Assessment of the Relation Between Average Aortic Valve Sclerosis Score Index and Severity of Coronary Artery Disease in Patients with Acute Coronary Syndrome

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Abstract

Objectives: This study aimed to evaluate the relation between average aortic valve (AV) sclerosis score index (AVSSI) and severity of coronary artery disease (CAD) in patients with acute coronary syndrome (ACS).

Patients and methods: A total of 100 patients with ACS were studied. They were classified into 2 equal groups of 50 patients each. Group (1) involved patients with average AVSSI >1, and group (2) involved patients with average AVSSI ≤ 1, were not matched in age and sex. For these patients electrocardiography (ECG), conventional echocardiography, coronary angiography and SYNTAX score were determined.

Results: The study found that there is a strong correlation between CAD and average AVSSI (r=0.791, p<0.001). There is increase in the incidence of average AVSSI with increase of CAD risk factors such as hypertension, diabetes mellitus, dyslipidemia, male gender, aging, family history, smoking, increased blood calcium and body mass index (BMI). Also there is decrease in LVEF % in group 1 (43.6 ± 7.14) compared to group 2 (51.2 ± 6.98) with statistically significant difference (p<0.001), while there is increase in E/e' in group 1 (9.68 ± 3.58) compared to group 2 (5.68 ± 3.27), p<0.05. The prevalence of three-vessel CAD was higher in group 1 (24%) than in group 2 (8%), p<0.001. SYNTAX score was higher in average AVSSI>1 (16.4 ± 9.67) than average AVSSI ≤ 1 patients (8.92 ± 10.1), p<0.001.

Conclusion: It is concluded that there is a strong relationship between average AVSSI and coronary artery disease severity, and is consistent with other high-risk echocardiographic findings.

Keywords
Coronary artery disease; Aortic valve sclerosis; A cute coronary syndrome

Introduction

Aortic valve sclerosis (AVS) is a disease of AV which involving about 25% of population at the age more than 65 years. AVS incidence is increased in elderly people and by widespread using of noninvasive techniques [1]. The definition of AVS is aortic valve calcification without a significant trans-valvular pressure gradient or impairment in leaflet excursion [2]. The disease begins with progression of calcium deposition gradually which can finally convert to aortic stenosis (AS) with impairment of blood flow from left ventricle. Severe form of AS ultimately results in remodeling of ventricle and blood circulation changes leading to increase morbidity and mortality rates if not controlled. It has been considered that progressive wear and tear results in an occasional age related degenerative process, there is evidence related to AVS that challenges this assumption [1].

Through conventional echocardiography, aortic sclerosis is defined as a micro-calciﬁcation focal region and a trileaflet aortic valve thickening, without presence of commissural fusion and/or ventricular outflow obstruction (ante-grade velocity across the valve <2.5 m/s). Disease frequency is increased by the age: 21–29% of adults aged >65 years manifest sclerosis of aortic valve, whereas the frequency is increased to 48% in individuals >84 years [3].

Novel perceptions have demonstrated that the AVS progression and AS may include, atherosclerotic lipoproteins deposition, chronic inﬁammatory ﬁltrates and calcification. The characterstic features of AVS, involving histological predominance of calcium, gradually progress, and high pressure location which acts as a gateway from the heart to the systemic circulation. Some researchers have declared either AVS or AS frequent coexistence in CAD patients [4].

Many researches have shown that risk factors in the progression of CAD, like hypertension, male gender and dyslipidemia, may also impact development of AVS and its progression to AS [5]. These notices not only marking the many participating features of AVS and CAD but have also encouraged researchers to test the medical techniques effect which may have useful impacts on both conditions[1].

In the egyptians, heart disease is the leading cause of death. The most of these deaths are due to CAD. Revascularization, statins and angiotensin inhibitors (ACEI) are used for improving CAD to allow larger number of patients living with CAD [6]. Understanding the underlying similarities in AVS and CAD pathophysiology, a lot of associated clinical questions remain not answered [7]. For example, Should AVS existence propose CAD presence or progression? Could we consider AVS a new risk factor for CAD progression? Is AVS presence enough for careful beginning and titration of treatment with changing life style similar to present lines used for diabetes mellitus treatment? We try to answer these questions in this study.

Aim

This study aimed to evaluate the relation between average aortic valve sclerosis score index and severity of coronary artery disease in patients with acute coronary syndrome.
Patients and Methods

Study design and population

The study was performed in Benha university hospital in the period of one year from March 2018 to March 2019 on 100 patients with ACS of them 50 patients with average AVSSI>1 represent group (1) and 50 patients with average AVSSI ≤ 1 represent group (2).

Inclusion criteria included patients presented with ACS represent the population of this study classified into two equal groups as mentioned above.

Exclusion criteria included patient refusal, heart muscle disease (severe heart failure and cardiomyopathy), severe myocarditis, significant arrhythmia , previous pacemaker implantation, or cardiac surgery . The ethics committee of the hospital approved the protocol.

All participants included in this study were subjected to:

- Informed consent: each participant has to perform written consent
- Full history taking: including history of hypertension, diabetes mellitus and smoking habit.
- General and local examinations of the heart
- 12 leads ECG
- Routine laboratory tests including: complete blood picture, liver functions, renal functions, serum calcium and lipid profile.
- Conventional echocardiography was performed for all the participants within 24 hours of admission by the same operator.
- Coronary angiography was performed for all patients.

Conventional echocardiographic diagnosis of AVS

Echocardiography was performed on all patients within 24 hour of admission. The presence of AVS was assessed by echocardiography (Vivid 7 Dimension ultrasound framework, GE Healthcare, Waukesha, WI, USA) by a probe of 2.5 MHz frequency[8]. It also used for aortic valve magnification along parasternal axis view. Three cardiac cycles and three loops for each one were registered confirming that the leaflets of aortic valve are seen during diastole. Grades of sclerosis were registered based on the sclerosis visual score (VSS) that appointed to every valve according to the parasternal short axis 2D appearance [9].

0=normal
1=slight increase in reflectance of the cusp bodies or margins
2=mild increase in overall reflectance and cusp thickness
3=generalized hyper-reflectance, cusps markedly thickened with markedly hyper-reflective masses.

For subsequent analysis goal, the finding of AVS was marked as an average aortic valve sclerosis score index (AVSSI) of ≥ 1. Doppler echocardiography was used to assess velocity in the LV outflow tract and through the aortic valve [6].

Other echocardiographic parameters

The left ventricular ejection fraction (LVEF) and variables of left ventricular diastolic function and filling pressure, such as transmural pulsed Doppler early diastolic velocities (E wave), early diastolic tissue Doppler mitral annular velocities (e'), and E/e' ratio, were also determined.

Coronary angiography

Coronary angiography was done in many views according to the typical techniques of Judkins or Sones . The left coronary artery acquired 2 orthogonal views and the right acquired at least 2 orthogonal views within at least five views. The angiographers explained the results of angiography and they didn't have any knowledge about findings of conventional echocardiography. The goal of applying coronary angiography is to detect plaques (twenty percent at least) which indicate atherosclerosis existence. Reduction in the internal diameter of left main vessel about 50% or more than 70% reduction in the internal diameter of other vessels (left anterior descending artery, left circumflex artery and right coronary artery) indicates presence of significant CAD. According to the Surgical Coronary Artery Study criteria, the 1-, 2- or 3-vessel disease was defined.

N.B: SYNTAX score (SS)

The synergy between Percutaneous Coronary Intervention with Taxus and Cardiac surgery (SYNTAX) score (SS) is an angiographic way to assert the degree of CAD intensity and complexity and allows more explaining assessment of the coronary lesion characters [11].The CAD complexity is evaluated by SS. Coronary arteries with diameter more than 1.5 mm and ≥ 50% of stenosis were embraced for assessment. The SS was measured by the last updated version online (accessed in October 2014) (2.11). There were two groups of SSs (high SYNTAX: ≥ 22, low SYNTAX: <22). Two cardiologists didn’t know the study data (ST, UA), calculated all angiographic variables. The definitive decision was taken by assent in case of disagreement [12].

Statistical Analysis

Measurable investigation was performed utilizing Statistical Package for Social Sciences (SPSS) variant 23.0 for windows (SPSS Inc., Chicago, IL, USA). Numerical values are recorded as sample size ratios or means ± SD. Study and control group comparisons were done for categorical information by Chi square test and Student's t-test to detect continuous data. ANOVA test estimated inter- and intra-observer differences. The association of CAD significance with other coronary risk factors and AVS were measured by multiple logistic regression analysis (backward stepwise). Significant p value was <0.05 and non-significant p value was >0.05.

Results

This study included 100 patients with signs of acute coronary syndrome, of them 50 with average AVSSI>1 (group 1), they were 36 (72%) of them males and 14 (28%) females, and 50 with average AVSSI ≤ 1 (group 2), they were 30 (60%) males and 20 (40%) females . There were significant differences as regard age and gender between the two groups. (Table 1).

Assessment of cardiovascular risk factors

All risk factors in this study (hypertension, diabetes mellitus, smoking, dyslipidemia, family history, Body Mass Index and calcium) showed a statistically significant difference (p<0.05) as presented in Table(2).
Patients' clinical conditions
There was a statistical non-significant difference as regard presence of STEMI, non-STEMI and unstable angina in the two groups (p>0.05) as shown in Table (3).

Aortic valve sclerosis grading in the studied groups
There was statistically highly significant difference in each grade of AVS (p<0.001) in group (1) compared to group (2) as illustrated in Table (4).

Conventional echocardiographic parameters of the studied groups
There was a statistical significant difference (p<0.001) as regard the left ventricular ejection fraction (LVEF) percent which decreases in group (1) compared to group (2), and also there is a statistical significant difference (p<0.05) as regard E/e' ratio that increase in group (1) compared to group (2). (Figure 1) Table (5).

Coronary angiography findings in the studied groups
There was a statistically highly significant difference (p<0.001) in the prevalence of 3 vessels CAD in group (1) compared to group (2) that illustrated in Table (6).

SYNTAX score (SS) of the studied groups
There was a statistical significant difference as regard the mean SS in group (1) compared to group (2) Table (7).

Table 1: Age and sex distribution of the studied groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>AVSSI&gt;1 (N=50)</th>
<th>AVSSI ≤ 1 (N=50)</th>
<th>Statistical test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 60</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>&gt; 60</td>
<td>12</td>
<td>29</td>
<td>χ²-test = 4.60</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
<td></td>
<td>p value = 0.018</td>
</tr>
<tr>
<td>Males</td>
<td>38</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>14</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05=significant.

Table 2: Risk factors in the studied groups.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>AVSSI&gt;1 (n=50)</th>
<th>AVSSI ≤ 1 (n=50)</th>
<th>Statistical test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>38</td>
<td>42</td>
<td>χ²-test = 5.24</td>
</tr>
<tr>
<td>Diabete mellitus</td>
<td>32</td>
<td>19</td>
<td>p value = 0.026</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>28</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>34</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td>24</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>BMI (Kg/m²):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 20</td>
<td>8</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>&gt; 20</td>
<td>42</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Calcium:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>6</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>2–3</td>
<td>44</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05 is a statistically significant value. BMI: body mass index.

Table 3: Patients clinical conditions in the studied groups.

<table>
<thead>
<tr>
<th>Patients clinical conditions</th>
<th>AVSSI&gt;1 (n=50)</th>
<th>AVSSI ≤ 1 (n=50)</th>
<th>Statistical test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI</td>
<td>20</td>
<td>21</td>
<td>F-test = 0.173</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>20</td>
<td>16</td>
<td>p value = 0.256</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>10</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

*p=0.05 is a statistically non-significant value, STEMI: ST segment elevation myocardial infarction, NSTEMI: non-STEMI.

Table 4: Average AVSSI by conventional echocardiography in the studied groups.

<table>
<thead>
<tr>
<th>Grade</th>
<th>AVSSI&gt;1 (n=50)</th>
<th>AVSSI ≤ 1 (n=50)</th>
<th>Statistical test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.49 ± 0.43</td>
<td>0.79 ± 0.28</td>
<td>χ²-test = 26.201</td>
</tr>
</tbody>
</table>

*p<0.001 is a statistically highly significant value. AVSSI: aortic valve sclerosis score index. AVSSI: aortic valve sclerosis score index.
Table 5: Conventional echocardiographic parameters of the studied groups.

<table>
<thead>
<tr>
<th>Variable (Mean ±SD)</th>
<th>AVSSI&gt;1 (n=50)</th>
<th>AVSSI ≤ 1 (n=50)</th>
<th>t-test</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF (%)</td>
<td>43.6 ± 7.14</td>
<td>51.2 ± 6.98</td>
<td>8.554</td>
<td>0.001</td>
</tr>
<tr>
<td>E wave (m/s⁻¹)</td>
<td>0.642 ± 0.17</td>
<td>0.651 ± 0.18</td>
<td>0.324</td>
<td>0.117</td>
</tr>
<tr>
<td>Avg e' (cm/s⁻¹)</td>
<td>6.78 ± 1.92</td>
<td>7.76 ± 1.94</td>
<td>7.225</td>
<td>0.027</td>
</tr>
<tr>
<td>E/e'</td>
<td>9.68 ± 3.58</td>
<td>5.68 ± 3.27</td>
<td>7.951</td>
<td>0.011</td>
</tr>
</tbody>
</table>

* p<0.05 is a statistically significant, LVEF%: left ventricular ejection fraction percentage, Avg: average, E/e': transmitral peak early diastolic velocity/mitral annular early diastolic velocity.

Table 6: Relation between CAD by coronary angiography and average AVSSI groups.

<table>
<thead>
<tr>
<th>Number of obstructive vessels (Lesion &gt;70%)</th>
<th>AVSSI&gt;1 (m=50)</th>
<th>AVSSI ≤ 1 (m=50)</th>
<th>Statistical test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>N %</td>
<td>N %</td>
<td>χ²-test</td>
<td>p value</td>
</tr>
<tr>
<td>0 0.0</td>
<td>10 20.0</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>1 36.0</td>
<td>18 36.0</td>
<td></td>
<td>0.00</td>
</tr>
<tr>
<td>2 40.0</td>
<td>18 36.0</td>
<td></td>
<td>2.55</td>
</tr>
<tr>
<td>3 24.0</td>
<td>4 8.00</td>
<td></td>
<td>10.62</td>
</tr>
</tbody>
</table>

* p<0.001 is a statistically highly significant

Table 7: SYNTAX score in the studied groups.

<table>
<thead>
<tr>
<th>SYNTAX score</th>
<th>AVSSI&gt;1 (n=50)</th>
<th>AVSSI ≤ 1 (n=50)</th>
<th>Statistical test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>N %</td>
<td>N %</td>
<td>χ²-test</td>
<td>p value</td>
</tr>
<tr>
<td>Low (&lt;22)</td>
<td>24 48.0</td>
<td>48 96.0</td>
<td>13.372</td>
</tr>
<tr>
<td>High (&gt;22)</td>
<td>26 52.0</td>
<td>2 4.00</td>
<td>2.719</td>
</tr>
</tbody>
</table>

* p<0.001 is a statistically highly significant, ^ calculated by t-test.

Discussion

Higher realization of optimum heart function state in middle age to older age is correlated with lower appearance of AV disease in old age, realization of optimum heart state and disease of heart valves are still not recognized [13].

The Statistics Committee and the American Heart Association Strategic Planning Task Force stated the goal of optimum heart health as the realization of four health aspects (healthy food, smoking cessation, body mass index <25 kg/m² and physical activity) and three health agents (fasting blood sugar <100 mg/dL, total cholesterol <200 mg/dL, blood pressure <120/<80 mmHg) [14].

This study included 100 patients with signs of acute coronary syndrome, of them 50 with average AVSSI>1 (group 1), they were 36 (72%) of them males and 14 (28%) females, and 50 with average AVSSI ≤ 1 (group 2), they were 30 (60%) males and 20 (40%) females. There were significant differences as regard age and gender between the two groups.

This was coincides with Shavelle et al. [15] who found 67% of AVSSI were males and Milin et al. [1] found 66% male patients had AVS. Korkmaz et al. [16] and Milin et al. [1] considered male gender as a risk factor for AVS.

In this study most of patients were above 60 years of age. This was in agreement with Soydinc et al. [10] stated that male gender (72%) and Sengelov et al. [13] who reported that average AVS increased with age. They reported increased prevalence of average AVS above 80 years of age. Soydinc et al. [10] stated significant positive correlation between age and AVS as they found that patients with average AVS were older than those without it (p<0.001). Bhatt et al. [7] show AVS prevalence increase
with older age, particularly in patients more than 71 years old. AVS has been usually associated with older age and seems to be sensitive degenerative changes marker due to hemodynamic overload in heart [11].

In this study, there was increase in the incidence of average AVS with increase of CAD risk factors such as hypertension (76%), diabetes mellitus (64%), dyslipidemia (56%), family history (48%), smoking (68%), increased blood calcium (80%) and body mass index (BMI) (84%). This was similar to many authors such as Shavelle et al. [15] who found hypertension (67%), smoking (40%), DM (35%), hyperlipidemia (42%) and family history (42%) as risk factors for AVS. Korkmaz et al. [16] found risk factors for AVS as hypertension (88%), DM (1%), smoking (16%), and dyslipidemia (26%), however they mentioned that they were insignificant which opposing to the results of this study.

In another study Soydinc et al. [10] declared that smoking (50%), hypertension (44%) and diabetes mellitus (32%) were more prevalent also in group two than one (p=0.006, 0.004, 0.027 and 0.029, in order). Regarding estimation of serum lipid levels, LDL cholesterol levels (130 ± 23.35 vs. 107.34 ± 19.31; p=0.001) and total cholesterol level (206.02 ± 29.9 vs. 180.3 ± 34.06 mg/dl; p=0.001) were lower in the control than AVSSI patients in that study. Body mass index and HDL levels were the same in the two groups.

Regarding patients conditions (STEMI, NSTEMI and unstable angina), there was no a significant difference between the two groups as p=0.05. As regard high SYNTAX Score (SS) in this study, there was high statistically significant difference between group (1) and (2). SS was high in 26 patients (52.0%) of AVSSI>1 group (1) with mean of 16.4 ± 9.67 and only in 2 patients (4%) of AVSSI ≤ 1 group (2), with mean of 8.82 ± 10.1, p value was highly significant (<0.001).

In agreement with this study Topcu et al. [12] reported that AVS positivity was significantly high in the high SS group in comparison with low SS group (31.3% vs. 10.6%, p<0.001 and OR=3.8, 95% CI: 2.4–6.1) because there were 237 AVS-negative and 28 AVS positive cases in the group of low SS, there were 191 AVS-negative and 87 AVS-positive cases in the group of high SS.

Opposing to the results of this study Bhatt et al. [7] reported that AVS presence was not related to SYNTAX score (p=0.684). They reported that interpretation of coronary angiography lesion characters and score of SYNTAX (using an algorithm) were restricted to cardiologist with intervention experience, which removes the inter-observer variability.

The existence of CAD can be detected by AVS estimation by conventional echocardiography and the relevant CAD severity at rest is determined by a noninvasive procedure which needs only a few minutes [10].

In this study there was a statistical significant difference (p<0.001) as regard the left ventricular ejection fraction (LVEF) percent which decreases in patients with AVSSI>1 (group 1) compared to patients with AVSSI ≤ 1 (group 2), from mean ± SD of 43.6 ± 7.14 to 51.2 ± 6.98 percent, respectively, and also there is a statistical significant difference (p<0.05) as regard E/e’ ratio that increase in group (1) with mean of 9.68 ± 3.58 compared to group (2) with a mean of 5.68 ± 3.27.

These results coincide with Topcu et al. [12] who stated that LVEF was lower in group 1 (median, 47) than in group 2 (median 55) which was statistically highly significant (p<0.001).

There is a statistically highly significant correlation between severity of CAD and number of affected vessels (multivessel lesion) with average aortic valve sclerosis index (p<0.001). In this study, existence of ACS, its severity and AVSSI are related to each other.

In agree with these results, in a study of 160 patients, Soydinc et al. [10] reported that the existence of triple vessel CAD was linked to AVS presence and was independently related to Gensini score. Regarding the 50 patients with AVS, CAD patients were 45 in comparison with 88 of the 110 patients without AVS. Higher incidence of 3-vessel disease was found in AVSSI patients. (non-AVS vs AVS group: 13.6 vs. 40%) (p=0.001). However, regarding AVS and the existence or absence of 1- or 2-vessel disease, there was no significant difference.

Also, Mazzone et al. [3] declared that 49% of 415 patients of acute coronary syndrome had AVS after follow-up for one year.

Oposing to this study Bhatt et al. [7] reported that AVS existence was not related to obstructive vessels number (p=0.831), more than seventy percent stenotic lesions in minor (p=0.1) and major (p=0.849) epicardial arteries, 50-70% stenotic lesions in minor (p=0.237) and major (p=0.267) epicardial arteries or SYNTAX score (p=0.684). They also determined that AVS should not be used in isolation from cardiac risk factors as coronary artery atherosclerosis noninvasive indicator and its use as an indicator of CAD with severe obstruction remains a subject of debate.

A study of 230 patients from Fazlinezhad et al. [17] showed that AVS can predict obstructive coronary disease independently.

In a cohort major study of more than 2000 AVS patients, aortic stenosis developed in 16%, mild stenosis in 10.5% and severe stenosis in 2.5%, over eight years interval [18]. A smaller group of patients had been observed with a similar percentage, however only a small aortic sclerosis patient percent is proceed to aortic stenosis: 2-4% of age over 65 years [19].

From the above results and studies, CAD and average AVSSI had a strong relation between them. AVS and atherosclerosis similarities are suggested by the following mechanisms: 1) Atherosclerosis incidence is increased by AVSSI, 2) There is similar histopathological properties between AVSSI and atherosclerosis, and 3) there was a relation between AVSSI, CAD and systemic atherosclerosis, like relation between peripheral disease of arteries, carotid artery disease and atherosclerosis [20,21].

Conclusion

In conclusion, average AVSSI and severity of coronary artery disease have a strong relationship, and is proportionate with other echocardiographic findings of high risk.

Limitations

The major limitations of this study is the lack of control (normal) group which may be useful for comparison of diseased and normal values, the small number of study which may give inaccurate statistical comparison between the two studied groups and lastly the limited duration of this study that may affect the studying of all parameters and risk factors.
References