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Coronary artery and aortic valve calcification evaluated with cardiac computed tomography in patients with chest pain: Prognostic value in clinical practice

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ABSTRACT

Objective: To determine the relationship between coronary artery calcification (CAC) and aortic valve calcification (AVC) and the development of adverse events in the follow-up of patients with suspected coronary artery disease (CAD).

Methods: All consecutive patients referred for coronary computed tomography angiography (CCTA) to evaluate for chest pain were included. Clinical data were collected at the time of the referral. CAC and AVC were quantified by means of the Agatston method. The patients were clinically followed for adverse events (cardiovascular death, acute coronary syndrome, stroke and hospitalization for congestive heart failure).

Results: The cohort included 304 patients. Both, CAC and AVC were related to age > 65 years, male sex, hypertension and diabetes mellitus. CAC was also related to smoking habits and dyslipidemia. CAC and AVC were not related to each other (Intraclass correlation coefficient = 0.455 [0.345–0.554]). Patients were followed for a median of 840 days [483–1267] and 23 adverse events were detected. CAC was associated with an increased rate of events, whereas AVC was not.

Conclusions: Among patients with chest pain and suspected CAD, both CAC and AVC are correlated with several cardiovascular risk factors (CVRF). CAC but not AVC identifies patients with a worse mid-term prognosis.

1. Introduction

Coronary artery calcification (CAC) is one of the manifestations of atherosclerotic disease in the coronary arteries [1]. Cardiovascular risk factors (CVRF) are key in its development and if they are controlled or corrected, the rate of adverse events decreases [2]. In recent years CAC quantification is used in daily clinical practice as it can be accurately assessed with non-invasive techniques, such us computed tomography (CT) [3,4]. Several studies found that patients with acute coronary syndromes (ACS) had higher CAC scores. CAC itself does not indicate plaque instability, but it is an important prognostic determinant for cardiovascular events [5,6].

Aortic valve calcification (AVC) is a common finding especially in the elderly. AVC can lead to variable degrees of valvular dysfunction with adverse clinical consequences. Observational studies have found a relationship between AVC and some risk factors for the development of atherosclerosis, such as smoking habits, hypertension, dyslipidemia and diabetes mellitus [7]. However, it is not clear if the control of these factors will reduce or limit the extent of AVC or valvular dysfunction [8].

Many studies regarding aortic sclerosis have assessed AVC with echocardiography. The reason is that is a widely available technique with reduced costs. However, we should not forget that it is operator-dependent and only provides a qualitative assessment. In contrast, CT

Abbreviations: CAC, coronary artery calcification; AVC, aortic valve calcification; CVRF, cardiovascular risk factors; CCTA, coronary computed tomography angiography; ACS, acute coronary syndrome; CAD, coronary artery disease.

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Table 1
Frecuency of different clinical characteristics and risk factors in all study subjects.

	n (%)
Gender	
Male	133 (44)
Female	171 (56)
Smoking	118 (39)
Obesity	58 (18)
Hipertension	181 (59)
Diabetes mellitus	48 (16)
Dyslipidemia	139 (46)
Chronic renal failure	3 (1)
Arteriopathy	9 (3)
Stroke	7 (2)
Chronic obstructive pulmonary disease	20 (6)

can accurately detect and quantify coronary artery and aortic valve calcification [9–11].

Previous research suggests that AVC identified by CT can predict cardiovascular outcomes in patients without known cardiovascular disease [12]. Therefore, assessing AVC whilst performing a coronary computed tomography angiography (CCTA) should improve the prognostic stratification of the patients. To assume this, we should previously prove that AVC score adds prognostic information in patients referred for CCTA in clinical practice. The aim of this work is to study AVC in patients with suspected CAD referred for CCTA and to determine if it enhances the risk assessment in this group of patients.

2. Methods

All consecutive patients referred between January 2009 and March 2013 for CCTA to evaluate for CAD were included. Patients with prosthetic valves, prior CAD or poor quality images were excluded. Epidemiological data were collected from the clinical history of the patients.

CCTAs were performed by using a 64-slice multidetector row CT (General Electric LightSpeed TC VCT®) using prospective ECG gating. Images were analyzed at our Corelab (ICICORELAB, www.icicorelab.es) by an expert in cardiac and coronary CT. CAC and AVC were quantified using the Agatston method. Furthermore, an analysis of the angiography was performed defining the presence of atherosclerotic plaques, its location, composition (fibrotic, fibrofatty, calcific), length and severity. Finally, a clinical follow-up was done. Adverse events were defined as the presence of cardiovascular death, ACS, stroke or hospitalization for congestive heart failure.

2.1. CT acquisition protocol

Intravenous betablockers were administered if needed before the examination to lower the heart rate and avoid arrhythmia for an improved image quality and dose reduction. Data acquisition was performed in the supine position and in craniocaudal direction. A topogram was used for planning the examination and determining the craniocaudal distance to be covered (from tracheal carina to diaphragm). A non-enhanced calcium scoring sequence is then performed during breath hold, electrocardiography (ECG)-gated (2.5 mm slice thickness, 25 cm field of view, 100 kV, 300 mA, rotation time: 0.35 s). CCTA is acquired afterwards. Intravenous nitroglycerin is administered to dilate the coronary arteries. An 85 mL dose of non-ionic iodinated contrast material is injected at approximately 4 mL/s through an antecubital vein. A saline solution bolus is also given. Scanning is triggered once contrast material is seen in the aortic root. (Sequence parameters: 25 cm Field of view, 100–120 kV, 600–700 mA, rotation time: 0.35 s, slice thickness: 0.625 mm). The images are reconstructed by using a medium soft-tissue kernel with retrospective ECG-gating.

3. Statistical methods

Discrete variables are expressed as absolute value (n) and percentage. Continuous variables are expressed as mean (SD; standard deviation) or median [IQR; interquartile range]. Normal distribution was verified with the Kolmogorov–Smirnov test. Relationship between CAC and AVC (categorized) and CVRF and clinical events was assessed with the use of the chi square test of Pearson or Fisher's exact test when the expected frequencies were less than 5. Relationship between CAC and AVC (non categorized) and CVRF and clinical events was assessed with the Mann–Whitney U test. CAC and AVC association was analyzed with the intraclass correlation coefficient. The Kaplan–Meier survival curves were compared with the log-rank test. A p value < 0.05 was used as a cutoff for statistical significance. Data were analyzed with the use of the SPSS V 20.0 software package (SPSS, Chicago, Ill).

4. Results

A total 304 patients were included; of these, 151 (56%) were female. Mean age was 62 (SD 11) years. The most important demographic features are shown in Table 1.

The relationship between CAC, AVC and CVRF was analyzed. We found a statistically significant correlation between CAC and age > 65 years old, male sex, smoking habits, hypertension, diabetes mellitus and dyslipidemia. A significant correlation was also identified between AVC and age > 65 years old, male sex, hypertension, diabetes mellitus and peripheral arterial disease (Table 2).

In patients with CAC median Agatston score was 85 [16–382], with a maximum value of 5471. In patients with AVC median Agatston score was 52 [14–133], with a maximum value of 5412. Significant CAD was identified in 82 patients (27%). The remaining patients had non-significant CAD. To study the correlation between CAC and AVC, patients with an Agatston score of 0 were excluded (84 patients). In the remaining 220 patients a significant correlation between CAC and AVC was not found (intraclass correlation coefficient = 0.455[0.345–0.554], Fig. 1).

Table 2
Baseline characteristics and risk factors according to the presence or absence of CAC and AVC.

	CAC			AVC		
CVRF	=0 (n 115)	>0 (n 189)	p-Value	=0 (n 166)	>0 (n 138)	p-Value
Age ≥ 65	26 (23%)	102 (54%)	<**0.001**	36 (22%)	92 (67%)	<**0.001**
Gender (Male)	39 (34%)	94 (50%)	**0.007**	82 (49%)	51(37%)	**0.029**
Smoke	35 (30%)	83 (44%)	**0.019**	65 (39%)	53 (38%)	0.894
Obesity	17 (15%)	37 (20%)	0.280	31 (19%)	23 (17%)	0.669
Hypertension	53 (46%)	128 (68%)	<**0.001**	84 (51%)	97 (70%)	<**0.001**
Diabetes	10 (9%)	38 (20%)	**0.008**	13 (8%)	35 (25%)	<**0.001**
Dyslipidemia	40 (35%)	99 (52%)	**0.003**	68 (41%)	71 (51%)	0.068
Chronic renal failure	0 (0%)	3 (2%)	0.294	1 (1%)	2 (2%)	0.591
Arteriopathy	1 (1%)	8 (4%)	0.161	1 (1%)	8 (6%)	**0.013**
Stroke	2 (2%)	5 (3%)	0.715	5 (3%)	2 (2%)	0.463
Chronic obstructive pulmonary disease	8 (7%)	12 (6%)	0.830	10 (6%)	10 (7%)	0.667