Prognostic factors of 28 days survival rate in patients with a first acute myocardial infarction based on gender in Isfahan, Iran (2000-2009)

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Original Article

Abstract

BACKGROUND: Determinant prognostic factors of 28 days survival rate in patients with a first acute myocardial infarction (AMI) based on gender in teen year's period in Isfahan, Iran, was the aim of this study.

METHODS: This study is a prospective hospital-based study that consisted, all patients with AMI admitted to all hospitals (private and universal hospitals) in Isfahan and Najafabad (Iran) during 2000-2009. To determinant the prognostic factors of 28 days survival rate in patients based on gender, analysis conducted separately for male and female. In analysis, we use of t-test, log Rank tests, Kaplan–Meier method, and univariate and multivariate Cox regression model.

RESULTS: Short-term (28 days) survival rate was 92.5% in male and 86.7% in female ($P < 0.001$). The adjusted hazard ratio (HR) of death for age group 80 years and older was 12.7 [95% confidence interval (CI): 5.14-31.3] in male and 8.78 (95% CI: 1.2-63.1) in female. HR for acute transmural MI of the unspecified site in male was 8.9 (95% CI: 4.68-16.97) and in female 9.33 (95% CI: 4.42-19.7). HR for receive of streptokinase in male was 1.11 (95% CI: 0.94-1.31) and in female was 0.69 (95% CI: 0.56-0.84).

CONCLUSION: Short-term survival rate in male was a higher than female. In male age, anatomic location of MI and hospital status and in female streptokinase use and anatomic location of MI was the most important prognostic factors of survival in-patient with AMI in Isfahan.

Keywords: Myocardial Infarction, Survival Rate, Gender, Isfahan (Iran)

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Introduction

Cardiovascular disease is one of the first causes of death in the world and Iran.[1] These diseases have increasing trends particularly in low-and moderate-income countries.[2] According to international reports, mortality from acute myocardial infarction (AMI) have rising trend,[3] and coronary artery disease (CAD) will remain among the three main causes of the global burden of disease to 2030.[4] According to the first national burden of disease study in Iran, CAD was the third factors of disability-adjusted life years in all ages and two genders (16% of total burden of disease). That led to 1 billion years of life lost resulted of premature mortality and 500

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thousand years lived with disability.[5] Despite a significant reduction in the amount of prevalence of coronary heart disease (CHD) in many countries[6] and advances in the treatment of patients,[7] case fatality rate (CFR) the following the incidence of AMI in both genders has remained high.[8] On the other hand, death from cardiovascular disease is the primarily cause of mortality in Iran.[1,9]

Accordingly, identifying predictive factors of mortality in patients could be an important role in reducing deaths from the disease, partially in countries such Iran that scattered reports have about the factors affecting the survival of patients with AMI. In studies that conducted in different parts of the world, factors such as diabetes mellitus, smoking, age, sex, hyperlipidemia, hypertension, previous MI introduced as the predictor of survival from AMI.[10,11]

In this study, in addition the demographic variables, we assess the role of type of AMI base on International Classification of Diseases version-10 (ICD-10), cardiac enzymes, symptoms, type of hospital, the first referral center for health services and streptokinase use as predictor of survival after first AMI, which less attention has paid to them in other studies. Thus, the aims of this study are determination of prognostic factors of 28 days (short-term) survival rate in patients with the first AMI based on gender in 10-year period in Isfahan, Iran.

Materials and Methods

This study is a prospective hospital-based study that consisted all patients with first AMI during 2000-2009 in the Isfahan and Najafabad (Iran). At the time, the study was performed about 13 hospitals were admitting and managing CHD patients in Isfahan.

In this registry, all possible CHD events were registered with ignoring MONICA age limitation. The MONICA MI diagnostic criteria were applied.[12] Diagnostic criteria are based on a collection of standardized information including past history of MI or ischemic heart disease, symptoms at onset, maximum levels of serum enzymes in admitted 1st day in the hospital, and relevant electrocardiograms (coded according to the Minnesota codes).[13] The World Health Organization (WHO) MONICA Project is concerned with events, not persons. Events are classified as first or recurrent.[12] In this study, only first events are included.

Hospital intensive care unit (ICU), coronary care unit (CCU), and cardiology ward admission and discharge lists were used for case finding. Records of patients hospitalized in cardiology wards, CCUs or in other wards but under complete or partial supervision of cardiologists were evaluated for possible signs and symptoms of CHD events. This evaluation was done by three experienced registered nurses trained in this regard before the study. They summarized proper records in special checklists containing information in age, sex, event date and hospitalization date, symptoms, history of previous MI, enzymes, admission electrocardiogram, whether the event was iatrogenic, survival status in discharge and after 28 days follow-up, and whether thrombolytic were used during hospitalization. The filled records were checked by an expert nurse with special training for the MONICA registration system. Moreover, 10% of the checklists was randomly chosen and refilled by the expert nurse from the original hospital records and compared with ones registered nurses had filled to see if any mistakes occurred. The patients investigated after admission to hospitals and patients with AMI related to different event locations assigned a specific code according to ICD-10, these codes were I21.0 (acute transmural MI of anterior wall), I21.1 (acute transmural MI of inferior wall), I21.2 (acute transmural MI of other sites), I21.3 (acute transmural MI of unspecified site), I21.4 (acute subendocardial MI) and I21.9 (AMI, unspecified), considering categorized AMI.[14]

MONICA and the WHO protocol defined AMI as a 28 days repeated attack, not considered as separate attacks but in fact related to the first AMI; however, following the first night of the 27th day after the attack it is considered as a new attack. Patients who died during the first 28 days are considered as death due to first AMI.[15] After collecting basic information about patients, their survival or death during the 28 days after the AMI were evaluated. For discharged patients, follow-up was the first executed by telephone but when their survival rates were not determined after three telephone calls, we went to the patients' homes. When previous efforts in terms of getting information about survival rate failed, using the national organization for civil registration and Isfahan cemetery, we tried to find out if the patient had died; we found the cause of death and exact date and location of the burial.[16] A detailed description of the methods used in this project was provided in previous reports.[16-24]

Overall, 14450 patients (10334 men and 4116 women) with first AMI, that inhabitants in Isfahan

and Najafabad entered in the study, 886 patients (564 men and 322 women) were excluded because their AMI type was not determined according to the ICD-10. In addition, 118 patients (82 men and 36 women) exclude from the study, because died during the 28 days after the first attack without mention of any cardiovascular disease due to accident, suicide, homicide, chronic obstructive pulmonary disease (COPD), cancer, liver cirrhosis, rheumatic heart disease, vascular disease, or atherosclerosis. In addition, 418 patients (292 men and 126 women) were excluded because outcome was unknown, and 128 patients (89 men and 39 women) was excluded from the study, Because the exact date of the occurrence or death from the disease was not specified and the 28 days duration after the attack could not be calculated in these cases,[15] also 85 patient (47 men and 38 women) were excluded because symptom or cardiac enzymes was not recorded. Therefore, 12815 patients, 9307 (72.6%) men and 3508 (27.4%) women, remained in the study (Tables 1 and 2).

Table 1. Clinical survival predictive factors in male with acute myocardial infarction

Variables	Total patients	Alive patients	Deaths patients	*Survival rates	**Adjusted HR (95% CI)	P
Age in male (year)						
39 year and lower	399	394	5	98.75	R	-
40-49	1629	1587	42	97.42	2.24 (0.88-5.66)	0.091
50-59	2525	2423	102	95.96	3.48 (1.41-8.55)	0.007
60-69	2343	2150	193	91.76	7.00 (2.87-17.00)	< 0.001
70-79	1886	1629	257	86.37	10.54 (4.34-25.60)	< 0.001
80 year and older	525	427	98	81.33	12.7 (5.14-31.30)	< 0.001
Streptokinase						
Receiving	5181	4864	317	93.88	R	-
Not receiving	4126	3746	380	90.79	1.11 (0.94-1.31)	0.340
ICD-10						
Acute subendocardial MI	752	736	16	97.87	R	-
Acute transmural MI of other sites	232	225	7	96.98	1.42 (0.58-3.47)	0.299
Acute transmural MI of inferior wall	2759	2650	109	96.05	1.74 (1.02-3.00)	0.035
Acute transmural MI of anterior wall	3187	2974	213	93.32	3.02 (1.78-5.11)	< 0.001
Acute MI, unspecified	2266	1938	328	85.53	5.90 (3.54-9.86)	< 0.001
Acute transmural MI of unspecified site	106	82	24	77.36	8.92 (4.68-16.97)	< 0.001
The first center was referred						
Non-specialized hospitals	638	573	65	89.81	2.11 (1.23-3.75)	0.011
Specialized hospital	8137	7547	590	92.75	1.50 (0.89-2.51)	0.200
Unknown	235	208	27	88.51	2.17 (1.11-4.00)	0.027
Health network or clinic	297	282	15	94.95	R	-
Symptoms						
Typical	7773	7250	523	93.27	R	-
A typical	1085	993	92	91.52	1.06 (0.85-1.36)	0.391
Others	414	339	75	81.88	1.67 (1.29-2.63)	< 0.001
Miss	6	5	1	83.33	1.87 (0.87-4.00)	0.094
***Cardiac enzymes						
A typical	1087	1026	61	94.39	R	-
Typical	7080	6597	483	93.18	1.27 (0.97-1.67)	0.078
Others	825	780	45	94.55	0.96 (0.65-1.40)	0.880
Not clear	315	207	108	65.71	4.81 (3.46-6.67)	< 0.001
Hospital						
Privative hospitals	763	716	47	93.84	R	-
Academic hospitals	8544	7894	650	92.39	1.45 (1.12-1.96)	0.018

*Survival rates at 28 days after the occurrence of the disease (percent). **Every variable adjusted for other variables. ***LDH (lactate dehydrogenase), CPK (creatine phosphokinase) and troponin.
HR: Hazard ratio; ICD: International classification of disease-10; CI: Confidence interval; MI: Myocardial infarction

Table 2. Clinical survival predictive factors in female with acute myocardial infarction

Variables	Total patients	Alive patients	Deaths patients	*Survival rates	**Adjusted HR (95% CI)	P
Age in female (year)						
39 year and lower	41	40	1	97.56	R	-
40-49	234	224	10	95.73	1.86 (0.23-14.11)	0.553
50-59	611	569	42	93.13	2.55 (0.35-18.63)	0.318
60-69	1038	920	118	88.63	4.39 (0.61-31.50)	0.123
70-79	1152	962	190	83.51	6.01 (0.84-43.00)	0.060
80 year and older	432	327	105	75.69	8.78 (1.20-63.10)	0.025
Streptokinase						
Receiving	1483	1260	223	84.96	R	-
Not receiving	2025	1782	243	88.00	0.69 (0.56-0.84)	< 0.001
ICD-10						
Acute subendocardial MI	438	426	12	97.26	R	-
Acute transmural MI of other sites	87	78	9	89.66	2.46 (1.02-5.90)	0.043
Acute transmural MI of inferior wall	901	819	82	90.90	2.27 (1.22-4.12)	0.009
Acute transmural MI of anterior wall	1069	945	124	88.40	3.09 (1.68-5.67)	< 0.001
Acute MI, unspecified	969	749	220	77.30	6.36 (3.53-11.45)	< 0.001
Acute transmural MI of unspecified site	44	25	19	56.82	13.12 (6.28-27.39)	< 0.001
The first center was referred						
Non-specialized hospitals	238	185	53	77.73	1.65 (0.94-2.90)	0.136
specialized hospital	3080	2697	383	87.56	0.83 (0.50-1.38)	0.344
Unknown	80	66	14	82.50	1.25 (0.60-2.61)	0.621
Health network or clinic	110	94	16	85.45	R	-
Symptoms						
Typical	2855	2489	366	87.18	R	-
A typical	408	367	41	89.95	0.83 (0.60-1.16)	0.250
Others	226	171	55	75.66	1.52 (1.12-2.03)	0.021
Miss	19	15	4	78.95	1.35 (0.52-3.63)	0.736
***Cardiac enzymes						
A typical	546	491	55	89.93	R	-
Typical	2464	2175	289	88.27	1.05 (0.77-1.40)	0.447
Others	318	281	37	88.36	1.37 (0.90-2.08)	0.186
Not clear	180	95	85	52.78	4.58 (3.24-6.54)	< 0.001
Hospital						
Privative hospitals	278	246	32	88.49	R	-
Academic hospitals	3230	2796	434	86.56	1.23 (0.85-1.77)	0.229

*Survival rates at 28 days after the occurrence of the disease (percent). **Every variable adjusted for other variables. ***LDH (lactate dehydrogenase), CPK (creatine phosphokinase) and troponin.
HR: Hazard ratio; ICD: International classification of disease-10; CI: Confidence interval; MI: Myocardial infarction

Variables that considered in the study include, age that divide in six sub-group (39 years and lower, 40-49, 50-59, 60-69, 70-79, and 80 and older), streptokinase use (receiving or not receiving), type of AMI based ICD-10, that include six categories (acute subendocardial MI, acute transmural MI of other sites, acute transmural MI of inferior wall, acute transmural MI of anterior wall, AMI, unspecified, acute transmural MI of unspecified site), the first center that patient referred forget medical care (non-specialized hospitals, specialized hospital, unknown, health network or clinic), symptoms (typical, A typical, others, not clear), cardiac enzymes (A typical, typical, others, not clear) and hospital status (privative hospitals and academic hospitals).

In this study, continuous variables are presented as mean ± standard deviation (SD). To compare average age in two genders, we use of the independent t-test. Time-dependent event (survival) rates were estimated by Kaplan-Meier method and P values were determined by use of log-rank statistics. The assumption of proportional hazards assessed by graphing the log-minus-log. Furthermore, to calculate the hazard ratio (HR) of death in 28 days of onset AMI, multivariate Cox regression analyses were used for calculation adjusted HR and category that have the lowest mortality, considered as reference group. In

calculate of adjusted HR every variable adjusted for other variables. Statistical significance was assumed if P < 0.050. All reported P values are two-sided. Statistical analyses were performed using SPSS software (version 15, SPSS Inc., Chicago, IL, USA).

Results

In this study, the average age of the patient in the time of disease occurrence was (12815 patients) 61.8 ± 12.6, in male (9307 patients) 60.0 ± 12.5 and in female (3508 patients) 66.7 ± 11.3, that this different was statically significant (P < 0.001). Sex ratio (male/female) was 2.65. Short-term (28 days) survival rate in study period was 90.9%, in male 92.5% and in female 86.7% (P < 0.001).

In male, the HR of death in the first 28 days after the occurrence of MI increased, so in 50-59 years age group HR was 3.48 [95% confidence interval (CI): 1.41-8.55, (P < 0.001)], in 60-69 years age group was 7 [95% CI: 2.87-17.00, (P < 0.001)], in 70-79 years age group was 10.54 [95% CI: 4.34-25.60, (P < 0.001)], and in 80 years and older was 12.7 [95% CI: 5.14-31.30, (P < 0.001)]. HR of death for other variables is presented in table 1.

HR for patients that referred to non-specialized hospitals as the first center for getting medical care was, 2.11 [95% CI: 1.23-3.75, (P = 0.011)], for unknown status was 2.17 [95% CI: 4.68-16.97, (P < 0.001)]. For patients with symptom other than typical, and A typical was 1.67 [95% CI: 1.29-2.63, (P < 0.001)]. In patients with cardiac enzymes [creatine phosphokinase (CPK) and lactic dehydrogenase] unclear was 4.81 [95% CI: 3.46-6.67, (P < 0.001)] and for patents in Academic hospitals was 1.45 [95% CI: 1.12-1.96, (P = 0.018)]. HR of death within 28 days after the occurrence of MI for other variable and sub variables in male was not statistical significant (Table 1).

In Female, HR of death in the first 28 days after the occurrence of MI were statistical significantly, only in 80 years and older age group that was 8.78 [95% CI: 1.20-63.10, (P = 0.025)]. HR of death for other variables is presented in table 2.

For patients with symptom other than typical, and A typical was 1.52 [95% CI: 1.12-2.03, (P = 0.021)]. In patients with cardiac enzymes (CPK and lactate dehydrogenase (LDH)] unclear was 4.58 [95% CI: 3.24-6.54, (P < 0.001)]. HR of death within 28 days after the occurrence of MI for other variable and sub-variables in female was not statistically significant (Table 2).

Discussion

In overall, from 12815 patients with AMI that included in the study, 9307 (72.6%) were males, and sex ratio was 2.65, a higher proportion of men than women in the disease has been observed in other studies.[25-28] The mean age at the time of occurrence of the disease in female, in average was 6.64 ± 3.04 years higher than male. In other studies observed, that the average age in time of occurrence of the disease is higher in female than male.[11,29,30] Short-term (28 day) survival rate in the entire study period is 90.9%, for males 92.5% and for females 86.7%. Perhaps higher mortality during the first 28 days after the occurrence of MI in female resulting from to higher age, higher prevalence of diabetes, higher ratio of female with poor prognosis who survived to the hospital and due to the fact that aging is reduced pain perception and response to pain.[20,29,31-37] Also, in recent years improvement in health care and the use of new technology and treatment can improve the survival rate. Of course, in Isfahan the Isfahan Healthy Heart Program (IHHP) in survival rates over time can be efficient.[38]

As expected, in both sexes with increasing age-adjusted HR of mortality is increased compared to baseline group, in a study that conducted by Stevenson et al. age was one of important determent factors in six-month survival rate in patients with AMI.[39] However, The risk of death increased with rising age has been observed in other studies.[40,41]

According to the ICD-10, MI divided into six categories. In this study, for the determent HR of mortality from AMI, considered group of patients who had the higher survival rate, as base group (acute subendocardial MI) and HR other groups, determined compared to this group. In two genders, acute, acute transmural MI of unspecified site have the highest HR compare basic group and after AMI, unspecified.

In both sexes, acute transmural MI of anterior wall has higher HR compare acute transmural MI of inferior wall. Thus, in this study the anatomic location of MI was a significant predictor of survival. In a number of studies, prognosis of MI based location was different, So that the anterior surface infarction has a worse prognosis compared to inferior level.[11,40,42] However, according to the method of data analysis in this study, difference in adjusted HR between various MI cannot caused by a variety of factors such as: gender, age, type of hospital, receive or did not receive streptokinase and type the first center to receive medical care. On

the other hand, because correct data about the differences among the mean interval between the occurrence of MI and go to health centers was not available, cannot image that this variable was ineffective, in the difference between the HRs among different types of MI.

Streptokinase is the first fibrinolytic drug, which widely used in the word. This drug is derived from the group A streptococcus. Patients may have or produce antibodies against it microorganism or drug, respectively. If a patient has antibody agent this, antibody led to increased incidence of allergic reactions (severe type of anaphylaxis). In addition, the presence of antibodies against the drug can lead to streptokinase thrombolytic effectiveness reduced. In England, overall 82.0% of hospitals used streptokinase for treatment of patients that for the first time suffering from AMI and have medical conditions of receiving this drug.[43] In this study not receiving streptokinase therapy in male, is not led to higher HR for death in the first 28 days after the occurrence of the disease, compared to the group receiving streptokinase (Table 1), but in female patients who received treatment (streptokinase therapy), compared to the group not receiving the drug has a lower HR (HR = 69%, 95% CI: 56-84), that is statistically significant.

In the present study, the HR of occurrence of death in both sexes in public hospitals is higher than private hospitals. Nevertheless, it should be note that the HR was statistically significant only in males. In a study that conducted with Chen et al.[44] in American with name, "Do 'America's best hospitals' perform better for AMI?" That conducted on 149, 177 patients with MI, the odds ratio (OR) for hospital mortality for the hospital with high rank was [relative risk (RR) = 76%, 95% CI: 69-84] against other hospitals. Survival was higher in patients admitted in this hospitals after entering variables such as disease severity and demographic characteristics of the patients, but after entering treatment quality indicators, adjusted OR was weaker and in terms of statistical not significant, so that its OR was equals (RR = 92%, 95% CI: 82-1.04) which is not significant, in actually shows that higher use of drugs such as beta blockers and aspirin in high-rank hospitals in American, lead to lower mortality.[44]

In calculation of the adjusted HR in this study, variables such as age, type of MI, receiving and not receiving the streptokinase, etc., that can be confounding role, considered. So cannot postulate that difference in survival rates due to differences in this variable, but we have not correct information about the differences between patients for receiving aspirin therapy. This article extracted from research project with code 84130 in 2011 in Isfahan Cardiovascular Research Institute.

Limitations

A difficulty of this study is a lack of complete, community-based case ascertainment, which contains through procedures for finding community fatal and nonfatal MI cases who are not admitted to the hospitals. Most important is the lack of data about out of hospital fatal cases, such as MI cases that managed at homes or in health centers. This figure might be unimportant since MI event is considering an emergency in Iran health care organization and total hospitals should admit such patients regardless of their insurance status. In Danish MONICA population, this number was measured to be not as much of as 0.1% of total MI cases in a year.[45] Therefore, the missing these patients would not lead to sham decline in MI CFR. However, in this study due to lack of data about confounding variables such as diabetes, hypertension, smoking higher ratio of female with poor prognosis who survived to the hospital and due to the fact that aging is reduced pain perception and response to pain, are not included in the statistical model. Probably, perhaps higher mortality during the first 28 days after the occurrence of MI in female resulting from to higher age, a higher prevalence of diabetes, higher ratio of female with poor prognosis who survived to the hospital and due to the fact that aging is reduced pain perception and response to pain.[20,29,31-37] Furthermore, in recent years improvement in health care and the use of new technology and treatment can improve the survival rate. Of course, in Isfahan the IHHP in survival rates over time can be efficient.[38]

Conclusion

The short-term survival rate in male was higher than female. In male age, anatomic location of MI and hospital status and in female streptokinase use and anatomic location of MI was the most important prognostic factors of survival in-patient with AMI in Iran.

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Conflict of Interests

Authors have no conflict of interests.

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