

# Frequency of Ischemic Mitral Regurgitation after First-Time Acute Myocardial Infarction and its Relation to Infarct Location and In-Hospital Mortality

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Received 30 July 2013; Accepted 13 July 2014

## Abstract

**Background:** Ischemic mitral regurgitation (IMR) is a common complication after acute myocardial infarction (AMI). We aimed to investigate the frequency of IMR following first-time AMI and its association with infarct location, in-hospital mortality, and complications.

**Methods:** From September 2011 to November 2012, all patients with a diagnosis of first-time acute ST-elevation MI were enrolled in the study. Patients with previous MI and heart failure, organic mitral valve disorders, and previous mitral surgery were excluded from the study. The patients' baseline characteristic, echocardiographic parameters, and complications were recorded. The frequency of IMR after AMI and its relation to infarct location and in-hospital mortality were evaluated.

**Results:** Altogether, 250 patients (180 male) at a mean age of  $60.21 \pm 12.90$  years were studied. IMR was detected in 114 (45%) patients. There was no association between the presence of MR and gender, systemic hypertension, smoking, diabetes mellitus, or body mass index; however, serum LDL-cholesterol and triglyceride levels were significantly higher in the patients with IMR.

The most frequent territory of MI was anterior in the patients without MR, while the anterolateral territory was the most common one in the patients with IMR. The patients with IMR had more reduced left ventricular ejection fraction, more elevated left ventricular end-diastolic pressure, and higher pulmonary arterial pressure ( $p$  values  $< 0.001$ ,  $< 0.001$ , and  $< 0.001$ , respectively). Stage III diastolic dysfunction was more frequent in the patients with IMR. All the deaths occurred in the IMR patients, who also had more complicated AMI.

**Conclusion:** IMR following AMI is highly prevalent, and it complicates about half of the patients. Regarding its relation to the AMI complications, assessment of the MR severity is necessary to make an appropriate decision for treatment.

*J Teh Univ Heart Ctr 2014;9(4):160-165*

**This paper should be cited as:** Fazlinezhad A, Dorri M, Azari A, Bigdelu L. Frequency of Ischemic Mitral Regurgitation after First-Time Acute Myocardial Infarction and its Relation to Infarct Location and In-Hospital Mortality. *J Teh Univ Heart Ctr 2014;9(4):160-165.*

**Keywords:** Mitral valve insufficiency • Myocardial infarction • Hospital mortality • Prognosis • Echocardiography, Doppler

## Introduction

Ischemic mitral regurgitation (IMR) is one of the most

important coronary artery disease complications and, in particular, myocardial infarction (MI).<sup>1</sup> IMR can occur during acute or chronic MI, and it is defined as mitral

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regurgitation (MR) secondary to regional wall motion abnormality or papillary muscle dysfunction in the territory of significant coronary artery disease and structurally normal mitral valve leaflets and chordae tendineae. IMR is common during the acute and chronic phases of MI and appears to have an adverse prognostic effect.<sup>2</sup> The risk stratification of AMI patients during the early stage can identify high-risk patients, who require more advanced treatment and whose outcome can be improved through early intervention.

In the present study, we sought to investigate the frequency of IMR following AMI and its association with infarct location and in-hospital mortality.

## Methods

This study was conducted in a referral teaching hospital. All patients with a diagnosis of first-time acute ST-elevation MI, according to the American College of Cardiology criteria,<sup>3</sup> were enrolled in this prospective observational study, carried out from September 2011 to November 2012. The exclusion criteria included previous history of MI, heart failure, organic mitral valve disorders (rheumatic heart disease, chronic autoimmune disease, and mitral valve prolapse), and previous mitral surgery. The patients' demographic information, coronary artery risk factors, Killip class, MI territory with respect to electrocardiographic and echocardiographic changes, medical treatment/therapeutic modalities, myocardial complication, and in-hospital mortality were recorded. Coronary risk factors were defined as follows: 1) male gender; 2) diabetes mellitus (DM) (defined as symptoms of diabetes plus a random plasma glucose concentration > 200 mg/dL or prior diagnosis of DM before admission); 3) hyperlipidemia (total cholesterol level > 200 mg/dL or triglyceride level > 150 mg/dL within the first 24 hours from admission); 4) history of hypertension (systolic blood pressure of at least 140 mmHg or diastolic blood pressure of at least 90 mmHg within the first 24 hours from admission); and 5) history of smoking (defined as pipes, cigarettes, cigars, and tobacco use).

Echocardiograms were obtained using Philips Envicor-C with a 2.5-3.5 MHz probe by experienced echocardiologists within the first day of hospitalization. The sizes of the left ventricle and left atrium were measured in the parasternal view in M mode. The left ventricular ejection fraction was calculated in the parasternal view in M mode and in the apical two- and four-chamber views in two-dimensional mode using the Simpson rule. IMR was defined as MR in the presence of normal leaflet and chordal structures with one or more regional wall motion abnormality which had a significant coronary artery disease in a territory supplying the wall motion abnormality.<sup>4</sup> The MR grade was assessed using the proximal isovelocity surface area method, effective regurgitant orifice area, color Doppler flow mapping, jet

eccentricity, and integrating jet expansion within the left atrium (jet area to atrial area). The regurgitant volume, fraction, and orifice area were calculated via the volumetric or the proximal isovelocity surface area method.

MR was classified into one of the following five categories: no MR (including trace MR); mild ischemic MR; moderate ischemic MR; severe ischemic MR; and flail mitral valve. The left ventricular ejection fraction was classified as normal ( $\geq 55\%$ ), mildly reduced (45%-54%), moderately reduced (30%-44%), or severely reduced ( $< 30\%$ ).<sup>5</sup>

The left ventricular diastolic function was evaluated using the mitral inflow velocities (E, A) pattern, which usually can be defined as various stages of diastolic dysfunction. Myocardial relaxation by tissue Doppler imaging was also evaluated. Both of the above methods were employed for the grading of diastolic dysfunction. The ratio of transmitral Doppler early filling velocity to tissue Doppler early diastolic mitral annular velocity (E/ $\dot{e}$ ) was utilized to estimate the filling pressure. The pulmonary capillary wedge pressure will be  $\geq 20$  mmHg or more if the E/ $\dot{e}$  is  $\geq 15$  and will be normal if the E/ $\dot{e}$  is  $< 8$ . When the E/ $\dot{e}$  is  $\geq 8$  but  $< 15$ , pulmonary vein flow velocities and Valsalva maneuver were used to estimate the pulmonary capillary wedge pressure.<sup>6</sup> The systolic pulmonary arterial pressure (SPAP) was measured via echocardiographic parameters and divided into four groups: 1) normal if the SPAP was  $\leq 35$  mmHg; 2) mild pulmonary hypertension if the SPAP was 36-45 mmHg; 3) moderate pulmonary hypertension if the SPAP was 46-65 mmHg; and 4) severe pulmonary hypertension if the SPAP was  $> 65$  mmHg.

For the statistical analyses, the statistical software SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL) was used. All the data are presented as mean  $\pm$  standard deviation (SD) for the continuous variables. The baseline demographics and clinical characteristics were compared between the two groups using the independent samples t-test, Mann-Whitney U test, chi-squared test, and/or Fisher exact test, as appropriate. Bivariate correlations were assessed using the Pearson and Spearman correlation coefficients for the normally and non-normally distributed data, respectively. A p value  $< 0.05$  was considered significant for all the data analyses.

## Results

Altogether, 250 patients were enrolled in this study, and 72% of the patients were male. Echocardiography was performed during the hospital stay. There were no significant differences between the patients with IMR and those without MR regarding age ( $59.9 \pm 13.7$  years and  $60.77 \pm 12$  years, respectively; p value = 0.6). IMR was detected in 114 (45%) patients. There were 80 (70%) patients with mild, 18 (16%) with moderate, and 9 (8%) with severe MR. Flail mitral

valve was detected in 6 patients. Table 1 depicts the results of a comparison between the patients with IMR and those without MR as regards the frequency of the risk factors and baseline characteristics. The clinical characteristics indicate that the patients with any degree of MR had higher serum low density lipoprotein (LDL)-cholesterol and triglyceride levels (p value = 0.009 and p value = 0.000, respectively) and were more likely to present in a higher Killip class (p value = 0.000). No association was found between the presence of MR and gender, systemic hypertension, smoking, DM, or body mass index. The most frequent territory of MI was the anterior territory in the patients without MR (35.3% vs. 3.5% in those with IMR) and the anterolateral territory in those with IMR (64.0%) (Table 1).

The echocardiographic findings of the patients indicated that those with IMR had a lower ejection fraction, higher right ventricular systolic pressure, and higher left ventricular

end-diastolic pressure compared to their counterparts without MR (p value < 0.001) (Table 2).

The majority of the patients with IMR had a severely reduced left ventricular ejection fraction (41 vs. one with no MR; p value < 0.001). In contrast, most of the patients without MR had a normal left ventricular ejection fraction (63 vs. 3 with IMR; p value < 0.001). Stage I diastolic dysfunction was more frequent in the patients with no MR in contrast to those with IMR (89 vs. 31, respectively; p value < 0.001). Stage III diastolic dysfunction was more frequent in the patients with IMR in contrast to those with no MR (26 vs. one, respectively; p value < 0.001). In the no-MR group, SPAP was significantly lower than that in the IMR group (Table 2). The end-diastolic pressure was significantly different between the patients with IMR and those without MR (p value = 0.000), and the patients with IMR had a higher end-diastolic left ventricular pressure (Table 2). There

Table 1. Frequency of risk factors, baseline characteristics, and MI location in the patients with IMR and the patients with no MR\*

	IMR group (n=114)	No MR group (n=136)	P value
Gender (Male)	101 (74.3)	80 (70.2)	0.380
Hypertension	52 (38.2)	54 (47.4)	0.094
Smoking	96 (70.6)	30 (26.3)	0.481
LDL-C > 100 mg/mL	35 (25.7)	47 (41.2)	0.009
Diabetes mellitus	29 (21.3)	34 (29.8)	0.155
Hypertriglycerdemia	17 (12.5)	35 (30.7)	0.000
BMI (kg/m <sup>2</sup> )			0.455
< 25	10 (7.4)	13 (11.4)	
25-30	93 (68.4)	71 (62.3)	
> 30	33 (24.3)	30 (26.3)	
Killip class			< 0.001
I	67 (58.8)	133 (97.8)	
II	20 (17.5)	3 (2.2)	
III	22 (19.3)	0	
IV	5 (4.4)	0	
Myocardial infarction territory			< 0.001
Anterior	4 (3.5)	48 (35.3)	
Inferior	4 (3.5)	21 (15.4)	
Anterolateral	73 (64.0)	28 (20.6)	
Inferior + right	9 (7.9)	13 (9.6)	
Inferior + posterior	13 (11.4)	20 (14.7)	
Inferior + posterior + right	7 (6.1)	3 (2.2)	
Inferior + lateral	3 (2.6)	1 (0.7)	

\*Data are presented as n (%)

MI, Myocardial infarction; MR, Mitral regurgitation; IMR, Ischemic mitral regurgitation; BMI, Body mass index; LDL-C, Low-density lipoprotein cholesterol



Table 2. Echocardiographic parameters in the IMR group and the no-MR group\*

	(n=114) IMR group	(n=136) No MR group	P value*
LVEF (%)			< 0.001
> 55	13 (11.4)	63 (46.3)	
45-55	29 (25.4)	50 (36.7)	
35-44	31 (27.1)	22 (16.1)	
< 35	41 (35.9)	1 (0.7)	
End-diastolic pressure (mmHg)			0.000
< 10	36 (80.1)	101 (74.3)	
10-15	53 (46.5)	33 (24.3)	
> 15	25 (21.9)	2 (1.5)	
Pulmonary arterial pressure (mmHg)			0.000
< 35	46 (40.4)	109 (80.1)	
35-45	46 (40.4)	27 (19.9)	
46-64	21 (18.4)	0	
> 65	1 (0.9)	0	
Stage of diastolic dysfunction			< 0.001
Normal	0	10 (7.3)	
I	31 (27.1)	89 (65.4)	
II	57 (50.0)	36 (26.4)	
III	26 (22.8)	1 (0.7)	

\*Data are presented as n (%)

IMR, Ischemic mitral regurgitation; MR, Mitral regurgitation; LVEF, Left ventricular ejection fraction

Table 3. Frequency of electrical complications following myocardial infarction regarding the presence or absence of MR

	IMR group (n=114)	No MR group (n=136)	P value*
Electrical Complications			
Ventricular tachycardia	47 (41.2)	19 (14.0)	0.001
Ventricular fibrillation	33 (28.9)	5 (3.7)	0.001
Atrial fibrillation or SVT	11 (9.6)	6 (4.4)	0.087
Bundle branch block	11 (9.6)	1 (0.7)	0.001
Atrioventricular block	9 (7.9)	17 (12.5)	0.129
Mechanical complications			
Left ventricular aneurysm	2 (1.8)	1 (0.7)	0.652
Left ventricular clot	1 (0.9)	1 (0.7)	0.201
Ventricular septal rupture	4 (3.5)	0	0.028
Free wall rupture	5 (4.4)	0	0.014
Death during hospitalization	17 (14.9)	0	0.000

MR, Mitral regurgitation; IMR, Ischemic mitral regurgitation; SVT, Supraventricular tachycardia

were no significant differences between the two groups in terms of the MR severity (i.e. effective regurgitant orifice area) and the MI territory.

There were no statistically significant differences in the therapeutic methods between the IMR group and the no-MR group. The patients were treated medically and underwent thrombolytic therapy (mainly Streptokinase) or mechanical revascularization with percutaneous coronary intervention/coronary bypass grafting. No differences were noted for the treatment with beta blockers (p value = 0.45), statins (p value

= 0.45), angiotensin-converting enzyme inhibitors (p value = 0.96), diuretics (p value = 0.76), and Digoxin (p value = 0.89).

Most of the mechanical and electrical complications of AMI were significantly higher in the IMR group than in the no-MR group. These complications included ventricular tachycardia (p value < 0.001), ventricular fibrillation (p value < 0.001), bundle branch block (p value < 0.001), ventricular septal rupture (p value = 0.028), and free wall rupture (p value = 0.014) (Table 3). Compared to the no-MR group,

the patients with IMR had marked excess mortality rates ( $p$  value = 0.000).

## Discussion

We conducted this study to evaluate the incidence of IMR following AMI and its relation to the complications and mortality of AMI. IMR was found in 45% of our patients. Although there are still uncertainties concerning the exact prevalence of MR after MI, all the studies published to date suggest that MR following MI is common. In angiographic studies, the frequency of MR in the wake of MI varies from 1.6% to 19%.<sup>7</sup> The frequency tends to be higher in color Doppler echocardiographic series, where it ranges from 8% to 74%.<sup>8,9</sup> In addition to the impact of the technique used, these discrepancies are also related to the timing of the imaging. Indeed, while some studies have investigated MR a few hours after the onset of MI,<sup>9</sup> others have extended the time of diagnosis to days following the infarction.<sup>10</sup>

In our study, male was the dominant sex regarding frequency (72%). In the Carrabba et al. study,<sup>11</sup> 70% of the patients were male. Among the patients with ischemic MR, 80, 18, and 9 patients (70%, 16%, and 8%) had mild, moderate, and severe MR, respectively. Additionally, 6 (6%) patients had flail mitral valve. Aronson et al.,<sup>12</sup> using echocardiography in 1190 patients admitted for AMI, demonstrated that mild and moderate or severe ischemic MR was present in 39.7% and 6.3% of the patients, respectively. In contrast, in the Carraba et al.<sup>11</sup> study, MR was not detected by color Doppler echocardiography in 63 (34%) patients and mild MR was present in 83 (45%) patients. Moreover, moderate MR was present in 29 (16%) patients, and moderate-severe MR was detected in 9 (5%). We think that the differences between the groups regarding the IMR severity are related to different baseline characteristics, coronary artery risk factors, and time of performing echocardiography.

According to our study, the anterior and anterolateral walls were the most frequent territories of MI in the patients with no MR and those with IMR, respectively. In the Yosefy et al.<sup>13</sup> study, moderate to severe MR occurred in 9% of 234 patients with only anteroapical MI versus 17% of 242 with inferoapical extension ( $p$  value < 0.001).

The present study demonstrated that majority of the patients with no MR had a left ventricular ejection fraction > 55%. In contrast, most of the patients with IMR had a left ventricular ejection fraction < 35%. In the Aronson et al.<sup>12</sup> study, after adjusting for the ejection fraction and clinical variables (age, sex, Killip class, previous infarction, hypertension, DM, anterior infarction, and coronary revascularization), compared with the patients without MR, the hazard ratios for heart failure were 2.8 (95% confidence interval [CI], 1.8-4.2;  $p$  value < 001) and 3.6 (95% CI, 2.0-6.4;  $p$  value < 001) in the patients with mild and moderate or severe ischemic

MR, respectively.

In our study, the majority of the patients with no MR and IMR had grade I and grade III diastolic dysfunction, respectively, and the patients with IMR had a higher end-diastolic left ventricular pressure. In the Lamas et al.<sup>10</sup> study, the patients with IMR and those without MR had similar left ventricular filling pressures (left ventricular end-diastolic pressure,  $23 \pm 9$  vs.  $22 \pm 9$  mmHg;  $p$  value = 0.110). In our investigation, the patients with IMR had higher SPAP than those with no MR, and SPAP was related directly to the severity of MR.

Our results demonstrated that ventricular tachycardia, ventricular fibrillation, and bundle branch block were more frequent in the patients with IMR than in those with no MR.

In our study population, ventricular septal rupture and papillary muscle rupture were not detected in the patients without MR, but there were 4 patients with ventricular septal rupture and 5 patients with papillary muscle rupture in the IMR group.

Finally, the mortality rate was significantly higher in the IMR group than in the no-MR group.

We would think that the discrepancies between the results of our studies and those mentioned above stem from differences in study designs, inclusion criteria, and times of performing echocardiography.

## Conclusion

IMR following AMI is highly prevalent and complicates about half of the patients. Color Doppler echocardiography is the preferred initial modality to investigate this complication. Given the relation between IMR and the electrical and mechanical complications and mortality rates, well-informed decision-making to adopt an appropriate course of treatment requires a thorough assessment of the MR severity.

## Acknowledgements

We appreciate the suggestions on statistical analysis by Dr. Mohammad Taghi Shakery, Mashhad University of Medical Sciences. This manuscript is based on a dissertation for the degree of specialty in cardiology, and it was approved and supported by Mashhad University of Medical Sciences, Mashhad, Iran.

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