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Early Mitral Regurgitation after Acute Myocardial Infarction Does Not Contribute to Subsequent Left Ventricular Remodeling

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Summary

Background: It is well known that mitral regurgitation may lead to left ventricular dilation; however, the relationship between progressive left ventricular dilation after acute myocardial infarction (MI) and mitral regurgitation has not yet been clarified.

Hypothesis: This study tested the hypothesis that early mitral regurgitation contributes to left ventricular remodeling after acute MI.

Methods: We prospectively evaluated 131 consecutive patients by serial two-dimensional and Doppler echocardiography on Days 1, 2, 3, and 7, after 3 and 6 weeks, 3 and 6 months, and 1 year following acute MI. Patients were divided into two groups: those with mitral regurgitation in the first week after acute MI (Group 1, n = 34) and those without mitral regurgitation (Group 2, n = 81).

Results: Over 1 year, a significant increase in end-diastolic volume index (from 62.1 ± 12.9 to 70.5 ± 23.6 ml/m^2, p = 0.001) with a strong linear trend (F = 15.1, p < 0.001) was noted. Initial end-diastolic volume index was higher in Group 1 (65.6 ± 13.3 vs. 60.4 ± 12.5 ml/m^2, p = 0.047), but this difference remained constant throughout the study (F = 1.76, p = NS). Therefore, the pattern of end-diastolic volume changes was similar in both groups during the period of observation.

Conclusions: These data indicate that early mitral regurgitation after acute MI does not contribute to subsequent left ventricular remodeling in the first year after myocardial infarction.

Key words: left ventricular remodeling, myocardial infarction, mitral insufficiency

Introduction

After acute myocardial infarction (MI) progressive left ventricular (LV) dilation occurs, beginning in the early phase of the disease and continuing for months and years, a process known as remodeling.[1] Remodeling is affected by numerous factors, including infarct location, infarct-related artery patency, and therapy.[2–7] On the other hand, it has been found that the incidence of mitral regurgitation after MI is high and that it is associated with higher mortality.[8–11] Although it is well known that mitral regurgitation may lead to LV dilation, the relationship between progressive LV dilation after acute MI and mitral regurgitation has not yet been clarified.

The aim of this study was to determine the impact of early mitral regurgitation on LV remodeling after acute MI.

Methods

Study Population

We prospectively evaluated 131 patients with first acute MI who met the following criteria: (1) age ≤ 70 years, (2) chest pain lasting > 30 min, (3) ST-segment elevation ≥ 2 mm at least in two electrocardiographic leads, (4) transient elevation of creatine kinase and/or MB isoenzyme, and (5) echocardiogram performed within 24 h of onset of pain.

The initial study population was divided into three groups: patients who developed mitral regurgitation in the first week after acute MI (Group 1), patients without mitral regurgitation (Group 2), and patients who developed mitral regurgitation later in the course of the disease (Group 3). Group 3 was excluded from the analysis of the impact of early mitral regurgitation on LV remodeling. Left ventricular volumes were not

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measurable in three patients from Group 2 because of poor quality of echocardiographic studies. Therefore, the remaining 115 patients, 34 in Group 1 and 81 in Group 2, represent the final study group.

Echocardiograms

Patients were serially evaluated by two-dimensional and Doppler echocardiography in the following sequence: on admission (Day 1), on Days 2, 3, 7, after 3 and 6 weeks, 3 and 6 months, and 1 year after infarction. All examinations were performed with an Acuson 128 machine (Mountain View, Calif.) using a 2.5 MHz transducer; they were stored on VHS video tapes for later analysis. Left ventricular end-diastolic and end-systolic volumes and ejection fraction were determined from apical two- and four-chamber views using the Simpson's biplane formula.[12] Tracing of endocardial borders in end-diastole and end-systole was performed on the Acuson 128 machine in the technically best cardiac cycle. The volumes were normalized for body surface area and expressed as indices. Anteroposterior left atrial diameter was measured in end-systole, in the parasternal long-axis view at the aortic valve level, as a distance from the trailing echo of the posterior aortic wall to the leading echo of the posterior left atrial wall.[12]

Pulsed-wave and color Doppler flow mapping were used for the detection of mitral regurgitation. Severity of mitral regurgitation was assessed semiquantitatively according to the length of the turbulent flow jet into the left atrial cavity, using scale 0–4+.[13]

Coronary Angiography

Coronary angiography was performed before hospital discharge in 96 of 115 patients and perfusion of the infarct-related artery was assessed using TIMI criteria.[14] Successful reperfusion was defined as Thrombolysis in Myocardial Infarction (TIMI) grade 2 or 3. Significant stenosis was defined as > 70% stenosis of the major epicardial coronary artery.

Statistical Analysis

Unpaired *t*-tests and chi-square tests were used to test the differences between patient groups; comparisons between initial ventricular volumes and volumes after 12 months were performed with paired *t*-tests. Changes of LV and left atrial size over time were assessed using repeated measures of analysis of variance.

Results

Groups 1 and 2 were similar with regard to age, gender, infarct site, history of hypertension, diabetes, cigarette smoking, peak creatine-kinase level, Killip class, and administration of thrombolytic therapy; however, multivessel coronary artery disease was more frequent in patients with early mitral regurgitation (Table I).

TABLE I Characteristics of patients enrolled in the study

	Group 1 (n = 34)	Group 2 (n = 81)
Age (years, mean ± SD)	56 ± 8	54 ± 9
Sex (female)	7	21
Hypertension	13	27
Cigarette smoking	20	42
Diabetes	6	14
Infarct site (anterior)	8	33
Q-wave infarction	30	73
Peak CK level	1159 ± 563	881 ± 129
Killip class >1	9	13
Thrombolysis	18	53
Multivessel CAD	19/29	24/67[a]
TIMI 0–1	10/29	21/67
Died	5 (14.7%)	5 (6.2%)

[a] $p < 0.05$ between the groups.

Abbreviations: CAD = coronary artery disease, CK = creatine-kinase, Group 1 = patients with early mitral regurgitation, Group 2 = patients without mitral regurgitation, SD = standard deviation, TIMI = The Thrombolysis in Myocardial Infarction Trial.

Early Mitral Regurgitation and Left Ventricular Remodeling

In Group 1, 33 patients had 1+ or 2+ mitral regurgitation and 1 patient had 3+ mitral regurgitation. Overall, the study group demonstrated a significant increase in end-diastolic volume index (from 62.1 ± 12.9 to 70.5 ± 23.6 ml/m^2; p = 0,001) with a strong linear trend (F = 15.1; $p < 0.001$) over 1-year follow-up. End-diastolic volume index was higher in Group 1 than in Group 2 already on Day 1 (65.6 ± 13.3 vs. 60.4 ± 12.5; p = 0.047); however, as shown in Figure 1, this difference remained constant throughout the study (F = 1.76; p = NS). End-systolic volume index was higher in Group 1 than in Group 2 on Day 1 (37.8 ± 13.8 vs. 32.8 ± 12.2; p =

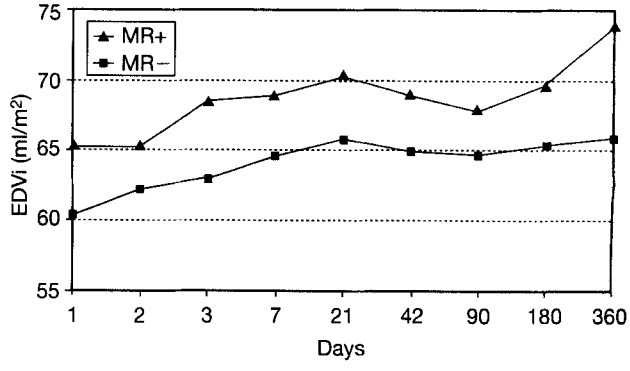

FIG. 1 Impact of early mitral regurgitation on left ventricular end-diastolic volume changes during the follow-up period. EDVi = end-diastolic volume index, MR+ = patients with early mitral regurgitation, MR− = patients without mitral regurgitation.

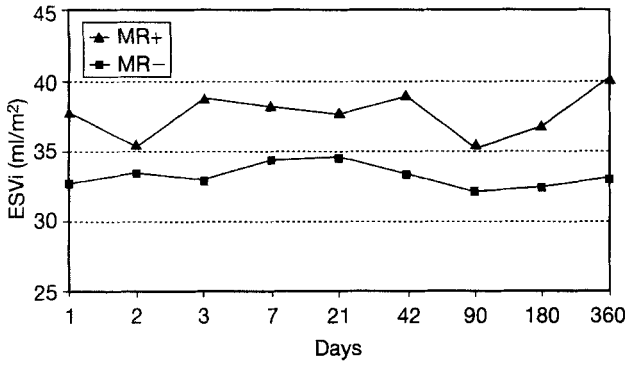

FIG. 2 Impact of early mitral regurgitation on left ventricular end-systolic volume changes during the follow-up period. Abbreviations as in Figure 1.

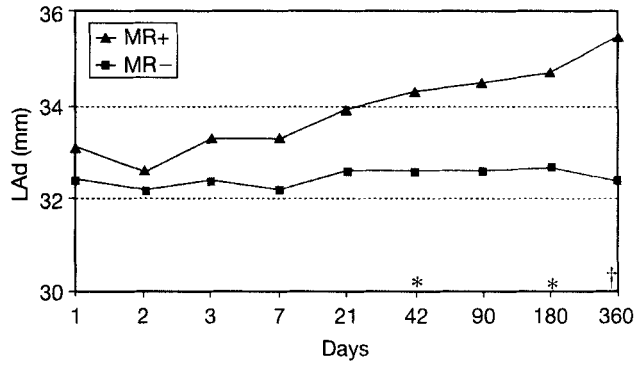

FIG. 3 Left atrial diameter changes in patients with and without early mitral regurgitation during the follow-up period. LAd = left atrial diameter, MR+ = patients with early mitral regurgitation; MR− = patients without early mitral regurgitation; * = $p<0.05$, † = $p<0.01$.

0.06), but the difference did not reach statistical significance. Similar to end-diastolic volume index changes over time, pattern of end-systolic volume index changes (Fig. 2) in Groups 1 and 2 remained similar during the follow-up period ($F = 1.02$; p = NS). Thus, no difference in the pattern of end-diastolic and end-systolic volume index changes was found between the groups over 1 year.

Left Atrial Size

Changes in left atrial diameter in both groups over the follow-up period is shown on Figure 3. Left atrial diameter was significantly greater in Group 1 at 6 weeks (34.3 ± 5.1 vs. 32.6 ± 2.8; p = 0.049), 6 months (34.7 ± 5.3 vs. 32.7 ± 3.1; p = 0.035), and 1 year (35.5 ± 5.5 vs. 32.4 ± 2.8; p = 0.002) than in Group 2.

Discussion

Since 1933, when Castex reported eight patients with inferior infarction and apical regurgitant systolic murmur consistent with mitral regurgitation,[15] this problem has been extensively studied using various techniques.[10, 11, 16–19] In 1967, in a prospective study that included 195 patients, Heikkila made some brilliant statements and reached conclusions that have been confirmed during the following decades.[8] However, results of the subsequent studies on mitral regurgitation after MI were frequently controversial. These differences may be related to two major reasons: (1) The nature of mitral regurgitation after acute MI, which can appear at different times in the course of infarction, and can be transient and can change its severity over time; and (2) nonuniformity of the entry criteria and methods for the detection of mitral regurgitation.

To our knowledge, there are no studies on consecutive postmyocardial infarction patients, with serial echocardiographic follow-up of mitral regurgitation during the first year after infarction. Previously published echocardiographic studies that analyzed data obtained in few examinations, either in the acute or in the chronic phase of MI, could not provide precise answers regarding the incidence, associated factors, natural history, or the impact of mitral regurgitation on postmyocardial infarction LV remodeling.[16–18, 20] Serial echocardiographic follow-up allowed us to collect more accurate data.

Although it has been recognized that mitral regurgitation in the setting of MI is associated with higher mortality, the reason for this increased mortality, except for acute severe mitral regurgitation, remained incompletely understood.[10, 11] Our data also showed a tendency toward higher 1-year mortality in Group 1 patients compared with Group 2 patients (14.7 vs. 6.2%), although, probably because of the relatively small number of patients, this difference did not reach statistical significance. In our study, mitral regurgitation was mild or moderate in the majority of patients. Considering this fact, one could presume nonmeasurable influence of mitral regurgitation on postmyocardial infarction LV volumes. However, we hypothesized that early mitral regurgitation, although mild to moderate, may contribute to LV dilation. This could be particularly important in the early phase, when hemodynamic changes are most prominent. Since it is well known that LV dilation after acute MI is one of the strongest predictors of long-term mortality,[21] evidence of mitral regurgitation-related increase of LV remodeling could be an attractive explanation for poor prognosis of these patients.

Our data showed that LV dilation occurred regardless of the presence of early mitral regurgitation. On the other hand, comparing parameters of LV systolic function in patients with and without mitral regurgitation, it can be noted that patients in Group 1 had higher end-diastolic and end-systolic volumes throughout the follow-up period. Furthermore, multivessel coronary artery disease was more frequent in Group 1 patients. These data indicated more profound LV dysfunction and greater portion of myocardium at risk, presumably leading to higher risk for future cardiac events. However, comparison of sequential changes of end-diastolic and end-systolic volumes during the 1-year follow-up period in patients with and without early mitral regurgitation revealed no significant difference

in the pattern of LV dilation between the groups. According to these data, it seems that increased risk and higher mortality in patients with early mitral regurgitation after MI is rather the consequence of greater LV damage and more severe coronary artery disease than the result of mitral regurgitation itself.

In addition, initial left atrial size was similar between groups. However, from 6 weeks and thereafter the left atrium was larger in Group 1. Recently, it has been shown that any absolute volume increase, such as the presence of mitral regurgitation, would have more striking impact on left atrial rather than on LV size.[22] Thus, although mitral regurgitation in our patients did not alter the process of LV remodeling, it could have caused minimal difference in left atrial size between Group 1 and Group 2 patients.

Conclusions

Early mitral regurgitation after acute MI was detected more frequently in patients with larger initial LV volumes and multivessel coronary artery disease. However, the pattern of subsequent LV dilation was similar in patients with and without early mitral regurgitation. These data indicate that early mitral regurgitation does not influence the pattern of LV remodeling during the first year after MI, and that increased mortality in patients with mitral regurgitation post MI is possibly related to more severe LV dysfunction and more severe coronary artery disease than to the effect of mitral regurgitation itself.

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