Mitral valve regurgitation is a powerful factor of left ventricular hypertrophy

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INTRODUCTION

Although occurrence of valvular heart disease is less frequent than coronary artery disease or arterial hypertension, it remains an important clinical issue. Valvular disease is still a common pathology characterized by a progressive course which in advanced stages may require surgical intervention. However, early administered appropriate treatment may improve the patients' survival and the quality of their lives. On the other hand, incomplete diagnostic evaluation or inappropriate therapy may lead to chronic heart failure and shorter survival.

OBJECTIVES

The aim of the present study was to evaluate hemodynamic consequences of MR both for the cardiac chambers and hypertrophy.

METHODS

The study included 1432 patients (mean age 54 ±15 years, male – 55%) with MR recorded in the transthoracic echocardiography database. Associations between the stage of MR and other variables in these patients were analyzed.

RESULTS

More advanced grades of MR were associated with progressive enlargement of left ventricular (LV) systolic and diastolic dimensions. LV ejection fraction (LVEF) was significantly decreasing with increased MR severity. A significant increase in the left atrial dimension and LV mass was observed. In multivariate regression analysis the grade of MR (p <0.0001), age (p <0.0001), endsystolic stress of LV (p <0.0001), LV fractional shortening (p <0.0001) and LVEF (p <0.05) were found to be independently associated with LV mass. The strongest linear correlations were found between LV mass and endsystolic stress of LV (r = 0.52, p <0.0001), the grade of MR (r = 0.32, p <0.0001) and ejection fraction (r = −0.29, p <0.0001).

CONCLUSIONS

MR alters cardiac dimensions and function parameters and is also one of the strongest factors that increase LV hypertrophy.

KEY WORDS

cardiac hypertrophy, mitral valve regurgitation

INTRODUCTION

Mitral valve regurgitation (MR) is a common abnormality found on echocardiography which in its advanced stage is a major cause of congestive heart failure. Cardiac remodeling associated with MR is caused by volume overload, dilatation and enlargement of the left ventricle and atrium.

OBJECTIVES

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CONCLUSIONS

MR alters cardiac dimensions and function parameters and is also one of the strongest factors that increase LV hypertrophy.
Mitral valve regurgitation is a powerful factor of left ventricular hypertrophy. In MR, hemodynamic disorders result from retrograde flow of blood from the left ventricle to the left atrium. It causes volume overload, enlargement and distension of both left chambers of the heart and the increase in mass of left ventricular (LV) muscle, which is the result of the hypertrophy of existing cardiomyocytes rather than hyperplasia. Increasing volume overload in MR causes myocyte lengthening by sarcomer replication in series, and increases ventricular mass. These changes are initially compensatory, but chronic hypertrophy may be deleterious, because it increases the risk for the development of heart failure and premature death.

The present paper assesses the relationship between MR and the degree of LV hypertrophy. This issue seems to be very important because of the occurrence of MR in the general population and serious clinical implications of cardiac hypertrophy, e.g. as an independent risk factor for cardiac morbidity and mortality. LV hypertrophy is a predictor of sudden cardiac death, myocardial infarction and heart failure.

**Patients and Methods**

Echocardiographic examinations were conducted from January 1997 to December 2003 in the 2nd Chair and Department of Cardiology, the Medical University of Lodz, Poland. The analysis included 1432 patients hospitalized in the Department for MR. In the study group there were 788 males (55%) and 644 females (45%) aged from 16 to 88 years (mean age was 54 ±15 years). Patients with arterial hypertension and aortic stenosis were excluded from the study. Each patient underwent full physical examination with blood pressure measurement on the day of the echo examination. In the study group a percentage of concomitant diseases obtained from a medical history of each patient was as follows: ischemic heart disease (68%), a history of myocardial infarction (59%), heart failure (20%), atrial fibrillation (10%), chronic obstructive pulmonary disease or asthma (9%), chronic renal failure (8%), a stroke (7%), thyroid disease (5%). Patients were taking statins (95%), antiplatelet drugs (acetylsalicylic acid, ticlopidin) (93%), angiotensin-converting enzyme inhibitors (89%), β-blockers (88%), long-acting nitrates (35%), calcium antagonists (20%), diuretics (25%), antiarrhythmic drugs (13%).

Transsthoracic echocardiography with evaluation of all anatomical and functional cardiac parameters was performed according to the recommendations of the American Society of Echocardiography (ASE) with the use of the Acuson Sequoia, Acuson 128 XP, Vivid. The investigation conformed with the principles outlined in the Declaration of Helsinki.

The degree of mitral valve insufficiency was estimated with the 4-grade ASE scale. The study group was divided into four subgroups according to the degree of regurgitation. The subgroup with the 1st degree of MR consisted of 59% of cases, the 2nd degree – 27%, the 3rd – 11%, the 4th...
**TABLE**  Selected echocardiographic parameters in the study group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study group</th>
<th>1st degree of MR</th>
<th>2nd degree of MR</th>
<th>3rd degree of MR</th>
<th>4th degree of MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1432</td>
<td>845</td>
<td>386</td>
<td>158</td>
<td>43</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54 ±15</td>
<td>54 ±14</td>
<td>52 ±14</td>
<td>57 ±16</td>
<td>49 ±15</td>
</tr>
<tr>
<td>Diameter of LV in systole (mm)</td>
<td>38 ±10</td>
<td>36 ±9</td>
<td>36 ±9</td>
<td>45 ±12</td>
<td>48 ±14</td>
</tr>
<tr>
<td>Diameter of LV in diastole (mm)</td>
<td>49 ±9</td>
<td>48 ±8</td>
<td>48 ±8</td>
<td>57 ±10</td>
<td>62 ±12</td>
</tr>
<tr>
<td>Systo-diastolic difference (mm)</td>
<td>12 ±3</td>
<td>12 ±2</td>
<td>12 ±3</td>
<td>11 ±4</td>
<td>13 ±7</td>
</tr>
<tr>
<td>Diameter of left atrium (mm)</td>
<td>41 ±13</td>
<td>40 ±15</td>
<td>39 ±5</td>
<td>50 ±9</td>
<td>58 ±12</td>
</tr>
<tr>
<td>Diameter of aorta (mm)</td>
<td>32 ±3</td>
<td>32 ±4</td>
<td>31 ±3</td>
<td>33 ±3</td>
<td>33 ±4</td>
</tr>
<tr>
<td>Diameter of right ventricle (mm)</td>
<td>23 ±4</td>
<td>22 ±2</td>
<td>22 ±3</td>
<td>26 ±6</td>
<td>30 ±7</td>
</tr>
<tr>
<td>Diameter of IVS in systole (mm)</td>
<td>13 ±2</td>
<td>13 ±2</td>
<td>13 ±2</td>
<td>12 ±2</td>
<td>13 ±2</td>
</tr>
<tr>
<td>Diameter of IVS in diastole (mm)</td>
<td>11 ±2</td>
<td>11 ±2</td>
<td>11 ±2</td>
<td>10 ±2</td>
<td>10 ±2</td>
</tr>
<tr>
<td>Diameter of posterior wall in systole (mm)</td>
<td>13 ±2</td>
<td>13 ±1</td>
<td>14 ±2</td>
<td>13 ±2</td>
<td>13 ±2</td>
</tr>
<tr>
<td>Diameter of posterior wall in diastole (mm)</td>
<td>11 ±2</td>
<td>10 ±1</td>
<td>11 ±2</td>
<td>11 ±2</td>
<td>11 ±2</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>238 ±83</td>
<td>221 ±69</td>
<td>235 ±77</td>
<td>292 ±105</td>
<td>338 ±131</td>
</tr>
<tr>
<td>End systolic stress (10³ dyn/cm²)</td>
<td>82 ±33</td>
<td>77 ±28</td>
<td>78 ±31</td>
<td>107 ±45</td>
<td>112 ±50</td>
</tr>
<tr>
<td>EF (%)</td>
<td>55 ±14</td>
<td>59 ±10</td>
<td>55 ±14</td>
<td>41 ±18</td>
<td>42 ±19</td>
</tr>
<tr>
<td>ECG – sinus rhythm (number of patients)</td>
<td>1084</td>
<td>756</td>
<td>264</td>
<td>42</td>
<td>22</td>
</tr>
<tr>
<td>ECG – atrial fibrillation (number of patients)</td>
<td>348</td>
<td>98</td>
<td>122</td>
<td>116</td>
<td>21</td>
</tr>
</tbody>
</table>

Values are presented as standard deviation ±mean or number of patients.

Abbreviations: EF – ejection fraction, IVS – interventricular septum, LV – left ventricle, MR – mitral valve regurgitation

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- 3%. Degenerative changes of the valve were the most frequent cause of MR observed in about 71% of cases. Mitral valve prolapse was diagnosed in about 13% of patients. Ischemic heart disease was the cause of MR in about 12% of patients. Left ventricular ejection fraction (LVEF) was calculated according to the 2-dimensional Simpson's rule. LV hypertrophy was expressed as LV mass (g) which can be evaluated using the Penn's equation: $1.04 \times [(IVS + LVEDD + PWT)^3 – LVEDD^3 – 13.6]$, where IVS is interventricular septal wall thickness, LVEDD = left ventricular enddiastolic dimension, PWT = posterior wall thickness.

Endsystolic stress $[10^3 \text{ dyne/cm}^2] = 0.334 \times \text{SBP} \times \text{LVESD/PWT} \times (1 + \text{PWT/LVESD})$, where SBP = systolic blood pressure, LVESD = left ventricular enddiastolic diameter, PWT = posterior wall thickness.

**RESULTS** In the study group patients with the 1st degree of MR were the largest subgroup (59%). The 2nd degree of MR was recognized in 27% of patients, the 3rd in 11% and the 4th in 3% (TABLE, FIGURE 1). The measurements showed that in particular the diameter of the left atrium (mean ± standard deviation [SD]) was for the 1st degree 39 ±15 mm, the 2nd – 39 ±5 mm, the 3rd – 50 ±9 mm, and the 4th – 58 ±14 mm, respectively (TABLE, FIGURE 2). Diameters of the LV were measured in systole and diastole. The LV diameter was increasing in subsequent degrees of MR both in systole and diastole (TABLE). Ejection fraction (EF) was reduced in patients with more advanced stages of MR (TABLE, FIGURE 3). Mass of LV muscle (mean ± SD) was increasing with a rise of MR degree. In the subgroup with the 1st degree of MR the average mass was 222 ±69 g, the 2nd – 241 ±78 g, the 3rd – 292 ±105 g, and the 4th – 338 ±128 g, respectively (TABLE, FIGURE 4).

The multivariate regression analysis revealed that the degree of MR (p < 0.0001), age (p < 0.0001), endsystolic stress of the LV...
DISCUSSION  Currently, valvular heart disease is usually diagnosed at the very early stage, in an asymptomatic period, what is related to the development and widespread availability of transthoracic and transoesophageal echocardiography. In the present study patients with the 1st grade of MR were the largest subgroup, whereas patients with the 4th grade of MR constituted the smallest one. It should be emphasized that in subjects with MR the most important is an early diagnosis of LV dysfunction and regular check-up of patients. The watchful waiting strategy may lead to the necessity of performing corrective procedures before the development of chronic LV failure. In the study group the distribution of MR causes is consistent with data from the Euro Heart Survey on Valvular Heart Disease where degenerative valve changes were the major cause of mitral valve defects, followed by rheumatic heart disease and then ischemic heart disease.

Data from many trials indicate that increased LV mass is the strongest and independent risk factor for mortality and morbidity from cardiovascular causes. The present study found a statistically significant relation between the degree of MR and the mass of the LV. It was observed that the LV mass is greater when a greater retrograde blood flow occurs. According to the measurements of LV mass the significant hypertrophy of the left ventricle was observed in patients with the 3rd and the 4th degree of MR. Increased mass of the left ventricle in MR is a sign of LV hypertrophy caused by volume overload.

Greater LV mass in more advanced stages of MR is the evidence that this condition has an influence not only on the left atrium and pulmonary circulation, but also on the left ventricle with its consequences like a decrease in EF. In the current study, lower EF was observed in the 2nd and more severe stages of MR. It is consistent with observations presented in the study by Carabello et al. who revealed that when MR exists even slightly decreased EF can be a signal of a severe dysfunction of the LV muscle. Furthermore, a decrease in LVEF occurring as early as in mild and moderate stages of MR may be primary to ischemic etiology of MR – about 12% of patients from the study group had ischemic etiology of MR.

According to Gaash et al. during the transition from compensated to decompensated MR, the ventricle progressively enlarges and systolic function declines. Despite this fact, LVEF tends to remain “normal” within the broad range. Some patients experience fatigue, a limited exercise tolerance or dyspnea during this transition, but sometimes patients may proceed through this stage with very mild or even no symptoms. The present study demonstrated that with the increase of MR degree the dimensions of the left ventricle increased. It indicates that MR has an influence on the geometry of the left ventricle.

According to previous studies, the left atrial diameter over 50 mm should be considered as an indicator of its marked enlargement. In the present study only in subgroups of patients with the 3rd and 4th degrees of MR the left atrium was significantly enlarged. It is an important observation that leads to the conclusion that a small backflow has little influence on the function and dimensions of the left atrium. At the same stage the left ventricle is already overloaded – it has a bigger mass and diameter, and EF is reduced. It confirms that only advanced stages of MR (3rd and 4th degree) significantly influence the dimension of the left atrium. The study by Gerds et al. is the first to report that MR is a predictor of left atrium enlargement which should raise awareness about the risk of subsequent atrial fibrillation.

**FIGURE 4** Mass of left ventricular (LV) muscle in subgroups with consecutive degree of mitral valve regurgitation (n = 1432)

**FIGURE 5** Association between left ventricular (LV) mass and endsystolic stress (n = 1432)
Using the multivariate regression analysis the current study identified predictors that could affect the mass of the LV. It was observed that statistically significant for an increase in LV mass were: the degree of MR (p < 0.0001), endystolic stress of the LV (p < 0.0001), LV fractional shortening (p < 0.0001) and LVEF (p < 0.05). All these parameters can be estimated on echocardiography. Moreover, there was a strong association between LV hypertrophy and age (p < 0.0001). The observations presented in the current study are consistent with the results of the Framingham Heart Study where LV volume-overload stages in MR resulted in increased LV dimensions and mass. No other statistical correlations of LV mass and other potential risk factors mentioned in previous papers were observed in the present study.

Limitations of the study Although the analysis described in this paper was the retrospective evaluation of consecutive patients with MR listed in the echo database, the authors hope that a large number of included subjects should provide reliable data concerning evaluated correlations. Echocardiography was performed by several echocardiographers, which may have influence on subjective evaluation of ultrasound examinations. However, all the echocardiographers were from one cardiologic center and had a similar approach towards recording and interpreting ultrasound examination.

The key issue arising from the discussed study is that MR is one of the strongest factors correlated with the increase in LV mass. The study confirmed that lower EF and endystolic stress of LV are associated with increased mass of the LV. It also documented that the degree of MR potently affects dimensions of the left atrium and the LV, and the parameters of cardiac function.

FIGURE 6 Association between left ventricular (LV) mass and ejection fraction (n = 1432)

REFERENCES