the cohort phase (No. = 1081) were reviewed for this investigation using the medical records from the baseline study.

Palabras clave: Hiperostosis esquelética idiopática difusa Calcificación vascular Enfermedades cardiovasculares Síndrome X metabólico Hombres Estudios epidemiológicos Download English Version:

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