Original Article

Presentation, Management and Early Mortality of Patients with Acute Coronary Syndrome in a Large Sample Study of a Middle East Country

Saeide Bahrani[1,2], Masoumeh Sadeghi[3], Zahra Teimouri-jervekani[3], Fatemeh Nouri[4], Nizal Sarrafzadegan[4]

[1]Student Research Committee, Isfahan University of Medical Sciences, Isfahan, Iran, [2]Hypertension Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran, [3]Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran, [4]Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Background: Due to lack of contemporary data on the presentation, management, and mortality of acute coronary syndrome (ACS) admissions in Iran, in this prospective registry study, we aimed to evaluate the presentation, management, and mortality as the outcome of patients with ACS in Isfahan, Iran, 2001–2016 to address treatment and healthcare depletions. **Methods:** Data of 62,276 patients admitted with the diagnosis of ACS from 2001 to 2016 prospectively were obtained by Surveillance Unit of Isfahan Cardiovascular Research Center, Isfahan, Iran, in 13 hospitals of Isfahan province. We evaluated data on presentation, management, and in-hospital and 28-day mortality. **Results:** Nearly half of the patients ranged in age from 51 to 70 years (32050, 51.5%), which did not differ among ACS types (ST-segment myocardial infarction (STEMI): 53.9%; non-STEMI: 53.4%; unstable angina: 51.9%). In-hospital, anti-platelets use was high (84.9%). Thrombolytic were used in 48.1% of STEMI, 3.8% of non-STEMI, and 1.1% of unstable angina. Discharge medication rates were suboptimal. In-hospital and 28-day mortality were highest for STEMI (6.5 and 12.6%, respectively). **Conclusions:** These data represent the large ACS registry in Iran. Data revealed the various presentations of ACS and demonstrated opportunities for improving ACS management by focusing on increasing use of recommended drugs especially after discharge due to suboptimal medical treatment in these patients. The high mortality rate needs to be taken into consideration in ACS patients.

Keywords: *Acute coronary syndrome, management, outcome, registry*

Introduction

Ischemic heart disease (IHD) is the most common cause of death and burden of disease worldwide. About 800,000 new cases of acute myocardial infarction was reported annually in the United States, of which 27% resulted in death.[1] It is also the most common cause of the disease burden in developing countries.[2] Prevalence of readmission due to cardiovascular outcomes including re-infarction, heart failure, and stroke are more prevalent in women.[3,4] The pattern of distribution and outcomes of IHD in Iran is the same as the other countries of middle east, but Iranian patients are older and female patients suffer more maybe due to the prevalence of more co-morbid conditions in women.[5] The manifestations of IHD, its management, and consequences are very different. Treatment of patients varies according to the time of the patients' arrival to the medical center. The mortality of these patients depends on several factors, including age and sex,[5] the underlying disease, onset of symptoms,[6] heart rate on arrival,[7,8] and even the type of treatment strategy considered.[9,10] Secondary prevention of ischemic heart diseases has been less considered in developing countries, while this type of prevention can significantly reduce morbidity and mortality and consequently decrease the burden of disease.[11] Acute Coronary Syndrome (ACS) management quality improvement programs have been reviewed in different countries and leads to improvement in the management during and after hospitalization significantly and thus the short-term and long-term outcomes improve, consequently.[12-14] outcomes of ACS could lead to morbidity or death, independently. ACS complications are divided into three categories including nosocomial, short-term, and long-term complications. Due to the fact that the prevention of each of these complications improves patients' survival, in this registry study, we aimed to evaluate the presentation, management, and early

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Address for correspondence:
Dr. Zahra Teimouri-Jervekani, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: Zahra.teimouri@med.mui.ac.ir

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mortality as the outcomes of patients with ACS admitted in hospitals of Isfahan, a city in the center of Iran, an Eastern Mediterranean country, Iran, from 2000 to 2017.

Methods

Patients setting

This study was held up in Surveillance Unit of Isfahan Cardiovascular Research Center, Isfahan, Iran, from April 2001 to March 2016 by registering Acute Coronary Syndrome ACS as one of the main units of Isfahan Cardiovascular Research Center (ICRC) from 13 hospitals in Isfahan province. Isfahan is an industrial city located in central Iran and the second most populous metropolitan area in Iran after Tehran. Most large cities in Iran are similar regarding socioeconomic status, population density, age distribution, men to women ratio, demographic picture, and health profile.[15,16] The registry was performed using the methodology of the "World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease" diagnostic categories (WHO-MONICA).[17,18] In this study, we reported the case-fatalities of ACS in Isfahan, Iran; this was done through gleaning information from the disease registration covering all hospitalized IHD patients. More than 75% with the diagnosis of ACS were managed in four public hospitals and the rest in the remaining nine private hospitals. Except for military hospitals, which did not allow access to their patients' records, other hospital records were evaluated. All patients older than 18 years, who were admitted with the diagnosis of ACS (I24.9) according to the International Classification of Diseases 10 (ICD-10) in 13 hospitals of Isfahan province was enrolled. Participants who died before reperfusion or treatment and patients with incomplete data were excluded from the study. Patients' privacy was protected at all times. Ethics Committee of Isfahan University of Medical Sciences approved all steps of the study (IR.MUI.MED.REC.1399.822).

Outcome measurement

Patients' IHD records and baseline demographics were assessed by trained medical personnel who was familiar with the ICD10 and WHO-MONICA assessment systems. Variables including sex, date of birth, date of hospitalization, name of hospital, risk factors, history of IHD, diagnostic categories related to clinical diagnosis (CD) based on (ICD) -10, CD-ICD-10, and WHO-MONICA were obtained from medical records. Data were supplemented by patient interviews, when necessary. The research team involved in the program consisted of cardiologists and general practitioners, a number of nurses trained in receiving and recording patients' information, and professional biostatistician and epidemiologist. In-hospital management, in-hospital mortality, and for discharge medical treatment was obtained from medical records. All patients were followed up for 28 days after discharge from the hospital to determine their mortality. Details of the early mortality (in-hospital and 28-day mortality), diagnosis of death, certificate, and autopsy findings were evaluated in a fatal event committee after recruitment of medical documents by a trained nurse. An expert nurse with special training in the MONICA registration system checked the filled records. Moreover, 10% of the checklists were randomly chosen and refilled by the expert nurse using the original hospital records and compared with those completed by registered nurses to see if any mistakes occurred. Detailed descriptions of the methods used in this project have been provided in previous reports.[19]

Statistical analysis

Data entry was done from April 2001 to March 2016 in a software designed under Fox pro. Information related to 2000 has been entered with software designed under Linux. In order to maintain a full confidentiality of the patients' information, a registration code, (as inspired by Hoffman's phonetic rule)[20] based on the first four digits of the family, the first two digits of the name, the last two digits of the year of birth, and an additional digit to avoid duplication of codes with identical characteristics, was assigned to be used for research purposes. In general, we use the mean ± standard deviation for quantitative data and the number (percentage) for grouping variables. Descriptive statistics have been used to report the initial characteristics of patients such as gender, age, place of residence (urban/rural), receiving lytic therapy, and the location of heart attack by years studied. In order to compare age average in the study, *t*-test and analysis of variance (ANOVA) were used. The significance level for this study was set to less than 0.05. The mentioned analyses were performed with STATA software (Stata/IC 12.0, Stata Corp LP, and College Station, TX, USA).

Results

In total, 62,276 patients with ACS with male dominancy were included in this study. Patient's demographics and clinical characteristics are presented in Table 1. Middle-aged patients (51–70 years old) were admitted more compared to patients younger than 50 or older than 70 years of age. Patients were more likely to present with unstable angina (43316, 69.5%) than with STEMI (7187, 11.5%), or Non-STEMI (1091, 1.75%). Prior history of diabetes, hypertension, and dyslipidemia were more common in patients presenting with Non-STEMI compared with STEMI and unstable angina, whereas smoking was more common in STEMI patients compared to non-STEMI and unstable angina. Heart rate of STEMI (88.98 ± 17.18) patients was higher compared to Non-STEMI (85.92 ± 16.36) and unstable angina (84.41 ± 14.97, $P < 0.001$) at the time admission, but systolic and diastolic blood pressure was higher in unstable angina (136.61 ± 26.28) and Non-STEMI (136.23 ± 26.98) patients compared to STEMI patients (133.15 ± 27.27). Most of patients

Table 1: Patient characteristics based on presentation

	Valid sample size	Total (*n*=62276)	STEMI (*n*=7187)	Non-STEMI (*n*=1091)	Unstable angina (*n*=43316)	*P*
Sex (male), *n* (%)	62202	34675	4970 (77.4)	426 (65.1)	22358 (51.7)	<0.001
Age	62200					
<50 years, *n* (%)		14496	1360 (21.2)	94 (14.4)	10671 (24.7)	<0.001
51-70 years, *n* (%)		32050	3462 (53.9)	349 (53.4)	22464 (51.9)	
>70 years, *n* (%)		15654	1600 (24.9)	211 (32.3)	10172 (23.4)	
History of Hypertension, *n* (%)	62265	6088	469 (7.3)	185 (28.3)	4691 (10.8)	<0.001
History of Diabetes mellitus, *n* (%)	62267	3829	328 (5.1)	125 (19.1)	2906 (6.7)	<0.001
History of Dyslipidemia *n* (%)	62269	3526	280 (4.4)	104 (15.9)	2803 (6.5)	<0.001
History of smoking *n*(%)	35846	9939	1708 (46.1)	114 (26.4)	6281 (24.7)	<0.001
Heart rate, mean±SD	53322	53322	88.98±17.18	85.92±16.36	84.41±14.97	<0.001
Systolic blood pressure (mmHg), mean±SD	54835	54835	133.15±27.27	136.23±26.98	136.61±26.28	<0.001
Ejection Fraction ≤30%, *n* (%)	8696	856	156 (20.2)	31 (13.4)	464 (6.9)	<0.001

with severe systolic dysfunction (LVEF <30%) was in STEMI group (20.02%, $P < 0.001$) compared to Non-STEMI (13.4%) and unstable angina (6.9%) group.

Thrombolytic therapy was done in 48.1% of patients with STEMI, which was significantly higher than patients with non-STEMI (3.8%). Approximately, more than half of STEMI patients received reperfusion therapy (thrombolysis and PCI). In-hospital medical treatments including anticoagulants, anti-platelets, and beta blocker was used commonly in Non-STEMI patients ($P < 0.001$). Calcium channel blockers and diuretics were used less commonly and nitrates was prescribed less often in patients with ACS. Given that nitrates do not alter the survival, they may be prescribed just in symptomatic patients with chest pain. A similar trend was seen in post-discharge prescription of anti-platelets and beta blocker. Nitrates was prescribed more at the time of discharge. Anti-arrhythmic drugs were used more significantly in STEMI patients either in hospital and after discharge [Table 2].

In STEMI patients, the unadjusted in-hospital mortality rate (6.5%) was significantly higher, compared with non-STEMI (4.4%, $P < 0.001$) and unstable angina (0.9%) patients. Incidence of 28-day mortality was significantly higher in patients with STEMI (12.6%) compared with non-STEMI and unstable angina patients (10.4% and 5.3%, respectively) ($P < 0.001$) [Table 3].

Table 4 demonstrates the odds ratio of in-hospital and 28-day mortality before and after adjustment. Patients presenting with STEMI had a higher risk of in-hospital mortality [odds ratio (OR) (95% confidence interval) 7.37 (6.2, 8.7)] and 28-day mortality [OR 2.3 (2.1, 2.6)] than patients presenting with unstable angina, even after adjustment for potential confounders. Patients presenting with non-STEMI had a higher risk of in-hospital mortality [OR 2.9 (1.8, 5.1)] and 28-day mortality [OR 1.4 (0.97, 1.9)] than patients presenting with unstable angina, even after adjustment for potential confounders.

Discussion

This large sample registry revealed the high incidence of ACS in Iranian population with various presentations. The highest portion of unstable angina was remarkable. The early mortality rate in ACS patients, especially in STEMI patients was high and needs more considerations. Patients with ACS were medically treated with a high degree of commitment to Guideline-directed medical therapy in hospitals, but they were discharged with a suboptimal prescription.

Demographics and medical characteristics

According to our findings, the most common clinical presentation of ACS in our registry was unstable angina and it was followed by STEMI (11.5%), which was lower than previous studies in IRAN (25.7%), Arabian countries around Persian Gulf (45.6%), India (60%), and even Latin America.[21-23] This incidence was as same as developed European countries.[24,25] This study has a larger sample size in comparison to IPACE2 study, which was held up in 2005, Iran.[26] Male dominancy was seen in almost all studies in this field. It may be due to less intensive evaluation of women according to the perception of coronary artery disease as a male disease. However, ischemic heart events showed a gender-specific difference in many studies such as GUSTO IIb (Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes),[27] TIMI IIIB (Thrombolysis In Myocardial Infarction),[28] and the Euro Heart Survey.[29] Women present more frequently with unstable angina and non-STEMI in contrast to the higher frequency of men with ACS presented as STEMI.[30] Our patients were mostly middle aged, 51–70 years as same as IPACE2 and other Arabian countries.[26] The mean age of our patients at the time of presentation was lower than developed countries.[31] It may be due to higher incidence of co-morbid conditions in our population or genetic differences. ACS in younger population is associated with more co-morbidities including diabetes, smoking, sedentary behavior (low HDL-cholesterol), cocaine use, and obesity.[32]

Table 2: In-hospital diagnostic evaluations, in-hospital medical and interventional treatments, and Discharge medical therapy prescriptions based on acute coronary syndrome type

	Valid sample size	Total (*n*=62276)	STEMI (*n*=7187)	Non-STEMI (*n*=1091)	Unstable angina (*n*=43316)	*P*
In-hospital medical therapy						
Thrombolysis, *n* (%)	55007	4008	2597 (48.1)	21 (3.8)	427 (1.1)	<0.001
Anti-arrhythmic, *n* (%)	55065	2632	726 (13.4)	32 (5.7)	988 (2.5)	<0.001
Anticoagulant, *n* (%)	55061	49228	4736 (87.6)	528 (94.6)	35551 (90.9)	<0.001
Anti-platelets, *n* (%)	55068	52872	5304 (98.1)	549 (98.4)	37763 (96.6)	<0.001
Beta-blocker, *n* (%)	55069	45674	4619 (85.4)	482 (86.4)	32781 (83.8)	0.004
Calcium channel blockers, *n* (%)	55066	9169	477 (8.8)	118 (21.1)	6797 (17.4)	<0.001
Diuretic, *n* (%)	55064	9644	925 (17.1)	128 (22.9)	6444 (16.5)	<0.001
Nitrates, *n* (%)	3484	87	22 (6.8)	0 (0)	45 (2.1)	<0.001
Anti-hypertensive, *n* (%)	55066	29125	3292 (60.9)	336 (60.2)	20637 (52.8)	<0.001
Discharge medications						
Anti-arrhythmic, *n* (%)	2390	172	32 (1.4)	2 (0.5)	99 (0.6)	<0.001
Anticoagulant, *n* (%)	23917	836	72 (3.1)	10 (2.6)	596 (3.4)	0.529
Anti-platelets, *n* (%)	23923	20197	2051 (87.5)	324 (84.8)	14867 (84.5)	0.001
Beta-blocker, *n* (%)	23920	14216	1515 (64.7)	240 (62.8)	10315 (58.7)	<0.001
Calcium channel blockers, *n* (%)	23915	2929	125 (5.3)	52 (13.6)	2254 (12.8)	<0.001
Diuretic, *n* (%)	23916	2332	241 (10.3)	41 (10.7)	1635 (9.3)	0.209
Nitrates, *n* (%)	23921	13174	1357 (57.9)	236 (61.8)	9452 (53.8)	<0.001

Table 3: In-hospital and 28-day mortality rate, based on acute coronary syndrome type

	Valid sample size	Total (*n*=62276)	STEMI (*n*=7187)	Non-STEMI (*n*=1091)	Unstable angina (*n*=43316)	*P*
In-hospital mortality, *n* (%)	62276	831 (1.6%)	419 (6.5%)	29 (4.4%)	383 (0.9%)	<0.001
28-day Mortality, *n* (%)	57916	3175 (6.3%)	809 (12.6%)	68 (10.4%)	2298 (5.3%)	<0.001

Table 4: Odds ratio of in-hospital and 28-day mortality rate before and after adjustment

	Unstable angina	STEMI OR (95%CI)	Non-STEMI OR (95%CI)
In-hospital mortality			
Model crude	Ref.	7.8 (6.8,9)	5.2 (3.5,7.6)
Model1*	Ref.	8.3 (7.1,9.6)	4.4 (3,6.5)
Model2**	Ref.	7.35 (6.2,8.7)	3 (1.8,5.1)
Model3***	Ref.	7.37 (6.2,8.7)	2.9 (1.8,5.1)
28-day Mortality			
Model crude	Ref.	2.57 (2.35,2.8)	2.07 (1.6,2.67)
Model1*	Ref.	2.57 (2.35,2.8)	1.67 (1.28,2.17)
Model2**	Ref.	2.35 (2.1,2.6)	1.27 (0.91,1.8)
Model3***	Ref.	2.3 (2.1,2.6)	1.4 (0.97,1.9)

*Adjusted by age, sex. **Adjusted by age, sex, Systolic Blood Pressure, Heart Rate. ***Adjusted by age, sex, Systolic Blood Pressure, Heart Rate, Diabetes Mellitus, Hypertension, dyslipidemia

In-hospital and discharge diagnostics and management

According to our data, 98.1% of patients with STEMI and 98.4% of the patients with NSTEMI received anti-platelets during the hospital stay for ACS as same as recent ACS registries.[33-35] These findings are compatible with appropriate compliance with guideline-directed medications at the time of admission in patients with ACS, which demonstrates the proper knowledge, attitude, and practice of Iranian physicians. Post-discharge medication of anti-platelets are almost as high as in-hospital rate of prescription. The lower rate of anti-platelet therapy at discharge in STEMI and NSTEMI group may be due to missing data of medical records. Anticoagulation with therapeutic dosage administered in all three groups of patients and more frequent in non-STEMI group during hospital stay. The lower rate of anticoagulant prescription in patients with STEMI may be due to reperfusion therapy in more than half of them, which leads to postpone the anticoagulation. Patients with non-STEMI received diuretics more, maybe due to higher frequency of co-morbid conditions. About 16.9% of patients with STEMI underwent

coronary angiography and 8.2% received percutaneous coronary intervention, which is significantly lower than developed countries in various registries.[8,36,37] These findings are lower in comparison to ACTION[9,38] and Euro Heart Survey ACS I and II,[9,29] although the frequency of coronary angiography and percutaneous intervention were slightly higher than other middle east countries.[39] In our registry, 48.1% of patients with the diagnosis of STEMI received thrombolysis, which was lower than CREATE Registry whereas the inappropriate use of thrombolysis in non-STEMI (3.8%) was as same as CREATE (3.4% thrombolysis use in non-STEMI patients).[22] Recently, national program named 24/7 were enrolled. According to this protocol, full-time provision of revascularization services should be available 24 hours a day, 7 days a week (24/7) in conjunction with a fully coordinated pre-hospital emergency system and equipped centers with experienced medical teams. It seems that this strategy will manage the problem of maximal revascularization in lesser time for STEMI patients.

In-hospital and 28-day mortality

In-hospital and 28-day mortality rates of patients with STEMI (6.5% and 12.6%, respectively) were higher than GRACE registry (7%).[24] In-hospital and 28-day mortality rates for non-STEMI patients (4.4 and 10.4%, respectively) was higher than other registries of developed countries. In addition, in comparison to unstable angina, STEMI is the most important risk factor of in-hospital mortality in patients with ACS (7.37 times). NSTEMI is the second most important risk factor. The risk of mortality decreases after discharge but still STEMI has the higher odds ratio during the first month of post-discharge (2.3 times) in comparison to unstable angina. This finding is in agreement with Polish registry,[25] which showed an adjusted worse long-term prognosis in patients with STEMI than in patients with NSTEMI. The reasons for higher mid-term non-cardiac mortality in patients with NSTEMI might be older age and higher prevalence of major diseases including diabetes mellitus, hypertension, and dyslipidemia, and less optimal revascularization therapies.

Limitations

First, this study was conducted over 17 years; and during this period although some procedures were gradually expanded and standard treatment options were updated, details are not specified in this study. Second, the details of drugs, especially in the field of antiplatelet administration due to changes in the treatment process, were not mentioned. Third, because of the observational nature of the study, there is an inherent selection bias. Finally, patients who had Out of Hospital Cardiac Arrest (OHCA) were not included in the study.

Conclusions

In conclusion, this study with a large sample size in Iran revealed that the composition of ACS presentation in Iranian population is relatively similar to developed European countries and different from developing countries. We found that patients with ACS were treated in hospitals with a high degree of commitment to Guideline-directed medical therapy but at discharge, medical treatments were suboptimal. However, STEMI is associated with higher risk of in-hospital and 28-day mortality. Moreover, Iranian patients with non-STEMI were delayed a long time before presenting to the hospital, and this delay increased the MACE in patients. Finally, this study demonstrates opportunities for improving the quality of ACS management by focusing on increasing use of recommended drugs especially at the time of discharge and finding better strategies to decline the mortality rate.

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Conflicts of interest

There are no conflicts of interest.

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