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Temporal trend of short-term mortality in acute myocardial between 2000-2017: A multi-centric Iranian registry

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Original Article

Abstract

BACKGROUND: The study explores the enduring challenges of cardiovascular disease mortality, emphasizing myocardial infarction rates as a proxy for cardiovascular disease in Iran. It analyzes the 28-day mortality trends after Acute Myocardial Infarction (AMI) from 2000 to 2017.

METHODS: This retrospective cohort study is based on data from a multi-centric hospital-based registry in Isfahan. Univariate and multivariate frailty Cox regression analyses were performed to identify Hazard Ratios (HRs) for the 28-day mortality rate of AMI based on age, gender, and living region.

RESULTS: The study enrolled 121,284 patients with an average age of 62.00±12.82 years. Older age than 65 years was found to be associated with an increased risk of AMI (HR: 3.2, 95% CI: 2.7-3.8 from 2000 to 2002 and HR: 4.6, 95% CI: 3.7-5.7 for 2015-2017). There was also an association between living in the urban region and a decreased risk of AMI from 2000 to 2005 (HR: 0.64, 95% CI: 0.46-0.90), from 2000 to 2002 (HR: 0.55, 95% CI: 0.43-0.71 for 2003-2005). Results showed that the trend of change in 28-day mortality declined more significantly from 2006 to 2017 compared to 2000-2002. Younger age (61.76±12.69 vs 71.12±11.73), female gender (HR:0.77, 95%CI: 0.67,0.89), and living in urban regions (HR: 0.69, 95%CI: (0.52,0.94) were the protective factors for the 28-days mortality rate of AMI.

CONCLUSION: It can be concluded that 28-day mortality had a descending trend from 2006 to 2017. Older age, male gender, and living in a rural region were the risk factors that affected the 28-day mortality rate of AMI.

Keywords: Acute Myocardial Infarction; Epidemiology; Heart Failure; Mortality; Trend

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Introduction

While cardiovascular disease (CVD) related mortality has notably decreased in recent years, the decline is less prominent in developing nations like Iran[1,2]. According to the World Health Organization (WHO), myocardial infarction (MI), which serves as a common manifestation of cardiovascular diseases (CVDs), can be utilized as a proxy for assessing CVD rates in epidemiological research[3]. Studying MI rates within a country informs decision-making, resource allocation, and health system planning, aiding in understanding causes, risk factors, and evaluating CVD prevention strategies[4]. In the last forty years, healthcare for those with acute myocardial infarction (AMI) has evolved due to improved early diagnosis and treatments, leading to a significant decrease in cardiovascular disease-related mortality[5]. The trend of AMI has been decreasing in recent years in many regions, and this decrease is due to the decrease in the main risk factors and the improvement of the

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treatment process, especially Primary Percutaneous Coronary Intervention (PPCI)[2,6]. However, it is not available as a first-line treatment in several regions of Iran[7]. To the best of our knowledge, no study has investigated the time trend of 28-day mortality of AMI across years after 2009 in Iran[8]. The goal of this study was to look at the time trends of changes in AMI both subgroup ST-elevation myocardial infarction (STEMI) and Non-ST acute coronary syndrome (NST-ACS) 28-day mortality from 2000 to 2017, as well as the factors that contributed to this variation.

Materials and methods

Study population

This study is a retrospective cohort study based on data from a multi-centric hospital-based registry in 13 hospitals in Isfahan, Iran, from 2000 to 2017[9]. In this registry, all probable coronary heart disease (CHD) events were documented according to the Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA). Only the first AMI episodes and patients classified as AMI, according to ICD-10 were included. The research team for the program included cardiologists, general practitioners, nurses who were trained to collect patients' information, professional biostatisticians, and epidemiologists.

Measurements

Records of patients admitted to the cardiology wards, coronary care units, or other wards but under the complete or partial supervision of cardiologists, were reviewed for suspected signs and symptoms of CVD events. The cases were identified through the hospital discharge list and finally, a cardiologist identified and separated patients with AMI based on ICD-10. Trained nurses collected basic information based on a predefined checklist by interviewing patients or obtaining information from their hospital records. Symptoms and cardiac enzyme codes were assigned similarly to the MONICA project[10]. The checklist included information on age, gender, and living region, as well as cardiovascular risk factors including, history of previous MI, ischemic heart disease, diabetes mellitus, hypertension, hyperlipidemia, smoking, event, and hospitalization dates, symptoms, enzymes, admission electrocardiogram, survival status and after 28-days follow-up, and whether thrombolytic therapy was used during hospitalization. In addition, some other information such as heart rate, systolic blood pressure, cardiopulmonary arrest before admission, cardiopulmonary arrest at admission, and ejection fraction were collected. For quality assessment and checking the accuracy of data, 10% of the checklists were randomly selected and refilled to see if any mistakes occurred. Then, the final data was collected at the Isfahan Cardiovascular Research Center (ICRC). To assess the MI survival rate in Isfahan, only records from residents of Isfahan and Najafabad were included in the study. All patients were followed up 28 days after admission by phone calls, and if not available, reached through their address. The patients or close family members were asked about the patient's health status. If a patient had died during the first 28 days after the event, the cause/causes were asked. Details of the methodological aspects of this project have been provided in previous studies[11].

Ethical issues

This study was approved by the Ethical Committee of the Isfahan University of Medical Science (Ethical code: IR.MUI.MED.REC.1399.75). Written informed consent was obtained at the beginning of enrollment in the cohort study after explaining the study protocol.

Statistical analysis

Data were presented as a mean ± standard deviation for continuous variables, or as counts and percentages for categorical variables. Continuous variables were compared using the independent sample t-test. Categorical variables were compared using the Chi-square test. Univariate and multivariate frailty Cox regression analyses were performed to identify hazard ratios (HRs) for the 28-day mortality rate of AMI based on age, gender, and living region. All data were expressed as HR with a 95% confidence interval (CI) for HR. The study period, from 2000 to 2017, was divided into six 3-year periods (2000-2002, 2003- 2005, 2006-2008, 2009-2011, 2012-2014 and 2015-2017). The first period (2000-2002) was considered as a reference, and other periods were compared with this group. In the analysis, two models were used; model 1 was adjusted for age and

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Table 1. Baseline characteristics of patients with acute myocardial infarction between 2000 to 2017

Age		62.00±12.82
Gender	male	66225 (54.6%)
	female	55059 (45.4%)
Risk factors	Smoking[1]	5646 (18.2%)
	Ischemic heart diseases[1]	16223 (52.2%)
	Diabetes mellitus[1]	7243 (23.3%)
	Hypertension[1]	11418 (36.8%)
	Hyperlipidemia[1]	6657 (21.4%)
Living region	Rural	5995 (4.9%)
	Urban	115289 (95.1%)
Heart rate (bpm) [1]		86.50±15.30
Systolic blood pressure (mmHg) [1]		136.18±26.00
Ejection fraction[1]		49.94±12.08

Data are shown as mean ± SD or frequency (percentage)

[1] Data were available since 2014.

Table 2. Time trend of acute myocardial infarction based on age, gender, and living region

Years	**Age (ref: ≤65 years of age)**			**Gender (ref: male)**			**Living region (ref: rural region)**		
	HR	**95%CI**	**P-value**	**HR**	**95%CI**	**P-value**	**HR**	**95%CI**	**P-value**
2000-2002	3.2	2.7-3.8	<0.001	1.07	0.92-1.25	0.38	0.64	0.46-0.90	0.01
2003-2005	3.4	2.9- 3.9	<0.001	1.13	0.99-1.26	0.06	0.55	0.43-0.71	<0.001
2006-2008	3.9	3.3-4.6	<0.001	0.97	0.82-1.13	0.65	0.74	0.54-1.01	0.06
2009-2011	3.6	3.1-4.3	<0.001	0.95	0.81-1.11	0.54	0.97	0.71-1.33	0.87
2012-2014	4.5	3.8-5.4	<0.001	0.93	0.80-1.1	0.35	0.85	0.62-1.17	0.31
2015-2017	4.6	3.7-5.7	<0.001	1.11	0.9-1.3	0.27	0.76	0.48-1.22	0.27

Univariate Cox regression was performed.

Data are shown as HR and 95% CI for HR.

gender. Model 2 was adjusted for age, gender, and living region. All statistical analysis was performed by STATA (Stata/IC 12.0, Stata Corp LP, and College Station, TX, USA). A P-value of < 0.05 was considered statistically significant.

Results

The study enrolled 121,284 patients with AMI referred to hospitals in Isfahan, Iran from 2000 to 2017. The average age of the patients was 62.00±12.82 years, 66,225 (54.6%) were male and 115289 (95.1%) of them were from urban regions. The demographic details of patients are available in Table 1.

As shown in Table 2, patients over the age of 65 were found to be at a higher risk for AMI (HR: 3.2, 95% CI: 2.7-3.8 from 2000 to 2002 and HR: 4.6, 95% CI: 3.7-5.7 for 2015-2017). Although no associations were found between gender and risk of AMI from 2000 to 2017, there was an association between living in the urban region and a decreased risk of AMI from 2000 to 2005 (HR: 0.64, 95% CI: 0.46-0.90 for 2000 to 2002 and HR: 0.55, 95% CI: 0.43-0.71 for 2003-2005). However, since 2005, the results revealed no associations between the living region and the risk of AMI.

Figure 1 and Table 3 indicate the trend of change in the 28-day mortality rate of patients with AMI from 2000 to 2017. The trend declined from 2006 to 2017 compared to 2000-2002. The mean age of patients with 28-day mortality was significantly older than the survivors (71.12±11.73 vs 61.76±12.69). The results also showed that females, compared to males, were less likely to have 28-day mortality (HR:0.77, 95%CI: 0.67,0.89). Moreover, living in the urban region was a protective factor for 28-day mortality in the population (HR: 0.69, 95%CI: (0.52,0.94) (Table 4).

Discussion

In this retrospective cohort analysis across multiple centers in Isfahan city, a decrease was noted in

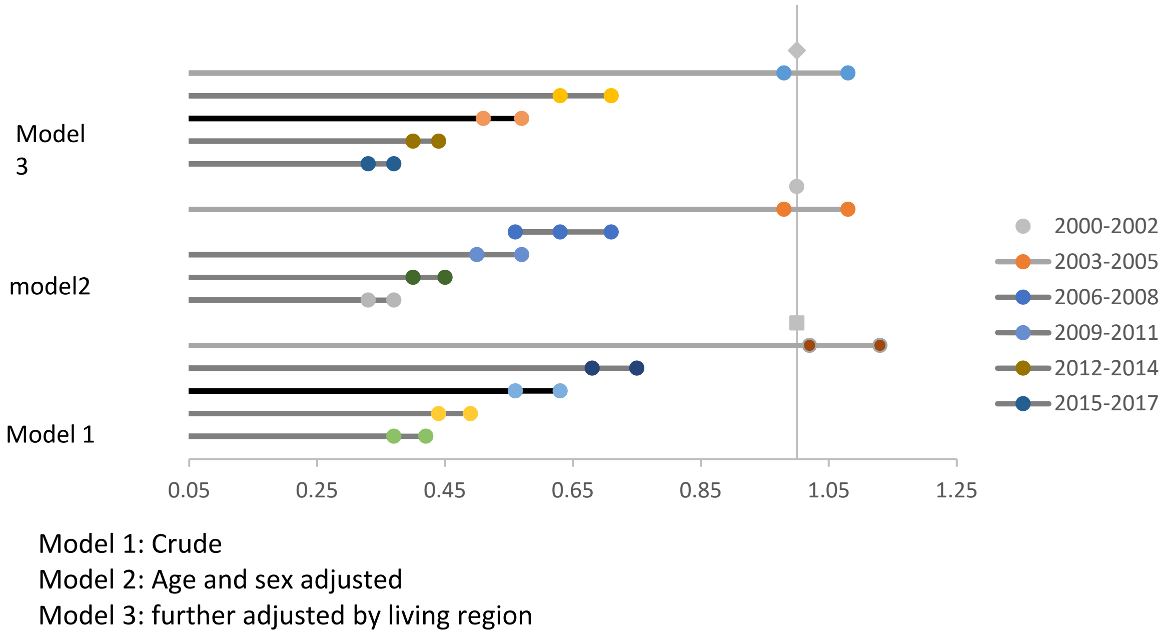

Figure 1. Trend of changes in the 28-day mortality rate of AMI patients from 2000 to 2017, multi-centric hospital-based registry in Isfahan, Iran.

Table 3. Trend of change in 28-days mortality for patients with acute myocardial infarction between 2000 to 2017

Years	Crude HR(95%CI)	Model 1 HR(95%CI)	Model 2 HR(95%CI)
2000-2002	Ref	Ref	Ref
2003-2005	1.02 (-0.92,1.13)	0/98(-0/89,1/08)	0/98(-0/89,1/08)
2006-2008	0/68(-0/61,0/75)	0/63(0/56,0/71)	0/63(-0/56,0/71)
2009-2011	0/56(-0/5,0/63)	0/51(-0/45,0/57)	0/51(-0/45,0/57)
2012-2014	0/44(-0/39,0/49)	0/4(-0/35,0/45)	0/4(-0/35,0/44)
2015-2017	0/37(-0/33,0/42)	0/33(-0/29,0/37)	0/33(-0/29,0/37)

Univariate and multivariate Cox regression analysis were performed.
Data are shown as HR and 95% CI for HR.
Model 1: Adjusted for age and gender
Model 2: Adjusted for age, gender, and living region

Table 4. Determining factors for 28-day mortality for patients with acute myocardial infarction between 2000 to 2017

Variables		Survivors	Death within 28 days	HR(95%CI)	P-value
Age		61.76±12.69*	71.12±11.73*	1.11(1.03,1.15)***	<0.001
Gender	**female**	49003(96.2%)**	1957 (3.8%)**	0.77(0.67,0.89)***	<0.001
Living region	**urban**	4897(95.2%)**	249 (4.8%)**	0.69(0.52,0.94)***	0.02

short-term (28-day) mortality rates for both men and women following their first acute myocardial infarction (AMI). Notably, the reduction was more significant among women. Factors such as being male, older age, and residing in a rural area were identified as contributing to a higher risk of 28-day AMI mortality. These findings align with earlier studies on the Iranian population, where the age range was 54.8 to 67.1 years[12,13]. A literature review of previous studies of patients with AMI revealed that there is a rising trend in the age of patients with AMI. Rajaei Behbahani et al. reported that the mean age of men and women with AMI were 59.70 ± 0.80 and 66.13 ± 0.10, respectively[14], while the mean age of AMI patients after 2000 is much closer to 60 to 65 years of age [4,12,13,15]. The results also showed that patients older than 65 years had 3.2 to 4.6 times the chance of AMI than those less than 65 years of age, in 2000-2002 and 2015-2017, respectively. In this retrospective cohort analysis across multiple centers in Isfahan city, a decrease was noted in short-term (28-day) mortality rates for both men and women following their first acute myocardial infarction (AMI). Notably, the reduction was more significant among women. Factors such as being male, older age, and residing in a rural area were identified as contributing to a higher risk of 28-day AMI mortality. These findings align with earlier studies on the Iranian population, where the age range was 54.8 to 67.1 years[12,13]. A literature review of previous studies of patients with AMI revealed that there is a rising trend in the age of patients with AMI. Rajaei Behbahani et al. reported that the mean age of men and women with AMI were 59.70 ± 0.80 and 66.13 ± 0.10, respectively[14], while the mean age of AMI patients after 2000 is much closer to 60 to 65 years of age[4,12,13,15]. The results also showed that patients older than 65 years had 3.2 to 4.6 times the chance of AMI than those less than 65 years of age, in 2000-2002 and 2015-2017, respectively.

In this study, 66,225 (54.6%) patients were male and 55,059 (45.4%) were female, thus the overall proportion of males to females was about 1.2. Therefore, AMI in Iran, similar to the rest of the world, has a higher incidence in men than women. According to several reports, the male to female ratio was 70/30, 67/33, 53-85/47-15, 65.5/34.5, 70/30, and 56/44 in Japan[16], Korea[17], various states in the United States[18], Taiwan[19], Switzerland[20], and Oman[21], respectively. However, no significant associations were found between gender and the risk of AMI from 2000 to 2017, the 28-day mortality rate is so high in men rather than women. This is inconsistent with the findings of the Mohammadian et al. study which confirms the higher 28-day case fatality rate from AMI in women from 2000 to 2009[8]. Moreover, Carine Milcent et al. in the French Hospitals Database reported a higher rate of hospital mortality in women than men (14.8% vs. 6.1%; P < 0.0001)[22]. This difference may be partly due to the higher average age of men at the time of the AMI event, and the higher prevalence of comorbidities in men[22-24].

In this study, 115,289 (95.1%) of AMI patients were from urban regions. Furthermore, it was demonstrated that there was an association between living in the urban region and a protective factor against AMI from 2000 to 2005, however, this significant association diminished after 2006. Another study also reported a lower rate of CVD-related mortality in all American regions in rural areas than in urban ones[25]. Urban-rural differences in CVD-related death have also been observed in studies across several nations[24,26,27]. The changes in lifestyle and risk factors of CVD in rural regions, as well as urban regions, could be a reason as the prevalence of risk factors for CVD, such as high blood pressure, diabetes, obesity, smoking, and inactivity, is high in both rural and urban areas. Another reason might be the differences between healthcare systems and facilities in urban and rural areas. The improvement in the rural health and medical system over time has most likely resulted in lowering the 28-day mortality rates of AMI after 2006. According to Molaei Qelichi et al., the intensity of health and medical systems in central and northern Iran, particularly Isfahan and Tehran, has increased in recent years, implying rapid urbanization in these areas, which has a direct impact on lifestyle and non-communicable disease risk factors[28]. Moreover, living in the rural region was the risk factor for 28-day mortality in our population (HR: 0.69 95%CI: 0.52,0.94 ref: rural population). This finding may be due to increasing tobacco exposure[29], uncontrolled non-communicable disease including Hypertension, Hyperlipidemia, and Diabetes Mellitus, and cardiovascular risk factors[30], as well as the long distance for the first cardiology hospital where emergent percutaneous coronary intervention (PCI) is applicable[31]. It is in agreement with some previous studies that implied that urban and rural differences in prevalence and mortality of AMI gradually narrowed[32].

The 28-day mortality of Acute Myocardial Infarction (AMI) showed a descending trend from 2006 to 2017. The rates of 28-day mortality revealed an approximately 60% decline in 2014-2017 compared to 2000-2002. These advances, endorsed by scientific evidence, have been incorporated by successive good practice guidelines and early intervention for AMI patients in the healthcare system[33,34]. For example, the treatment strategy for AMI has developed to Primary Percutaneous Coronary Intervention (PPCI) since 2006 in just one referral hospital (Chamran heart center) and gradually PCI-capable hospitals had been increasing during the last decades[35]. This decrease in 28-day mortality of AMI patients during the study was remarkable compared with the result of a similar study from 2000 to 2009 that demonstrated a 29.46% reduction in 28-day mortality[8].

The data analyzed in the present study were obtained from registries, meaning that it is not possible to ensure that the sample is representative of Iranian hospitals, as only hospitals in Isfahan have participated. Also, another difficulty was the lack of complete, community-based case ascertainment, which includes protocols for finding community fatal and non-fatal MI cases who are not admitted to hospitals. However, this figure is not less concerning since the MI event is considered an emergency in the Iranian healthcare system, and all hospitals should admit such patients regardless of their insurance status.

Furthermore, as it was noted in Table 1, a part of the data was available since 2014. Moreover, the way that some of the variables were defined has changed over time, i.e., hypertension, hyperlipidemia, diabetes, AMI, etc., which could explain some of the changes observed. Although this limitation is common in publications of this type and has previously been discussed[36].

Conclusions

From the findings of this study, it can be concluded that the number of patients older than 65 years with Acute Myocardial Infarction (AMI) was rising from 2000 to 2017. Being male, older age, and living in rural areas were found to be associated with a higher risk of 28-day AMI mortality rate. There was an association between living in the urban region and an increased risk of AMI from 2000 to 2005. Moreover, it was demonstrated that the 28-day mortality had a descending trend from 2006 to 2017.

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Conflict of Interest

The authors report no conflicts of interest.

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Author's Contributions

MS, ZTJ, and NS conceived the study and designed the methodology. HR, FN, and SN conducted the statistical analyses and ensured quality control. MHP and FBY wrote the first draft. All authors contributed to reviewing the draft, providing comments, and approving the final version.

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