

Original Article

Early Improvement of Infarct-Associated Mitral Valve Regurgitation and Likelihood of Successful Thrombolysis: Color Doppler Echocardiographic Study

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ABSTRACT

Objective: To determine whether early successful thrombolysis can improve infarct-associated mitral valve dysfunction

Design: Cohort study conducted between February 1997 and January 2004

Setting: Coronary care unit and non-invasive cardiac laboratory, Department of Medicine, Farwania hospital, Kuwait

Subjects : One hundred and twenty five patients with ST segment elevation and acute myocardial infarction associated mitral valve regurgitation/mitral regurgitation (MR) were included in the study.

Interventions: Cardiac enzymes and 12-lead electrocardiogram were done for all patients. Transthoracic echocardiography, pulsed Doppler and color Doppler echocardiogram were done on admission and within 24 hours after thrombolytic therapy.

Main Outcome Measures: Infarct-associated MR in hospital outcome.

Results: Predictive indices revealed that the early improvement of infarct-associated MR after thrombolytic therapy is an indicator to predict successful thrombolysis status. The sensitivity was 86%, specificity = 79%, accuracy = 83%, positive predictive value = 62% and negative predictive value = 38%. Stepwise logistic multivariate analysis revealed a significant correlation between the age of the patients, chest pain to thrombolytic therapy interval and the early improvement of MR after thrombolytic therapy of acute myocardial infarction ($p < 0.05$). Patients with post-thrombolysis improvement in MR had a significantly lower incidence of in-hospital post-infarction angina, reinfarction, sustained ventricular tachycardia and congestive heart failure than patients without improvement ($p < 0.05$).

Conclusion: Early improvement of infarct-associated MR in patients with acute myocardial infarction treated with thrombolytic therapy suggests successful thrombolysis.

KEY WORDS: acute myocardial infarction, mitral valve function, thrombolytic therapy

INTRODUCTION

Mitral valve regurgitation/mitral regurgitation (MR) is a frequent complication of acute myocardial infarction and has several etiologies^[1]. In the setting of acute myocardial infarction, MR is most commonly due to valvular dysfunction without structural disease and may result from altered ventricular geometry, incomplete mitral leaflet coaptation, papillary muscle dysfunction and regional wall motion abnormalities^[2]. The functional MR after acute myocardial infarction is not related to left ventricle chamber size, ejection fraction, or regional wall motion abnormalities. Left ventricle sphericity is a primary determinant of the etiology of functional MR^[3]. The past decade has witnessed tremendous growth in the understanding of the mechanisms underlying acute infarction, accompanied by the development of chemical and mechanical techniques designed to

abort the process and lessen the extent of necrosis. It is possible that the same processes that lead to myocardial salvage during reperfusion may limit or reverse mitral valve incompetence^[4]. The coronary revascularization with percutaneous transluminal coronary angioplasty or coronary bypass grafting may be useful in restoring mitral valve competence, improving hemodynamics and increasing survival in patients with ischemic MR^[5].

We hypothesized that early improvement of MR after thrombolytic therapy for acute myocardial infarction predicts successful thrombolysis and better in-hospital outcome.

The aim of the study was to:

1. Investigate the relation between the early improvement of infarct-associated mitral valve regurgitation after thrombolytic therapy and the likelihood of successful reperfusion.
2. Study the association between the early

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improvement of infarct-associated mitral valve regurgitation after thrombolysis and the in-hospital course of the patient sample.

PATIENTS AND METHODS

Study patients:

One hundred and twenty-five patients with acute myocardial infarction associated MR were included in the study. All patients were admitted by their physicians to the coronary care unit in Farwania hospital. All patients were evaluated clinically by looking at history and doing a physical examination, 12-leads ECG, plain chest X-ray and routine laboratory investigations.

Exclusion criteria included patients with rheumatic heart disease, mitral valve prolapse, previous myocardial infarction, intraventricular conduction disturbances, atrial fibrillation, acute pulmonary edema, severe MR, patients with one of the following contraindications to thrombolytic therapy: history of bleeding diathesis, recent (< 6 months) cerebrovascular accident (CVA), active peptic disease, recent (< 6 weeks) surgery or trauma or severe hypertension (> 180 mmHg systolic or > 120 mmHg diastolic blood pressure). None of the patients had a revascularization procedure before the qualifying myocardial infarction.

Exclusion was based on: medical history, physical examination and 12-lead electrocardiogram.

Thrombolytic therapy:

Seventy-eight patients received i.v. streptokinase infusion (1.5 million U over 60 minutes) followed by i.v. heparin infusion. Patients with history of previous use of streptokinase were excluded. Forty-seven patients were treated with 100 mg of rt-PA administered i.v. over 90 minutes. Immediately before the initiation of rt-PA therapy, an i.v. bolus of 5000 IU of heparin was administered and followed by continuous infusion of 1000 IU/h for at least five days. Aspirin was given on admission to CCU and continued at a daily dose of 100 mg.

Cardiac enzymes:

Blood samples were obtained every eight hours during the 1st day and once daily from the second day for determination of total serum creatine kinase (CK), MB isoenzyme (CK-MB) fraction and troponin I.

Electrocardiogram:

Standard 12-lead ECG was recorded on admission to CCU and every three hours thereafter during the 1st 24 h after admission. Beyond the 1st 24 h, a 12-lead ECG was recorded daily throughout the hospital stay. All ECGs were recorded with identical (marked) positions of the chest leads.

Voltage criteria for diagnosis of AMI was the presence of new > 0.2 mV (> 2 mm) ST segment elevation in two or more ECG leads.

Transthoracic echocardiography:

Two-dimensional and M-mode echocardiography was performed for all patients of the study with the use of Toshiba Power Vision or GE vivid 7 and a 3.5 MHZ phased array transducer. The leading edge to leading edge convention was used. Left ventricular dimensions were measured at or immediately below the tips of mitral leaflets and averaged over five heart cycles. Left ventricular end-diastolic volume, end-systolic volume and ejection fraction were determined from apical two and four chamber views using Simpson's formula. Tracing of endocardial borders in end diastole and end-systole was performed in the technically best cardiac cycle. Left ventricular segmental wall motion score index was calculated by using a 16 segment model. Wall motion for each segment was graded as normokinesia = 1, hypokinesia = 2, akinesia = 3 and dyskinesia = 4. Wall motion score index was calculated by summing the scores for each segment and dividing by the number of analysed segments^[6].

Pulsed and color-coded Doppler was obtained from the standard apical four chamber view. The transducer was then manipulated to obtain the maximal flow velocity as assessed by the auditory and spectral outputs. The Doppler measurements were made during at least three cardiac cycles using the darkest part of the spectral recording and were then averaged. MR was considered present, if blue, green or mosaic signals were seen originating from the mitral valve and spreading into the left atrium during systole. For each patient the maximal area of the regurgitant jet and regurgitant jet area/left atrial area in all three planes (left parasternal long axis, apical four chamber and apical two chamber views) were measured.

Severity of MR was graded on the basis of the method described by Helmcke *et al*^[7], which correlates Doppler color flow findings with angiographic scoring. No regurgitation was classified as grade 0; a MR jet occupying 5 - 19%, 20 to 39% and \geq 40% of the left atrial area represented, respectively, mild (grade 1), moderate (grade 2) and severe (grade 3) MR.

The study subjects were divided into two groups:

Group I: included 75 patients with early improvement of infarct-associated MR (within 24 hours after thrombolysis).

Group II: included 50 patients without early improvement of infarct-associated MR.

Coronary angiography:

Coronary cine angiography was performed for all study patients either in Egypt, India, Syria or Kuwait. Coronary stenoses were quantified visually to detect the extent and severity of the coronary lesions and to detect the culprit lesion with residual coronary stenosis. The luminal narrowing of > 50% was considered a hemodynamically significant coronary artery lesion.

Infarct related artery flow was quantitated using the Thrombolysis in Myocardial Infarction (TIMI) flow grades: TIMI 0 (no perfusion) = no flow beyond the occlusion; TIMI 1 (penetration without perfusion) = slow and incomplete opacification of the vascular bed by contrast material; TIMI 2 (partial perfusion) = slow but complete opacification of the vascular bed by contrast material with slower clearance and TIMI 3 (complete perfusion) = prompt and complete opacification of the vascular bed by contrast material with rapid clearance as in an uninvolved artery^[8].

Statistical analysis:

Continuous variables are summarized as a mean \pm standard deviation (SD). Comparison between two groups was performed with t-test for continuous variables and chi-square test for categorical variables. A p-value < 0.05 was considered statistically significant and a p-value < 0.01 was considered statistically highly significant. A stepwise multivariate regression model was used to identify possible independent variables associated with early improvement of MR after thrombolysis of acute myocardial infarction. The strength of the association with early reversion of MR after thrombolysis was presented as 95% confidence intervals. Potential confounding of clinical variables was entered as independent variables.

The validity of early improvement of MR after acute myocardial infarction to detect successful thrombolysis was assessed by estimating the predictive indices and Kappa coefficient to determine the overall agreement with the data obtained from the coronary angiography.

Kappa coefficient value (k) = (Observed frequency of agreement - Expected frequency of agreement) / (Total observed - Expected frequency of agreement). Predictive indices such as true positive (TP), true negative (TN), false positive (FP), false negative (FN), sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated.

Receiver operating characteristic (ROC) curve (grade of sensitivity versus false positive) was used to identify the sensitivity and false positive of certain value of the variable with area under

curve and probability of error with sensitivity 100% to detect usefulness of early MR improvement after acute myocardial infarction for prediction of successful thrombolysis in patients with TIMI flow 2 & 3.

The agreement between the two observers was verified by using the method of Bland and Altman^[9]. Mean of the difference between two observers and SD were calculated to obtain limits of agreements. Upper limit of agreement = mean of difference + 2SD. Lower limit of agreement = mean - 2SD. For good agreement at least 95% of values must lie within the limits of agreement.

RESULTS

Clinical characteristics:

With regards to the age of the patients, there was no significant difference between both groups of the study (48.34 ± 6.29 versus 49.2 ± 4.13 years, respectively, $p < 0.13$). There was no significant difference between both groups as regards their gender [65 (86%) versus 41 (82%) males, ($p < 0.07$) and 10 (7%) versus 9 (5%) females, ($p < 0.11$) respectively]. There was no significant difference between both groups regarding the percentage of patients with history of smoking, hypertension, diabetes mellitus and hypercholesterolemia [48 (64%) versus 36 (72%) patients, ($p < 0.1$), 26 (34%) versus 21 (42%) patients, ($p < 0.08$), 24 (32%) versus 20 (40%) patients, ($p < 0.1$) and 16 (21%) versus 14 (28%) patients, ($p < 0.11$)] respectively. There was a significant increase in the heart rate on admission in patients from group II than those from group I (108.15 ± 6.63 versus 89.5 ± 7.92 beats/minute, $p < 0.05$) but there was no significant difference in the systolic and diastolic blood pressure between patients from both groups (134.8 ± 13.63 versus 125.22 ± 9.31 mmHg, $p < 0.09$ and 92.8 ± 6.30 versus 87.94 ± 8.14 mmHg, respectively, $p < 0.07$).

There was no significant difference between the patients of both groups with regards to the time between chest pain and the initiation of thrombolytic therapy in CCU (80.6 ± 15.3 versus 99.3 ± 17.4 minutes, $p < 0.06$). There was no significant difference between the patients from both groups who received either streptokinase or r-tPA with regards to the time between chest pain and the initiation of thrombolytic therapy (72.5 ± 12.3 versus 83.9 ± 14.3 minutes, $p < 0.07$).

Presenting ECG:

The ECG of all patients from both groups showed sinus rhythm without ectopics and intraventricular conduction defects. There was no significant difference between both groups as regards the electrical axis deviation, PR interval and heart rate corrected QT interval ($+36^\circ \pm 8.2^\circ$ versus $+46^\circ \pm$

Table 1: Coronary angiography in both groups of the study

Variables	Group I n (%)	Group II n (%)	p-Value
Culprit lesion of IRA:			
Proximal LAD	55 (73)	33 (67)	NS
Mid LAD	20 (27)	17 (33)	NS
Single vessel disease	46 (61)	30 (60)	NS
Two vessel disease	20 (27)	14 (28)	NS
Three vessel disease	9 (12)	6 (12)	NS
Residual coronary stenosis	60.9 ± 15.1	75.4 ± 12.2	<0.05
Coronary collaterals	45 (60)	17(33)	<0.01

IRA = infarct related artery, n = number of patients, NS = not significant

9.4°, $p = NS$, 144.1 ± 13.9 versus 139.4 ± 8.5 msec, $p = NS$, and 345.3 ± 13.8 versus 367.6 ± 11.4 msec, $p = NS$, respectively).

All patients presented with ST segment elevation > 2 mm in the chest leads from V3 to V6 or inferior leads. Five patients in group I versus seven patients in group II had ST segment elevation in V3 to V5. There were 27 patients in group I versus 20 patients in group II who had ST segment elevation in lead I, aVL, V5 and V6. There were 43 patients in group I versus 23 patients in group II who had ST segment elevation in inferior leads. There was a non-significant difference between both groups as regards ST segment elevation on admission (3.4 ± 1.1 versus 2.9 ± 1.4 mm, $p < 0.11$).

ECG after thrombolysis:

There was a non-significant difference between both groups as regards ST segment elevation after thrombolysis (1.3 ± 0.5 versus 1.6 ± 0.7 mm, $p < 0.10$). No significant change was noted as regards electrical axis deviation, QT interval, QT dispersion ECG before and ECG after thrombolysis between both groups. No patients had new left or right bundle branch block after thrombolysis in both groups. Only six patients in group I versus 11 patients in group II had persistent ST segment elevation > 2 mm at time of transfer to chest hospital for coronary angiography ($p < 0.13$).

Coronary angiography:

There was no significant difference in the number of the patients who had single vessel disease in the group I versus those of the group II [49 (61%) versus 30 (60%), $p < 0.07$]. As regards two and three vessel disease, there was no significant difference in the number of the patients in both groups ($p < 0.11$). There was significantly more residual coronary stenosis in the patients with early reversion of infarct-associated MR than those without early reversion of MR after thrombolysis (60.9 ± 13.7 % versus 75.4 ± 11.2 %, $p < 0.05$), but there was a

non-significant difference between both groups as regards the site of culprit lesion in LAD ($p < 0.06$). There were significantly more coronary collaterals in patients from group I compared with those of group II (45 (60%) versus 17 (33%), respectively, $p < 0.01$), Table 1). As regards the infarct related artery, there was no significant difference between both groups with reference to LAD (56% versus 49%, $p < 0.06$). There were significantly more patients in group II who had left circumflex coronary artery culprit lesion than the patients from group I (60% versus 27%, $p < 0.05$), but there were significantly more patients in group I who had right coronary artery culprit lesion than the patients in group II (73% versus 40%, $p < 0.05$), Fig. 1).

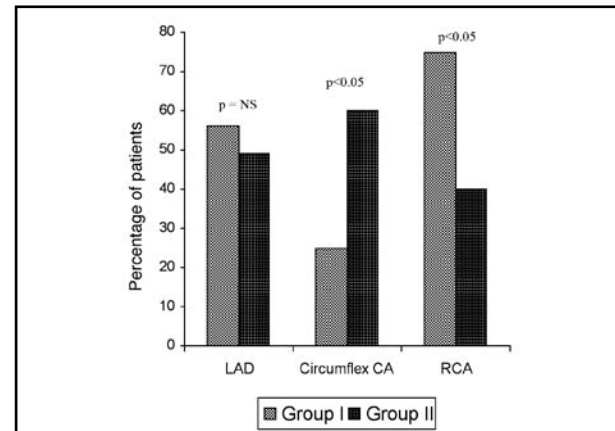


Fig. 1: Percentage of the patients with early improvement of MR after thrombolysis of acute myocardial infarction versus those without, as regards the infarct-related artery

In group I, 65 (86%) patients achieved TIMI 2-3 flow and 10 (14%) patients achieved TIMI 0-1 flow. In group II, 11 (22%) patients achieved TIMI 2-3 flow and 39 (78%) patients achieved TIMI 0-1 flow.

Echocardiography and Doppler study:

There was a non-significant difference with regards to the left ventricular end-systolic dimension and left ventricular ejection fraction in the patients of both groups (43.8 ± 5.2 versus 48.8 ± 4.6 mm, $p < 0.10$ and 54.3 ± 4.6 versus 50.7 ± 6.9 %, $p < 0.12$) respectively). There was a significant decrease in MR jet area / left atrial area ratio and left ventricle segmental wall motion score index in the patients of group I than those of group II (15.81 ± 5.92 versus 25.61 ± 4.73 and 1.32 ± 0.41 versus 1.91 ± 0.53 , respectively, $p < 0.05$, Table 2).

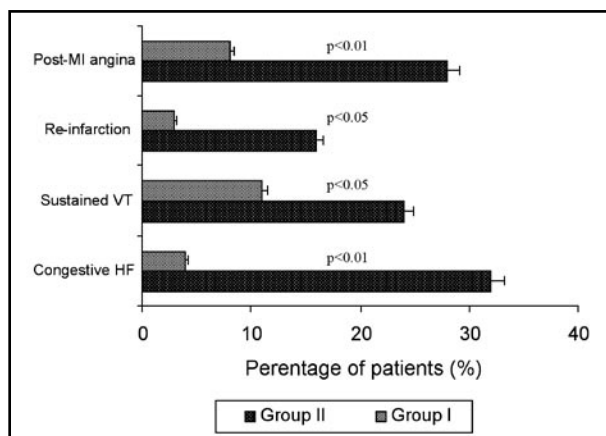
Grading of MR:

Out of 75 patients from group I, 58 patients presented with MR grade I which reverted to MR grade zero within 24 hours (reduction in MR jet area / left atrial area ratio by < 15%), and out of 17 patients presented with MR grade II, 14 patients had reversion of MR to grade I and only three

Table 2: Echocardiography and Doppler study in both groups on admission

Variables	Group I	Group II	p-Value
LV end-systolic dimension (mm)	43.8 ± 5.2	48.8 ± 4.6	NS
Left ventricular EF (%)	54.3 ± 4.6	50.7 ± 6.9	NS
LVSWM score index	1.32 ± 0.41	1.91 ± 0.53	< 0.05
Left atrium dimension (cm)	3.3 ± 0.4	3.9 ± 0.9	NS
MR jet area / LA area ratio (%)	15.81 ± 5.92	25.61 ± 4.73	< 0.05

EF = ejection fraction, LVSWM = left ventricle segmental wall motion, mm = millimeter, msec = millisecond, MR = mitral regurgitation

**Fig. 2:** In-hospital clinical outcome in both groups of the study

patients had a reversion of MR to grade zero within 24 hours (reduction in MR jet area / left atrial area ratio by > 15%).

On discharge, there were only 14 patients with MR grade I and three patients with MR grade II in group I, but in group II, there were 22 patients with MR grade II and 28 patients with MR grade I.

There were no patients in both groups who developed mechanical complications such as pericardial effusion, cardiac tamponade, ventricular septal defect, or intracardiac thrombus.

In-hospital outcome:

There was a significant decrease in the percentage of patients in group I who had post-MI angina, re-infarction, sustained ventricular tachycardia and congestive heart failure as compared with those from group II [6 (8%) versus 12 (28%), 2 (3%) versus 8 (6%), 8 (11%) versus 12 (24%) and 3 (4%) versus 16 (32%) respectively, $p < 0.05$, Fig. 2]. There was no patient in both groups who had hemorrhagic complications after thrombolytic therapy.

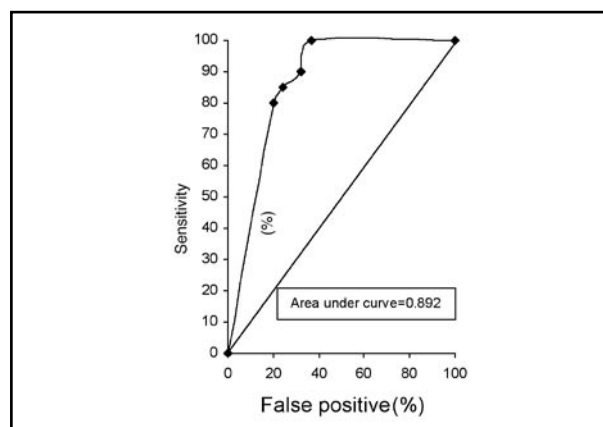
Forward stepwise logistic analysis:

Multivariate analysis revealed a significant relation between age of the patients ($R = 0.2134$ & 95% CI = 1.025 - 4.091, $p < 0.05$), residual coronary stenosis ($R = 0.3753$ & 95% CI = 1.511 - 3.091, $p < 0.05$), chest pain to thrombolytic therapy interval ($R = 0.4212$ and 95% CI = 1.390 - 2.118, $p < 0.05$) and

Table 3: Stepwise logistic multivariate analysis of patients with early improvement of infarct-associated MR versus those without as regards age, gender, ECG based site of infarction, residual coronary stenosis, chest pain to admission time, fibrin specific thrombolytic therapy and ACE inhibitors.

Variables	Coefficient	p-value	95% CI
Age	0.2134	< 0.05	1.025 - 3.191
Gender	0.0215	NS	0.221 - 1.407
Site of infarction (ECG-based)	0.1877	NS	0.325 - 1.421
Residual coronary stenosis	0.3753	< 0.05	1.511 - 3.091
Chest pain to thrombolytic therapy	0.4212	< 0.05	1.390 - 2.118
Fibrin specific thrombolysis	0.1711	NS	0.682 - 1.490
ACE inhibitors	0.1072	NS	0.399 - 1.260

ACE = angiotensin converting enzyme

**Fig. 3:** Receiver operating characteristic (ROC) curve data of early MR improvement after acute myocardial infarction for prediction of successful thrombolysis in the patients with TIMI flow grade 2-3. 100% sensitivity has a 37% error.

the early improvement of MR after thrombolytic therapy of acute myocardial infarction. However there was no significant relation with regards to gender, diabetes mellitus status, site of infarction (ECG based) and fibrin specific thrombolytic therapy (Table 3).

Agreement and reliability:

Table 4 shows that there was an agreement between TIMI flow and early improvement of MR after thrombolysis with Kappa coefficient = 0.625. The predictive indices showed that early improvement of infarct-associated MR after thrombolytic therapy is valid for prediction of patients with successful thrombolysis status as sensitivity was 86%, specificity = 79%, accuracy = 83%, positive predictive value = 63% and negative predictive value = 38%.

Receiver operating characteristic (ROC) curve:

ROC curve data of early improvement for prediction of successful thrombolysis in the patients with reduction of MR jet area / left atrium area

Table 4: Agreement of the coronary angiogram (TIMI flow) and the early improvement of infarct-associated MR as regards the prediction of successful thrombolysis

	Angio +ve	Angio -ve	Total
Early improvement of MR	65	10	75
No early improvement of MR	11	39	50
Total	76	49	125

Kappa Coefficient value (k) = 0.625; MR = mitral regurgitation

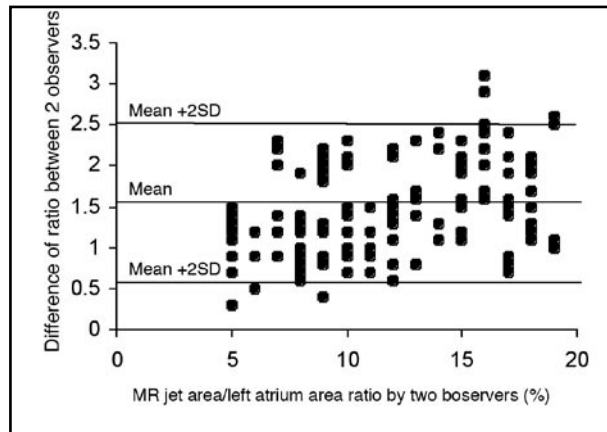


Fig. 4: Plot of the mean values obtained by two observers versus the difference of these values.

ratio, revealed that the sensitivity was 90%, false positive = 32% (specificity = 68%), in cases with 10% reduction in MR jet area / left atrium area ratio. The sensitivity was 80%, false positive = 20% (specificity=80%), in cases with 40% reduction in MR jet area / left atrium area ratio (Fig. 3).

Reproducibility:

There was no significant difference in inter-observer variability and intra-observer variability with regards to measurement of MR jet area / left atrium area ratio ($p < 0.08$, Table 5) and there was a good agreement between MR jet area / left atrium area ratio measurements by both observers as $> 95\%$ of the measurements were between the upper and lower limits of agreement (mean + 2SD & mean - 2SD, Fig. 4).

DISCUSSION

It is widely recognized that MR can develop during the course of acute myocardial infarction. The previously published frequency of this complication varies with the techniques used for detection but ranges from 10 to 55%^[10]. Lehmann *et al* reported a 13% prevalence of MR within the first seven hours of symptom onset^[11]. This valvular lesion was more common in patients with anterior infarction, but it did not correlate with peak creatine kinase levels or early ventricular dilation. Moreover, the early presence of MR was

Table 5: Intra-observer and inter-observer variability in measurement of MR jet area after acute myocardial infarction

	Intra-observer variability (1)	Inter-observer variability (2)	Variability
Absolute difference	1.4%	1.3%	1.5%
p-value	NS	NS	NS

the strongest predictor of cardiovascular mortality, with relative risks of 7.3 at 10 days (95% confidence interval (CI) 1.4 to 38.4) and 12.2 at one year (95% CI 3.5 to 42.0). It is logical to hope that timely restoration of valvular competence may improve this otherwise poor prognosis.

Optimal restoration of valvular function requires an understanding of the underlying pathogenesis. Unfortunately, the mechanisms involved in this complication appear to be multifactorial. At one extreme is frank papillary muscle rupture, leading to immediate hemodynamic compromise and often to a quick demise^[12]. At the other is a more subtle disruption of the complex architecture that comprises the valve and its supporting sub-valvular apparatus^[13]. Further, controversy exists as to whether mitral valve incompetence is largely a problem of restricted papillary muscle and leaflet motion, leading to incomplete valve closure, or to exaggerated leaflet movement beyond the line of closure, producing valve prolapse^[14].

The classic interventional approach to mitral valve dysfunction in this setting has been surgical replacement or repair, usually in conjunction with coronary artery bypass procedures. Uncontrolled series have suggested a survival benefit over that of medical treatment alone, although perioperative mortality can range up to 41%^[15]. Because of this high surgical risk, an effective alternative approach to restoring valve competency would clearly be preferable^[16].

In theory, re-establishing perfusion in the infarct related artery early in the course of an evolving myocardial infarction might restore the functional integrity of the mitral valve without surgery. Several investigators have reported anecdotal evidence that supports this this concept. Shawl *et al* were apparently able to reverse moderate and severe acute MR in five patients undergoing emergency coronary angioplasty during infarction, as evidenced by a significant improvement in pulmonary capillary wedge pressure after reperfusion. Follow-up contrast ventriculography at a mean of 35 months revealed no MR in three out of four patients tested^[17]. This same technique was successfully applied by Heuser *et al* to three patients with severe regurgitation, two of whom were in cardiogenic shock at the time of the procedure^[18].

The mean pulmonary wedge pressure decreased from 34 to 10 mmHg after successful coronary dilation in these three patients, with no clinical heart failure or auscultatory evidence of MR observed at one-year follow up. Hickey *et al* retrospectively reported on nine patients undergoing angioplasty within 24 h of the onset of infarction. Six of the nine patients experienced complete reversion of MR after successful reperfusion^[19].

Previous studies after reperfusion with thrombolytic therapy demonstrated a positive correlation between the severity of the residual lesion^[20] or the TIMI perfusion grade^[21] of the culprit vessel and the likelihood of recurrent angina or reinfarction, or both.

Our results showed a significant statistical difference in vessel patency after thrombolysis in patients with early reversion of infarct-associated MR than those without. Out of 125 patients with mild / moderate MR in our study, only 75 patients (60%) had an early reversion after successful thrombolytic therapy, and this is in agreement with the study of Tenenbaum *et al*^[22]. The effect of thrombolysis on the incidence and severity of MR is controversial. Although it was shown to improve contraction of the posterobasal segment and reduce the incidence of significant MR in patients with inferior myocardial infarction, it had no effect on restoring valvular competence in another study^[16].

The results of this study confirm those of the angiographic study by Lamas *et al*, which focused on the outcome of mild MR in a large group of patients^[13]. The presence of moderate and severe MR was shown to identify a high risk group of patients who often progress early to congestive heart failure and have more extensive coronary atherosclerosis.

Although early improvement of MR after acute myocardial infarction was associated in the present study with a significantly higher patency rate of the infarct related artery, absence of early reversion of infarct-associated MR did not exclude patency of the infarct related artery. However, even if reperfusion occurred among patients without early reversion, a more severe residual stenosis and lower TIMI perfusion grade might be anticipated with less myocardial salvage and with a higher incidence of in-hospital complications, especially reinfarction and congestive heart failure. Thus, early reversion of infarct-associated MR is not accounted for by any degree of reperfusion but requires for its occurrence adequate reperfusion, which results in significant myocardial perfusion and salvage. Therefore, patients without early reversion of infarct-associated MR must be monitored very carefully and designed for catheterization at any sign of recurrent ischemia^[23].

CONFOUNDERS

1. With regards to coronary collaterals, there was a significantly more increase in the number and percentage of the patients in group I compared with those of group II, and this may confound the results.

2. The reperfusion injury after the thrombolytic therapy in successful revascularization may also confound our results.

LIMITATIONS OF THE STUDY

1. Relatively small number of patients.
2. Patients with severe MR were not included in the study.
3. Coronary angiography was not performed early (within 90 minutes) after thrombolysis.
4. Myocardial contrast echocardiogram was not done as it detects myocardial blood flow and perfusion.
5. The study was not completely blind to observers.

CONCLUSION

We conclude that in spite of limitations and confounders of our study, early improvement of infarct-associated MR in patients with acute myocardial infarction treated with thrombolytic therapy suggests successful thrombolysis, better epicardial coronary artery perfusion grade and left ventricular function and a better in-hospital course.

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