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In-Hospital Case Fatality Rate and Cox Proportional-Hazards Model for Risk Factors of Mortality Due to Myocardial Infarction in Iran's Hospitals: A National Study

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ABSTRACT

Background: To date, no hospital-based national study with large sample size has been conducted to determine the predictive factors of in-hospital mortality among patients with Myocardial Infarction (MI) in Iran.

Objectives: This study aimed to determine in-hospital Case Fatality Rate (CFR) and hazard ratio of the factors associated with mortality in the patients with MI diagnosis in Iran.

Patients and Methods: In this nationwide, hospital-based, prospective study, the researchers made use of the data of 20750 new MI cases registered by Iranian Myocardial Infarction Registry (IMIR) in 31 provinces between April 2012 and March 2013. Demographic, clinical, and laboratory variables were obtained from the medical records of patients with confirmed acute MI. Cox regression was done by Stata software, version 12 using univariate and multiple analyses through Breslow method. $P < 0.05$ was considered as statistically significant.

Results: In-hospital mortality rate was 12.1% (N = 2511) and female/male ratio of CFR was 1.36 (95% CI: 1.2 - 1.4). Besides, in-hospital CFR was 8.36: 7.81 - 8.94 in females and 6.12: 5.83 - 6.43 in males. Hazard ratio of mortality for ST segment Elevation Myocardial Infarction (STEMI), chest pain resistant to treatment, and Right Bundle Branch Block (RBBB) was 1.32, 4.06, and 2.45, respectively ($P < 0.01$). Using Percutaneous Coronary Intervention (PCI) decreased the risk of death in the patients (HR: 0.68). Overall, 83.7% of the patients with STEMI died.

Conclusions: In Iran, identifying the risk factors of mortality due to MI could contribute to detecting high-risk individuals and improving healthcare by relevant planning and interventions in clinics and communities.

►*Implication for health policy/practice/research/medical education:*
The findings of the present study could be conducive to planning in health systems as well as to monitoring and improving patients' care and treatment.

1. Background

Despite decrease in mortalities due to Myocardial Infarction (MI) in many countries, this disease is the leading cause of mortality in developing countries, including Iran (1, 2). MI is the most important and prevalent coronary heart disease. Coronary heart disease is the reason for one per six deaths in the United States (3). According to the report by Iran's Ministry of Health, Treatment, and Medical Education in 2011, the mortality rate due to MI was 103 per 100000 deaths (4). Additionally, mortality rate due to

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MI prior to arriving at hospitals is high and is estimated to be approximately 20% in Iran. In-hospital mortality rate due to MI varies between 7.7% and 19.2% worldwide. One-year mortality rate due to MI also varies from 23% to 25.3% (5, 6). Coronary heart disease is a multifactorial disorder for which more than 250 risk factors have been introduced so far (7-9). Aging, male gender, hypertension, diabetes, smoking, and dyslipidemia are considered as important risk factors for MI. Furthermore, in-hospital mortality rate is higher among women compared to men. Yet, controversial results have been obtained regarding the above-mentioned factors (10, 11). Identifying the predictive factors of mortality contributes greatly to decreasing the mortality rate in patients. Up to now, no hospital-based, national study with large sample size has been conducted to determine the predictive factors of in-hospital mortality in the patients with MI in Iran.

2. Objectives

This study aims to determine in-hospital Case Fatality Rate (CFR) and hazard ratio of the factors associated with mortality in the patients with MI diagnosis in Iran.

3. Patients and Methods

In this nationwide, hospital-based, prospective study, the researchers made use of the data of 20750 new MI cases registered by Iranian Myocardial Infarction Registry (IMIR) in 31 provinces between April 2012 and March 2013. IMIR collects the data from Cardiac Care Units (CCUs) of all the hospitals across the country (12). This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences. MI diagnosis was based on the definitions provided by World Health Organization (WHO), World Heart Federation, and International Classification of Diseases (codes I21, I22, I24.9, and I25) (13). The patients with no definite diagnosis of MI by a cardiologist were excluded from the study. The underlying and predictive data were gathered for demographic variables, such as age, gender, province of residence, and length of hospital stay, as well as the, risk factors and clinical and laboratory history, including type 2 diabetes, hypertension, smoking, history of heart disease, Coronary Artery Bypass Surgery Graft surgery (CABG), Percutaneous Coronary Intervention (PCI), dyslipidemia, ischemic pain pattern, place of MI, cardiac blocks, complications of MI, ventricular arrhythmias, and troponin. In-hospital mortality due to MI was set as the dependent variable. Duration of exposure to risk of in-hospital mortality was calculated using the date of hospitalization and the date of discharge or death. The variables with $P < 0.2$ were entered into multiple Cox regression model using univariate analysis through Breslow method. Then, the presuppositions were investigated and confirmed by Schoenfeld residuals (Phtest). All data analyses were performed using Stata software (Stata Corp. 2011. Stata Statistical Software: Release 12. College Station, TX: Stata Corp LP).

4. Results

In this study, follow-up was from definite diagnosis of MI to death. The prospective cohort of the patients was defined in view of the date of diagnosis, hospitalization, and discharge (recovery or in-hospital death due to MI). Overall, 20750 patients with MI at risk of in-hospital death with total hospitalization of 3724983 person-years were studied. Among these patients, 15033 (72.4%) were male and the rest were female. Mean age at MI incidence was significantly lower in males than in females ($P = 0.001$). Demographic variables and clinical risk factors of the deceased and survived patients have been presented in Tables 1 and 2. Accordingly, hypertension and diabetes were significantly more prevalent in the deceased patients compared to the survived ones. Besides, 83.7% of the patients with ST segment Elevation Myocardial Infarction (STEMI) died. The frequency of PCI use was higher in the survived patients than in the deceased ones. Furthermore, 37.15% of the survived patients and only 7.29% of the deceased ones had used thrombolytic therapy. In-hospital mortality rate was 12.1% (N = 2511). In addition, in-hospital fatality rate was 6.74 (95% CI: 6.48 - 7); 6.12 (95% CI: 5.83 - 6.43) in males and 8.36 (95% CI: 7.81 - 8.94) in females. Besides, female/male ratio of fatality was 1.36 (95% CI: 1.2 - 1.4). In-hospital fatality rate due to MI based on age and gender

Table 1. Demographic Characteristics and Medical History of the Study Population

Characteristics	Total	Survived	Deceased	P value
Age (year) [a]	61.2 ± 13.4	60.65 ± 13	65.2 ± 15.2	0.001
Hospital stay (day) [a]	6.5 ± 14.6	6.57 ± 14.6	6.43 ± 14.4	0.647
Gender [b]				
Male	15033 72.4%	13377 64.6%	1656 7.9%	0.001
Female	5717 27.6%	4862 23.4%	855 4.12%	0.001
Smoker [b]	5443 26.2%	4667 25.6%	776 30.9%	0.001
Hypertension [b]	7376 35.5%	6426 35.2%	950 37.8%	0.011
Diabetes mellitus [b]	4612 21.9%	22.2% 610	4002 24.3%	0.008
Hyperlipidemia [b]	3710 17.8%	3268 17.9%	442 17.6%	0.699

[a] Mean ± SD, [b] Frequency and percentage

Table 2. Clinical Characteristics of the Study Population

Characteristics	Total	Survived	Deceased	P value
VF	511	371	140	0.001
	2.5%	2%	5.5%	
VT	1198	934	264	0.001
	5.8%	5.1%	10.5%	
Lateral MI	990	817	173	0.001
	4.8%	3.94%	0.83%	
Anterior MI	4332	3765	567	0.025
	20.9%	18.14%	2.73%	
Inferior MI	7179	6354	825	0.05
	34.6%	30.62%	3.98%	
Posterior MI	853	744	109	0.536
	4.2%	3.59%	0.53%	
STEMI	15729	13626	2103	0.001
	75.8%	16.2%	83.7%	
Non-STEMI	5021	4613	408	0.001
	24.2%	25.2%	16.2%	
PCI	1431	1354	77	0.001
	6.9%	7.4%	3.07%	
CABG	539	469	70	0.523
	2.6%	2.5%	2.8%	
Lack of thrombolytic therapy	9222	7709	1513	0.001
	44.5%	37.15%	7.29%	
Chest pain	2229	1356	873	0.001
	10.7%	6.53%	4.21%	

Abbreviations: VF, ventricular fibrillation; VT, ventricular tachycardia; MI, myocardial infarction; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non ST-segment elevation myocardial infarction; PCI, percutaneous Coronary Intervention; CABG, coronary artery bypass grafting

has been shown in Table 3.

In univariate analysis, age, gender, education level, smoking, hypertension, type 2 diabetes, PCI, chest pain, heart failure, heart rupture, troponin, and laterality of MI were yielded as significant ($P < 0.03$) and were entered into the Cox regression model. The final model of death determinants in the patients has been presented in Table 4. In univariate analysis, the hazard ratio was 3.27 for STEMI. In multivariate analysis, however, the hazard ratio decreased to 2.88 in presence of other variables and after controlling the confounding variables.

5. Discussion

The present study was done based on the registered data of MI patients in Iran. This was the first national study investigating the predictive risk factors of in-hospital mortality in Iran. Based on the study findings, the most important risk factors of in-hospital mortality due to MI were age, female gender, education level, type 2 diabetes, smoking, PCI, Right Bundle Branch Block (RBBB), STEMI, Ventricular Tachycardia (VT), and lack of thrombolytic therapy. Up to now, no study has comprehensively examined the predictive factors of short-term survival after MI in Iran. Thus, it could be argued that this study is the first one in this field with a large sample size, based on the population of all provinces of Iran, and with definite diagnosis of MI based on WHO's criteria. The results of the present study showed that 72.4% of the patients were male and the rest were female, and male/female ratio was 2.69. In a study in France, 23.5% of the patients with MI were female and 76.5% were male. In that study, the patients' mean age was 62.6 years, which is similar to our study, and mortality rate was 9% in females and more than 4% in males. In addition, age at MI incidence was 8 years earlier in males, while the risk factors were more prevalent in females (14). In a study by Uchiyama in Japan, 78.5% of the patients were male (15), which is relatively similar to the gender ratio in our study.

According to the current study findings, men developed

Table 3. In-Hospital Mortality Rate with 95% Confidence Interval and Case Fatality Rate due to MI in Iran's Hospitals

Gender	Age Group	Number MI (CFR %)	IMR [a]: 95% CI
Female	< 65 years	2690(47)	6.49 : 5.79 - 7.28
	≥ 65 years	3027(53)	9.84 : 9.05 - 10.68
	Total females	5717(27.6)	8.36 : 7.81 – 8.94
Males	< 65 years	9814(65.3)	5.3 : 4.96 - 5.65
	≥ 65 years	5219(34.7)	7.5 : 7.02 – 8.1
	Total males	15033(72.4)	6.12: 5.83 - 6.43
Total		2511(12.1)	6.74: 6.48 - 7

[a] in 100 person years

Table 4. The Hazard Ratios of the Factors Associated with Mortality in Total Patients

Factor	Univariate Analysis		Multiple Cox Model	
	HR: 95% CI	P value	HR: 95% CI	P value
Age	1.32:1.26 - 1.37	0.001	1.31: 1.25 - 1.37	0.001
Female gender	1.38:1.27 - 1.5	0.001	1.22: 1.12 - 1.34	0.001
Education level				
Illiterate	1.41:1.18 - 1.67	0.001	1.27: 1.06 - 1.52	0.394
Primary	1.05:0.87 - 1.27	0.557	0.85: 0.70 - 1.03	0.093
Secondary	0.81:0.67 - 0.98	0.037	0.77: 0.63 - 0.93	0.012
Academic	Ref.	-	-	-
Diabetes mellitus	1.1: 1 - 1.2	0.039	1.06: 0.97 - 1.17	0.154
Smoker	1.31: 1.2 - 1.42	0.001	1.13: 1.04 - 1.23	0.004
VT	2.19: 1.93 - 2.49	0.001	1.82: 1.46 - 1.90	0.001
STEMI	3.27: 3.01 - 3.55	0.001	1.32: 1.18 - 1.48	0.001
RBBB	2.81: 2.23 - 3.55	0.001	2.45: 1.94 - 3.11	0.001
Chest Pain	4.68: 4.3 - 5.08	0.001	4.06: 3.73 - 4.43	0.001
Lack of TT	1.91: 1.77 - 2.07	0.001	1.57: 1.44 - 1.72	0.001
PCI	0.42: 0.34 - 0.53	0.001	0.68: 0.54 - 0.86	0.001

Abbreviations: EL, educational level; VT, ventricular tachycardia; STEMI, ST-segment elevation myocardial infarction; RBBB, right bundle branch block; TT, thrombolytic therapy; PCI, percutaneous coronary intervention

MI about 5.2 years earlier compared to women, which is in line with the results of some other studies conducted on the issue. However, mean age at in-hospital death was lower in our study than in Uchiyama's study. In that study, mean age at MI incidence was 67.9 years and mean age at death was 76.1 years (15).

In our study, the risk of in-hospital death due to MI was 1.2 times higher in women than in men, which is consistent with other studies. For instance, Randall reported that the risk of mortality was higher in women compared to men. In another study in Norway, mortality rate increased with age and in-hospital mortality rate was reported as 3.8%. Besides, mortality rate was higher in women (19%) than in men (13.9%) (16-18). In-hospital mortality and post-MI survival are highly associated with the disease severity. In addition, quality of healthcare and the type of treatments used by the patients contribute greatly to the patients' survival. The positive effects of thrombolytic drugs and PCI have been reported by different studies (19, 20). In the present study, the patients with no thrombolytic therapy were at a higher risk of death in comparison to those receiving PCI. Nevertheless, the frequency of PCI use seems to be lower in Iran compared to other countries. Infrequent use of this treatment and lower administration of thrombolytic drugs seem to explain the higher mortality rate in Iran. Smoking was another predictive factor of death in the patients in our study, which is consistent with the results of other studies. In addition, type of MI was an important determinant of death, which is in agreement with the previous researches conducted in this regard. In several studies, an association was reported between smoking and mortality due to MI. One study indicated that smoking decreased the risk of death in the patients (HR: 0.85; 95% CI: 0.76-0.95; P = 0.005). In that study, mortality rate was 5.4% in smokers and 9.9% in non-smokers. Besides, smoking was associated with a 48% decrease in the risk of mortality for all reasons within one year after acute MI (20). Our study was not consistent with the aforementioned one and showed that smoking increased the risk of death in the patients. On the other hand, it was in line with a study in Turkey reporting that smoking and diabetes increased the risk of death in the patients (21). Our study was also in agreement with a study in India reporting gender, ventricular fibrillation, and heart failure as mortality-associated factors in the patients and diabetes, hypertension, and smoking as the main risk factors in the patients with MI (22). Moreover, another study demonstrated that the used treatments, including CABG and PCI, decreased mortality in the patients with MI. In the study in India, 52.3%, 15.3%, and 7.5% of the patients used thrombolytic therapy, PCI, and CABG, respectively. Nonetheless, these treatments are used less frequently in Iran. Other studies also indicated that the rate of mortality was higher in the patients not receiving the above-mentioned treatments.

In the present study, illiteracy was another risk factor of death in the patients, which is in agreement with other works (22-24).

5.1. Conclusion

Our study reported in-hospital fatality rate with hazard ratios in the patients with MI across Iran. The results indicated that female gender, smoking, low education level, illiteracy, type 2 diabetes, VT, STEMI, RBBB, lack of thrombolytic therapy and angioplasty (PCI), and chest pain resistant to treatment were the most important determinants of death due to MI in Iran. The findings of the present study could be conducive to planning in the health system as well as to monitoring and improving patients' care and treatment (25-27).

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Authors' Contribution

Study concept and design: Ahmadi, Soori and Khaledifar.

Acquisition of data: Ahmadi. Analysis and Interpretation of data: Ahmadi, Soori and Khaledifar. Critical revision of the manuscript for important intellectual content: Ahmadi, Soori and Khaledifar. Drafting of the manuscript: Ahmadi, Soori and Khaledifar. Administrative, technical, and material support: Khaledifar and Ahmadi.

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There is no financial disclosure.

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