Baseline characteristics, management practices, and long-term outcomes among patients with first presentation acute myocardial infarction in the Second Gulf Registry of Acute Coronary Events (Gulf RACE-II)

Abdulaziz U. Joury [a,b], Ahmed S. Hersi [a], Hussam Alfaleh [a], Khalid F. Alhabib [a], Tarek Seifaw Kashour [a,*], Gulf Registry of Acute Coronary Events Investigators [a]

[a] King Fahad Cardiac Center, College of Medicine, King Saud University, Riyadh
[b] King Salman Heart Center, King Fahd Medical City, Riyadh

[a,b] Saudi Arabia

Background and objectives: **Limited data are available highlighting the different clinical aspects of acute coronary syndrome (ACS) patients, especially in Gulf countries. In this study, we aimed to compare patients who presented with acute myocardial infarction (AMI) as the first presentation of patients who have a history of ACS in terms of initial presentation, medical history, laboratory findings, and overall mortality.**

Methods: **We used the Second Gulf Registry of Acute Coronary Events (Gulf RACE-II), which is a multinational observational study of 7930 ACS patients.**

Results: **Among all patients, 4723 (59.6%) patients presented with AMI. First presentation AMI patients were older (mean age, 55 years vs. 53 years; $p < 0.001$) and had lower risk factors than patients with a history of ACS. Higher laboratory readings of cardiac markers and all aspects of mortality were significantly higher among patients with first presentation AMI. After adjustments for baseline variables, congestive heart failure [odds ratio (OR) = 1.08; 95% confidence interval (CI), 0.73–1.57], reinfarction (OR = 1.16; 95% CI, 0.58–2.30), cardiogenic shock (OR = 1.51; 95% CI, 0.74–3.08), stroke (OR = 2.30; 95% CI, 0.29–17.99), and overall mortality (OR = 1.16; 95% CI = 0.74–1.83) were independent predictive factors for first presentation AMI.**

Conclusions: **First presentation AMI patients tend to be older and to have lower rates of risk factors. Adverse clinical outcomes such as congestive heart failure, reinfarction, cardiogenic shock, and stroke were higher among patients with first presentation AMI compared to patients with a history of ACS.**

Keywords: Acute coronary syndrome, Acute myocardial infarction, Middle East, Mortality

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* Corresponding author at: P.O. Box 7805, Riyadh 11472, Saudi Arabia.
E-mail address: tkashour@ksu.edu.sa (T.S. Kashour).

P.O. Box 2925 Riyadh – 11461KSA
Tel: +966 1 2520088 ext 40151
Fax: +966 1 2520718
Email: sha@sha.org.sa
URL: www.sha.org.sa

Peer review under responsibility of King Saud University.
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Introduction

Acute coronary syndrome (ACS) has always been the leading cause of death worldwide [1,2]. Symptoms of acute myocardial infarction (AMI) often include a wide variety of symptoms; however, chest pain is considered to be the main manifestation [3–7]. It is well known that early diagnosis and treatment of AMI is a cornerstone to better outcomes and positive prognosis [8]. The prevalence of coronary artery disease in the Gulf countries is alarming [9], and based on the Saudi ACS registry, 41.5% of ACS patients presented with ST-segment elevation myocardial infarction (STEMI) [10]. The Second Gulf Registry of Acute Coronary Events (Gulf RACE-II) represents distinct racial and sociodemographic characteristics of ACS patients in Gulf country regions. A previous study compared Gulf RACE-II registry with the well-known Global Registry of Acute Coronary Events (GRACE), and the authors found a significant difference in age, with almost a decade difference between the two cohorts [11]. In the National Registry of Myocardial Infarction, a large and prospective US registry, the authors correlated atherosclerotic risk factors and short-term mortality after first AMI, and the results showed higher mortality among patients with diabetes mellitus [12]. The French MONICA registry of ACS patients found that higher fatality rate was associated with poor prognosis [13]. However, to the best of our knowledge, there was no previous study that correlated the different clinical characteristics of patients who presented with first AMI and compared it with patients who had a history of ACS. In our study, we aimed to investigate the clinical presentation, variety of demographic differences, laboratory findings, and hospital outcomes of patients who presented with first AMI compared to patients with a history of ACS.

Abbreviations

ACS	acute coronary syndrome
AMI	acute myocardial infarction
Gulf RACE-II	Gulf Registry of Acute Coronary Events

Methods

Study structure and design

The Gulf RACE-II registry is a large prospective multinational registry of patients with ACS. It recruited consecutive patients from six different Gulf countries (Saudi Arabia, Bahrain, Qatar, United Arab Emirates, Oman, and Yemen). ACS patients were enrolled from October 2008 until June 2009 in 65 hospitals. Further details have been described in previously published articles [14,15].

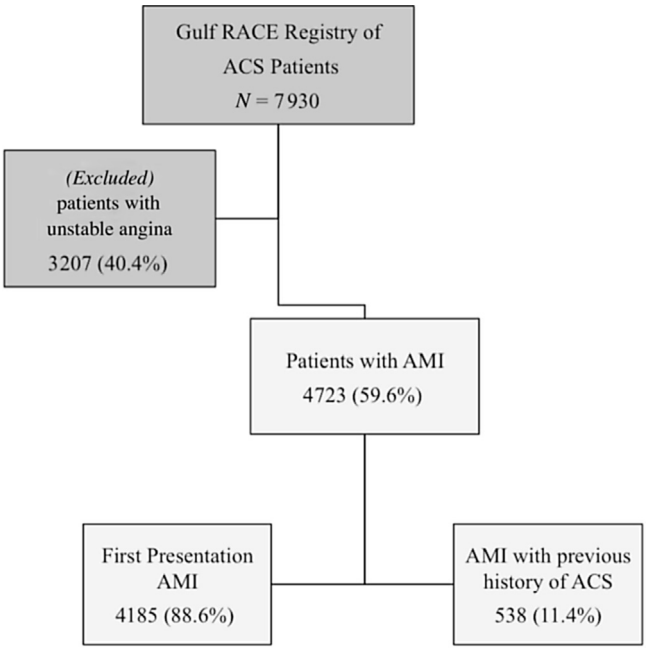

Figure 1. Flow chart of the groups analyzed in the study. Patients with unstable angina were excluded. ACS = acute coronary syndrome; AMI = acute myocardial infarction; RACE = Registry of Acute Coronary Events.

Table 1. Demographic and clinical characteristics of the study cohort stratified by history of first AMI.

Variable	Overall $N = 4723$	First presentation AMI n (%), 4185 (88.61)	AMI with previous ACS n (%), 538 (11.39)	p
Demographics				
Mean age (y)	56.43 ± 12.80	55.53 ± 12.59	52.91 ± 11.62	<0.001
Male	3992 (84.52)	3533 (84.42)	459 (85.32)	0.613
Initial presentation				
Typical ischemic chest pain	4512 (95.53)	4004 (95.68)	508 (94.42)	0.186
Atypical chest pain	211 (4.47)	181 (4.32)	30 (5.58)	
SBP (mmHg)	134.3 ± 29.66	133.9 ± 27.99	135.7 ± 26.35	0.155
DBP (mmHg)	81.24 ± 18.50	81.62 ± 17.59	82.30 ± 17.24	0.402
HR (beats/min)	85.29 ± 20.74	83.92 ± 18.07	82.30 ± 17.93	0.050
Atrial fibrillation	62 (1.31)	58 (1.39)	4 (0.74)	0.218
Medical history				
Diabetes mellitus	1690 (35.78)	1468 (35.08)	222 (41.26)	0.018
Congestive heart failure	162 (3.43)	143 (3.42)	19 (3.53)	0.299
Hyperlipidemia	1309 (27.72)	1038 (24.80)	271 (50.37)	<0.001
Hypertension	1885 (39.91)	1607 (38.40)	278 (51.67)	<0.001
Peripheral arterial disease	59 (1.25)	53 (1.27)	6 (1.12)	0.743
Chronic renal failure	124 (2.63)	111 (2.65)	13 (2.42%)	0.571
Smoking status				
Never smoked	1895 (40.12)	1686 (40.29)	209 (38.85)	0.811
Ex-smoker	762 (16.13)	674 (16.11)	88 (16.36)	Reference
Smoker	2066 (43.74)	1825 (43.61)	241 (44.80)	Reference
GRACE Risk Score				
Low GRACE Risk Score	1853 (39.81)	1590 (38.60)	263 (49.07)	<0.001
Intermediate GRACE Risk Score	1843 (39.59)	1652 (40.11)	191 (35.63)	<0.001
High GRACE Risk Score	959 (20.60)	877 (21.29)	82 (15.30)	<0.001

Data are presented as n (%) or mean ± SD.
ACS = acute coronary syndrome; AMI = acute myocardial infarction; DBP = diastolic blood pressure; GRACE = Global Registry of Acute Coronary Events risk score; HR = heart rate; SBP = systolic blood pressure; SD = standard deviation.

Study cohort participants

All prospective patients with ACS were enrolled in the registry; however, for the purpose of this study, we excluded patients with unstable angina. The study cohort participants were stratified into two main groups: patients who presented with AMI as first presentation and patients who presented with AMI and known to have a history of ACS (Fig. 1). Demographic characteristics, medical history, final diagnosis, different laboratory investigations, in-hospital management, and outcomes were collected using case report forms. Filling of these case report forms was initiated upon admission with a provisional diagnosis of ACS, and verified cardiologists or research assistants filled these forms. To prevent double-counting of patients, the patients' national identification number and registry number were used instead of any other identifier. To ensure patients' confidentiality, only registry numbers were included for the data analysis.

Study measurements

Diagnosis of the different types of ACS was based on the American College of Cardiology clinical data standards [16]. Diabetes mellitus was defined as having a history of diabetes mellitus, on current diabetes treatments, or having blood glucose of more than or equal to 7 mmol/L. Dyslipidemia was defined as the presence of elevation of plasma cholesterol, triglycerides, or both, or patients being treated with lipid-lowering agents. The definition of hypertension was having a history of hypertension diagnosed and treated with medications or lifestyle modifications, a systolic blood pressure of > 140 mmHg, or a diastolic blood pressure > 90 mmHg on at least two occasions, or being treated with any antihypertensive medications. Smoking status was defined as smoking cigarette or water pipe within 1 month of admission. Patients were stratified into different risk groups based on percentile of the calculated baseline Global Registry of Acute Coronary Events (GRACE) risk score [17]. Ethical approvals were obtained from institutional ethical bodies in all participating hospitals.

Statistical analysis

Continuous data were summarized as mean and standard deviation. Categorical data were

Table 2. Laboratory and echocardiographic findings, in-hospital outcome/procedures and mortality stratified by history of first AMI.

Variable	Overall *N* = 4723	First presentation AMI *n* (%), 4185 (88.61)	AMI with previous ACS *n* (%), 538 (11.39)	*p*
Laboratory findings				
Positive serum troponin	4272 (90.55)	3800 (90.87)	472 (88.06)	0.071
Peak creatinine kinase MB (ng/mL), median (IQR)	510.5 (12.87)	602.0 (13.62)	302.0 (11.72)	<0.001
Total cholesterol (mmol/L), median (IQR)	4.89 (1.85)	4.92 (1.80)	5.00 (1.87)	0.305
Triglyceride (mmol/L), median (IQR)	1.53 (1.10)	1.58 (1.11)	1.70 (1.29)	0.003
High-density lipoprotein cholesterol (mmol/L), median (IQR)	0.99 (0.39)	0.98 (0.38)	1.00 (0.35)	0.525
Low-density lipoprotein cholesterol (mmol/L), median (IQR)	3.16 (1.58)	3.22 (1.52)	3.10 (1.61)	0.018
Random serum glucose (mmol/L), median (IQR)	8.70 (6.53)	8.40 (6.18)	8.97 (6.51)	0.248
HbA1c (%), median (IQR)	7.10 (3.40)	6.90 (3.20)	7.60 (3.50)	0.063
Serum creatinine (μmol/L), median (IQR)	88.00 (33.00)	88.00 (31.60)	84.00 (33.60)	0.032
Left ventricle findings in echocardiography				
Mild dysfunction	1899 (50.48)	1702 (51.17)	197 (45.18)	Reference
Moderate dysfunction	771 (20.49)	682 (20.51)	89 (20.41)	Reference
Sever dysfunction	297 (7.89)	257 (7.73)	40 (9.17)	0.053
Normal left ventricle function	795 (21.13)	685 (20.60)	110 (25.23)	Reference
In-hospital outcomes/procedures				
Congestive heart failure	518 (10.97)	466 (11.14)	52 (9.67)	0.305
Recurrent ischemia	767 (16.24)	674 (16.11)	93 (17.29)	0.484
Reinfection	109 (2.31)	95 (2.27)	14 (2.60)	0.629
Cardiogenic shock	259 (5.48)	242 (5.78)	17 (3.16)	0.012
Stroke	27 (0.57)	24 (0.57)	3 (0.56)	0.963
Major bleeding	22 (0.47)	18 (0.43)	4 (0.74)	0.315
Percutaneous coronary intervention	724 (21.03)	594 (19.53)	130 (32.34)	< 0.001
Coronary artery bypass graft surgery	123 (2.61)	99 (2.37)	24 (4.46)	<0.001
Mortality				
In-hospital	207 (4.38)	193 (4.61)	14 (2.60)	0.032
1 mo	316 (7.77)	293 (8.18)	23 (4.75)	0.008
1 y	426 (11.65)	392 (12.15)	34 (7.91)	0.010

Data are presented as *n* (%) unless otherwise indicated.
ACS = acute coronary syndrome; AMI = acute myocardial infarction; IQR = interquartile range; MB = myocardial B fraction.

Table 3. Crude and adjusted odds ratios (OR) for medical history and for developing adverse hospital outcomes and overall mortality in patients with first presentation of AMI.

Outcome	Crude OR (95% CI)	*p*	Adjusted OR (95% CI)	*p*
In-hospital outcomes				
Congestive heart failure	1.17 (0.86–1.58)	0.305	1.08 (0.73–1.57)	0.706
Recurrent ischemia	0.92 (0.72–1.17)	0.485	0.93 (0.69–1.25)	0.650
Reinfarction	0.87 (0.49–1.53)	0.629	1.16 (0.58–2.30)	0.676
Cardiogenic shock	1.88 (1.14–3.10)	0.013	1.51 (0.74–3.08)	0.256
Stroke	1.03 (0.31–3.43)	0.964	2.30 (0.29–17.99)	0.429
Major bleeding	0.58 (0.19–1.71)	0.321	0.65 (0.13–3.07)	0.583
Overall mortality	1.59 (1.10–2.30)	0.013	1.16 (0.74–1.83)	0.511

Adjustment done for age, medical history (diabetes, hypertension and hyperlipidemia, GRACE score, creatinine and triglyceride).
AMI = acute myocardial infarction; CI = confidence interval; GRACE = Global Registry of Acute Coronary Events risk score; OR = odds ratio.

reported as absolute number and percentages. Univariate comparisons of patient different characteristics, initial presentation, and medical history were conducted using Wilcoxon rank-sum or chi-square tests. Cox proportional hazards models were conducted to compare the mortality hazards. A multivariable adjusted model was built; we controlled the baseline characteristics and other clinical presentation variables. Logistic regression modeling was used to more systematically examine the differences in risk of adverse in-hospital outcomes and overall mortality between the two groups. Potential confounding demographic and clinical characteristics were controlled.

Results

From a total of 7930 patients with a confirmed diagnosis of ACS in the registry, we excluded 3207 patients because they were diagnosed with unstable angina (Fig. 1). Of the total number of patients with AMI in the registry, 88.6% have had AMI as first presentation of ACS.

Initial presentation between the two groups were almost similar; however, patients in the first presentation AMI group were older with a statistical significant association ($p < 0.001$) (Table 1). Comparison of the two groups in terms of medical history showed that patients with a history of ACS had a significantly higher rate of diabetes mellitus, congestive heart failure, hyperlipidemia, and hypertension. However, those in the first presentation AMI group showed higher frequency of intermediate and high GRACE risk score categories with a p value of <0.001.

Laboratory investigations showed almost similar results between the two groups, with higher results of cardiac markers in the first presentation AMI group (Table 2). Interestingly, mild and moderate left ventricle dysfunction was higher in the first presentation AMI group. In-hospital outcomes were insignificantly variable between the two groups. However, invasive procedures such as percutaneous coronary intervention and coronary artery bypass graft surgery were more likely to be conducted among patients with a history of ACS ($p < 0.001$). All aspects of mortalities including in-hospital, 1-month, and 1-year mortality occurred significantly more frequently in first presentation AMI patients (Table 2).

Moreover, in order to explore the association and avoid confounding measures, we conducted a multivariate logistic regression of first presentation AMI as an independent variable. Dependent variables include congestive heart failure, recurrent ischemia, reinfection, cardiogenic shock, and overall mortality (Table 3).

Discussion

This study is the first to compare the demographic characteristics, initial presentation, and medical history of patients with first presentation AMI and patients with a history of ACS. Patients with first AMI were relatively older and had lower risk factors for coronary artery disease than patients with a history of ACS. Comparing Gulf RACE-II with GRACE registries, the average age among ACS patients in Gulf RACE-II was a decade younger than that in GRACE [11]. This significant difference might be attributed to the difference in the coronary risk factor profile between the two cohorts. Diabetes mellitus and smoking habit were more prevalent in Gulf RACE-II, and this might accelerate the underlying coronary atherosclerosis.

Although first presentation AMI patients have had lower ACS risk factors, the level of cardiac markers in their blood was significantly high. The level of cardiac troponin was more than eight times higher in patients with first AMI, and the

level of creatinine kinase myocardial B fraction (MB) was doubled in the same group compared to the second group. This might be attributed to different reasons, including the fact that the massive myocardial infarction that happened to the first AMI group led to leakage of cardiac markers in high values. However, the elevated level of cardiac markers could be referred to different noncardiac etiology [18,19].

Generally, in-hospital outcomes were nonsignificantly different between the two groups. However, cardiogenic shock was statistically significantly more common among patients with first AMI. The correlation between the levels of cardiac troponin in the first AMI group with more prevalent cardiogenic shock might explain this observation. In-hospital outcomes including congestive heart failure, recurrent ischemia, reinfection, cardiogenic shock, and major bleeding were slightly more prevalent among patients with a history of ACS. Long-standing risk factors among patients who have a history of ACS might explain this observation. The patients with a history of ACS were more likely to undergo percutaneous coronary intervention or coronary artery bypass graft surgery. Having a history of ACS might make the odds of having another ACS episode more likely; thus, the decision of revascularization therapy is more likely to happen. The overall rate of revascularization therapy was low, and this is because the different hospitals that participated in the Gulf-RACE registry were not equipped to handle advanced revascularization therapy such as percutaneous coronary intervention and coronary artery bypass grafting.

In-hospital, 1-month, and 1-year mortality rates were significantly higher among patients with first AMI compared to those with a history of ACS. These high mortality rates, which were almost double in pattern across the mortality aspects, were surprising. Taking into consideration the extreme values of cardiac troponin and cardiac creatinine kinase-MB among patients with first AMI is an acceptable explanation for these high mortality rates. The correlation between the level of cardiac markers and the mortality rates has been discussed previously and showed a positive correlation [20,21].

The Gulf RACE registry included a large number of hospitals, and treatment, management, and patient care is not similar across all these hospitals. The higher mortality rates among patients with first AMI indicate an urgent need to implement a policy to detect AMI among patients with no previous ACS and start management immediately. These findings yield several implications regarding healthcare regulations in Gulf countries. Further studies examining the discrepancy between the effects of different risk factors of ACS among patients presented with their first AMI are needed.

Our study has several limitations, including the fact that the voluntary involvement of patients to this cohort registry might not reflect an accurate representation of clinical practice in participating hospitals. However, the wide variety of participating hospitals based on geographic location creates a reasonable representation of ACS medical care in the area. There are no available data regarding remission for reinfection, ischemia, or repeated revascularization procedures, which can result in underreporting of the long-term benefit of the treatment provided. Although long-term mortality rates were reported, it was limited to mortality rate alone without other potential factors such as medications, compliance, and recurrent ischemia or reinfarctions. Finally, being diagnosed with AMI as the first presentation of ACS was based on patients' history upon admission, and this carries the risk of recall bias.

Conclusions

Cardiac patients who presented with AMI as the first presentation of their coronary artery disease were relatively older and had fewer risk factors compared to patients who have a history of ACS. Major bleeding and the likelihood to undergo revascularization procedures including percutaneous coronary intervention or coronary artery bypass graft surgery were more prevalent among patients with a history of ACS. In-hospital, 1-month, and 1-year mortality rates were higher among first presentation AMI patients.

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Authors' contributions

AJ conducted the data analysis and drafted the manuscript; NA proposed the idea participating in writing the protocol; AH conduct the analysis; TK is the author of correspondence, supervised the whole project from writing the protocol and drafting the manuscript.

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