Mitral annular calcification: a marker of severe coronary artery disease in patients under 65 years old

S Atar, D S Jeon, H Luo, R J Siegel

Background: Mitral annular calcification has been associated with various systemic and cardiac diseases, with a higher prevalence in women and patients over 70. A possible association between mitral annular calcification and coronary artery disease has recently been suggested.

Objective: To determine the prevalence of severe coronary artery disease in younger patients with mitral annular calcification.

Methods: Consecutive patients aged ≤ 65 years with and without mitral annular calcification as detected by echocardiography were identified from a prospective clinical database. Only patients with a coronary angiogram done within one year of their qualifying echocardiogram were analysed. Severe coronary artery disease was defined as ≥ 70% stenosis of at least one major epicardial coronary artery.

Patients: 17 735 patients were screened. Of these, 6207 (35%) had mitral annular calcification and 885 (5%) were also < 65 years old; coronary angiography was done in 100 of the latter (64 men; 36 women), mainly for anginal symptoms or a positive stress test. A control group (n = 121; 88 men, 33 women) was identified from 2840 consecutive patients screened. There was no significant difference between the groups in patient characteristics, indication for angiography, or atherosclerotic risk factors.

Results: Angiography showed a higher prevalence of severe coronary artery disease in patients with mitral annular calcification than in those without (88% v 68%, p = 0.0004), and a higher prevalence of left main coronary artery disease (14% v 4%, p = 0.009) and triple vessel disease (54% v 33%, p = 0.002). The positive predictive value of mitral annular calcification for finding severe coronary artery disease was 92%.

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, especially when associated with anginal symptoms.

The clinical significance of mitral annular calcification in a selected population of younger patients has not yet been defined. Our aim in this study was to determine whether there is a correlation between the presence of mitral annular calcification on echocardiography and the finding of significant obstructive coronary artery disease on cardiac catheterisation in patients aged less than 65 years. In such a relatively young group of patients, mitral annular calcification may serve as an important and specific marker of severe coronary artery disease.

METHODS

The Institutional Review Board of Cedars-Sinai Medical Center approved the study.

We screened the computer database of the echocardiography laboratory from January 1995 to December 1998 for patients with a diagnostic code of mitral annular calcification and from these we selected patients aged ≤ 65 years. We then studied only patients who had a coronary angiography within one year of the qualifying echocardiogram. A control group (patients without mitral annular calcification) was selected from the same database using the same methods. In the selection procedure, the absence of mitral annular calcification was the only criterion that differed between the groups.

The diagnosis of mitral annular calcification was by M mode and cross sectional transthoracic echocardiography. Three highly experienced echocardiologists interpreted the echocardiograms. On M mode echocardiography the diagnosis
The control group comprised 121 consecutive patients from the same database. These patients (33 women, 88 men; mean age 56 (8) years, range 29–65 years, median 58 years) had no mitral annular calcification, were ≤ 65 years old, and underwent angiography within one year of the diagnostic transthoracic echocardiography.

The patients’ clinical characteristics are presented in table 1. There were no significant differences between the groups in risk factors or clinical presentation (71% of the control group and 79% of the index group had angina pectoris as an indication for angiography, p = 0.18). Other indications for angiography (evaluation of heart failure and cardiomyopathy and assessment before valvar or major vascular surgery) were not different between the two groups.

Thirty-five patients in the control group had undergone angiography for indications other than chest pain or unstable angina, compared with 21 patients in the index group. Only six of the asymptomatic control patients (15%) had obstructive coronary artery disease, compared with 15 (72%) in the index group (p < 0.0001). Moreover, 99 of 111 patients with angina (89%) had mitral annular calcification, compared with only 71 of 110 without angina (64%) (p < 0.0001). Patients in the control group had undergone significantly more percutaneous coronary interventions than patients in the index group (40% v 24%, p = 0.024).

### Angiographic findings

We found significantly more obstructive coronary artery disease in patients in the index group than in the control group (88% v 68%, p = 0.0004). As shown in table 2, patients in the index group had a higher prevalence of significant left main coronary artery stenosis (14% v 4%, p = 0.009) and a higher prevalence of triple vessel coronary artery disease (54% v 33%, p = 0.002). The prevalence of double and single vessel disease was not different between the two groups.

### Table 1 Clinical characteristics of the patients with and without mitral annular calcification

<table>
<thead>
<tr>
<th>Variable</th>
<th>MAC (n=100)</th>
<th>No MAC (n=121)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean (SD))</td>
<td>59 (7)</td>
<td>56 (8)</td>
<td>0.22</td>
</tr>
<tr>
<td>Male sex</td>
<td>64 (64)</td>
<td>88 (73)</td>
<td>0.16</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>34 (34)</td>
<td>30 (25)</td>
<td>0.13</td>
</tr>
<tr>
<td>Hypertension</td>
<td>42 (42)</td>
<td>58 (48)</td>
<td>0.38</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>37 (37)</td>
<td>54 (45)</td>
<td>0.25</td>
</tr>
<tr>
<td>Smoking</td>
<td>18 (18)</td>
<td>31 (26)</td>
<td>0.17</td>
</tr>
<tr>
<td>CRF</td>
<td>9 (9)</td>
<td>6 (5)</td>
<td>0.23</td>
</tr>
<tr>
<td>CABG</td>
<td>39 (39)</td>
<td>42 (33)</td>
<td>0.51</td>
</tr>
<tr>
<td>PCI</td>
<td>26 (26)</td>
<td>49 (40)</td>
<td>0.024</td>
</tr>
<tr>
<td>Chest pain</td>
<td>79 (79)</td>
<td>86 (71)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Values are n (%) unless specified.

CABG, coronary artery bypass graft; CRF, chronic renal failure; MAC, mitral annular calcification; PCI, percutaneous coronary intervention.

### Table 2 Angiographic findings in patients with and without mitral annular calcification

<table>
<thead>
<tr>
<th>Variable</th>
<th>MAC (n=100)</th>
<th>No MAC (n=121)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LM stenosis</td>
<td>14 (14)</td>
<td>5 (4)</td>
<td>0.009</td>
</tr>
<tr>
<td>TVD</td>
<td>54 (54)</td>
<td>40 (33)</td>
<td>0.002</td>
</tr>
<tr>
<td>DVD</td>
<td>17 (17)</td>
<td>12 (10)</td>
<td>0.12</td>
</tr>
<tr>
<td>SVD</td>
<td>17 (17)</td>
<td>30 (25)</td>
<td>0.16</td>
</tr>
<tr>
<td>No significant CAD</td>
<td>12 (12)</td>
<td>39 (32)</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

Values are n [%].

DVD, double vessel disease; LM, left main coronary artery; MAC, mitral annular calcification; SVD, single vessel disease; TVD, triple vessel disease.
Mitral annular calcification according to sex

We analysed our data according to sex and did not find that mitral annular calcification was a predictor of significant coronary artery disease in men. There were 34 women in the index group, and of those only six (18%) had non-significant coronary stenosis or angiographically normal coronary arteries, compared with 18 of 33 women in the control group (54%) (p = 0.002). Thus the absence of mitral annular calcification was a significant marker for the absence of obstructive coronary artery disease in women but not in men. There were no significant differences between the two groups of women with regard to age or risk factor profile.

Multivariate analysis

As presented in table 3, we found on multivariate analysis that hyperlipidaemia (p = 0.002), mitral annular calcification (p = 0.02), chest pain (p = 0.02), smoking (p = 0.05), age ≥ 60 (p = 0.04), and male sex (p = 0.02) were independent predictors of the presence of significant coronary artery disease. The presence of mitral annular calcification on trans-thoracic echocardiography was found to have a 92% positive predictive value for the presence of significant coronary artery disease, while the absence of mitral annular calcification had a 49% negative predictive value.

DISCUSSION

The main finding of our study is that mitral annular calcification is an independent predictor of the presence of severe stenosis (≥ 70% diameter stenosis) in at least one major epicardial coronary artery on angiography in patients presenting with chest pain under the age of 65. Moreover, mitral annular calcification is a marker of a higher prevalence of triple vessel disease or significant left main coronary artery stenosis in this specific group of patients. In women under 65 years of age, the absence of mitral annular calcification was an indicator of the absence of obstructive coronary artery disease.

The prevalence of both mitral annular calcification and coronary artery disease is known to increase with age. In 1992, Benjamin and colleagues first reported an increased incidence of coronary artery disease from the Framingham database. They found that patients with mitral annular calcification had a higher prevalence of coronary artery disease than a control group (28.8% v 17.4%, p = 0.006). Subsequently, it was shown that patients with mitral annular calcification had a significantly higher prevalence of aortic atheroma than matched controls.17 Protruding atheromas and an atheroma thickness > 4 mm were also more prevalent in individuals with mitral annular calcification. These findings may in part explain the increased risk of stroke in the presence of mitral annular calcification. It was then hypothesised that various calcification processes (for example, aortic valve calcification, mitral annular calcification, coronary artery calcification, and aortic atheroma) may all be a part of the spectrum of atherosclerosis.
the presence of severe coronary artery disease needs to be determined in a large prospective study.

Conclusions
Our findings suggest that in patients aged 65 years or less, mitral annular calcification is associated with an increased prevalence of severe and extensive obstructive coronary artery disease. In women, the absence of mitral annular calcification seems to infer a lower risk of obstructive coronary artery disease. Mitral annular calcification may be an easily detected echocardiographic marker of the presence of obstructive coronary artery disease, especially when associated with anginal symptoms.

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REFERENCES

IMAGES IN CARDIOLOGY
Spontaneous coronary artery dissection: stent it or wait for healing?

S ponstantaneous coronary artery dissection is an extremely rare cause of unstable angina and acute myocardial infarction or other ischaemic manifestations. It is more prevalent in young women, particularly in the peripartum period. There are a number of associated conditions such as inborn errors of metabolism and collagen synthesis, atherosclerotic disease, oral contraceptive use, and intense physical exercise, but the complete pathogenesis remains unclear. Treatment usually involves stent implantation or less commonly surgical repair.

A 67 year old woman with a history of hypertension, diabetes mellitus type II, and chronic obstructive pulmonary disease was admitted with acute pulmonary oedema that prompted resolution with conventional medical treatment. The ECG showed a regular rhythm without acute ischaemic changes, and the peak creatine kinase-MB (CK-MB) concentration was 5 ng/dl. Two days after admission the patient experienced chest pain. She was transferred to the coronary care unit and intravenous heparin and glyceryl trinitrate were administered, following which the symptoms resolved. ECG and CK-MB concentration remained unchanged. One day later the patient was brought to the catheterisation laboratory and angiography revealed a large dissection containing thrombus, which involved the mid and distal portion of the right coronary artery, but no evidence of atheroma and TIMI 3 flow (left panel). Since the patient was asymptomatic with clinical management (furosemide, enalapril, nitrates, heparin, and aspirin), it was decided to switch her from unfractionated heparin to enoxaparin treatment (1 mg/kg subcutaneously, twice a day), and to bring her back to the cath lab in a week. Subsequent angiography (right panel) revealed a completely normal vessel.

To our knowledge, this is the first case reported in which a patient received low molecular weight heparin treatment in the context of spontaneous coronary artery dissection with complete angiography and clinical resolution.

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