

Improved Posterobasal Segment Function After Thrombolysis Is Associated With Decreased Incidence of Significant Mitral Regurgitation in a First Inferior Myocardial Infarction

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Objectives. This study was designed to investigate the association between wall motion abnormalities and the occurrence of ischemic mitral regurgitation in patients with a first inferior or posterior myocardial infarction and to reassess the role of thrombolytic treatment in these patients.

Background. We previously demonstrated that thrombolytic therapy reduces the incidence of significant mitral regurgitation in patients with a first inferior myocardial infarction, but the mechanisms responsible for this decrease were not clear.

Methods. Wall motion score on two-dimensional echocardiography (16 segments) and mitral regurgitation grade (0 to 3) on Doppler color flow imaging were assessed in 95 patients (in 47 after thrombolysis) at 24 h, 7 to 10 days and 1 month after myocardial infarction. Significant mitral regurgitation was defined as moderate or severe (grade 2 or 3).

Results. Multivariate analysis revealed that the presence of an

advanced wall motion abnormality of the posterobasal segment of the left ventricle was the most significant independent variable associated with significant mitral regurgitation: odds ratio (OR) 15.0, 90% confidence interval (CI) 1.4 to 165.6 at 24 h; OR 2.8, CI 0.9 to 9.3 at 7 to 10 days; OR 4.2, CI 1.2 to 11.4 at 1 month. Thrombolysis reduced the prevalence of advanced wall motion abnormalities in the posterobasal segment at 24 h (55% vs. 75%, OR 0.5, CI 0.2 to 0.99), 7 to 10 days (44% vs. 73%, OR 0.3, CI 0.1 to 0.7) and 1 month (36% vs. 56%, OR 0.4, CI 0.2 to 0.9).

Conclusions. There is a strong association between advanced wall motion abnormalities in the posterobasal segment and significant mitral regurgitation. In this study group, thrombolysis reduced the prevalence of advanced wall motion abnormalities in the posterobasal segment and thereby reduced the incidence of significant mitral regurgitation.

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New mitral regurgitation in acute myocardial infarction, defined as valve incompetence with no primary leaflet or chordal abnormalities, is associated with the development of hemodynamic deterioration and increased mortality (1-7). This disorder is a relatively common complication of acute ischemia and frequently occurs in patients with inferior or posterior myocardial infarction (4,5,8). Recent reports (3-5,9-11) suggest that the incidence of ischemic mitral regurgitation is 9% to 56%. Ischemic mitral regurgitation has traditionally been ascribed to "papillary muscle dysfunction." Originally, Burch et al. (12) proposed that papillary muscle dysfunction could be due to either mitral valve prolapse or incomplete mitral valve closure. Subsequent studies suggested additional mechanisms for mitral valve incompetence in acute myocardial infarction: mitral annulus dilation (5,13) and left ventricular dilation (5,11,14) or

dysfunction (5,10). The role of regional myocardial dysfunction in the development of ischemic mitral regurgitation has been controversial (15-20) and has not yet been thoroughly elucidated.

We (9) previously demonstrated that thrombolytic therapy reduces the incidence of significant mitral regurgitation in patients with a first inferior myocardial infarction, but the mechanisms responsible for this decrease were not clear.

The current series of analyses were undertaken to investigate the possible association between segmental wall motion abnormalities and the occurrence of ischemic mitral regurgitation in patients with a first inferior or posterior myocardial infarction and to reassess the role of thrombolytic treatment in these patients.

Methods

Study patients. During the 18-month study period from December 5, 1989 to June 4, 1991, 462 patients were admitted to the intensive coronary care unit at Sheba Medical Center with a documented myocardial infarction. As indicated in our previous communication (9), our study patients were patients <76 years of age with acute inferior, inferoposterior, infero-

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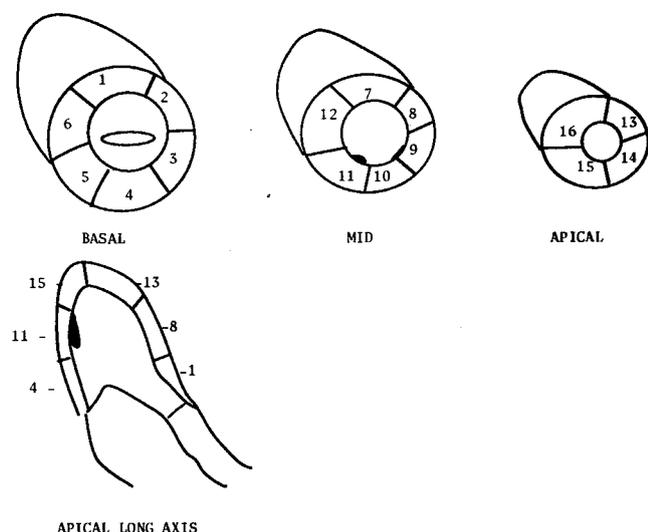


Figure 1. Diagrammatic representation of 16-segment regional wall motion analysis in the standard two-dimensional echocardiographic views. 1 and 2 = anteroseptal; 3 = lateral; 4 = posterobasal; 5 = inferobasal; 6 = inferoseptal; 7 and 8 = anteroseptal; 9 = lateral; 10 = posterior; 11 = inferior; 12 = inferoseptal; 13 = anterior; 14 = lateral; 15 = inferior; 16 = septal. Modified from the recommendations of the American Society of Echocardiography reported by Schiller et al. (24).

lateral or extensive posterior (inferoposterolateral) wall myocardial infarction.

Definitions of inferior, posterior or right ventricular myocardial infarction as well as the thrombolytic protocol and the noninvasive criteria for reperfusion are based on accepted criteria (4,9,21,22). Exclusion criteria were 1) a history of prior myocardial infarction; 2) the presence of rheumatic heart disease or heart failure or a history of cardiac surgery or percutaneous transluminal coronary angioplasty; 3) a history of organic mitral valve disease; 4) inadequate echocardiographic images.

Echocardiography. Each patient underwent three echocardiographic examinations: 1) within 24 h after the onset of chest pain; 2) at 7 to 10 days after infarction, and 3) at 1 month (28 to 30 days) after infarction (9).

All two-dimensional echocardiographic studies included pulsed Doppler and color flow imaging. Severity of mitral regurgitation was graded according to the method of Helmcke et al. (23): No regurgitation was classified as grade 0; a mitral regurgitation jet occupying 5% to 19%, 20% to 39% and $\geq 40\%$ of the left atrial area represented, respectively, mild (grade 1), moderate (grade 2) and severe (grade 3) mitral regurgitation.

To assess regional wall motion, one of us (A.T.) retrospectively reviewed all echocardiograms in blinded manner without knowledge of the interpretation of the mitral regurgitation grading. The left ventricle was divided into 16 segments according to the recommendation of the American Society of Echocardiography (24) with slight modification in terminology and the addition of an apical long-axis view (Fig. 1). For each

segment, wall motion was graded as follows: normal = 0, hypokinetic = 1, akinetic = 2, and dyskinetic = 3. When the wall motion scores obtained from the long- and the short-axis views differed, we always selected the score with more significant regional abnormalities.

To assess interobserver and intraobserver variability, 40 randomly chosen echocardiograms (640 segments) were analyzed several weeks later by two observers (Z.V. and A.T.), one of whom had scored those echocardiograms earlier. On a segment by segment basis, these reproducibility studies showed a concordance of 93% in the assessment of wall motion score between two observers, and of 95% between the two studies scored by the same observer.

End points. The primary end points of this study were the development of advanced wall motion abnormalities: akinesia or dyskinesia, and significant mitral regurgitation (grade 2 or 3). Secondary end points were the presence of all types of wall motion abnormalities (hypokinesia, akinesia or dyskinesia), development of mitral regurgitation of any grade and in-hospital and follow-up events.

Statistical methods. As a measure of association between the levels of segmental wall motion abnormalities and grade of mitral regurgitation severity, the Spearman rank correlation coefficient was used. Univariate analysis methods included the chi-square test for categorical variables. To estimate the odds ratio for the tables with zero entries, 0.5 was added to each cell. In this case the estimation of confidence interval was based on the log odds ratio. Multivariate analysis was performed by using a logistic regression model with a stepwise selection of factors.

The model for prediction of mitral regurgitation included age, gender, congestive heart failure, administration of thrombolytic therapy and the development of advanced wall motion abnormalities (akinesia/dyskinesia); thrombolytic therapy and advanced wall motion abnormalities were forced into the model. The model with wall motion abnormalities as the dependent variable included age, gender, congestive heart failure and administration of thrombolytic therapy. Odds ratios attributable to the factors were estimated from coefficients of logistic regression.

The statistical analysis system (SAS) software was used, especially FREQ, CORR and LOGISTIC procedures (25).

Results

Ninety-five patients met the criteria for eligibility in the study. At study 2 (7 to 10 days), a technically adequate echocardiogram was obtained in 89 patients. Three patients died after the second examination period; two patients missed the second study, but one of them was included in the last follow-up. Thus, at the 1 month study, echocardiograms of 85 patients were analyzed.

Clinical characteristics. Table 1 presents the baseline clinical characteristics of the 95 patients with a first inferior myocardial infarction included in the study. The majority (78%) were male. Electrocardiographic criteria for posterior

Table 1. Clinical Characteristics of the 95 Patients Included in the Study

Age (yr)	60 ± 11
Female	22 (23%)
Diabetes mellitus	13 (14%)
Hypertension	21 (22%)
Posterior MI	55 (58%)
Right ventricular MI	23 (24%)
LVEF (n = 70) (%)	52.5 ± 8%
Complete AV block	19 (20%)
Arrhythmias	32 (34%)
Post MI ischemia	40 (42%)
Heart failure	14 (15%)
Mortality	3 (3%)
Revascularization (PTCA or CABG)	10 (10.5%)
Thrombolytic treatment	47 (49.5%)
Cardiac catheterization	20 (21%)

Data are presented as number (%) of patients or mean value ± SD. AV = atrioventricular; CABG = coronary artery bypass grafting; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

wall involvement were present in 58% of patients and for right ventricular involvement in 24%. Intravenous thrombolytic therapy was administered to 47 patients within 3.3 ± 2.7 h (mean ± SD) after the onset of chest pain. Thirty-five patients (74%) were judged to have successful reperfusion by clinical criteria. Forty-eight patients did not receive thrombolytic therapy because of contraindications to thrombolysis or late arrival (>6 h) after the onset of chest pain. Between the second and third follow-up examinations, 10 patients (10.5%) underwent revascularization (percutaneous transluminal coronary angioplasty in 8 patients, coronary artery bypass grafting in 2); 5 of the 10 patients had received thrombolytic therapy.

Univariate Spearman correlation analysis. Significant correlation coefficients ($r > 0.2$) between echocardiographic segmental wall motion abnormality score and mitral regurgitation grade were present only for the posterobasal, inferobasal, midposterior, midinferior and posterolateral regions (Table 2). The correlation between mitral regurgitation grade and wall motion abnormality score of the posterobasal segment was the most significant of these correlations at all study periods after myocardial infarction. Because the correlation coefficients between the five segments themselves was very high ($r = 0.56$ to 0.93), only the posterobasal segment wall motion score was included in the multivariate logistic analyses.

Association between advanced wall motion abnormalities of the posterobasal segment and the incidence of mitral regurgitation. Table 3 shows the correlation between the incidence and severity of mitral regurgitation and the presence or absence of advanced wall motion abnormalities (akinesia/dyskinesia) of the posterobasal segment. Such abnormalities were present in 62 patients (65%) at 24 h, in 53 patients (60%) at 7 to 10 days and in 39 patients (46%) at 1 month. The presence of mitral regurgitation of any grade was correlated with these advanced abnormalities.

Clinical significance of advanced wall motion abnormalities of the posterobasal segment as a predictor of mitral regurgitation. Stepwise logistic regression analysis disclosed that the presence of advanced wall motion abnormalities of the posterobasal segment was a strong, independent and significant predictor associated with the presence of any grade of mitral regurgitation at any study period (Table 4). The association between these advanced abnormalities and the presence of significant mitral regurgitation at 7 to 10 days was of borderline significance (OR 2.8, 90% CI 0.9 to 9.3). An especially strong association was noted between these abnormalities and the presence of significant mitral regurgitation (grade 2 or 3) at 24 h: All the patients with significant mitral regurgitation had advanced wall motion abnormalities of the posterobasal segment.

Influence of posterobasal segment dyskinesia on the prevalence of significant mitral regurgitation. At 24 h, there were nine patients with posterobasal segment dyskinesia, three (33%) of whom had significant mitral regurgitation. At 7 to 10 days, seven patients had posterobasal segment dyskinesia, five (71%) of whom had significant mitral regurgitation; and of the eight patients with posterobasal segment dyskinesia at 1 month, 7 (87%) had significant mitral regurgitation (Fig. 2).

Severe mitral regurgitation (grade 3) was found only in one patient at 24 h, in five patients at 7 to 10 days and in four patients at 1 month.

Influence of thrombolysis on the prevalence of posterobasal advanced wall motion abnormalities in a first inferior myocardial infarction (Table 5). Patients receiving thrombolytic therapy had a reduced prevalence of advanced wall motion abnormalities (akinesia/dyskinesia) in the posterobasal segment at 24 h (55% vs. 75%, OR 0.5, 90% CI 0.2 to 0.99), at 7 to 10 days (44% vs. 73%, OR 0.3, 90% CI 0.1 to 0.7) and at 1 month (36% vs. 56%, OR 0.4, 90% CI 0.2 to 0.9).

Effect of revascularization procedures on the presence of advanced wall motion abnormalities in the posterobasal segment and the severity of mitral regurgitation. Between the studies at 7 to 10 days and 1 month, eight patients underwent angioplasty (four patients had received thrombolysis) and two underwent coronary artery bypass grafting (one of whom had received thrombolysis). Angioplasty was performed in the left anterior descending coronary artery in one patient, in the left circumflex coronary artery in four patients and in the right coronary artery in three. Six of these eight patients had

Table 2. Significant Spearman Correlation Coefficients (r) Between the Grade of Mitral Regurgitation and Segmental Wall Motion Abnormalities in the Study Patients

Wall Motion Abnormality	24 h (n = 95)	7-10 days (n = 89)	1 month (n = 85)
Posterobasal	0.306, p = 0.003	0.342, p = 0.001	0.373, p = 0.0004
Inferobasal	0.24, p = 0.02	0.285, p = 0.007	0.297, p = 0.006
Midinferior	0.27, p = 0.07	0.255, p = 0.02	NS
Midposterior	NS	0.268, p = 0.01	0.355, p = 0.0008
Posterolateral	NS	NS	0.330, p = 0.002

Table 3. Association Between Posterobasal Advanced Wall Motion Abnormalities and the Incidence and Severity of Mitral Regurgitation

	All Pts	Mitral Regurgitation				Total MR
		None (grade 0)	Mild (grade 1)	Moderate (grade 2)	Severe (grade 3)	
At 24 h						
With AWMA	62 (100%)	37 (59.7%)	14 (22.6%)	10 (16.1%)	1 (1.6%)	25 (40.3%)
Without AWMA	33 (100%)	26 (78.8%)	7 (21.2%)	0 (0%)	0 (0%)	7 (21.2%)
Total	95 (100%)	63 (66.3%)	21 (22.1%)	10 (10.5%)	1 (1.1%)	32 (33.7%)
At 7-10 days						
With AWMA	53 (100%)	24 (45.3%)	14 (26.4%)	10 (18.9%)	5 (9.4%)	29 (54.7%)
Without AWMA	36 (100%)	26 (72.2%)	6 (16.7%)	4 (11.1%)	0 (0%)	10 (27.8%)
Total	89 (100%)	50 (56.2%)	20 (22.5%)	14 (15.7%)	5 (5.6%)	39 (43.8%)
At 1 month						
With AWMA	39 (100%)	20 (51.3%)	10 (25.6%)	3 (7.7%)	6 (15.4%)	19 (48.7%)
Without AWMA	46 (100%)	34 (73.9%)	8 (17.4%)	4 (8.7%)	0 (0%)	12 (26.1%)
Total	85 (100%)	54 (63.5%)	18 (21.2%)	7 (8.2%)	6 (7.1%)	31 (36.5%)

Data are presented as number (%) of patients. AWMA = advanced wall motion abnormalities (akinesia/dyskinesia) of the posterobasal segment; MR = mitral regurgitation; Pts = patients.

advanced wall motion abnormalities in a posterobasal segment and four had mitral regurgitation. Successful revascularization markedly improved posterobasal wall motion in five patients and reduced mitral regurgitation in three (from moderate to mild). The only patient with postinfarction angina in whom coronary angioplasty did not improve posterobasal wall motion or reduce the severity of mitral regurgitation had total occlusion of the left circumflex coronary artery and dilation was performed on the lesion in the left anterior descending artery (not the infarct-related vessel).

Discussion

We (9) have previously demonstrated that thrombolytic therapy during a first inferior myocardial infarction is associated with a reduced incidence and severity of ischemic mitral regurgitation. However, the exact mechanisms of the development of mitral regurgitation in acute inferior myocardial

infarction and its decreased severity after thrombolysis are not clear. The main finding of the present study is the strong association between advanced wall motion abnormalities (akinesia/dyskinesia) in the posterobasal segment of the left ventricle and the development of significant mitral regurgitation. The use of thrombolytic therapy during a first inferior myocardial infarction considerably reduced the incidence of these advanced abnormalities and, as a consequence, the incidence of significant mitral regurgitation.

Ischemic mitral regurgitation is a complex phenomenon (5,8,18) and has often been attributed to papillary muscle dysfunction leading to mitral leaflet eversion or prolapse into the left atrium (12,13,19,25-27).

Subsequent studies suggested additional mechanisms for mitral regurgitation after myocardial infarction—in particular, left ventricular and mitral annulus dilation in anterior (but not in inferior) myocardial infarction (5,10,14). In inferior myocardial infarction an alternative mechanism—namely, dyskinesia of the corresponding ventricular wall—was suggested (11,18,20). Moreover, several studies (15-17) suggested that

Table 4. Odds Ratios of Posterobasal Advanced Wall Motion Abnormalities for Development of Mitral Regurgitation in a First Inferior Myocardial Infarction

	Odds Ratio	90% Confidence Interval
At 24 h		
MR of any grade*	2.3	1.0-5.3
Significant MR†	15.0	1.4-165.6
At 7-10 days		
MR of any grade*	3.2	1.4-7.2
Significant MR*	2.8	0.9-9.3
At 1 month		
MR of any grade*	4.0	1.6-9.9
Significant MR*	4.2	1.2-11.4

*Odds ratio adjusted for use of thrombolytic treatment, patient age and gender and presence of heart failure. †Unadjusted odds ratio (all patients with significant mitral regurgitation had advanced wall motion abnormalities). MR = mitral regurgitation.

Figure 2. Influence of posterobasal segment dyskinesia on the prevalence of significant mitral regurgitation (MR). Data are presented as percent of patients. The number of patients with (solid line)/without (dotted line) posterobasal segment dyskinesia was 9/86 at T1 (24 h), 7/82 at T2 (7 to 10 days) and 8/77 at T3 (1 month).

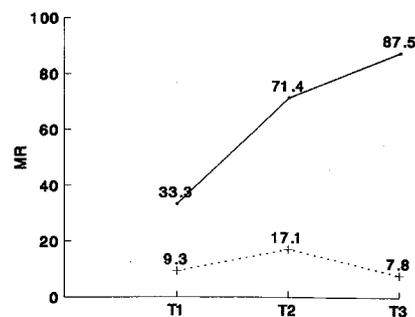


Table 5. Influence of Thrombolysis on the Prevalence of the Posterobasal Advanced Wall Motion Abnormalities in a First Inferior Myocardial Infarction

	Total Group	With Hypokinesia	With Akinesia/Dyskinesia
At 24 h			
Total group	95	33 (35%)	62 (65%)
With thrombolysis	47	21 (45%)	26 (55%)
Without thrombolysis	48	12 (25%)	36 (75%)
OR (CI), p value		0.5 (0.2-0.99), p = 0.04	
At 7 to 10 h			
Total group	89	36 (40%)	53 (60%)
With thrombolysis	41*	23 (56%)	18 (44%)
Without thrombolysis	48	13 (27%)	35 (73%)
OR (CI), p value		0.3 (0.1-0.7), p = 0.005	
At 1 month			
Total group	85	46 (54%)	39 (46%)
With thrombolysis	42	27 (64%)	15 (36%)
Without thrombolysis	43	29 (44%)	24 (56%)
OR (CI), p value		0.4 (0.2-0.9), p = 0.06	

Data are presented as number (%) of patients. *One patient receiving thrombolytic treatment failed to participate in the study at 7 to 10 days. CI = 90% confidence interval; OR = odds ratio adjusted for patient age and gender and presence of heart failure.

advanced wall motion abnormalities in areas of the myocardium supporting the papillary muscles (leading to the displacement of papillary muscles and retraction of the mitral leaflets) appear to be a sufficient condition for the development of ischemic mitral regurgitation even without ischemia of the papillary muscle.

The present study demonstrated a significant correlation between the grade of mitral regurgitation and wall motion abnormality score for posterobasal, inferobasal, midposterior, midinferior (area of posterior papillary muscle) and posterolateral regions. The most significant correlations at any study period were obtained for mitral regurgitation grade and posterobasal segmental wall motion score by both univariate and multivariate logistic analysis.

Severe mitral regurgitation (grade 3) was found in only one patient at 24 h, but it was present in five patients at 7 to 10 days, one of whom later died, thus leaving four of these patients at the 1-month study. In all cases severe mitral regurgitation was associated with dyskinesia of the posterobasal segment of the left ventricle. When severe mitral regurgitation developed, it did not resolve spontaneously.

It is now well established (28-30) that thrombolytic therapy administered soon after acute myocardial infarction preserves left ventricular function and improves regional wall motion. Although this treatment has been widely accepted in patients with anterior wall myocardial infarction, its value in patients with inferior or posterior wall myocardial infarction has been controversial (31-33). Our data show that thrombolysis in a first inferior myocardial infarction preserves posterobasal left ventricular function and significantly decreases the number of patients with advanced wall motion abnormalities (akinesia/dyskinesia) in this region.

There are sparse and discordant data regarding the effect of thrombolysis on the development of postinfarction mitral

regurgitation. In accordance with preliminary reports from the Thrombolysis in Myocardial Infarction (TIMI) I trial (7), acute ischemic mitral regurgitation is independent of coronary artery patency before or after thrombolysis and cannot be successfully treated by reperfusion of the infarct-related artery with late thrombolytic therapy. In contrast, several studies have demonstrated a beneficial effect of intracoronary (34) or intravenous (9) thrombolysis and emergency angioplasty on ischemic mitral regurgitation (35,36).

In our study, the prevalence of postinfarction mitral regurgitation was associated with advanced posterobasal wall motion abnormalities in the total study group. However, there were fewer patients with posterobasal akinesia/dyskinesia in the group with than in the group without thrombolysis. Therefore, the incidence of mitral regurgitation was significantly lower among patients who received thrombolytic therapy. On the basis of these data, we suggest that successful reperfusion after thrombolysis protects against advanced wall motion abnormalities in the posterobasal left ventricular region (area of myocardium supporting the posteromedial papillary muscle) and thus reduces the incidence and severity of mitral regurgitation.

Limitations of the study. The major limitation of our study is the lack of immediate coronary angiography in most patients. This procedure would have helped to correlate the prevalence and severity of mitral regurgitation with the objective proof of successful thrombolytic therapy, early patency of the infarct-related artery and possible value of its late spontaneous recanalization. Another shortcoming is the absence of data on left ventricular and mitral ring sizes. However, most of the previous studies (10,14) demonstrated an association between left ventricular or mitral annulus size and mitral regurgitation for anterior, but not for inferior, myocardial infarction. In the present study we used echocardiography to assess

regional left ventricular function. The improved yield of two-dimensional echocardiography in quantifying regional wall motion abnormalities in comparison with that of contrast or radionuclide ventriculography, or both, has been widely discussed and is now well established (28-30).

Conclusions and clinical implications. This study demonstrated a strong association between advanced wall motion abnormalities (akinesia/dyskinesia) in the posterobasal segment of the left ventricle and the development of significant postinfarction mitral regurgitation. Administration of thrombolytic therapy during a first inferior myocardial infarction considerably reduced the incidence of advanced posterobasal segmental dysfunction and may protect against the development of significant mitral regurgitation. On the basis of these findings, we strongly support the use of thrombolytic therapy in patients with a first inferior myocardial infarction, especially in those with advanced posterobasal wall motion abnormalities on echocardiography.

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