

Association of Aortic Valve Sclerosis with Previous Coronary Artery Disease and Risk Factors

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Abstract

Background: Aortic valve sclerosis (AVS) is characterized by increased thickness, calcification and stiffness of the aortic leaflets without fusion of the commissures. Several studies show an association between AVS and presence of coronary artery disease.

Objective: The aim of this study is to investigate the association between presence of AVS with occurrence of previous coronary artery disease and classical risk factors.

Methods: The sample was composed of 2,493 individuals who underwent transthoracic echocardiography between August 2011 and December 2012. The mean age of the cohort was 67.5 ± 15.9 years, and 50.7% were female.

Results: The most frequent clinical indication for Doppler echocardiography was the presence of stroke (28.8%), and the most common risk factor was hypertension (60.8%). The most prevalent pathological findings on Doppler echocardiography were mitral valve sclerosis (37.1%) and AVS (36.7%). There was a statistically significant association between AVS with hypertension ($p < 0.001$), myocardial infarction ($p = 0.007$), diabetes ($p = 0.006$) and compromised left ventricular systolic function ($p < 0.001$).

Conclusion: Patients with AVS have higher prevalences of hypertension, stroke, hypercholesterolemia, myocardial infarction, diabetes and compromised left ventricular systolic function when compared with patients without AVS. We conclude that there is an association between presence of AVS with previous coronary artery disease and classical risk factors. (Arq Bras Cardiol. 2014; 103(5):398-402)

Keywords: Heart Valve Disease/physopathology; Coronary Artery Disease; Risk Factors; Echocardiography, Doppler.

Introduction

Aortic valve sclerosis (AVS) is characterized by increased thickness, stiffness and calcification of the aortic leaflets without fusion of the commissures. Evaluation of AVS can be performed with Doppler echocardiography, and its presence can result in aortic valve stenosis, which is reflected by increased aortic systolic velocities¹⁻⁴.

In contrast, acute myocardial infarction (AMI) is one of the main causes of death worldwide. This pathology is characterized by accumulation of lipid layers on the coronary artery walls through a process of atherosclerosis, resulting in limitation of blood flow to the cardiac tissue, which may cause hypoxia of this tissue and, in more critical situations, lead to cardiac muscle death^{4,5}.

The relationship between these two pathologies is explained by a progressive release in AVS of oxidized

low-density lipoprotein that accumulates in the valves and extend through the coronary ostia towards the arteries where they are deposited, leading to coronary disease. This hypothesis is consistent with findings of histologic and immunohistochemistry studies and, even though the mechanism is not yet totally known, AVS can be used as a possible significant marker of obstructive coronary artery disease (CAD). It is also considered that this association may be explained by the involvement of risk factors common to both pathologies, such as age, gender, arterial hypertension (AH), smoking, hyperlipidemia and diabetes mellitus (DM)⁶.

Even though the etiological mechanisms of the aortic valve disease and the coronary disease have been documented for many years, the relationship between these two pathological entities only started to be more sharply investigated in the beginning of the 90s after observations, conducted mainly with radiological images, of calcification in the coronary vasculature and in the aortic valve^{7,8}.

The main aim of this study is to verify whether there is an association between the presence of AVS and CAD.

Methods

This is a transversal, retrospective and descriptive study, based on a convenience sample obtained from a database of

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the ultrasonography laboratory of Hospital do Espírito Santo de Évora. The study included 2,493 individuals with mean age of 67.5 ± 15.9 years, 50.7% of which were female, who underwent transthoracic Doppler echocardiography between August 2011 and December 2012.

The inclusion criteria for the selection of the sample were all patients undergoing transthoracic Doppler echocardiography during the period mentioned above when the aortic valvular system was evaluated. Exclusion criteria were defined as all individuals undergoing transthoracic Doppler echocardiography outside the period mentioned above, individuals undergoing transesophageal echocardiography and individuals without information regarding this variable.

The diagnoses of the pathologies that served as clinical indications for the exam, such as heart failure, pulmonary disease, AMI and stroke, were conducted by physicians based on clinical history, physical examination and diagnostic tests. Evaluations with bidimensional and Doppler echocardiogram were conducted with two ultrasonography equipments manufactured by Philips®, models IE33 and HD11 XE. AVS was defined as an increase in echogenicity and thickness of the aortic leaflets without restriction in mobility. Left ventricular systolic function was considered compromised when its value, calculated by the Simpson method, was lower than 55% of the ejection fraction. Finally, it was defined as dilatation of the left heart chambers when a left ventricular diastolic diameter was superior to 32 mm/m² and the increase in left atrial diameter was above 40 mm⁹.

As for the risk factors, AH was defined as systolic pressure above 140 mmHg, diastolic pressure above 90 mmHg, or use of medication for treatment of AH. Presence of diabetes was defined as a level of glucose above 125 mg/dl or treatment for diabetes, without distinction between types I and II diabetes. It was defined as smoker an individual with current use of tobacco and as previous smoker, those who had not used tobacco for more than one year. Dyslipidemia was defined as presence of total cholesterol level above 200 mg/dl or use of medications to treat dyslipidemia⁶.

Statistical analysis of all collected data was computerized with SPSS® (Statistical Package for the Social Science) for Windows®, version 20.0. Initially, a description and characterization of the studied variables was performed in order to establish a general profile of the sample. Later, an analysis of the results was conducted with a descriptive and correlative statistical analysis.

Continuous variables were defined as mean \pm standard deviation ($\bar{X} \pm DP$) and categorical variables as number (n) and percentage (%).

The chi-square test of independence was conducted to correlate categorical variables, and the chi-square test of goodness of fit was performed to evaluate significant differences between the prevalences observed in our study with those from other studies.

The level of statistical significance used for interpretation of the tests was $p \leq 0.05$ for a confidence interval of 95%.

The study was conducted with approval from the Ethics Committee of Escola Superior de Saúde Dr. Lopes Dias and Hospital Espirito Santo de Évora.

The investigation team declares that the study was conducted without external financial sources and with all the expenses paid by the authors.

Results

The sample of this study was composed of a total of 2,493 individuals with mean age of 67.5 ± 15.9 years ($\bar{X} \pm DP$), of which 50.7% were females (Table 1).

In Table 2, we may observe the frequencies of the main studied variables in patients diagnosed with AVS (only main clinical indications are displayed).

As shown in Table 2, the most frequent clinical indication was stroke with 28.8%. Of the risk factors, the most frequent was AH with 60.8%, followed by hypercholesterolemia with 27%. As for the pathological results of Doppler echocardiography, mitral valve sclerosis (MVS) was the most frequent with 37.1%, followed by AVS with 36.7%.

After dividing the sample into two groups of patients with and without AVS, the chi-square test was conducted as previously described. The group with AVS was composed of 915 individuals, whereas the group without AVS had 1,578 individuals. The variables related to the clinical indications, risk factors and results of Doppler echocardiography were then compared between both groups.

Following statistical analysis and as shown in Table 3, there were important significant associations with the variables AH ($p < 0.001$), AMI ($p = 0.007$), compromised left systolic function ($p < 0.001$) and compromised segmentar mobility ($p < 0.001$). In contrast, there was no significant association with hypercholesterolemia, stroke and smoking. There was also no significant association with gender, with males showing a prevalence of AVS of 17.3% and females of 19.4%.

It is observed, therefore, a significant relationship between presence of AMI, AH, DM and compromised left systolic ventricular in patients with AVS when compared with patients without AVS.

Discussion

As already shown in several studies, AVS may be used as a risk marker for coronary disease. Even though its biochemical mechanism has not been completely clarified, this relationship is already widely known. Inflammatory and degenerative processes are thought to affect coronary vases adjacent to this valve system and attack the arteries walls, aggravating pre-existent atherosclerotic processes^{1-3,6}.

In the studied cohort, we could observe a balance between the prevalence of AVS in males and females (17.3% / 19.4%), which is consistent with findings from other studies. Also, the advanced mean age observed (67.5 years) confirms that AVS, as a degenerative pathology, affects mainly older age groups¹⁰.

Table 1 – Characterization of the sample relative to gender

	Male	Female
Frequency	1,228	1,265
Percentage	49.3%	50.7%

Table 2 – Frequencies of the main studied variables (n = 2,493)

Variable	Frequency (n/%)	
Clinical Indication	Cardiac failure	329 (13.2%)
	Stroke	717 (28.8%)
	Pulmonary Disease	383 (15.4%)
	Myocardial Infarction	202 (8.2%)
	Others	862 (34.4%)
Risk Factors	AH	1,515 (60.8%)
	Hypercholesterolemia	673 (27%)
	DM	500 (20.1%)
	Smoking	120 (4.8%)
	Atrial Fibrillation	303 (12.2%)
Pathological Results on Doppler echocardiography	Compromised LVSF	88 (3.5%)
	Enlarged CD	203 (8.1%)
	MVS	914 (37.1%)
	AVS	915 (36.7%)

AH: Arterial hypertension; DM: Diabetes mellitus; LVSF: Left ventricular systolic function; CD: Left cavity dimensions; MVS: Mitral valve sclerosis; AVS: Aortic valve sclerosis.

Table 3 – Results of statistical tests comparing variables between both groups (n = 2,493)

Variable	Group with AVS (n = 915) %(N)	Group without AVS (n = 1,578) %(N)	p value	
Clinical Indication	Cardiac failure	15% (137)	12.2% (192)	0.046
	Stroke	30.7% (281)	27.6% (436)	0.101
	Pulmonary Disease	14.5% (133)	15.8% (250)	0.383
	Myocardial Infarction	10.1% (92)	7% (110)	0.007
Risk Factors	AH	68.5% (627)	56.3% (888)	< 0.001
	Hypercholesterolemia	27.3% (250)	26.8% (423)	0.780
	DM	23% (210)	18.4% (290)	0.006
	Smoking	3.1% (28)	5.8% (92)	0.002
	Atrial Fibrillation	11% (101)	12.8% (202)	0.194
Pathological Results on Doppler echocardiography	Compromised LVSF	9.5% (87)	0.1% (1)	< 0.001
	Enlarged CD	1.9% (17)	11.8% (186)	< 0.001
	MVS	45.6% (404)	32.3% (510)	< 0.001

AVS: Aortic valve sclerosis; AMI: Acute myocardial infarction; AH: Arterial hypertension; DM: Diabetes mellitus; LVSF: Left ventricular systolic function; CD: Left cavity dimensions; MVS: Mitral valve sclerosis.

As for the prevalences found in this study and comparing them with other reference scientific articles regarding AVS, there was a relevant prevalence of stroke in almost one third of the sample (28.8%), which is much higher than the rate found by Otto and cols. (1999) in which the prevalence of stroke in individuals with AVS was 8%. Despite the difference in values from both studies, there was no significance in this study ($p = 0.101$) in contrast to the study by Otto et al¹¹ ($p = 0.003$). The prevalence of AMI in that same study was 8.6%, which is almost identical to the prevalence of 8.2% in our cohort. In both studies, there was a statistical significance in comparison with the control group. As already mentioned, the sclerotic process that affects the aortic valve is similar to the atherosclerotic process in which the worsening in aortic degeneration may accelerate the development of atherosclerotic plaques in the coronary arteries located peripherally to the valvular system, thus leading to the occurrence of symptoms associated with CAD^{6,11}.

In the rates associated with risk factors, AH presented a prevalence of 60.8%, which is slightly inferior to 69% found by Hsu et al⁷, but superior to 51.7% reported by Otto et al¹¹. As for the statistical significances between the group with and without AVS, Hsu et al⁷ did not observe a significant association in this variable, in contrast to the ones observed in this study ($p < 0.001$) and in the study by Otto et al¹¹. The influence of AH in the development of AVS may be explained by the fact that the aortic valve in patients with AH is subjected to higher stress due to the elevated pressure exerted on the aortic leaflets, leading to damage on the endothelium of the leaflets, similar to what occurs in atherosclerotic lesions^{3,12}.

The prevalence of hypercholesterolemia registered in this study was 27%, much lower when compared with the prevalence of 45% found in the study by Hsu et al⁷. In both studies, this variable did not present statistical significance. Comparing with the study by Otto et al¹¹, the prevalence of DM was 13.1%, without statistical difference when compared with the control group ($p = 0.9$), whereas the value found in this study was 20.1%, which showed a strong statistical significance when compared with the control group ($p = 0.006$). The absence of significance in hypercholesterolemia was a surprise, since the presence of cholesterol is an important factor in the process of valvular degeneration. This may have occurred due to the absence of muscular tissue in the aortic valves and to the fact that the deposition of cholesterol occurs differently than that in the coronary arteries. The absence of significance can also be explained by the low number of diagnoses established in the cohort^{13,14}.

In the pathological results found on Doppler echocardiography, a compromised left ventricular systolic function had a prevalence of 9.5%, inferior to that reported by Rosa et al¹⁰ who registered a prevalence of 17.2% with a strong statistical significance in both studies ($p < 0.001$).

Despite the absence of studies associating AVS and MVS, this last had a prevalence of 37.1% with a strong statistical significance. Since the organic tissues that compose the aortic valve are similar to those of the mitral valve, it would be expected that the processes that lead to the development of sclerosis could also occur in both the valves, even though

their repercussion in the coronary disease may be different due to their anatomical situation⁵⁻¹⁷.

Finally, the prevalence of AVS was 36.7%, which is superior to 25% observed by Rosa et al¹⁰.

Based on the information presented above comparing this and several reference studies, we observe that, with the exception of hypercholesterolemia, AH and compromised left ventricular systolic function, the prevalences found in this study are superior, reinforcing the existing link between AVS with DM, AMI and stroke.

These results suggest that patients with AVS have an increased tendency to develop these clinical conditions. Medical action should focus especially in these patients in order to enhance therapies and improve measures to prevent risk factors.

Conclusion

We conclude, therefore, that there is an association between the occurrence of AVS and previous occurrence of AMI, DM and compromised left ventricular systolic function. This confirms the main hypothesis of this study of an existing association between the presence of previous CAD and AVS, similar to the main studies in this area. This association may lead to an appreciation of the presence of AVS on ultrasonography exams, which can be considered a risk marker for suspicion of CAD^{6,18}.

A limitation of the study is that the sample was selected in a laboratory that assists mainly a stroke unit and internal medicine inpatients, which may have influenced the prevalence of stroke. Another limitation of the study refers to the absence of multivariate analysis, which did not show significant results. As a suggestion for future studies, we propose to investigate if MVS, like AVS, could influence the occurrence of AMI and if stroke would or would not be an influence. The investigation team suggests that there could be an advantage to perform a longitudinal study about this theme.

Author contributions

Conception and design of the research, Analysis and interpretation of the data, Statistical analysis and Critical revision of the manuscript for intellectual content: Marmelo FC, Mateus SMF, Pereira AJM; Acquisition of data and Obtaining financing: Marmelo FC, Mateus SMF; Writing of the manuscript: Marmelo FC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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