Correlation Between Aortic Valve Sclerosis and Coronary Artery Disease: A Cross-Sectional Study

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ABSTRACT

Introduction: Aortic valve sclerosis considered as a manifestation of coronary atherosclerosis. Recent studies demonstrated an association between aortic valve sclerosis and obstructive coronary artery disease. The purpose of this study was to evaluate the correlation between aortic valve sclerosis and obstructive coronary artery disease and the extent of coronary artery disease in patients hospitalized for chest pain.

Materials and Methods: A total of 230 consecutive patients were referred to the coronary angiography of Ghaem Medical Center and were subjected to transthoracic echocardiography for screening of aortic valve sclerosis and coronary risk assessment. The diagnostic value of obstructive coronary artery disease for aortic valve sclerosis was calculated.

Results: The patients with obstructive coronary artery disease had a higher prevalence of aortic valve sclerosis compared to those with no coronary artery disease (P<0.05). Aortic valve sclerosis was an independent predictor for obstructive coronary artery disease by multivariate analysis (P<0.05). Aortic valve sclerosis had sensitivity of 47% and specificity of 79% and positive predictor value of 92%.

Conclusions: Aortic valve sclerosis was an independent predictor for obstructive coronary artery disease in patients with chest pain and was strongly interrelated with the extent of coronary artery disease in these patients.

Introduction

Aortic valve sclerosis (AVS) is defined as a progressive calcification, increased thickening of aortic valve leaflets without valve obstruction and antegrade velocity across the valve less than 2.5 m/s (1). AVS presence is associated with an approximately 50% increase in cardiovascular mortality and myocardial infarction (2).

AVS’s predictive value among cardiovascular findings in these patients is limited (3). Echocardiography scanning of individuals without coronary artery disease (CAD) symptoms is cost-prohibitive so finding existing subgroups of cases with AVS at a high risk for heart disease was necessary. Over the last decade, different researchers evaluated the relationship between AVS and CAD (4) but studies about AVS’s importance as a single factor in classification of risk is limited. The association between CAD and AVS could be clearly seen in ischemic heart suspected patients who had coronary angiography (5). AVS was also documented as a strong predictor of obstructive CAD (obCAD) and it might be considered as a CAD risk stratification (6). Thus, the determination of the degree of AVS is the most imperative risk for CAD and should be investigated.

The purpose of this study was to evaluate whether the presence and severity of AVS in echocardiographic evaluation could be a predictor for obCAD severity. The extent of CAD in patients hospitalized for chest pain is of concern given the number and vital importance of the in-
volved vessels. We are looking to address the special importance in risk acceptance for patients who have had a moderate risk for CAD.

**Materials and Methods**

**Study population**

This cross-sectional study included 230 patients with chest pain who were known or clinically suspected cases of CAD and scheduled for coronary angiography between March 2008 and August 2009 in Ghaem University Hospital, Mashhad, Iran. Clinical history and laboratory data were collected from all patients. All patients underwent complete transthoracic echocardiography (TTE) prior to considering coronary angiography either on the same day or within 2 days of the procedure. Patients with aortic stenosis, aortic regurgitation more than mild, rheumatic valvular disease, congenital heart disease history and prosthetic valve replacement were excluded from the study. An informed consent form was obtained from all patients. All procedures were approved by ethics committee of Mashhad University of Medical Sciences (MUMS).

**Clinical data**

All patients’ demographic characteristics and atherogenic risk factors were determined before they underwent coronary angiography. Diabetes mellitus, systemic hypertension, hyperlipidemia and renal failure were defined as hyperglycemia more than 114 mg/dl fasting blood sugar or diabetes medications, blood pressure >140/90 mmHg or antihypertensive medications, LDL>160mg/dl and total cholesterol level > 200 mg/dl, and creatinine more than 1.3 mg/dl, respectively. Smoking was defined as active smoking within the past 12 months.

Electrocardiographic (ECG) changes including ischemic ST-T changes, Q-wave, bundle branch block and arrhythmia were evaluated and diastolic dysfunction rely on mitral valve filling pattern and mitral annular tissue Doppler imaging were classified into defined categories such as; impaired left ventricular relaxation, pseudo normalized and restrictive pattern.

**Echocardiographic Evaluation**

Complete TTE studies were performed according to the last ASE-AHA guidelines for all patients using commercially available system (VIVID7 dimension, GE, Horten Norway, 2007 with probe 2.5-3.5 MHZ) in lying down and left lateral positions. Two dimensional assessments of the aortic valve were made from the parasternal long axis, short axis and apical views with appropriate gain settings. Peak transaortic flow velocity was measured from the apical view by continuous wave Doppler. AVS was defined as a focal area of increased echogenicity and thickening of the aortic valve leaflets without restriction of leaflet motion and a transaortic flow velocity (<2.5 m.s) on TTE (2, 7). The thickness of sclerotic aortic cusps were determined from the end diastolic frozen echocardiographic images obtained in either short or long axis. Mild, moderate and severe AVS were classified as cusp thickness 2.3-9 mm, >4-6 mm and >6 mm, respectively (8, 9). Mitral annular calcification (MAC) was also evaluated and measured from the 2 and 4 chamber views. MAC was defined as thickness increment of mitral annulus >5 mm (8).

**Coronary angiography**

Coronary angiography in multiple views was performed according Judkins or Sones Standard technique (10). At least four views for evaluation of left main (LM) coronary artery, left anterior descending (LAD), left circumflex (LCX) and right coronary artery (RCA) were performed. Angiographic results were interpreted by angiographer who was blinded to echocardiographic findings. Significant CAD was defined as more than 50% reduction of internal diameter of at least one coronary artery. The definition of 1, 2- or 3-vessel disease was based on the criteria of Coronary Artery Surgery study (11).

**Statistical analysis**

Student's t-test or Mann-Whitney test was used to compare the continuous data, according to the presence and absence of AVS or ObCAD. Furthermore, group comparisons involving categorical data were made using chi-square analyses. Correlation between severity of ObCAD and other variables was investigated by Spearman’s correlation coefficient and ANOVA or Kruskal Wallis test. Multiple logistic regression analysis was applied to evaluate the association of significant ObCAD with AVS and other coronary risk factors. P value less than 0.05 was considered significant. Numerical data are expressed as mean ± SD or as proportions of the sample size.

**Results**

**Patient's clinical characteristics**

The baseline characteristics of patients underwent coronary angiography were presented in Table 1. The CAD group included 184 patients (123 male and 61 female; mean age 61.49 ±10.85 years) and the non CAD group included 44 patients (15 male and 19 female; mean age 57.41±9.8 years). There was a higher proportion of elderly patients (age more than 60 years old) in CAD group compare to non CAD group (P< 0.05). Diabetes mellitus, hypertension, hyperlipidemia, renal failure, smoking history and ECG ischemic changes were also more common in CAD patients. However, these increments were not significant. Cases with CAD had a higher prevalence...
Echocardiographic findings

Table 2 summarizes the clinical and laboratory characteristics of the cases with and without AVS. Echocardiographic findings revealed that among 103 patients who had AVS, 88 were found to have significant obCAD compared to 97 cases out of 127 patients without AVS (P<0.01). AVS prevalence in Age>60 years was significantly higher than younger patients (P<0.001).

Patients with AVS revealed higher prevalence of respected diastolic dysfunction stages (I, II and III stages, respectively) in comparison with patients without AVS (P<0.01) (Table2). The distribution of coronary artery involvement in different stages of AVS is shown in Fig 1.

There was significant difference in extent of coronary arteries between patients with AVS and without AVS (P<0.001). There was also significant increase in LCX and RCA involvement in AVS patients (P<0.05, <0.001, respectively) compare to patients without AVS.

Multiple logistic regression analysis

Multiple logistic regression analysis was conducted to determine the association between obCAD with some clinical variables including AVS, diastolic dysfunction, ECG ischemia, mitral annular calcium, and age>60 years. Data has been revealed in Table 3. The analysis presented AVS as a significant predictor of the CAD presence in patients with suspected ischemic heart disease. The prevalence of CAD in patients with AVS were 3 times higher than patients without AVS (OR=3.49).

Among aortic cusps involved in patients with AVS, RCC and LCC had the maximum and minimum of sclerosis, respectively (55.07% versus 12.5%). Univariate analysis revealed that RCC and NCC sclerosis and their severity had significantly correlated with obCAD (P<0.001). Likewise there was significant linear correlation between RCC, NCC, LCC sclerosis severity with severity of obCAD (P<0.001).

Figure 1. Distribution of coronary artery involvement in different stages of aortic valve sclerosis
LM (Left main), VD (Vessel Disease)

<table>
<thead>
<tr>
<th>Variables</th>
<th>No CAD (n=46)</th>
<th>CAD (n=184)</th>
<th>Odd ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (Male)</td>
<td>15 (24.1%)</td>
<td>123 (66.8%)</td>
<td>2.56</td>
<td>(0.18-0.82)</td>
<td>0.087</td>
</tr>
<tr>
<td>Age ≥ 60 y</td>
<td>15 (44.1%)</td>
<td>110 (61.1%)</td>
<td>1.99</td>
<td>(0.94-4.17)</td>
<td>0.09</td>
</tr>
<tr>
<td>Age (year)</td>
<td>57.41 ± 9.8</td>
<td>10.85 ± 61.49</td>
<td>2.03</td>
<td>(0.89-4.61)</td>
<td>0.089</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>10 (30.3%)</td>
<td>46 (25.4%)</td>
<td>0.78</td>
<td>(0.34-1.76)</td>
<td>0.520</td>
</tr>
<tr>
<td>HTN</td>
<td>17 (51.5%)</td>
<td>98 (54.1%)</td>
<td>1.11</td>
<td>(0.52-2.33)</td>
<td>0.850</td>
</tr>
<tr>
<td>HLP</td>
<td>14 (42.4%)</td>
<td>75 (41.4%)</td>
<td>0.96</td>
<td>(0.45-2.03)</td>
<td>1</td>
</tr>
<tr>
<td>Smoking</td>
<td>0 (0.0%)</td>
<td>3 (1.7%)</td>
<td>...</td>
<td>...</td>
<td>1</td>
</tr>
<tr>
<td>ECG Ischemic</td>
<td>21 (65.6%)</td>
<td>101 (59.4%)</td>
<td>0.76</td>
<td>(0.34-1.69)</td>
<td>0.56</td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td>5 (15.2%)</td>
<td>50 (29.5%)</td>
<td>2.29</td>
<td>(0.83-6.28)</td>
<td>0.079</td>
</tr>
<tr>
<td>MAC</td>
<td>2 (5.9%)</td>
<td>9 (4.9%)</td>
<td>0.818</td>
<td>(0.169-3.96)</td>
<td>0.682</td>
</tr>
<tr>
<td>AVS</td>
<td>7 (20.6%)</td>
<td>88 (47.6%)</td>
<td>3.49</td>
<td>(1.45-8.43)</td>
<td>0.004</td>
</tr>
<tr>
<td>Sclerotic RCC</td>
<td>6 (17.6%)</td>
<td>71 (38.6%)</td>
<td>2.93</td>
<td>(1.15-7.43)</td>
<td>0.019</td>
</tr>
<tr>
<td>Sclerotic NCC</td>
<td>6 (17.6%)</td>
<td>76 (41.3%)</td>
<td>3.28</td>
<td>(1.29-8.31)</td>
<td>0.011</td>
</tr>
<tr>
<td>Sclerotic LCC</td>
<td>2 (5.9%)</td>
<td>30 (16.3%)</td>
<td>3.11</td>
<td>(0.70-13.7)</td>
<td>0.184</td>
</tr>
<tr>
<td>EF</td>
<td>0.54±0.08</td>
<td>0.49±0.12</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Data were presented as mean± SD or percent of patients; CI= confidence interval; HTN= Hypertension; HLP= Hyperlipidemia; RF= Renal Failure; MAC= Mitral annular calcium; AVS= Aortic valve sclerosis; RCC= Right Coronary Cusp; NCC= Non Coronary Cusp; LCC= Left Coronary Cusp; EF= Ejection Fraction.
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AVS existence was effective on LCX, RCA and LM obstruction and the possibility of their obstructions were approximately 3.2-3.5 times higher in patients who had AVS compare to patients who did not represent AVS respectively (P<0.001).

Additionally, analysis showed that only sclerosis of RCC had relation with LAD obstruction (P<0.05) while sclerosis severity of all aortic trileaflets related significantly with LCX obstruction (P<0.01) and RCA obstruction (P<0.05).

Diagnostic value of AVS for CAD

Significant AVS had sensitivity and specificity of 47% and 79% for obCAD diagnosis, respectively (consider to mentioned criteria). Despite a low negative predictive value (21%), it was a high positive predictive value (PPV) (92%) for the presence of significant CAD.

Discussion

Our results indicated that AVS is a strong echocardiographic predictor for obCAD in patients with chest pain who underwent angiography. The chance of obstruction of coronary vessels in AVS patients is three times higher compare to patients without AVS.

Conte et al studied patients with chest pain and negative cardiac enzymes which are candidate for angiography.
phy (4). They found AVS by TTE in patients who had high risk acceptance for obCAD (4). Hsu et al. and Soydinc et al independently achieved the similar results (12, 13). Soydinc et al. also showed the significant relation between AVS with extent and severity of CAD according to Gensini score (13). Contrarily, Tolstrup and coworkers showed that the relation between AVS and obCAD was not significant (6).

Our results showed that AVS is more prevalent in patients older than 60 years. It was exhibited that the prevalence of AVS is high and associated with aortic atheromatous diseases in people older than 60 years and 50% risk increment of angina, stroke, congestive heart failure, myocardial infarction and death (6). It has been shown that AVS is detectable by echocardiography in 50% of the elderly patients (14). Prevalence of unassigned AVS in elderly cases without aortic stenosis is common and involved 21-26% cases older than 65 years (5-7, 14-17). Clinical factors were associated with AVS pathogenesis include age, sex, hypertension, hyperlipidemia, diabetes mellitus and current smoking (7,15-16). Ejection Fraction (EF) average in obCAD patients was lower than non obCAD group, as well. High PPV measurement of our data is parallel to rest of literature (92%) (4, 6, 12).

While Hsu et al. observed no significant correlation between the degree of aortic cusp thickening and the extent of CAD (11); our results indicate prognostic predictable value for the degree of aortic valve sclerosis in obCAD as well as a significant correlation with the extent of coronary artery involvement. In addition, between moderate and severe sclerosis, the most obCAD was observed in 2-vessel and left main involvement. We found that AVS had significant correlation to LM, RCA and LCX obstruction. Our study classified sclerosis according to leaflets thickness while with using of different kinds of morphological sclerosis better results could be achieved. Although morphological evaluation of AVS showed that this could be as obCAD predictor (8), studies about the relation between sclerosis leaflet involvement and obCAD severity are limited. Other associated factors to obCAD extent and number of involved arteries included: age more than 60 years old, male gender, ischemic changes of ECG and chronic renal failure.

Ootto et al. reported that in AVS often NCC becomes involved (2) while we found that RCC were the most involved cusp. Correspondingly we found that presence and severity of RCC and NCC sclerosis related to obCAD persistence. There was significant relation between the extent of coronary artery involvement with sclerosis of aortic leaflets and number of obstructed vessels. That meant that more than 40% of patients with NCC and RCC sclerosis had 3-VD involvement. Also, we evaluated aortic leaflet sclerosis in relation to the kind of involved vessel. We concluded that only RCC sclerosis severity was related to LAD obstruction while sclerosis of all trileaflets was associated to LCX and RCA. Stewart et al. showed that age increment and high LDL correlated with aortic sclerosis (7), while another presented only age and lower BMI related to AVS persistence (12). Our study presented that age more than 60 years old, ECG ischemic changes and diastolic dysfunction had significant relation to AVS persistence.

Conclusion

AVS is valuable independent predictor for obCAD and degree of sclerosis is a prognostic marker of CAD and also had a significant correlation with the extent of coronary artery involvement.

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Conflict of Interest: The authors declare no conflict of interest.

References


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