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Original Article

## Is female gender associated with worse outcome after ST elevation myocardial infarction?

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### ABSTRACT

**Objectives:** To investigate the impact of gender in outcomes of patients with ST segment myocardial infarction in a setting with limited access to primary percutaneous coronary intervention

**Methods:** In 1017 consecutive patients hospitalized with ST segment myocardial infarction during years 2008–2013, distribution of risk factors, therapeutic methods, heart failure and in-hospital mortality were compared between males and females. Association of gender and primary outcomes was determined after adjustment for confounding factors.

**Results:** Females were significantly older ( $66 \pm 12.1$  years vs.  $59.5 \pm 12.7$  years,  $p < 0.001$ ). Prevalence of hypertension, hyperlipidemia and diabetes was significantly higher in females (72.2% vs. 39%,  $p < 0.001$ , 36.1% vs. 20.3%,  $p < 0.001$ , 46.5% vs. 32.1%,  $p < 0.001$ , respectively). Presentation delay was similar in males and females. Females received reperfusion therapy more than males (63.2% vs. 55.8%,  $p = 0.032$ ). Development of heart failure and in-hospital mortality were significantly higher in females (36.5% vs. 27.2%,  $p = 0.003$  and 19.4% vs. 12.1%,  $p = 0.002$ , respectively).

However in multivariate analysis, female gender was not independently associated with increased rate of heart failure and in-hospital mortality

**Conclusion:** In a center with low rate of primary percutaneous coronary intervention, crude rates of heart failure and in-hospital mortality are higher in females; however, the association is lost after adjustment for baseline characteristics

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### 1. Introduction

ST segment elevation myocardial infarction (STEMI) remains the leading cause of morbidity and mortality worldwide despite widely use of evidence-based guidelines and novel reperfusion therapies.<sup>1</sup> Although males are generally at a greater risk for developing the disease, clinical complications and mortality of STEMI may be higher in females.<sup>2–5</sup> Whether biological characteristics or socioeconomic gender disparities lead to the different outcomes is a matter controversy.<sup>3,6–10</sup>

The rate of undergoing reperfusion therapies, which are one of the best therapeutic methods to improve the prognosis in STEMI, may vary between males and females. According to some studies, females are more likely to receive conservative therapy.<sup>8,11</sup> In line with this, the higher mortality rate of females after STEMI is

attributed to underutilization of standard treatments.<sup>11,12</sup> In contrary, similar rate of reperfusion therapies in males and females is also reported in literature.<sup>13,14</sup> Additionally, the trend of using treatment strategies may change over time.<sup>13</sup>

There is also a debate on the independent role of gender in clinical outcomes of patients with STEMI.<sup>3,9,15</sup> Although female gender was demonstrated as an independent risk factor for mortality after STEMI in some of the studies,<sup>7,9,15</sup> others have reported no independent impact of gender on clinical outcomes.<sup>2,3</sup> The fact that female patients are generally older with more concurrent diseases, higher mortality in females may result from other confounding factors, rather than gender itself.<sup>16,17</sup>

Considering the ambiguity of the evidence about the possible role of gender in clinical implications of the patients with STEMI, we designed this cohort study to investigate the potential differences in risk factor distribution, therapeutic approaches and clinical outcomes between males and females, treated for STEMI in our hospital. This study was took place in the main cardiovascular center of North-West of Iran, which is a middle-

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income country with low primary angioplasty rate at the time of present study. After adjusting for other co-morbidities, the association of gender with heart failure and in-hospital mortality was determined.

## 2. Methods and materials

### 2.1. Study sample

This is a retrospective registry based observational-analytical study of patients discharged from our cardiovascular hospital, the principal cardiac center in northwest of Iran, with a final diagnosis of STEMI during years 2008–2013. The study proposal was reviewed and approved by the Institutional Review Board at Tabriz University of Medical Sciences. The study was assigned proposal registration number 82/1231, and waiver of consent was granted due to its retrospective chart review design and absence of intervention. Extreme caution was taken to assure patient privacy during the whole study process. A total number of 1017 consecutive patients diagnosed with STEMI were included in the study. The mean age of study sample was  $61.41 \pm 12.93$  years. Among the study population, 729 out of 1017 patients (71.7%) were male and 288 out of 1017 patients (28.3%) were female.

### 2.2. Study variables

Complete demographic and serum biochemical data, coronary risk factors including history of hypertension, hyperlipidemia, diabetes, active smoking and family history of premature cardiovascular diseases, history of acute coronary syndrome, coronary artery bypass graft (CABG) surgery or percutaneous coronary intervention (PCI) and history of stroke were collected and entered into prepared questionnaires.

Based on first admission electrocardiogram (ECG) in the emergency department, the location of myocardial infarction was determined to confirm the registered data. Whether the patient received reperfusion therapy including intravenous fibrinolysis, primary PCI, rescue PCI or was managed conservatively was recorded. The rate of late in-hospital angioplasty during hospitalization was also investigated.

By evaluating all ECGs of the patients during hospitalization, development of arrhythmia and cardiac bundle branch blocks were all determined. Left ventricular ejection fraction (LVEF), presence of significant mitral regurgitation (MR) and any other post myocardial infarction cardiac abnormalities were recorded based on the reports of trans-thoracic echocardiographic examination performed after myocardial infarction.

Study primary endpoints, which were development of heart failure (HF) during hospitalization period and in-hospital mortality, were also documented for each patient.

STEMI was defined as documentation for the presence of cardiac chest pain lasting more than 30 min with ST elevation of more than 0.2 mV from the J point at least in two consecutive precordial leads or more than 0.1 mV in two limb leads on the admission ECG with an increase in cardiac enzymes. An increase of one point above the 99 percentile cut off point for MB isoenzyme of creatine kinase (CK-MB) and Cardiac-Troponin I (cTNI) was considered elevated cardiac enzymes.

### 2.3. Study design

Patients were allocated into two groups based on their gender. All recorded demographic data, risk factors, electrocardiographic disturbances, primary reperfusion therapy and clinical complications including emergence of heart failure and in-hospital mortality were compared between males and females. To

determine independent role of gender on study primary outcomes, adjustment for other confounding factors were performed.

### 2.4. Statistical analysis

The statistical analysis of the data was performed by statistical software SPSS (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago, United States). Continuous variables were presented as mean  $\pm$  standard deviation (SD). Categorical variables were stated as frequencies and percentages. Independent *t*-test or equivalent non-parametrical Mann-Whitney U-Test was used to compare continuous variables between two study groups. Fisher's exact test or Chi-square analysis was done as appropriate to compare the frequencies of the categorical variables.

Multivariate logistic regression analysis was performed to determine the independent role of gender on development of heart failure and in-hospital mortality after controlling for other confounding variables. Odds ratios with 95% confidence intervals for developing primary endpoints were stated for female gender. A *p*-value of less than 0.05 was considered statistically significant.

## 3. Results

### 3.1. Risk factors

Among 1017 patients, 729 (71.7%) were male and 288 (28.3%) were female. The mean age of females was significantly higher than males ( $66 \pm 12.1$  years vs.  $59.5 \pm 12.7$  years,  $p < 0.001$ ). Females had significantly higher prevalence of hyperlipidemia ( $p < 0.001$ ), hypertension ( $p < 0.001$ ) and diabetes ( $p < 0.001$ ). Active smoking was significantly less prevalent in females ( $p < 0.001$ ). Family history of premature cardiovascular diseases was similar in males and females. History of stroke and unstable angina were more common in females. The comprehensive data is presented in Table 1.

The mean hemoglobin level was significantly higher in males than females ( $14.54 \pm 3.96$  mg/dl vs.  $13.52 \pm 4.57$  mg/dl,  $p = 0.001$ ). Mean creatinine level was not significantly different between males and females ( $1.23 \pm 0.98$  mg/dl vs.  $1.21 \pm 1.05$  mg/dl,  $p = 0.7$ ).

### 3.2. Reperfusion therapy and pharmacologic treatments

In our study population, 589 out of 1017 patients (57.9%) treated with reperfusion therapy. Out of 1017 patients, only 51 (5.01%) had

**Table 1**  
Comparison of Demographic factors and Coronary Risk Factors in Males and Females.

	Total Patients N = 1017		P Value
	Male N = 729	Female N = 288	
Age	59.5 $\pm$ 12.7	66 $\pm$ 12.1	<0.001
Hyperlipidemia	148(20.3%)	104(36.1%)	<0.001
Hypertension	284(39.0%)	208(72.2%)	<0.001
Diabetes	234(32.1%)	134(46.5%)	<0.001
Smoker	277(38.0%)	23(8.0%)	<0.001
Family History	41(5.6%)	25(8.7%)	0.067
History of:			
CABG	16(2.2%)	3(1.0%)	0.221
Coronary Angioplasty	21(2.9%)	9(3.1%)	0.838
Stroke	22(3.0%)	19(6.6%)	0.015
Central Sleep Apnea	6(0.8%)	8(2.8%)	0.016
Unstable Angina	32(4.4%)	20(6.9%)	0.046
Myocardial Infarction	58(8.0%)	24(8.3%)	0.842

CABG; Coronary Artery Bypass Graft.

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