Mitral Inflow and Mitral Annular Motion Velocities in Patients with Mitral Annular Calcification: Evaluation by Pulsed Doppler Echocardiography and Pulsed Doppler Tissue Imaging


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**Aims:** We evaluated the relationship between the mitral inflow velocities by pulsed Doppler echocardiography and mitral annular motion velocities by pulsed Doppler tissue imaging in patients with mitral annular calcification.

**Methods and Results:** Fifty-three patients with mitral annular calcification were divided into two groups: severe mitral annular calcification (n=15, mitral annular calcification ≥5 mm in width) and mild mitral annular calcification (n=38, mitral annular calcification <5 mm in width). In addition, 20 patients with hypertensive heart disease (HHD group) and mild left ventricular hypertrophy but no mitral annular calcification and 30 normal individuals (normal group) were studied. The early diastolic mitral inflow velocity (E) was higher in the severe mitral annular calcification group (0.75 ± 0.26 m/s) than in the HHD and normal groups (mild mitral annular calcification, 0.65 ± 0.21; HHD, 0.57 ± 0.24; normal, 0.55 ± 0.15 m/s), and the late diastolic mitral inflow velocity (A) was higher in the severe mitral annular calcification group (1.24 ± 0.23 m/s) than in the other three groups (mild mitral annular calcification, 0.96 ± 0.20; HHD, 0.84 ± 0.23; normal, 0.75 ± 0.13 m/s). In contrast, the early and late diastolic annular velocities (Ea, Aa) were lower in the severe mitral annular calcification group (Ea: 5.7 ± 2.2; Aa: 11.9 ± 4.4 cm/s) than in the other three groups (Ea: mild mitral annular calcification, 8.3 ± 2.5; HHD, 7.7 ± 2.2; normal, 9.0 ± 1.8 cm/s; Aa: mild mitral annular calcification, 14.2 ± 4.1; HHD, 14.3 ± 2.8; normal, 14.2 ± 2.1 cm/s). Mitral valve area was smaller in the severe mitral annular calcification group (2.6 ± 1.0 cm²) than in the other three groups (mild mitral annular calcification, 3.1 ± 0.7; HHD, 4.1 ± 0.7; normal, 4.2 ± 0.9 cm²).

**Conclusion:** Patients with severe mitral annular calcification have higher mitral inflow velocities due to mitral annular restriction and lower mitral annular velocities caused by decreased mitral annular motion and abnormal left ventricular relaxation.

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**Key Words:** pulsed Doppler echocardiography; pulsed Doppler tissue imaging; mitral annular calcification.
whether the existence of mitral annular calcification affects the mitral inflow velocity and mitral annular motion velocity using pulsed Doppler echocardiography and pulsed Doppler tissue imaging.

Methods

Study Population

Of the 85 patients with echocardiographic evidence of mitral annular calcification evaluated between May 1998 and September 1999, we enrolled 53 patients (10 men and 43 women; mean age: 74 ± 10 years) in sinus rhythm who met the following inclusion criteria: (1) no evidence of moderate or severe valvular disease, (2) no evidence of ischemic or dilated cardiomyopathy, and (3) an echocardiographic left ventricular ejection fraction > 45% and a percent left ventricular fractional shortening > 25%.

The 53 patients included 13 patients with hypertensive heart disease, 13 with mild valvular disease, seven with angina pectoris, three with hypertrophic cardiomyopathy, and 17 with other diseases (paroxysmal atrial fibrillation (n=3), neurocirculatory asthenia (n=3), diabetes mellitus (n=3), chronic renal failure (n=3), anemia (n=2), first degree atrioventricular block (n=2), and complete right bundle branch block (n=1)). In addition, 20 age- and sex-matched patients (four men and 16 women; mean age 72 ± 9 years) with hypertensive heart disease who had left ventricular hypertrophy and no evidence of mitral annular calcification (HHD group) and 30 age- and sex-matched healthy individuals (normal group; six men and 24 women; mean age: 75 ± 8 years) were also studied. Informed consent was obtained from all participants.

M-mode and Two-Dimensional Echocardiography

Transthoracic M-mode and two-dimensional echocardiograms were recorded with Aloka SSD-2200 (Aloka, Tokyo, Japan) ultrasound system using a 2-5 MHz probe. We measured the maximum left atrial dimension, left ventricular end-diastolic dimension (LVIDd), left ventricular end-systolic dimension (LVIDs), end-diastolic ventricular septal thickness (VSTh), and end-diastolic left ventricular posterior wall thickness (PWTh) on the M-mode echocardiogram. The percent left ventricular fractional shortening and left ventricular wall thickness were calculated with the following equations:

\[ \text{Percent left ventricular fractional shortening} = \left( \frac{LVIDd - LVIDs}{LVIDd} \right) \times 100 \]

\[ \text{Left ventricular wall thickness} = \text{VSTh} + \text{PWTh} \]

Echocardiographic criteria for the diagnosis of mitral annular calcification included the presence of dense echoes, more than 3 mm thick, behind the posterior mitral leaflet and anterior to the left ventricular endocardium that moved parallel to the left ventricular posterior wall. The width of the mitral annular calcification behind the echoes originating from the mitral valve was determined by M-mode echocardiography. Intra-observer and inter-observer mean percentage error for the width of the mitral annular calcification were 6.4 ± 6.1 and 7.3 ± 6.5%. The patients with mitral annular calcification were divided into two groups: 15 patients with severe mitral annular calcification (three men and 12 women; mean age 77 ± 9 years; mitral annular calcification ≥ 5 mm in width), and 38 patients with mild mitral annular calcification (seven men and 31 women; mean age 74 ± 10 years; mitral annular calcification < 5 mm). In the correlation between the mitral inflow or mitral annular velocities and the severity of mitral annular calcification, the mitral annular calcification severity was defined by the width of the mitral annular calcification behind the echoes originating from the mitral valve by M-mode echocardiography (the width of mitral annular calcification in normal subjects was defined as 0 mm).

Transthoracic two-dimensional echocardiograms were also recorded. The shortest distance between the annulus of the anterior and posterior mitral leaflets at end-diastole measured in the parasternal long-axis view was defined as the mitral annular dimension. The aortic cross-sectional area was calculated from the midsystolic diameter of the aortic annulus in the parasternal long-axis view.

Pulsed Doppler Echocardiography

The sample volumes were set at the tips of the mitral leaflets and at the aortic annulus on the apical long-axis view (Fig. 1, left). Diastolic mitral inflow and systolic aortic flow velocity waveforms were acquired for these sample volumes. Based on the velocity patterns, the peak early and late diastolic velocities (E, A) and their time–velocity integrals, the isovolumic relaxation time, the aortic component of the second heart sound and the onset of the early diastolic wave, and the

Figure 1. Sample recording of the mitral inflow and aortic ejection flow velocity patterns (A, C) and the motion velocity pattern of the mitral annulus by pulsed Doppler tissue imaging (B) in the apical long-axis view of the left ventricle (left), and measurement of variables obtained from these recordings (right). The area enclosed by the baseline and the Doppler envelope (indicated by the bold white lines on the mitral inflow and aortic ejection flow velocity patterns) represents the time velocity integral. T, transducer; LV, left ventricle; RV, right ventricle; Ao, ascending aorta; LA, left atrium; IRT, isovolumic relaxation time; E, early diastolic mitral inflow velocity; A, late diastolic mitral inflow velocity; Ea, early diastolic annular velocity; Aa, late diastolic annular velocity.
time–velocity integral of the aortic flow velocity waveform were determined (Fig. 1, right). Based on the continuity equation\(^{[12]}\), mitral valve area was calculated as:

\[
\text{mitral valve area} = \frac{\text{aortic annular cross-sectional area} \times \text{TVIa}}{\text{TVIm}},
\]

where TVIa and TVIm represent the time–velocity integrals of the flow at the aortic annulus and the mitral orifice, respectively.

**Pulsed Doppler Tissue Imaging**

Pulsed Doppler tissue imaging was performed by activating the Doppler tissue imaging function on the same machine equipped with a 2·5 MHz probe. Using the apical long axis view, the sample volume was set at the mitral annulus in the left ventricular posterior wall, and the wall motion velocity patterns were recorded (Fig. 1, left). From these velocity patterns, the peak early and late diastolic annular velocities (Ea, Aa) were determined (Fig. 1, right).

**Statistical Analysis**

All results are expressed as the mean ± standard deviation. Differences in the observed frequencies between different groups were compared using the chi-square test. Differences in the mean values for different groups were evaluated by one-factor analysis of variance, and if the difference was significant, Fisher’s protected least significance difference test was performed. Pearson’s correlation coefficient was used to analyze the relationship between two parameters. A value of \(P<0·05\) was considered statistically significant.

**Results**

**Patient Characteristics and M-mode Echocardiographic Variables**

Table 1 summarizes the clinical characteristics and M-mode echocardiographic findings in each study group. Both left ventricular wall thickness and left atrial diameter were significantly greater in the mitral annular calcification and HHD groups than in the normal group. However, there were no differences in these variables between the mitral annular calcification and HHD groups. There were no significant differences in left ventricular diameter and percent fractional shortening between the four groups.

**Mitral Inflow and Doppler tissue imaging Variables**

Table 2 summarizes the mitral inflow, Doppler tissue imaging, and mitral valve findings. The mitral E velocity was significantly higher in the severe mitral annular calcification group than in the HHD and normal groups. However, there was no difference in the E velocity between the severe mitral annular calcification and mild mitral annular calcification groups. The mitral A velocity was significantly higher in the severe mitral annular calcification group than in the other three groups. In contrast, both the annular Ea and Aa velocities were significantly lower in the severe mitral annular calcification group than in the other three groups. The isovolumic relaxation time was significantly longer in the HHD group than in the mild mitral annular calcification and normal groups, whereas there was no difference between the severe mitral annular calcification and HHD groups.

**Mitral Valve Area and Mitral Annular Dimension**

The mitral valve area was significantly smaller in the severe mitral annular calcification group than in the other three groups, and smaller in the mild mitral annular calcification group than in the HHD and normal groups. In addition, the mitral annular dimension was significantly shorter in the severe mitral annular calcification group than in the other three groups.

**Correlations Between the Mitral Inflow or Mitral Annular Velocities and Other Echocardiographic Variables**

Table 3 shows the correlations between the mitral inflow or mitral annular velocities and other echocardiographic variables in patients with mitral annular calcification and healthy individuals. The mitral valve area correlated inversely with both the mitral E and A velocities (\(r = -0·372\) and \(r = -0·672\), \(P<0·01\)). In addition, the left ventricular wall thickness correlated inversely with the annular Ea velocity (\(r = -0·371\), \(P<0·01\)). The severity of mitral annular calcification, defined in Methods, correlated positively with both the mitral E and A velocities (\(r = 0·359\) and \(r = 0·654\), respectively, \(P<0·01\)), and correlated inversely with both the annular Ea (\(r = -0·449\), \(P<0·01\)) and Aa velocities (\(r = -0·241\), \(P<0·05\)).

**Discussion**

The M-mode and two-dimensional echocardiographic analysis of mitral annular calcification have characterized its appearance and simplified its diagnosis\(^{[4–9]}\). However, there have been few studies evaluating mitral inflow dynamics in patients with mitral annular calcification. In this study, we assessed mitral inflow velocity profile, mitral valve area, and the correlation of both parameters in patients with mitral annular calcification. The findings obtained from this study suggest that severe
Mitral annular calcification might cause restriction of mitral annular motion and an increase in mitral inflow velocity, and are compatible with the report that functional mitral stenosis is common in mitral annular calcification\(^{11}\). The pathogenesis of restriction of mitral annular motion in patients with mitral annular calcification includes (1) the combination of large mitral annular calcific deposits and a small, thick-walled, non-compliant left ventricle\(^{13}\) and (2) severe calcification of the annulus interferes with the active mitral annular

Table 1. Patient characteristics and M-mode echocardiographic variables.

<table>
<thead>
<tr>
<th></th>
<th>Severe MAC</th>
<th>Mild MAC</th>
<th>HHD</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=15)</td>
<td>(n=38)</td>
<td>(n=20)</td>
<td>(n=30)</td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>77±9</td>
<td>74±10</td>
<td>73±9</td>
<td>75±8</td>
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<tr>
<td>Female/male</td>
<td>12/3</td>
<td>31/7</td>
<td>16/4</td>
<td>24/6</td>
</tr>
<tr>
<td>LVWT (mm)</td>
<td>22.8±5.4**</td>
<td>20.9±4.7**</td>
<td>22.6±1.5**</td>
<td>17.0±1.7</td>
</tr>
<tr>
<td>LVD (cm)</td>
<td>4.6±0.8</td>
<td>4.8±0.9</td>
<td>4.7±0.5</td>
<td>4.5±0.4</td>
</tr>
<tr>
<td>%FS (%)</td>
<td>35.2±9.2</td>
<td>35.9±9.0</td>
<td>38.1±7.3</td>
<td>38.0±5.6</td>
</tr>
<tr>
<td>LAD (cm)</td>
<td>4.5±0.8**</td>
<td>4.3±0.6**</td>
<td>4.4±0.6**</td>
<td>3.7±0.6</td>
</tr>
</tbody>
</table>

*P<0.05 vs normal; **P<0.01 vs normal.

MAC, mitral annular calcification; HHD, hypertensive heart disease; LVWT, left ventricular wall thickness; LVD, left ventricular diameter; %FS, percent fractional shortening of the left ventricle; LAD, left atrial diameter.

Table 2. Variables of mitral inflow, Doppler tissue imaging, and mitral valve area.

<table>
<thead>
<tr>
<th></th>
<th>Severe MAC</th>
<th>Mild MAC</th>
<th>HHD</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=15)</td>
<td>(n=38)</td>
<td>(n=20)</td>
<td>(n=30)</td>
<td></td>
</tr>
<tr>
<td>Mitral inflow</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E (m/s)</td>
<td>0.75±0.26</td>
<td>0.65±0.21</td>
<td>0.57±0.24*</td>
<td>0.55±0.15**</td>
</tr>
<tr>
<td>A (m/s)</td>
<td>1.24±0.23</td>
<td>0.96±0.20**</td>
<td>0.84±0.23**</td>
<td>0.75±0.13**</td>
</tr>
<tr>
<td>IRT (msec)</td>
<td>92±22</td>
<td>84±20</td>
<td>98±15†</td>
<td>84±24§</td>
</tr>
<tr>
<td>DTI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ea (cm/s)</td>
<td>5.7±2.2</td>
<td>8.3±2.5**</td>
<td>7.7±2.2*</td>
<td>9.0±1.8**§</td>
</tr>
<tr>
<td>Aa (cm/s)</td>
<td>11.9±4.4</td>
<td>14.2±4.1*</td>
<td>14.3±2.8*</td>
<td>14.2±2.1*</td>
</tr>
<tr>
<td>Mitral valve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area (cm²)</td>
<td>2.6±1.0</td>
<td>3.1±0.7**</td>
<td>4.1±0.7**</td>
<td>4.2±0.9***</td>
</tr>
<tr>
<td>Annular dimension (cm)</td>
<td>2.5±0.2</td>
<td>2.9±0.3**</td>
<td>3.1±0.2**</td>
<td>3.1±0.2**‡</td>
</tr>
</tbody>
</table>

*P<0.05 vs severe MAC; **P<0.01 vs mild MAC; †P<0.05 vs normal; §P<0.05 vs HHD.

MAC, mitral annular calcification; HHD, hypertensive heart disease; E, early diastolic mitral inflow velocity; A, late diastolic mitral inflow velocity; IRT, isovolumic relaxation time; DTI, Doppler tissue imaging; Ea, early diastolic annular velocity; Aa, late diastolic annular velocity.

Table 3. Correlation coefficients between the mitral inflow or mitral annular velocities and other echocardiographic variables in patients with MAC and healthy individuals.

<table>
<thead>
<tr>
<th></th>
<th>E</th>
<th>A</th>
<th>Ea</th>
<th>Aa</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRT</td>
<td>-0.201</td>
<td>0.142</td>
<td>-0.2</td>
<td>-0.033</td>
</tr>
<tr>
<td>LVWT</td>
<td>0.024</td>
<td>0.334**</td>
<td>-0.371**</td>
<td>-0.156</td>
</tr>
<tr>
<td>LVD</td>
<td>0.012</td>
<td>-0.052</td>
<td>0.014</td>
<td>0.024</td>
</tr>
<tr>
<td>%FS</td>
<td>-0.034</td>
<td>0.102</td>
<td>0.193</td>
<td>0.278*</td>
</tr>
<tr>
<td>LAD</td>
<td>0.336**</td>
<td>0.319**</td>
<td>-0.154</td>
<td>0.024</td>
</tr>
<tr>
<td>MVA</td>
<td>-0.372**</td>
<td>-0.672**</td>
<td>0.387**</td>
<td>0.055</td>
</tr>
<tr>
<td>MAC severity</td>
<td>0.359**</td>
<td>0.654**</td>
<td>-0.449*</td>
<td>-0.241*</td>
</tr>
</tbody>
</table>

*P<0.05; **P<0.01.

E, early diastolic mitral inflow velocity; A, late diastolic mitral inflow velocity; Ea, early diastolic annular velocity; Aa, late diastolic annular velocity; IRT, isovolumic relaxation time; LVWT, left ventricular wall thickness; LVD, left ventricular diameter; %FS, percent fractional shortening of the left ventricle; LAD, left atrial diameter; MVA, mitral valve area; MAC, mitral annular calcification.

motion necessary for normal valvular function and the absence or reduction of normal annular dilation during diastole results in functional mitral stenosis[14]. In this study, there was no significant difference in left ventricular diameter between the groups, which does not substantiate the first pathogenetic mechanism.

Pulsed Doppler tissue imaging has been used to assess myocardial wall motion velocities[15]. Using pulsed Doppler tissue imaging, important information has been obtained for left ventricular myocardial function in patients with various heart diseases[16–19]. However, there have been no studies evaluating mitral annular dynamics in patients with mitral annular calcification using pulsed Doppler tissue imaging. In this study, we assessed mitral annular motion velocities by pulsed Doppler tissue imaging in patients with mitral annular calcification, and found that both the annular Ea and Aa velocities were lower in patients with severe mitral annular calcification than in the other three groups. It has been reported that patients with left ventricular hypertrophy have significantly lower annular Ea velocity than in patients without heart disease[16]. In this study, the annular Ea velocity was lower in the HHD group than in the normal group. These results support the hypothesis that the lower annular Ea velocity in patients with severe mitral annular calcification might reflect the impaired left ventricular relaxation associated with left ventricular hypertrophy. In patients without HHD, the left ventricular wall thickness correlated inversely with the annular Ea velocity in this study, which is in keeping with the findings of the previous study[16]. However, differences in the diastolic annular Ea velocity between patients with severe mitral annular calcification and patients with HHD suggest that lower mitral annular Ea velocity in patients with mitral annular calcification might result from both the limitation of mitral annular motion and abnormal left ventricular relaxation. This hypothesis is in keeping with the finding that the severity of mitral annular calcification correlated inversely with the annular Ea velocity. The annular Aa velocity is also reported to increase in patients with left ventricular hypertrophy and mitral inflow E/A ratio <1[16]. However, in this study, the annular Aa velocity was lower in patients with severe mitral annular calcification than in the HHD group. Thus, the decreased annular Aa velocity in patients with severe mitral annular calcification might result mainly from the limitation of mitral annular motion. Though the magnitude of the annular Ea and Aa velocities are altered by age[16,20], the patients in our study were age-matched.

This study has several limitations. First, patients with evidence of moderate or severe valvular disease were excluded because the mitral valve area determined using the continuity equation could differ from the true values in such patients. However, patients with mitral annular calcification frequently have mild mitral regurgitation[10,11], which might alter measurements of mitral inflow and annular velocities in this study. Second, the study population included many patients with cardiac or systemic diseases that can cause left ventricular diastolic function, and which make the determination of the direct effect of mitral annular calcification on diastolic left ventricular wall and flow dynamics difficult. Finally, we measured velocities only in the mitral annulus of the left ventricular posterior wall using pulsed Doppler tissue imaging. The motion velocity of the posterior annulus may provide insufficient information to evaluate global annular motion and left ventricular diastolic abnormalities. Further studies are needed to measure the velocities at various annular sites.

In conclusion, patients with severe mitral annular calcification have higher mitral inflow velocities caused by mitral annular restriction and lower mitral annular velocities due to both the limitation of mitral annular motion and abnormal left ventricular relaxation.

References


