Predictive factors of short-term survival from acute myocardial infarction in early and late patients in Isfahan and Najafabad, Iran

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Original Article

Abstract

BACKGROUND: Cardiovascular disease (CVD) is the primary cause of mortality in the world and Iran. The aim of this study was to determine the prognostic factors of short-term survival from acute myocardial infarction (AMI) in early and late patients in the Najafabad and Isfahan County, Iran.

METHODS: This hospital-based cohort study was conducted using the hospital registry of 1999-2009 in Iran. All patients (n = 14426) with an AMI referred to hospitals of Isfahan and Najafabad were investigated. To determine prognostic factors of short-term (28-days) survival in early and late patients, unadjusted and adjusted hazard ratio (HR) was calculated using univariate and multivariate Cox regression.

RESULTS: The short-term (28-day) survival rate of early and late patients was 96.64% and 89.42% (P < 0.001), respectively. In 80% of early and 79.3% of late patients, mortality occurred during the first 7 days of disease occurrence. HR of death was higher in women in the two groups; it was 1.97 in early patients was (CI95%: 1.32-2.92) and 1.35 in late patients (CI95%: 1.19-1.53) compared to men. HR of death had a rising trend with the increasing of age in the two groups.

CONCLUSION: Short-term survival rate was higher in early patients than in late patients. In addition, case fatality rate (CFR) of AMI in women was higher than in men. In both groups, sex, age, an atomic location of myocardial infarction based on the International Classification of Disease, Revision 10 (ICD10), cardiac enzymes, and clinical symptoms were significant predictors of survival in early and late patients following AMI.

Keywords: Myocardial Infarction; Survival Rate; Early; Late; Regression Analysis; Iran

Introduction

Cardiovascular disease (CVD) is the most important reason of death in residents of Iran.[1] Every month around 11500 decease owing to coronary heart disease happens in Iran, about 50% of this deaths occurs as a result of acute myocardial infarction (AMI).[2] This disease is the major cause of disability, morbidity, and mortality in Iran residents.[3-5] Age is one of the important factors that have a massive influence on decease after heart attack so that older individuals are at bigger hazard of mortality from AMI.

In several studies that conducted around the word and detected that the mean age of patients who deceased in 28 days afterward the incidence of AMI and patients who deceased beforehand getting hospital, respectively, in average were 10 and 7 years older than survived patients.[6,7] Clearly, the possibility of decease from AMI was higher in elderly. Moreover, albeit only about 10% of the entire patients with AMI are < 45 years old.[6,7] AMI

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is a common cause of disability and mortality in a lot of countries and causes additional disadvantages, especially when it occurs in early patients. In studies that have been conducted in different parts of the world, factors such as age, sex, type of AMI, electrokardiogram (EKG), symptom, cardiac enzymes (lactate dehydrogenase, creatine kinase, and troponin), hypertension, previous MI, diabetes mellitus (DM), hyperlipidemia, season of disease event, and smoking introduced as the predictor of death from AMI.[8-10]

Therefore, identifying prognostic factors of mortality in patients could have an important effect in decreasing deaths from the disease,[11-13] especially in countries such Iran that dispersed information has about the factors affecting the survival from AMI, particularly in early patients that this information is little or does not be existent. Therefore, the aims of this study are determent prognostic factors of 28-day survival rate after AMI in teen year's period in early (younger) and late (older) patients in Isfahan and Najafabad County, Iran.

Materials and Methods

This study is a hospital-based cohort study that implemented to determent predictive factors of 28-day survival rate from AMI in 10 year's period in Isfahan and Najafabad. The population entered in the study involved of all patients (census) that diagnosis with first AMI for the period of 1999-2009 in all infirmary and hospitals in Isfahan and Najafabad. All patients examined afterward admittance to hospitals, then patients by AMI related to unalike event locations allocated a specific code pursuant to International Classification of Diseases-version 10 (ICD-10) based on the final diagnosis of hospital cardiologist.

Trained nurses, who used special questioner for gathering evidence about the patients with an interview with patients or check the hospital records, gathered basic information related to demographic and clinical and laboratory characteristics of patients and then all documents collected in the Isfahan Cardiovascular Research Center.

By definition of MONICA and the World Health Organization (WHO) protocol, AMI as a 28-day repeated attack, and separate attacks not considered according to this definition, but in fact related the first AMI; however, following the primary night of the 27th day after the first attack, it is considered as a new attack. It should be mentioned patients who died along the first 28 days are considered as death due to first AMI.[14] Patients are divided into two categories: (1) Early patients group (male with age 50 years and below and female with 55 years and below) and (2) late patients group (male with 51 years and older and female with 56 years and older).

After gathering basic information of the patients, their survival or deaths during days after the AMI examined. For discharged patients, follow-up was first executed by telephone, but when he did not answer the phone 3 times, we went to the patient's homes. When previous trying to getting information about survival rate failed, using the National Organization for Civil Registration and Isfahan Cemetery, we tried to find out the cause of death if the patient had died; and precise date and place of the burial.

This study encompassed merely patients who were resident in Isfahan and Najafabad with primary AMI. Overall, 16259 patients (12046 male and 4213 female) with primary AMI, that inhabitants in Isfahan and Najafabad entered in the study, 997 patients (632 male and 365 female) omitted because their AMI kind undetermined according to the ICD-10. In addition, 152 patient (107 male and 45 female) exclude from the study because they were died along the 28 days after the first attack without mention any CVD due to accident, suicide, homicide, chronic obstructive pulmonary disease (COPD), types of cancer, cirrhosis, rheumatic heart disease, atherosclerosis, or vascular disease; and 438 patients (305 men and 133 female) omitted because outcome of disease was unknown. Furthermore, 145 patients (96 men and 49 female) excluded from the study because the unknown exact date of the occurrence or death from the disease and the 28-day duration after the attack could not calculate in these cases.[14] Moreover, 101 patients (56 men and 45 female) excluded because symptom or cardiac enzymes were not recorded. Therefore, 14426 patients, 10850 (75.2%) men and 3576 (24.8%) female, stayed in the study and 11.27% of patient censored. Detailed description of the material and methods utilized in this scheme provided in previous reports.[10,12,13,15-17]

Variables that considered in the study include age that divide in six subgroup (39 years and lower, 40-49, 50-59, 60-69, 70-79, and 80 and older); streptokinase use (receiving or not receiving); kind of AMI-based ICD-10 that include six categories: (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, (I21.9) AMI; unspecified, the

first center that patient referred for get medical care (non-specialized hospitals, specialized hospital, unknown, health network, or clinic); symptoms (typical, atypical, others, not clear); cardiac enzymes (atypical, typical, others, not clear); and hospital status (privative hospitals and academic hospitals).

In this study, continuous variables 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 the log-minus-log diagram. Furthermore, to calculate the hazard ratio (HR) of death in 28 days of onset AMI, multivariate cox regression was used for calculation adjusted HR and category that have the lowest mortality, considered as the reference group. In calculate of adjusted HR every variable adjusted for other variables. Statistical significance assumed in conditions that $P < 0.050$. All testified P values are two-sided. Statistical analyzes performed with using SPSS software (version 15, SPSS Inc., Chicago, IL, USA).

Results

In overall, 14426 patients with AMI throughout the study period admitted in Isfahan and Najafabad hospitals. From this patients, 10850 (75.2%) was male, and 3576 (24.8%) was female. Sex ratio (male/female) was 3.03. In this study, the mean age of the patients in the disease occurrence time was (14426 patients) 60.83 ± 12.22, in male (10850 patients) 58.96 ± 11.92, and in female (3576 patients) 66.50 ± 11.34 and that different between average age in two genders was statically significant ($P < 0.001$).

Short-term (28-day) survival rate in study period was 91.5% (93.0% in male and 86.8% in female) ($P < 0.001$). Short-term (28-day) survival rate in early patients was 96.6% and in late patients was 89.4% ($P < 0.001$), in early patients was 94.2 and 97.4% ($P = 0.556$) and in late patients 85.4 and 91.8% ($P < 0.001$), respectively, for female and male. Short-term (28-day) survival rates of the two groups (early and late patients) for each of the variables are presented in tables 1-3.

In patients with AMI, the highest probability of mortality was during the first 7 days after the disease occurrence. Therefore, that 80.0% of deaths in early patients occurs during the 1st week after the even (39.3% in the day of incidence disease and 40.7% in 1-7 days after the disease occurrence) and in late patients 79.3% (44.3% in the day of incidence disease and 35.0% in 1-7 days after the disease occurrence) (Table 1).

HR of decease in two genders, in female was higher than male. So, in early patients was HR = 1.97; confidence interval (CI) 95%: 1.32-2.92 and in late patients was HR = 1.35; CI 95%: 1.19-1.53. In two groups, HR of death increases with increasing age; so that, in the early patients in age group 40-44 years was HR = 1.46; CI 95%: 0.56-3.79, 45-49 years was HR = 2.71; CI 95%: 1.14-6.44 and in age group 50-55 was HR = 3.44; CI 95%: 1.49-7.92 compared by 39 years and lower age group that HR with 95% CI only for age group 40-44 years was not statistically significant.

Table 1. Patient's demographic and 28 days case fatality rate

Variables	Early patients			Late patients		
	Female < 55	Male < 50	Total	Female > 55	Male > 50	Total
Total [n (%)]	586 (14.1)	3571 (85.9)	4157 (100)	2990 (29.1)	7279 (70.9)	10269 (100)
Sex ratio (male/female)	6.09		-	2.43		-
Age (year) (mean ± SD)	48.5 ± 5.4	47.2 ± 6.2	47.38 ± 6.11	70.02 ± 8.5	64.73 ± 9.58	66.27 ± 9.59
Survival status						
Dead	34	106	140	437	650	1087
Alive	552	3465	4017	2553	6629	9182
CFR (%)	5.8	2.96	3.4	14.6	8.9	10.6
Survival rate (%)	94.2	97.4	96.6	85.4	91.1	89.4
Means for survival time (day)	26.06	27.31	27.21	24.47	25.93	25.5
CI 95%	26.12-27.6	27.18-27.45	27.08-27.34	24.15-24.78	25.77-25.65	25.36-25.65
Day of death after hospitalization and survival rate						
Day 0 [n (%)]	11 (32.4)	44 (41.9)	55 (39.6)	214 (49.0)	268 (41.2)	482 (44.3)
Days 1-7 [n (%)]	20 (58.8)	37 (35.2)	57 (41.0)	146 (33.4)	234 (36.0)	380 (35.0)
Days 8-14 [n (%)]	1 (2.9)	13 (12.4)	14 (10.1)	48 (11.0)	78 (12.0)	126 (11.6)
Days 15-21 [n (%)]	2 (5.9)	9 (8.6)	11 (7.5)	23 (5.3)	49 (7.5)	72 (6.6)
Days 22-28 [n (%)]	0 (0)	3 (1.9)	3 (1.8)	6 (1.4)	21 (3.2)	27 (2.5)

SD: Standard deviation; CI: Confidence interval; CFR: Case fatality rate

In late patients, in age group 60-69 years was HR = 2.03; CI 95%: 1.64-2.5, 70-79 years was HR = 2.88; CI 95%: 2.35-3.53, and in 80 years and older was HR = 3.85; CI 95%: 3.06-4.84 compared by 50-59 years age group.

In both groups, HR of death in patients with acute sub-endocardial MI was lowest and acute transmural MI of unspecified site was highest; so, in early patients was HR = 22.42; CI 95%: 4.24-118.37 and in late patients was HR = 10.52; CI 95%: 6.41-17.28 (Tables 2 and 3).

Receiving streptokinase therapy in predicting survival in early and late patients is not a determining factor so that the HR of occurrence of death in patients who have not received the drug, respectively, in early and late patients were HR = 1.01; CI 95%: 0.71-1.46 and HR = 1.09; CI 95%: 0.95-1.24 that is not statistically significant. HR for other variables presented in tables 2 and 3.

Discussion

In this study, 28-day survival rate was 91.5%, in early patients 96.6% and in late patients 89.4%, and the highest probability of mortality (80.0%) was during the first 7 days after the disease occurrence. HR of demise in female was higher than male and increases with increasing age; acute sub-endocardial MI has lowest and acute transmural MI of the unspecified site have highest HR for mortality in first 28 days of disease start.

From 14426 patients with AMI that entered in the study, 10850 (75.2%) were male and sex ratio (male/female) was 3.03, parallel results in this context found in other studies.[18,19] The average age of patients in disease occurrence time in female was 7/5 years upper than male and these results also been observed in other studies.[9,20,21] Short-term (28-day) survival rate in the entire patients in the study was 91.5% - for males 93.0% and females 86.8%; and in early patients were 96.6% and in late patients were 89.4%. In fact, the risk ratio of death in 28 days after the onset of disease in late patients is 3.2 times higher than early patients. In a study that conducted in Yazd, Iran, by Soltani et al.[22] on 815 patients with AMI, patients divided into two age groups: ≤ 45 years (young) and > 45 years (old). In two genders, young patients had less in-hospital mortality than old patients, so in male was 1.2 vs. 9.1% (P = 0.005) and in female was 10.0 vs. 19.9% (P = 0.300). Similar results observed in other studies.[7,12] Therefore, age has an important role in determining survival rate in the patients with AMI. So, in both group (early and late patients) with increasing age-adjusted HR of mortality increased compared to baseline group, in a study that conducted by Stevenson et al.,[23] age of patients was important determent factor in 6-month survival rate in patients with AMI. However, this result that the risk of death increased with rising age has been observed in other studies.[24,25]

HR of death in 28 days after the onset of disease in female are 2.23 and 1.78 time higher than male, respectively, for early and late disease type. Perhaps, higher death in the first 28 days after the happening of AMI in female, resulting from the higher age, higher prevalence of diabetes, higher ratio of female with poor prognosis who survived to hospital, and also, because aging is reduced pain perception and response to pain.[13,20,26-32] Nevertheless, in this study due to lack of availability of data on the above variables, we cannot analysis effect of this variable on survival based on gender.

According to ICD-10, MI divided into six groups. In this study, for determent the HR of mortality from AMI considered a group of patients who had the higher survival rate as a base group (acute subendocardial MI), HR of other groups determined. In two groups (early and late patients), acute transmural MI of the unspecified site has highest HR compare basic group and after, AMI, unspecified (Tables 1 and 2). Furthermore, in both groups (early and late patients), acute transmural MI of the 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 early and late patients. In a number of studies, the prognosis of MI-based location was different so that the anterior surface infarction has a worse prognosis compared to inferior level.[9,24,33]

However, according to the method of data analysis in this study, we adjusted difference in various types of MI, and after calculated adjusted HR. Therefore, difference between adjusted HR for mortality from AMI according to ICD-10 cannot cause by a variety of factors such as: gender, age, kind of hospital, receive or did not receive streptokinase, and also difference in symptoms (typical, atypical, others, and miss), cardiac enzymes (atypical, typical, other and not clear), and EKG (definite, probable, ischemic, other, impossible coding, miss).

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.[34]

Table 2. Predictive factors in 28-day survival rate in early patients with acute myocardial infarction in Isfahan

Variables	The number of patients alive at 28-day after the first MI (%)	The number of deaths occurred in the first 28-day after MI	Survival rates at 28-day after the occurrence of the disease (%)	HR for death in the first 28-day after a first MI with 95% CI (unadjusted)	HR for death in the first 28-day after a first MI with 95% CI (adjusted)[*]
Sex					
Male	3571	106	97.0	-	-
Female	586	34	94.2	1.98 (1.34-2.91)	1.97 (1.32-2.92)
Age group (year)					
39 year and lower	440	6	98.6	-	-
40-44	739	15	98.0	1.49 (0.57-3.84)	1.46 (0.56-3.79)
45-49	1124	38	96.6	2.49 (1.05-3.84)	2.71 (1.14-6.44)
50-55	1854	81	95.6	3.24 (1.41-7.42)	3.43 (1.49-7.92)
Streptokinase					
Receiving	2509	77	96.9	-	-
Not receiving	1648	63	96.2	1.24 (0.89-1.74)	1.01 (0.71-1.46)
ICD-10					
Acute subendocardial MI	331	2	99.4	-	-
Acute transmural MI of other sites	103	5	95.1	8.18 (1.58-42.20)	8.70 (1.66-45.63)
Acute transmural MI of inferior wall	1334	25	98.1	3.12 (0.73-13.17)	3.38 (0.77-14.75)
Acute transmural MI of anterior wall	1420	39	97.3	4.59 (1.10-19.00)	4.92 (1.15-21.06)
AMI, unspecified	932	64	93.1	11.70 (2.86-47.80)	11.62 (2.79-48.33)
Acute transmural MI of unspecified site	37	5	86.5	24.18 (4.69-124.66)	22.42 (4.24-118.37)
Symptoms					
Typical	3542	112	96.8	-	-
Atypical	477	17	96.4	1.12 (0.67-1.88)	0.99 (0.59-1.67)
Others	128	10	92.2	2.52 (1.32-4.81)	2.11 (1.08-4.10)
Miss	10	1	90.0	3.35 (0.46-24.03)	0.54 (0.06-4.28)
Cardiac enzymes					
Others	384	9	97.7	-	-
Typical	3189	93	97.1	1.24 (0.62-2.47)	1.40 (0.69-2.80)
Atypical	478	20	95.8	1.80 (0.82-3.96)	1.93 (0.87-4.26)
Not clear	106	18	83.0	7.96 (3.57-17.73)	7.27 (3.22-16.4)
EKG					
Ischemic	675	16	97.6	-	-
Probable	80	7	91.2	3.79 (1.55-9.21)	3.37 (1.36-8.36)
Other	39	1	97.4	1.07 (0.14-8.07)	1.03 (0.13-7.90)
Definite	3268	102	96.9	1.32 (0.78-2.23)	1.60 (0.91-2.81)
Impossible coding	50	10	80.0	9.59 (4.35-21.13)	6.73 (2.96-15.30)
Miss	45	4	91.1	3.90 (1.30-11.67)	5.57 (1.81-17.10)

[*]Every variable adjusted for other variables; ICD: International Classification of Disease; AMI: Acute myocardial infarction; EKG: Electrokardiogram; HR: Hazard ratio; CI: Confidence interval

Table 3. Predictive factors in 28-day survival rate in late patients with acute myocardial infarction in Isfahan

Variables	The number of patients alive at 28-day after the first MI (%)	The number of deaths occurred in the first 28-day after MI	Survival rates at 28-day after the occurrence of the disease (%)	HR for death in the first 28-day after a first MI with 95% CI (unadjusted)	HR for death in the first 28-day after a first MI with 95% CI (adjusted)*
Sex					
Male	7279	650	91.1	-	-
Female	2990	437	85.4	1.68 (1.49-1.90)	1.35 (1.19-1.53)
Age group (year)					
50-59	2893	126	95.6	-	-
60-69	3381	311	90.8	2.16 (1.76-2.66)	2.03 (1.64-2.50)
70-79	3038	447	85.3	3.54 (2.91-4.32)	2.88 (2.35-3.53)
80 and higher	957	203	78.8	5.26 (4.21-6.58)	3.85 (3.06-4.84)
Streptokinase					
Receiving	5118	497	90.3	-	-
Not receiving	5151	590	88.5	1.18 (1.05-1.33)	1.09 (0.95-1.24)
ICD-10					
Acute subendocardial MI	979	26	97.3	-	-
Acute transmural MI of other sites	263	14	94.7	2.04 (1.06-3.92)	1.67 (0.87-3.20)
Acute transmural MI of inferior wall	2839	175	93.8	2.36 (1.56-3.56)	1.73 (1.13-2.64)
Acute transmural MI of anterior wall	3391	317	90.7	3.63 (2.43-5.41)	2.81 (1.86-4.23)
AMI, unspecified	2674	513	80.8	7.86 (5.30-11.65)	5.40 (3.62-5.07)
Acute transmural MI of unspecified site	123	42	65.9	15.24 (9.34-24.86)	10.52 (6.41-17.28)
Symptoms					
Typical	8461	829	90.2	-	-
Atypical	1202	124	89.7	1.05 (0.87-1.27)	0.96 (0.79-1.16)
Others	555	123	77.8	2.41 (1.99-2.91)	1.52 (1.24-1.85)
Miss	51	11	78.4	2.36 (1.30-4.28)	1.61 (0.88-2.93)
Cardiac enzymes					
Atypical	1344	104	92.3	-	-
Typical	7602	726	90.4	1.23 (1.08-1.52)	1.29 (1.05-1.59)
Other	896	77	91.4	1.12 (0.83-1.50)	1.19 (0.88-1.60)
Not clear	427	180	57.8	7.03 (5.52-8.95)	5.17 (4.04-6.63)
EKG					
Other	49	2	95.9	-	-
Probable	187	26	86.1	3.57 (0.84-15.05)	2.27 (0.53-9.60)
Ischemic	1721	110	93.6	1.56 (0.38-6.33)	1.06 (0.26-4.32)
Definite	7954	859	89.2	2.69 (0.67-10.79)	2.07 (0.51-8.36)
Impossible coding	208	50	76.0	6.46 (1.57-26.58)	2.64 (0.64-10.89)
Miss	150	40	73.3	7.58 (1.83-31.30)	3.08 (0.74-12.83)

*Every variable adjusted for other variables; ICD: International Classification of Disease; AMI: Acute myocardial infarction; EKG: Electrokardiogram; HR: Hazard ratio; CI: Confidence interval

In this study, although short-term (28-day) survival rate in early and late patients that receive streptokinase are higher from not receiving group but adjusted HR for death in not receiving group and are not significant. So that, patients who not received treatment, compared to the group receiving the drug, respectively, in early and late patients have adjusted HR = 1.01; CI 95%: 0.71-1.46 and HR = 1.09; CI 95%: 0.95-1.24. Thus, it can be seen that in both groups, receive and not receiving streptokinase are not significant determinate of short-term (28-day) survival in AMI patients. This article extracted from a research project with code 84130 in 2011 in Isfahan Cardiovascular Research Institute.

Limitation

A trouble of this study is a shortage of complete, community-based case ascertainment, which contains through protocols for discovery community fatal and non-fatal MI patients who not admitted to the hospitals. Most important is the shortage of information about out of hospital fatal cases such as MI cases that receive care managed at the house or in health centers. This figure is unimportant because in Iran care system MI events consider as emergency condition and all hospitals must admit such patients irrespective of their insurance position. In the study in Danish MONICA population, this patient contains < 1% of total MI cases. Therefore, the missing these patients would not lead to severe changes in case fatality rate (CFR).

Conclusion

The short-term survival rate in early patients is higher than late. In addition, CFR from AMI in female is higher than male. The highest probability of mortality (80.0% in early and 79.3% in late patients) was during the first 7 days after the disease occurrence. In both groups (early and late patients): sex, age, anatomic location of MI-based ICD-10, cardiac enzymes, and clinical symptoms are significant prognostic factors of survival in patients following AMI.

Acknowledgments

Conflict of Interests

Authors have no conflict of interests.

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