Non-rheumatic annular mitral stenosis: prevalence and characteristics

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Aims To define the prevalence and characteristics of non-rheumatic annular mitral stenosis (AMS) in a general population as compared with rheumatic mitral stenosis (RMS).

Methods and results Clinical and echocardiographical variables were assessed in 70 patients with mitral stenosis. AMS and RMS patients were age- and gender-matched for the comparison of echocardiographic variables. Thirteen patients (18.5%) had AMS. Arterial hypertension and hypercholesterolemia were more prevalent in AMS (77 vs. 36% and 75 vs. 27%, respectively, P < 0.05). Mitral annulus calcification severity score (2.2 vs. 1.3, P < 0.05) and left ventricular mass (276 ± 73 vs. 209 ± 57 g, P < 0.05) were significantly higher in AMS. Mitral valve area (MVA) was higher and mean gradient was lower (2.25 ± 0.6 vs. 1.9 ± 0.6 cm², 4 ± 1.2 vs. 5.6 ± 3.5 mmHg, P = ns) in AMS. Pressure half-time (PHT) MVA and planimetry MVA had a better correlation in RMS than in AMS patients (r = 0.98 vs. 0.71, P < 0.05).

Conclusion AMS is more frequent than that is assumed and is associated with risk factors for coronary artery disease. AMS is generally mild and PHT may be less accurate for MVA calculation than in RMS.

KEYWORDS Mitral stenosis; Mitral annulus calcification; Echocardiography; Risk factors

Introduction Mitral stenosis (MS) is a common valvular condition, generally assumed to be of rheumatic aetiology. Mitral annulus calcification (MAC) is a degenerative calcific process of mitral valve (MV) support ring. It has been associated with coronary artery disease, stroke and chronic kidney disease and was shown to be an independent predictor of cardiovascular mortality and morbidity.1–5 Following first reports6–9 on the usefulness of this technique, echocardiography has subsequently been extensively used to describe MAC.

Generally associated with regurgitation,10 severe MAC may induce a diastolic gradient across the MV as well, even without significant restriction of the leaflets tips.11,12 MS caused by MAC has been rarely reported, mainly as case reports11–17 and little is known about this entity or its frequency.

The echocardiographic characteristics of rheumatic MS (RMS) as compared with that of calcific annular MS (AMS) have not been studied previously. With the increasing proportion of elderly patients with multiple risk factors, the frequency of MAC and, thus, of calcific, non-rheumatic AMS is expected to rise. We defined the prevalence and characteristics of AMS in consecutive patients diagnosed with MS by Doppler criteria and compared the echocardiographic characteristics of AMS with age-matched RMS patients.

Methods

Study population

Patients with MS were retrieved from the echocardiographic digitally archived data base of 7000 consecutive in- and outpatient studies performed between 1 October 2004 and 1 October 2005 at the Department of Cardiology, Royal Liverpool University Hospital. Seventy patients (age = 69 ± 11, range = 33–88 years, female gender = 52) were identified as having been diagnosed at the time of the study with MS by the presence of a turbulent antegrade flow with a mean diastolic gradient of > 2 mmHg through a native MV.18

The presence of risk factors and renal dysfunction was documented from the patient’s case file. Arterial hypertension (AHT) was defined as systolic or diastolic blood pressure of > 140 or > 90 mmHg, respectively, or current use of antihypertensive drugs. Diabetes mellitus (DM) was defined as two documented blood glucose levels > 7 mmol/L or postprandial serum glucose of > 11 mmol/L or known diabetes controlled with either diet or antidyseemic medications. Individuals with total cholesterol of > 5 mmol or using medication for this condition were classified as dyslipidemic.

Echocardiography parameters

All studies were reviewed by two investigators. AMS was diagnosed, if the increased transvalvular gradient was associated with MAC with normal or minimally reduced leaflets motion without tips restriction.
Figure 1 Early diastolic frame in apical four-chamber view in a patient with annular mitral stenosis. Note the heavy calcifications protruding in the valve orifice at both the anterior and posterior aspect of the annulus. The tips are relatively free and the leaflets open without doming restriction (arrows).

Figure 2 Patient with rheumatic mitral stenosis. Note the tips thickening and the typical doming of both leaflets with restricted diastolic opening (arrows).

(Tips restriction, thickening or diffuse leaflets thickness and restriction of the posterior mitral leaflet were indicative of RMS (Figure 2). MAC severity was scored as 1 (focal, limited calcification of mitral annulus), 2 (marked density >1/3 but <1/2 of the annulus) and 3 (marked echo density involving >1/2 of the annulus). MV area (MVA) was calculated by both pressure half-time (PHT) and planimetry. Mean and peak MV gradient was calculated by tracing the CW signal across the MV in apical four chamber view. Mitral regurgitation (MR) was assessed semi-quantitatively using the area of colour flow jet as compared with the area of LA in orthogonal views and graded as none or trivial, mild, moderate, and severe. Left ventricular (LV) mass was calculated from M-mode measurements using the Devereux convention. RMS and AMS patients were further age- and gender-matched for comparison of echocardiographic variables.

Statistical analysis

$t$-Test for continuous variables and $\chi^2$-test for categorical variables were used for group comparison. $P$-value was considered significant at $\alpha = 0.05$.

The study was approved by the local ethics committee.

**Table 1** Baseline characteristics of patient with annular mitral stenosis (AMS) and rheumatic mitral stenosis (RMS)

<table>
<thead>
<tr>
<th></th>
<th>AMS ($n=13$)</th>
<th>RMS ($n=57$)</th>
<th>$P$-value</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>72 ± 12</td>
<td>68 ± 11</td>
<td>ns</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>5 (38)</td>
<td>13 (23)</td>
<td>ns</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>10 (77)</td>
<td>19 (36)</td>
<td>$&lt;0.05$</td>
</tr>
<tr>
<td>Hypercholesteremia (%)</td>
<td>9 (73)</td>
<td>15 (27)</td>
<td>$&lt;0.05$</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m$^2$)</td>
<td>64 ± 25</td>
<td>63 ± 23</td>
<td>ns</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>5 (38)</td>
<td>10 (18)</td>
<td>ns</td>
</tr>
</tbody>
</table>

**Table 2** Echocardiographic findings age- and gender-matched patients with AMS and RMS

<table>
<thead>
<tr>
<th></th>
<th>AMS ($n=12$)</th>
<th>RMS ($n=12$)</th>
<th>$P$-value</th>
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<tbody>
<tr>
<td>LV mass (g)</td>
<td>276 ± 7</td>
<td>209 ± 57</td>
<td>$&lt;0.05$</td>
</tr>
<tr>
<td>MAC severity score</td>
<td>2.2</td>
<td>1.3</td>
<td>$&lt;0.05$</td>
</tr>
<tr>
<td>Grade II–III MR</td>
<td>2</td>
<td>4</td>
<td>ns</td>
</tr>
<tr>
<td>Mean grd (mmHg)</td>
<td>4 ± 1</td>
<td>5.6 ± 3</td>
<td>ns</td>
</tr>
<tr>
<td>PHT MVA (cm$^2$)</td>
<td>1.92</td>
<td>1.75</td>
<td>ns</td>
</tr>
<tr>
<td>Planimetry MVA (cm$^2$)</td>
<td>2.25</td>
<td>1.9</td>
<td>ns</td>
</tr>
<tr>
<td>PHT/planimetry</td>
<td>0.71</td>
<td>0.98</td>
<td>$&lt;0.05$</td>
</tr>
<tr>
<td>Mild MS (%)</td>
<td>8 (67)</td>
<td>4 (33)</td>
<td>ns</td>
</tr>
<tr>
<td>Aortic stenosis (%)</td>
<td>5 (42)</td>
<td>2 (17)</td>
<td>ns</td>
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**Results**

Out of 70 patients with MS, 13 (18.5%) were diagnosed with AMS and 57 (81.5%) were considered to have RMS. Demographic characteristics and prevalence of risk factors in the two groups are given in Table 1. AMS patients were older and showed a trend for higher diabetes prevalence. Serum creatinine levels were higher in AMS patients though the difference did not reach statistical significance and estimated glomerular filtration rate was similar in the two groups. AHT and hypercholesterolemia were much more frequent in AMS patients than in RMS patients.

The echocardiographic differences between age- and gender-matched AMS and RMS patients are summarized in Table 2. MAC severity score, LV mass, and frequency of concomitant aortic stenosis were significantly higher in AMS patients. Overall prevalence of MR was similar in the two groups but moderate or greater MR was more frequent in RMS patients though without reaching statistical significance. MV orifice area in parasternal short axis view could be accurately planimetered in nine out of 12 patients with AMS and in seven out of 12 patients with RMS MVA by both planimetry and PHT tended to be higher and mean gradient was lower in AMS patients though these differences did not reach statistical significance. MVA by PHT and planimetry had a better correlation in RMS patients than in AMS patients.

**Discussion**

In the Western world, rheumatic heart disease is on the decline but with increased life expectancy, there has been a raise of degenerative valvular heart disease. Though not
unexpected, the possible relationship between MAC and haemodynamic MS rather than mitral incompetence is infrequently acknowledged. Protruding calcification, reduction of normal mitral annular dilatation during diastole\textsuperscript{11,12} and impaired anterior mitral leaflet mobility,\textsuperscript{17} are possible mechanisms responsible for the increased mitral gradient caused by MAC.

We found that out of all patients reported as having MS, 18.5\% actually had AMS rather than RMS. The prevalence of this entity among patients generally diagnosed with MS has not been reported before. We also, for the first time to our knowledge, compared the echocardiographic features of AMS and RMS. As expected, MAC severity score was significantly higher in AMS patients. Compared with age- and gender-matched RMS patients, LV mass in AMS patients was also significantly higher. This may reflect the high prevalence of hypertension in AMS patients. Clinically significant MR was more likely to be found in rheumatic patients. Whether this represents a true difference in pathology or also more shadowing of the regurgitant jet by heavy calcification in AMS patients is not clear.

AMS patients were found to have mild MS with higher valvular areas and lower mean gradients than rheumatic patients. The average mean gradient in AMS patients in our study was 4 ± 1 mmHg. Muddassir et al.\textsuperscript{17} recently reported higher gradients in their patients with non-RMS. However, their subjects were preselected for severe MAC, of whom half had limited mobility of the anterior mitral leaflet, so they may represent the more severe end of this disease entity spectrum. Five out of 13 AMS patients in our study had severe MAC and four of them had MV gradient ≥ 5 mmHg.

We found that PHT and planimetry had a better correlation in RMS than in AMS. This may be related to both reduced accuracy of planimetry in the presence of heavy calcification and the known limitations of PHT for MVA calculation in patients with stiffer ventricles.\textsuperscript{21}

We had no information regarding these patients’ symptoms and cardiac functional class. The mild degree of MS and the coexistence of advanced age and other comorbidities, suggest, however, that AMS on its own may be less likely to induce dyspnoea or other cardiac symptoms than its rheumatic counterpart. This consideration only emphasizes the importance of differentiating between the two entities.

Limitations

The assignment of patients as having either rheumatic or non-rheumatic, AMS was done retrospectively, using somewhat arbitrary and not validated criteria. However, we believe that preserved mobility of mitral leaflets tips in the presence of significant MAC is a reasonable argument against rheumatic aetiology and a similar approach has been already used in the literature.\textsuperscript{9,11} Also, due to the small number of patient reported, the differences found in echocardiographic characteristics between the two groups of age- and gender-matched patients should be regarded as orientative and need further validation in larger cohort studies.

Conclusion

We found that AMS is more frequent than that assumed, occurring in almost one fifth of non-selected, consecutive patients diagnosed with MS and it is strongly associated with risk factors for coronary artery disease and with LV hypertrophy. When reporting MS, more attention should be paid to the presence or absence of ‘rheumatic markers’ such as typical tips and posterior leaflet involvement, in order to correctly identify the non-rheumatic cases. As compared with RMS, AMS tends to be rather mild by both area and gradient measurements. PHT derived MVA may be less accurate in AMS than in RMS and this limitation should be recognized when reporting MS due to MAC.

Conflict of interest: none declared.

References


