DOI: https://dx.doi.org/10.48305/arya.2024.42893.2985

In-hospital mortality of acute ST-elevation myocardial infarction (STEMI) and its predictors-using Yazd Cardiovascular Diseases Registry, YCDR

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Original Article

Abstract

BACKGROUND: The purpose of this study was estimate and identify in hospital mortality predictors factors for patients with acute ST elevation myocardial infarction (STEMI).

METHODS: This study is a retrospective cohort study based on data from the Yazd Cardiovascular Diseases Registry (YCDR) from 2015-2018 in Yazd Province, Iran, focusing on hospitalized patients with ST-elevation myocardial infarction (STEMI). The primary outcome was in-hospital mortality in STEMI patients. A total of 1861 patients with STEMI were analyzed. Multivariable logistic regression was used to determine death predictive factors for in-hospital mortality in STEMI patients. The significance level of the model was considered to be 5% and the software was used for analysis.

RESULTS: The study included 1,861 patients with STEMI. Among them, 103 (5.5%) individuals died during admission the hospital. After multivariable logistic regression, the following variables were identified as death predictive factors for in-hospital mortality of STEMI: having a history of CVA (OR: 5.6, 95% CI: 2.2-20.3), killip class IV (OR: 6.4, 95%CI: 1.5-11.2), lower ejection fraction (OR: 3.6, 95% CI: 1.2-9.8), lower HDL cholesterol (OR: 1.2, 95% CI: 1.01-2.3), and lower hemoglobin (OR: 1.4, 95% CI: 1.3-2.9).

CONCLUSION: This study found that lower ejection fraction, lower hemoglobin levels, Killip class IV, having a history of CVA, and low HDL cholesterol levels are important death predictive factors for hospital mortality in patients with STEMI. Health policy in STEMI management must consider these factors to improve hospital prognosis.

Keywords: STEMI, Acute Myocardial Infarction, Ischemia, Prognostic Factors

Date of submission: *2024-08-04*, ***Date of acceptance:*** *2024-10-09*

Introduction

Although the age-adjusted mortality rate due to chronic diseases has decreased in several developed countries in recent years, the rate of cardiovascular diseases has significantly increased in low- and middle-income countries[1-3]. One of the consequences of coronary heart disease (CAD) is a heart attack, which can sometimes result in death. The third global definition of a heart attack, which is considered the most up-to-date definition, describes the classification based on etiology. The classification definition based on the cause of myocardial infarction is as follows: Type 1 refers to cases that occur due to plaque rupture or erosion or atherothrombotic consequences, while

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Type 2 refers to cases that occur due to an imbalance of myocardial oxygen demand in the absence of atherothrombosis[4,5]. In recent years, there has been a decrease in mortality caused by cardiovascular diseases in North America, Western Europe, and Japan. The highest increase in mortality due to heart diseases was observed in countries located in South Asia and then East Asia. Additionally, countries like South Latin America and Australia have not shown any change in their mortality trends between 1990 and 2013. Every year, approximately 1 million people experience this event, and 33% of them die as a result of this complication[6].

In Iran, as well as in most West Asian countries, cardiovascular diseases are the leading cause of death. Approximately 46% of mortality in Iran is attributed to cardiovascular diseases[7]. The potential to reduce the mortality rate of acute myocardial infarction and other heart diseases lies in a combination of environmental changes, health promotion, and improvement of clinical care[8]. Research findings suggest that much of the mortality from cardiovascular diseases, which is most common in the early stages of the disease, can be prevented through individual interventions targeting high-risk populations. By creating models to identify and predict individuals at high risk for these diseases, timely and effective therapeutic interventions can significantly reduce mortality rates[9].

Most studies that have predicted mortality in individuals who have had a heart attack are from a decade ago when fibrinolysis was the primary treatment, and there was no information about new treatments such as PCI[10]. Information on the trend of hospital death rates is necessary to evaluate therapeutic interventions and prevention, but it is currently unavailable. Thus far, information on ischemic heart diseases has been calculated based on the death registration system. This method has presented challenges and inaccuracies, as it does not provide information on the hospitalization of patients. Therefore, having accurate and reliable statistics is crucial for understanding the significant health issues in the province of Yazd and developing policies to improve heart health. This study aims to identify death predictive factors related to patients with acute myocardial infarction using data from the Yazd Cardiovascular Diseases Registry (YCDR) in Yazd province. The results of this study will be utilized by healthcare professionals and cardiologists to identify high-risk patients and provide them with specialized care.

Methods

Study design

The present study utilized data from the Yazd Cardiovascular Diseases Registry (YCDR), which is a prospective cohort. Since 2015, the registry project for ischemic heart patients in Yazd province has been collecting comprehensive information on admitted patients with ischemic heart problems. Considering that hospital death risk assessment is helpful in choosing the type of treatment and patient management, and similar systems in the world help doctors in making diagnostic and treatment decisions, we also wanted to implement a native system for hospitals in Iran.

In this center, a committee has been responsible for quality control of the collected data. Also, the entire process of data collection has been carried out based on the designed guidelines. In addition, the researchers performed quality control of the data before the analysis stage. This data didn't contain preadmission mortalities. To collect data, the researchers used the acute myocardial infarction registry form, following the implementation protocol of the YCDR project. This form includes demographic information, previous disease history, drug history, risk factors (such as hypertension, diabetes, smoking and hookah smoking, hypercholesterolemia, and family history of cardiovascular disease), revascularization treatment, biochemical tests, medications administered within the first 24 hours, symptoms, echocardiography results, initial electrocardiogram findings, angiography during hospitalization, complications during hospitalization, and treatment outcomes at discharge. The patient's information is recorded during three evaluations conducted throughout their hospital stay. The outcome measured in this study was in-hospital mortality in patients with acute myocardial infarction (STEMI).

STEMI

Acute coronary syndromes lead to myocyte injury and subsequent death. In the clinical setting, their classification is based on electrocardiographic presentation; ST-segment elevation myocardial infarction (STEMI; ≥2 mm ST segment elevation

and prominent T waves on the electrocardiogram)[11].

Sample size

1,861 STEMI patients were included in the research from 2015-2018. The study focused on patients admitted with acute myocardial infarction in Yazd province.

Inclusion & exclusion criteria

The inclusion criteria in the YCDR was the diagnosis of MI, but in the present study, the inclusion criteria was the diagnosis of STEMI in teaching hospitals of Yazd province. Exclusion criteria included patients discharged to institutionalized care and co-existing terminal illness with palliative care for cancer, neurological illness (severe dementia, motor neuron disease, multiple sclerosis, Parkinson's disease). Other exclusion criteria were out-of-hospital death or death from other causes.

Statistical analysis

Descriptive analysis was performed using SPSS ver. 26. Logistic regression analysis was used for statistical analysis. All variables were included in the regression model simultaneously, and any variables that were not significant in the univariable analysis (P value >0.10)[12] were discarded. The remaining variables were then entered into multivariable analysis using the backward elimination method. Variables with a P value < 0.05 were retained in the model, while other variables were excluded.

Ethical Considerations

The current study received approval from the ethics committee of Yazd University of Medical Sciences, with the code IR.SSU.SPH.REC.1400.184. (This study was carried out as a sub-study of the main study of registering cardiovascular diseases leading to hospitalization in Yazd province, and after the implementation of this main study, the current research was carried out using its data. Therefore, in order to use patient data, it was necessary to obtain a new code of ethics.)

YCDR also obtained informed consent from the participants or their legal guardians to enter the study. All provisions of the Declaration of Helsinki were adhered to in this study, especially appropriate ethical and scientific review.

Results

In this study, data was collected on 3,247 patients who had an acute myocardial infarction, also known as a heart attack. Among these patients, 1,861 were diagnosed with STEMI. Of the total 1,861 patients with STEMI, 103 died and 1,758 patients were alive during hospitalization.

One of the findings was that mortality is higher in men than in women (P-value = 0.04). Looking at Table 1, it can be seen that the highest occurrence of heart attacks in the surviving group happened during the seasons of spring, autumn, winter, and summer, respectively. In contrast, for the deceased group, the highest occurrence was during autumn, spring, summer, and winter, respectively. The difference between the two groups is statistically significant (P-value < 0.001).

Furthermore, it has been observed that for the deceased group, the highest occurrence was during spring, autumn, summer, and winter, respectively. The difference between the two groups was not statistically significant, and in the surviving group, the highest occurrence was during autumn, spring, winter, and summer, respectively (P-value > 0.05).

It has been found that individuals with high Killip IV at arrival to the hospital had higher mortality compared to other patients (P-value < 0.001).

Overall, this study provides valuable insights into cardiovascular disease and its impact on patients with acute myocardial infarction.

According to Table 1, the average age was significantly higher in the deceased group compared to the alive group (75.7 vs 64.4) (P-value < 0.001). Moreover, the prevalence of CABG history, CVA history, alcohol use, diabetes mellitus history, and the average levels of blood sugar, hemoglobin, cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), creatine phosphokinase maximum (CPKMax), and MBpick (Isoform MB as cardiac specialized CPK) were higher in the deceased group compared to the surviving group, but the difference was not significant (Table 1).

According to the information provided in Table 2, the univariable logistic regression analysis showed that certain variables were significant in relation to cardiovascular disease. These variables include marital status (divorced/widowed), gender (male), smoking (quit smoking), CVA history, family history of MI, left

Table 1. Baseline characteristics of qualitative variables of patients with acute myocardial infarction (STEMI) in Yazd province from 2016 to 2018

Variables	Dead(N=103)	Alive(N=1758)	P-value
Age	75.7±12.0	64.4±13.6	0.001
Sex			
Male	54(52.4)	1364(78.1)	
Female	49(47.6)	384(21.9)	0.04
BMI	25.9±3.8	28.2±13.7	0.70
Height	159.8±8.4	164.8±12.2	0.14
Weight	66.9±14.5	73.91±13.2	0.86
Marital Status			
Single	2(1.9)	8(0.5)	
Married	88(85.4)	1636(94.3)	
Widowed/Divorced	13(12.6)	90(5.2)	0.62
Job			
Office job	6(5.8)	350(19.9)	
Not office job	1(1.0)	62(3.5)	0.15
Driver	1(1.0)	118(6.7)	
Unemployed/Retired/Housewife	95(92.2)	1228(69.9)	
Admission by season			
Spring	548(31.8)	29(29)	
Summer	398(23.1)	17(17)	
Autumn	420(24.4)	33(33)	
Winter	356(20.7)	21(21)	0.2
Blood Sugar (Mg/dl)	220.9±88.2	176.7±45.1	0.44
Hemoglobin (Mg/dl)	12.8±1.8	13.5±2.1	0.35
Cholesterol (Mg/dl)	169.3±35.2	167.8±31.2	0.92
HDL (Mg/dl)	43.8±4.3	41.0±8.4	0.69
LDL (Mg/dl)	111.3±30.2	103.5±20. 2	0.88
CPKMax	922.05±100.0	513.5±99.1	0.09
MBpick	111.0±40.1	57.1±9.6	0.12
CABG history	5(5.3)	78(4.5)	0.61
PCI history	4(4.7)	191(11.3)	0.36
CVA history	5(5.5)	28(1.6)	0.06
Other MI history	2(2.5)	191(11.9)	0.16
Smoking			
Yes	13(12.9)	535(30.6)	
Quit	6(5.9)	135(7.97)	0.40
Alcohol Use	1(1.0)	3(0.2)	0.92
Hookah history	1(1.0)	42(2.4)	0.62
Opium history	10(10.0)	375(21.5)	0.22
Diabetes Mellitus history	41(42.7)	520(30.5)	0.55
Family history (MI)	5(20.0)	453(36.3)	0.09
Killip Classification			
Killip I	14(45.3)	1196(93.2)	
Killip II	4(13.1)	33(2.6)	0.001
Killip III	3(14.6)	23(1.8)	
Killip IV	4(21.2)	6(0.5)	
Hypertension	17(70.8)	794(63.0)	0.28

*Independent T- test, **Chi-Square test, P<0.05, Abbreviation: HDL; High-Density Lipoprotein, LDL; Low-Density Lipoproteins

ventricular ejection fraction (LVEF), hypertension history, illness severity at arrival to the hospital (Killip class II, III, IV), syncope, dyspnea, blood sugar, hemoglobin, HDL, and creatinine (P-value > 0.10). In the final model, which included demographic, clinical, and laboratory variables, a multivariate logistic regression analysis was conducted to control for confounders. The analysis identified several influencing factors in the mortality of patients with acute myocardial infarction. These factors include having a history of CVA (OR: 5.6, 95% CI: 2.2-20.3), Killip class (III: OR: 3.32, 95% CI: 0.5-11.2; OR: 6.4, 95% CI: 1.5-11.2), lower ejection fraction (OR: 3.6, 95% CI: 1.2-9.8), lower HDL cholesterol (OR: 0.83, 95% CI: 0.6-0.9), and lower hemoglobin (OR: 0.72, 95% CI: 0.4-0.9) (Table 3).

Table 2. Death predictive factors (demographic, clinical and laboratory) for myocardial infarction (STEMI)-Logistic Regression-univariable

Variable name	Category	Crude OR	P_value
Job status	Office	Reference	
	Not office	1.90	0.65
	Driver	2.51	0.51
	Unemployed/Retired/Housewife	1.81	0.59
Marital Status	Single	Reference	
	Married	0.66	0.21
	Widowed/Married	0.48	*0.02
Sex	Female	Reference	
	Male	0.34	*<0.001
Smoking	No	Reference	
	Quit	3.13	*<0.001
	Yes	1.82	0.23
Opium history	No	Reference	
	Yes	1.79	0. 21
Hookah history	No	Reference	
	Yes	0.41	0.38
Alcohol	No	Reference	
	Yes	5.94	0.12
Ejection Fraction	>40	Reference	
	<40	6.62	*<0.001
CVA history	No	Reference	
	Yes	3.55	* 0.01
CABG history	No	Reference	
	Yes	1.18	0.72
Family history of MI	No	Reference	
	Yes	0.35	*<0.001
Hypertension history	No	Reference	
	Yes	1.54	*0.04
Other MI history	No	Reference	
	Yes	0.19	*0.02
Killip Classification	I	Reference	
	II	10.5	*<0.001
	III	11.3	*<0.001
	IV	15.5	*<0.001
Syncope	No	Reference	
	Yes	6.40	*<0.001
Sweating	No	Reference	
	Yes	1.12	0.66
Dyspnea	No	Reference	
	Yes	2.72	*<0.001
Blood sugar		1.06	*<0.001
Hemoglobin		0.78	*<0.001
Cholesterol		1.03	0.83
LDL cholesterol		1.02	0.25
HDL cholesterol		0.90	0.00
Creatinine		1.48	0.00
CPKMax		1.00	0.33
MBpick		1.02	0.56
***P<0.1**			

Discussion

This study was conducted with the aim of estimating and identifying the predictive factors for in-hospital mortality in patients with acute myocardial infarction, as well as the related factors using registry data of ischemic heart patients in Yazd province. The multivariable logistic model, which included demographic and clinical variables,

Table 3. Death predictive factors (demographic, clinical and laboratory) for myocardial infarction (STEMI)-Logistic Regression- multivariable

Variable name	Category	Adjusted OR	P_value
Job status	Office	Reference	
	Not office		
	Driver	-	-
	Unemployed/Retired/Housewife	-	-
Marital Status	Single	Reference	
	Married	0.72(0.4-1.9)	0.22
	Widowed/Married	0.32(0.2-1.6)	0.25
Sex	Female	Reference	
	Male	0.38(0.1-1.8)	0.55
Smoking	No	Reference	
	Quit	2.32(0.8-3.8)	0.45
	Yes	1.30(0.9-3.5)	0.30
Opium history	No	Reference	
	Yes	-	-
Hookah history	No	Reference	
	Yes	-	-
Alcohol	No	Reference	
	Yes	-	-
Ejection Fraction	>40	Reference	
	<40	3.61(1.2-9.8)	*0.04
CVA history	No	Reference	
	Yes	5.6(2.2-20.3)	*<0.001
CABG history	No	Reference	
	Yes	0.98(0.5-2.2)	0.55
Family history of MI	No	Reference	
	Yes	0.35(0.15-1.9)	0.26
Hypertension history	No	Reference	
	Yes	1.50(0.8-2.9)	0.80
Other MI history	No	Reference	
	Yes	0.13(0.1-1.8)	0.15
Killip Classification	I	Reference	
	II	2.96(0.31-27.9)	0.34
	III	3.32(0.5-11.2)	0.07
	IV	6.42(1.5-11.2)	*0.03
Syncope	No	Reference	
	Yes	1.10(0.7-4.1)	0.51
Sweating	No	Reference	
	Yes	-	-
Dyspnea	No	Reference	
	Yes	1.50(0.8-3.3)	0.44
Blood sugar		1.05(0.9-2.5)	0.08
Hemoglobin		0.72(0.4-0.9)	*0.03
Cholesterol		-	-
LDL cholesterol		-	-
HDL cholesterol		0.83(0.6-0.9)	0.05
Creatinine		1.19(0.8-2.8)	0.22
CPKMax		-	-
MBpick		-	-

***P<0.05**

revealed a significant association between illness severity, ejection fraction, marital status (married), family history, and dyspnea with STEMI mortality. Additionally, the model involving laboratory variables showed a significant association between fasting blood sugar, hemoglobin, and HDL level with STEMI mortality. However, in the final model that combined these variables, the adjusted odds

ratios of illness severity, dyspnea, and fasting blood sugar changed to insignificance.

Combining clinical and laboratory variables emphasizes the necessity to examine both demographic and clinical factors, as well as lab measurements, when studying patients with myocardial infarction (MI). Additionally, clinicians should consider the complex interaction between clinical variables and laboratory variables. While individual factors may show significant associations with MI mortality, the significance changes when considering all variables together.

Findings showed that the odds of mortality in patients with an EF less than 40 were 3.6 times higher than in patients with an ejection fraction greater than 40. Most of the previous studies determined the association between LVEF and mortality in patients with MI (myocardial infarction) and HF (heart failure). Most studies reported an increase in the odds of mortality with lower LVEF/EF scores or categories[13-19]. However, the study by Toma et al. reported a U-shaped association between LVEF and mortality of HF[20], and Solomon et al. reported that LVEF is an independent predictor of CV mortality even in patients with adequate treatment[21], which is consistent with findings. The compensatory response of the heart after a myocardial infarction (MI), with an elevated ejection fraction (EF), can contribute to ventricular remodeling. This can lead to weakening of the heart and, ultimately, heart failure, which further increases the risk of mortality[22, 23]. Although a high EF initially suggests preserved or enhanced cardiac pumping function, it can also coexist with diastolic dysfunction. This reduces the heart's ability to efficiently fill with blood during relaxation[24, 25]. Additionally, comorbidities such as hypertension, diabetes, or other underlying health conditions, which are common in MI patients, can worsen the adverse cardiovascular outcomes associated with a high EF[26].

Findings showed that the odds of mortality increased by 1.03 times with each unit decrease in HDL cholesterol level. Previous studies have also reported that HDL is a predictor of CHD diseases[27, 28]. Additionally, the study by Barter et al. showed that the severity of CVDs was higher in patients with low HDL levels, even when their LDL levels were low[29]. However, the study by Angeloni et al. reported that high HDL levels have no association with vascular events in CAD patients[30].

HDL's influence on MI mortality may result from reversing macrophage cholesterol transport[31]. Additionally, HDL may promote endothelial balance by increasing nitric oxide production and inhibiting pathways linked to vascular inflammation and endothelial cell apoptosis[32]. Moreover, low HDL levels may worsen heart muscle damage and severity, potentially leading to prolonged recovery and an increased risk of mortality in patients with MI[33].

This study also demonstrated that the odds of mortality decreased by 22% or 0.78 times with an increase in hemoglobin levels. This finding is consistent with previous studies that have shown an association between anemia and 1-year mortality in patients hospitalized for AMI[34-36]. Some studies have also shown an increase in the odds of cardiovascular mortality after 21 months[37], as well as all-cause mortality after 6 years of follow-up[38]. However, Reinecke et al. reported no association between hemoglobin concentration and mortality in patients following elective percutaneous coronary intervention[39].

Previous systematic reviews have reported a pooled prevalence of moderate-to-severe anemia of 21% in patients with cardiovascular diseases[40]. Therefore, it is crucial to pay attention to this variable in patients with myocardial infarction (MI). An important factor that contributes to increased mortality in anemic patients is their vulnerability to bleeding after cardiac events and revascularization procedures, which can have a long-term impact on their risk of mortality[41]. Additionally, cardiovascular diseases may decrease the heart's ability to tolerate low hemoglobin levels[42], and anemia-induced hypoxia may increase sympathetic activity and cardiac output, potentially reducing coronary reserve[43, 44].

Results showed that the odds of mortality were increased 5.6 times in patients with a history of CVA. These results are consistent with a previous systematic review[45]. The association between mortality in patients with myocardial infarction and a history of CVA may be due to different factors. Some similar risk factors, such as hypertension, diabetes, and smoking, can affect the severity of both conditions[46, 47]. Additionally, a history of CVA may disrupt rehabilitation after MI due to physical and psychological effects[48, 49]. Furthermore, inflammation

caused by CVA, the connections between different inflammatory pathways, and the adjustment of the immune system all affect the complexity of the patients[50, 51].

One limitation of this research is that some checklists were not completed due to the large number of variables. As a result, some data had to be excluded. However, the number of excluded data points was not significant enough to impact the results. Another limitation of this research is the lack of follow-up of heart attack patients after discharge from the hospital, which can underestimate the risk of overall mortality in patients with STEMI.

Conclusion

Several factors, including lower EF, low hemoglobin levels, history of CVA, marital status, and low HDL cholesterol levels, may predict mortality in patients with MI. It is recommended to take these variables into consideration when determining the care and treatment for these patients.

Acknowledgements

The Authors, would like to express their gratitude to the management and staff of the Registry of Cardiovascular Diseases Patients in Yazd Province and the reviewers of this study proposal, as well as the School of Public Health at Yazd University of Medical Sciences for their support in this project.

Conflict of Interests

The authors declare no conflict of interest.

Funding

There is no funding in this study.

Author's Contributions

SMN was as PI of YCDR and supervisor of this Ph.D. thesis who provided critical comments on this paper, MM and SMSBafighi, interpreted the data and provided critical comments on this paper. MAS, helped either the statistical analysis of the study and provided critical comments on this paper. MM was the lead editor of the project, contributed to the writing and provided critical comments on this paper. HD managed the data collection system. All authors read and approved the final manuscript.

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How to cite this article: Mohammadi M, Namayandeh SM, Mirzaei M, Askari Shahi M, Sadr Bafighi SM, Dehghan H. **In-hospital mortality of acute ST-elevation myocardial infarction (STEMI) and its predictors-using Yazd Cardiovascular Diseases Registry, YCDR.** ARYA Atheroscler. 2024; 20(6): 6-16.