Aortic Sclerosis and Cardiac Calcifications

P. Faggiano
Brescia - Italy
Aortic valve sclerosis (AVS) is present in > 25% of subjects > 65 years of age.

AVS is characterized by diffuse or focal thickening of the aortic cusps, leaflet calcification and absence of stenosis.

AVS was previously considered to be a benign condition, but several recent studies have found that a significant proportion of patients will develop AS.

However, the clinical significance of AVS extends beyond its time relation with significant AS.
In fact……

• A number of prospective and retrospective studies have established that AVS is an independent, incremental risk marker of mortality and cardiovascular events.

• It is largely accepted that the pathogenesis of AVS shares many features with the atherosclerotic process in several vascular beds.

• Other intracardiac calcium deposits, such as mitral annulus and papillary muscle calcification and ascending aortic wall thickening and hyperreflectivity, seem to reflect the atherosclerotic process in the coronary arteries and are frequently associated to it.
Normal tricuspid aortic valve

Calcific tricuspid aortic valve
Calcific deposits in
epicardial coronary arteries
mitral annular area
aortic valve cusps
left ventricular papillary muscles

“Thus, cardiac calcium is not good. It may narrow the coronary arteries, mitral valve orifice and aortic valve orifice and it may prevent either or both of these valvular orifices from closing completely. It is reasonable to believe that both mitral annular and aortic cuspal calcific deposits in the elderly have the same etiology as the coronary atherosclerotic plaques because the 3 are commonly present in the same heart and the predisposing factors of all 3 are the same.”
Aortic Valve Sclerosis - Epidemiology

Cardiovascular Health Study (5621 subjects > 65 years):
Aortic Sclerosis 29%, Aortic Stenosis 2%

Helsinki Ageing Study (577 subjects, age 55-86 years):
Aortic valve calcifications 53%

INSIGHT substudy (263 hypertensive subjects, age 52-79 years):
Aortic valve calcifications 54%

LIFE substudy (960 hypertensive subjects, age 55-80 years):
Initial study: Aortic Sclerosis 40.4%, Aortic Stenosis 1.6%
After 4 years follow-up: Aortic Sclerosis 63%, Aortic Stenosis 4%
PATHOGENESIS

Three factors responsible for the development of calcific aortic valve disease: **cardiovascular risk factors, genetic factors, and osteoblast regulatory pathways**
Calcific aortic valve disease: Pathogenesis

Key elements of the disease

Atherosclerosis Steps

LDL and ? Leucocytes Activated VICs

Inflammation Extracellular matrix remodelling Angiogenesis Calcification

Pathological Hallmarks

Stenosis

Akat K et al. Heart 2009 95: 616-623
Patients with AVS showed a markedly lower **Flow-Mediated Dilation** than those without AVS (2.2 ± 3.5% vs. 5.3 ± 5.3%, p< 0.01).

On multivariate analysis, only FMD was highly predictive of AVS, with an OR of 1.18 for each percent decrease in FMD (95% confidence interval 1.05 to 1.32; p<0.01).
### Clinical factors associated with calcific aortic valve disease

Stewart et Al. J Am Coll Cardiol 1997; 29;630-4

<table>
<thead>
<tr>
<th>Variable</th>
<th>p</th>
<th>OR</th>
<th>95% IC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt; 0.001</td>
<td>2.18</td>
<td>2.15, 2.20</td>
</tr>
<tr>
<td>Male gender</td>
<td>&lt; 0.001</td>
<td>2.03</td>
<td>1.7, 2.5</td>
</tr>
<tr>
<td>Lp(a)</td>
<td>&lt; 0.001</td>
<td>1.23</td>
<td>1.14, 1.32</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.001</td>
<td>0.84</td>
<td>0.75, 0.93</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>0.002</td>
<td>1.23</td>
<td>1.1, 1.4</td>
</tr>
<tr>
<td>Present smoking</td>
<td>0.006</td>
<td>1.35</td>
<td>1.1, 1.7</td>
</tr>
<tr>
<td>LDLc (mg/dl)</td>
<td>0.008</td>
<td>1.12</td>
<td>1.03, 1.23</td>
</tr>
</tbody>
</table>

“Clinical factors associated with aortic sclerosis and stenosis can be identified and are similar to risk factors for atherosclerosis”
CARDIOVASCULAR HEALTH STUDY

Rates and relative risk of cardiovascular mortality and morbidity among 4271 subjects without prevalent cardiovascular disease at entry according to presence or absence of aortic sclerosis.


Editorial. Aortic Sclerosis – A window to the coronary arteries?
Mitral Annular Calcification Predicts Cardiovascular Morbidity and Mortality. *The Framingham Heart Study*

1197 subjects with adequate echo; 14% had MAC.
16 years of follow-up.

For each 1-mm increase in MAC, the risk of incident CVD, CVD and all-cause death adjusted for relevant risk factors increase by $\approx 10\%$
Heart valve sclerosis predicts all-cause and cardiovascular mortality

Study of Health in Pomerania (SHIP)

All-cause mortality

Cardiovascular mortality

\[ p < 0.05 \]

\[ p < 0.05 \]

Atherosclerosis (2010);209: 606–610
Valvular Calcification Increases Mortality Risk in Peritoneal Dialysis Patients

* Determined by echocardiography.
† P<0.0005 vs no VC. ‡ P=0.05 vs no VC or AVD. § P<0.0001 vs no VC or AVD.

VC = valvular calcification; AVD = atherosclerotic vascular disease.

Relation of aortic valve sclerosis to carotid artery intima-media thickening in healthy subjects

Yamaura et Al  Am J Cardiol 2004; 94: 837

252 healthy volunteers, age 25 – 65 years

Aortic sclerosis in 27 subjects (11%)

<table>
<thead>
<tr>
<th>TABLE 3 Odds Ratios for Presence of Aortic Valve Sclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds Ratio (95% Confidence Interval)</td>
</tr>
<tr>
<td>--------------------------------------</td>
</tr>
<tr>
<td>IMT &gt; 1.0 mm</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
</tr>
<tr>
<td>Current smoking</td>
</tr>
<tr>
<td>Total cholesterol</td>
</tr>
<tr>
<td>Fasting blood sugar</td>
</tr>
</tbody>
</table>

![Bar chart showing the box plots for IMT (intima-media thickness) in different categories of AVS (Aortic Valve Sclerosis).](image)
Relation of Carotid Intima-Media Thickness and Aortic Valve Sclerosis (from the ISMIR Study [“Ispessimento Medio Intimale e Rischio Cardiovascolare”] of the Italian Society of Cardiovascular Echography)

Prevalence of aortic valve sclerosis, increased intima-media thickness (>0.80 mm), or both in the entire study population (n = 479)

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only increased IMT (&gt;0.80 mm)</td>
<td>221</td>
<td>46.1</td>
</tr>
<tr>
<td>Only AVS</td>
<td>18</td>
<td>3.8</td>
</tr>
<tr>
<td>Increased IMT and AVS</td>
<td>70</td>
<td>14.6</td>
</tr>
<tr>
<td>Neither increased IMT nor AVS</td>
<td>170</td>
<td>35.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Risk Factor</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased IMT (&gt;0.80 mm)</td>
<td>Hypertension</td>
<td>2.28</td>
<td>1.40–3.73</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Dyslipidemia</td>
<td>1.90</td>
<td>1.21–2.98</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Family history</td>
<td>2.12</td>
<td>1.31–3.41</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
<td>2.23</td>
<td>1.17–4.22</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>1.09</td>
<td>1.07–1.11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AVS</td>
<td>Age</td>
<td>1.09</td>
<td>1.06–1.12</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Increased IMT (&gt;0.80 mm) and AVS</td>
<td>Hypertension</td>
<td>4.11</td>
<td>1.58–10.65</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>1.12</td>
<td>1.08–1.16</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Mitral annular calcification: a marker of severe coronary artery disease in patients under 65 years old

Atar et Al – Heart 2003; 89: 161-164

Consecutive subjects ≤ 65 years with (100 pts) and without (121 pts) mitral annular calcification on 2-D Echo, undergoing coronary angiogram within one year for angina or positive stress test.

CONCLUSIONS: In patients aged ≤ 65 years, mitral annular calcification is associated with an increased prevalence of severe obstructive coronary artery disease. It may serve as a useful echocardiographic marker for the presence of obstructive coronary artery disease, specially when associated with anginal symptoms.
Clinical significance of calcification of the fibrous skeleton of the heart and aortosclerosis in community dwelling elderly. The Cardiovascular Health Study (CHS)

Barasch et Al. Am Heart J 2006; 151:39

Table IV. Odds ratios (95% CI) for the association of MAC, AAC, AVS, and all 3 combined with CVD adjusted for age, sex, and race

<table>
<thead>
<tr>
<th>Calcification category</th>
<th>MI, OR (95% CI)</th>
<th>Stroke, OR (95% CI)</th>
<th>Angina pectoris, OR (95% CI)</th>
<th>CHF, OR (95% CI)</th>
<th>Revascularization, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAC</td>
<td>1.70 (1.38-2.09)</td>
<td>1.84 (1.40-2.41)</td>
<td>1.29 (1.11-1.51)</td>
<td>1.69 (1.31-2.17)</td>
<td>1.50 (1.18-1.91)</td>
</tr>
<tr>
<td>AAC</td>
<td>1.17 (0.95-1.54)</td>
<td>1.13 (0.86-1.48)</td>
<td>1.21 (1.03-1.42)</td>
<td>1.75 (1.34-2.27)</td>
<td>1.33 (1.04-1.71)</td>
</tr>
<tr>
<td>AVS</td>
<td>1.27 (1.03-1.57)</td>
<td>1.16 (0.88-1.53)</td>
<td>1.24 (1.06-1.45)</td>
<td>1.02 (0.79-1.31)</td>
<td>1.07 (0.84-1.37)</td>
</tr>
<tr>
<td>MAC + AAC + AVS</td>
<td>1.86 (1.32-2.62)</td>
<td>1.95 (1.26-3.03)</td>
<td>1.60 (1.24-2.07)</td>
<td>2.04 (1.34-3.09)</td>
<td>1.85 (1.21-2.84)</td>
</tr>
</tbody>
</table>
62 patients aged > 40 years
Clinical picture of heart failure
left ventricular dilatation (end
diastolic diameter > 56 mm) and
systolic dysfunction [LVEF< 40%].

Echo Score
- Aortic valve thickening/calcification
  (no stenosis)
- Mitral Annulus calcification
- Papillary muscle fibrosis/calcification
- Ascending aortic wall thickening and echogenicity

Coronary arteriography

The sensitivity, specificity and positive predictive values of a calcium score ≥ 3 in identifying an ischaemic cardiomyopathy were 90%, 92%, 86%.,
Usefulness of Echocardiographic Assessment of Cardiac and Ascending Aorta Calcific Deposits to Predict Coronary Artery Calcium and Presence and Severity of Obstructive Coronary Artery Disease

Gaetano Nucifora, MD\textsuperscript{a,b}, Joanne D. Schuijf, PhD\textsuperscript{a}, Jacob M. van Werkhoven, MSc\textsuperscript{a}, J. Wouter Jukema, MD, PhD\textsuperscript{a,c}, Nina Ajmone Marsan, MD\textsuperscript{a}, Eduard R. Holman, MD, PhD\textsuperscript{a}, Ernst E. van der Wall, MD, PhD\textsuperscript{a,c}, and Jeroen J. Bax, MD, PhD\textsuperscript{a,*}

<table>
<thead>
<tr>
<th>Grade</th>
<th>Aortic Valve Sclerosis</th>
<th>Mitral Annular Calcium</th>
<th>Papillary Muscle Calcium</th>
<th>Ascending Aorta Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>1</td>
<td>Mild</td>
<td>&lt;5 mm</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
<td>5–10 mm</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
<td>&gt;10 mm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[ p \text{ for trend } <0.001 \]

Number of vessels with obstructive CAD

\[ N^0 \text{ of vessels with obstructive CAD} \]

<table>
<thead>
<tr>
<th>ECS</th>
<th>No. of vessels with obstructive CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>0.5 ± 0.8</td>
</tr>
<tr>
<td>3-5</td>
<td>1.4 ± 1.0</td>
</tr>
<tr>
<td>&gt;5</td>
<td>2.0 ± 1.1</td>
</tr>
</tbody>
</table>

\[ p \text{ for trend } <0.001 \]

Number of segments with obstructive CAD

\[ N^0 \text{ of segments with obstructive CAD} \]

<table>
<thead>
<tr>
<th>ECS</th>
<th>No. of segments with obstructive CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>0.7 ± 1.4</td>
</tr>
<tr>
<td>3-5</td>
<td>2.8 ± 2.7</td>
</tr>
<tr>
<td>&gt;5</td>
<td>4.5 ± 3.0</td>
</tr>
</tbody>
</table>
Cardiac calcification by transthoracic echocardiography in patients with known or suspected coronary artery disease

Anca I. Corciu a,b,* Valeria Siciliano b, Elisa Poggianni b, Christina Petersen b, Lucia Venneri b, Eugenio Picano b

ARS - (0-1)
Score: 0- normal echogenicity, wall thickness < 2.2 mm
1- enhanced echogenicity, wall thickness ≥ 2.2 mm

AVS - (0-6)
Score: 0- normal echogenicity
1- enhanced echogenicity
2- calcification

MAC - (0-3)
Score: 0- normal echogenicity
1- mild calcification (thickness < 2mm, length < 5mm)
2- moderate calcification (thickness >2mm, length >5mm)
3- severe calcification (“shadowing”)

CSI = ARS+AVS+MAC
(0-10)

0 1 2
RC
LC
NC

- Categorical graphs showing the distribution of calcification score index in low risk, average risk, and high risk groups.

- Box plots comparing calcification score index between No CAD and CAD groups.
Progression of Aortic Valve Sclerosis to Aortic Stenosis

Faggiano et Al. Am J Cardiol 2003; 91: 99-101

400 pts >50 yrs with aortic valve thickening/calcification and peak vel ≤ 2 m/s. During 44±30 months follow-up 131 pts (32.7%) developed some degree of aortic stenosis.

Rate of change in peak velocity (m/s/yr)  0.073 ± 0.17 (-0.49 to +1.49)
Rate of change in pressure gradient (mmHg/yr)  1.4 ± 3.5 (-7 to +31)
A pattern of rapid progression (rate of increase in peak aortic velocity 0.3 m/s/yr) was observed in 24/400 pts (6%).

Age, gender and body mass index did not influence the rate of progression.
The risk of the Development of Aortic Stenosis in Patients With “Benign” Aortic Valve Thickening

Cosmi et Al - Arch Intern Med. 2002;162: 2345-2347

2131 pts with aortic sclerosis. During 7.3 years of follow-up, 338 pts developed aortic stenosis (mild 10.5%, moderate 2.9%, severe 2.5%)

“Mitral annular calcification was independently associated with progression to aortic stenosis”
MetS was associated with a significant increase in incident (“new”) AVC, raising the possibility that MetS may be a potential therapeutic target to prevent AVC development.

AVS and therapeutic implications

• Statins
• Biphosphonates
• ACE inhibitors / Angiotensin II receptor antagonists

Controversial Evidence
SEAS study: negative effects of statin therapy

Intensive Lipid Lowering with Simvastatin and Ezetimibe in Aortic Stenosis

Stage-related effect of statin treatment on the progression of aortic valve sclerosis and stenosis

Retrospective not randomized study

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Statin group</th>
<th>Control group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve sclerosis (&lt;2 m/s)</td>
<td>0.04±0.04 (26)</td>
<td>0.08±0.06 (26)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Mild aortic stenosis</td>
<td>0.11±0.25 (63)</td>
<td>0.11±0.17 (63)</td>
<td>ns</td>
</tr>
<tr>
<td>Moderate aortic stenosis</td>
<td>0.24±0.27 (32)</td>
<td>0.24±0.23 (32)</td>
<td>ns</td>
</tr>
</tbody>
</table>

“in a large series of patients with long-term follow-up, statins were effective in slowing the progression of aortic valve disease in aortic sclerosis, but not in AS. These results suggest that statin therapy should be taken into consideration in the early stages of this common disease”

OT is strongly and independently associated with decreased progression of AS. This association warrants investigation in a larger, prospective study.
Reduced prevalence of vascular and valvular calcification in women ≥ 65 years and increased prevalence of CV calcification in younger women on treatment.
“Despite their previously shown effect on aortic valve calcium accumulation, ACEIs do not appear to slow AS progression”
Angiotensin-Converting Enzyme Inhibitors and Change in Aortic Valve Calcium

Arch Intern Med. 2005;165:858-862

- Retrospective, observational study
- Significant association between ACEI use and lower rate of AVC accumulation, as assessed by serial EBT

Fig 1. Association of ACEI use with lower rate of change in aortic valve calcium (AVC) scores

Fig 2. Association of ACEI use with lower likelihood of definite progression in AVC scores (Fisher exact test).
Intracardiac Calcifications on Echocardiogram

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Easily available</td>
<td>- Qualitative - semiquantitative approach (score)</td>
</tr>
<tr>
<td>- Routine exam</td>
<td>- Operator and/or machine dependence</td>
</tr>
<tr>
<td>- Simple and quick approach</td>
<td></td>
</tr>
<tr>
<td>- Safe</td>
<td></td>
</tr>
</tbody>
</table>
Aortic sclerosis and cardiac calcifications

Summary

• Common abnormalities
• Pathogenesis similar to atherosclerosis
• Prognostic role
• Diagnostic role → marker of subclinical atherosclerosis
• Progressive disease
• Therapeutic approaches still uncertain

Their role in risk stratification of asymptomatic subjects in order to suspect subclinical atherosclerosis needs to be carefully considered during every echo examination
Thanks for Your attention
The 1st SHAPE Guideline
Toward the National Screening for Heart Attack Prevention and Education (SHAPE) Program

Conceptual Flow Chart

Apparently Healthy At-Risk Population

Step 1
Test for presence of the disease

Atherosclerosis Test

Negative
- No Risk Factors
- Risk Factors

Positive
- +
- ++
- +++
- <75th Percentile
- 75th-90th Percentile
- ≥90th Percentile

Step 2
Stratify based on the severity of the disease and presence of risk factors

Step 3
Test based on the level of risk

- Lower Risk
- Moderate Risk
- Moderately High Risk
- High Risk
- Very High Risk
Calcification of the Aortic Arch. Risk Factors and association with coronary artery disease, stroke and peripheral vascular disease

Iribarren et Al. JAMA 2000; 283: 2810

Evaluation of aortic arch calcification on chest radiograph in 60393 women and 55916 men, aged 30 to 89 years

- Aortic arch calcification found in 1.9% of men and 2.6% of women.
- Independent association with age, smoking and hypertension.
- Multivariate-adjusted RR for CAD 1.27 (men) and 1.22 (women), for ischemic stroke 1.46 (women), non significant trend for peripheral disease.
Morphologic Characteristics of Aortic Valve Sclerosis by Echocardiography: Importance for the Prediction of Coronary Artery Disease

Tolstrup et Al. Cardiology 2002; 98: 154-158

4 morphologic types of Aortic Sclerosis:

I: localized, not nodular

II: localized, nodular

III: diffuse

IV: mixed (nodular and diffuse)

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD</td>
<td>3,7</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>4,4</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>3,3</td>
</tr>
</tbody>
</table>
FINDINGS ASSOCIATED TO A FASTER PROGRESSION

- Older age
- Smoking
- Hypertension
- Obesity /diabetes
- Lipid abnormalities
- Degenerative aortic stenosis
- Valve calcification and regurgitation
- Bicuspid valve
- Concomitant coronary artery disease
- Chronic renal failure and dialysis
- Mild-moderate stenosis at initial presentation
- Symptoms appearance or worsening
- Left ventricular systolic dysfunction and/or low cardiac output
- Hemodynamic changes during exercise

Faggiano et Al. Am Heart J 1996
“Progression of AS (absolute and percentage reduction in AVA/year) is accelerated in patients with milder degrees of aortic stenosis, in presence of smoking, hypercholesterolemia, elevated serum creatinine and calcium levels”.

Palta et Al. Circulation 2000; 101: 2497
The NCBPs have the potential to influence calcium homeostasis in CV tissue by several mechanisms:

• **Pleiotropic, statin-like effects**
  - inhibition of protein prenylation,
  - Inhibition of various inflammatory processes: IL-1β, IL-6, TNF-α, matrix metalloproteinases
  - Inhibition of vitamin K metabolism: inhibition of isoprenoid synthesis, which is required for vitamin K metabolism, affects several vitamin K-dependent bone regulatory proteins such as osteocalcin and matrix Gla protein
  - Reduction of serum lipids which accumulate in vessel walls and valve leafleets triggering calcification

• **Selective inhibition of bone resorption** by which calcium-phosphate mineral complexes released into the bloodstream are deposited in vascular and valvular tissues
Patients with abnormal compared with normal aortic valves throughout the study had a greater incidence of composite end points (16.8% vs 9.3%, p 0.05).

The risk for developing AV stenosis was greater in patients with AV sclerosis compared with those with normal AVs at baseline, after 1 year (2.8% vs 0.4%, p 0.001) and 4 years (6.9% vs 0.9%, p 0.001) of treatment.

The prevalence of AV sclerosis and mild AV stenosis increased continuously in this elderly, high-risk hypertensive population, and this progression was prevented by neither losartan-nor atenolol-based treatment.
## Association of Mitral Annulus Calcification, Aortic Valve Sclerosis and Aortic Root Calcification With Abnormal Myocardial Perfusion Single Photon Emission Tomography in Subjects Age ≤ 65 Years Old

*Doo-Soo Jeon et Al – JACC 2001; 38: 1988-93*

<table>
<thead>
<tr>
<th></th>
<th>No multiple calcium deposits</th>
<th>Multiple calcium deposits</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No DM or multiple CRF</td>
<td>DM or multiple cardiac risk factors</td>
</tr>
<tr>
<td>Total</td>
<td>1 2.37 (1.17-4.79)</td>
<td>2.59 (1.31-5.1)</td>
</tr>
<tr>
<td>Male</td>
<td>1 1.80 (0.75-4.33)</td>
<td>2.25 (0.94-5.37)</td>
</tr>
<tr>
<td>Older (age &gt; 55 yrs)</td>
<td>1 1.38 (0.36-5.34)</td>
<td>1.16 (0.35-3.84)</td>
</tr>
<tr>
<td>Younger (age ≤ 55 yrs)</td>
<td>1 2.21 (0.65-7.54)</td>
<td>3.40 (0.80-14.44)</td>
</tr>
<tr>
<td>Female</td>
<td>1 4.83 (1.12-20.82)</td>
<td>5.06 (1.25-20.42)</td>
</tr>
<tr>
<td>Older (age &gt; 55 yrs)</td>
<td>1 1.95 (0.27-13.98)</td>
<td>4.50 (0.81-24.97)</td>
</tr>
<tr>
<td>Younger (age ≤ 55 yrs)</td>
<td>1 13.3(1.28-138.8)</td>
<td>4.00 (0.31-51.03)</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** *When coronary risk factors are also taken into consideration, the presence of multiple calcium deposits in the mitral annulus, aortic valve or aortic root appears to be a marker of CAD in men ≤ 55 years old and women.*