



Clinical characteristics and outcomes of young adults with first myocardial infarction: Results from Gulf COAST



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ABSTRACT

Introduction: Limited data exists on the risk factor profile and outcomes of young patients suffering their first acute myocardial infarction (AMI).

Methods: We examined 1562 Gulf-Arabs without prior cardiovascular disease presenting with first AMI enrolled in the Gulf COAST prospective cohort. Clinical characteristics were compared in patients ≤ 50 years of age (young) vs. > 50 years (older). Associations between age group and in-hospital adverse events (re-infarction, heart failure, cardiogenic shock, cardiac arrest, stroke, and in-hospital death) or post-discharge mortality were estimated using logistic regression.

Results: Young patients represented 26.1% ($n = 407$) of first AMI cases and were more likely to be men (82.8% vs. 66.5%), current smokers (49.9% vs 19.0%), obese (38.3% vs 28.0%), and have family history of premature coronary artery disease (21.4% vs 10.4%) compared with older patients (all $P < 0.001$). Young patients were more likely to receive β -blockers (83.0% vs 74.4%; $P < 0.001$), clopidogrel (82.3% vs 76.0%; $P = 0.009$) and primary reperfusion therapy (85.6% vs. 75.6%; $P = 0.003$). Young adults had lower in-hospital death (adjusted odds ratio [aOR] = 0.37; 95%CI = 0.16–0.86) or any in-hospital adverse cardiovascular events (aOR = 0.53; 95%CI = 0.34–0.83). Young adults had lower likelihood of cumulative death at 12-month post-discharge (aOR = 0.34; 95%CI = 0.19–0.59) after adjusting for potential confounders.

Conclusion: Young patients with first AMI were more likely to be obese, smokers and have family history of premature coronary artery disease compared to older adults. Young patients were more likely to receive guideline-proven therapies and have better in-hospital and post-discharge mortality. These data highlight important age-related care gaps in patients suffering AMI for the first time.

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1. Introduction

Recent trends show an increasing burden of cardiovascular risk factors in young adults [1,2]. Consequently, the incidence of acute myocardial infarction (AMI) in young adults is on the rise [2]. Modifiable atherosclerotic cardiovascular disease (ASCVD) risk factors account for the majority of AMI risk in both the young and old [1,3,4]. However, these risk factors may remain undiagnosed or undertreated in young adults until the time of first AMI.

Data from the INTERHEART (The Effect of Potentially Modifiable Risk Factors Associated with Myocardial Infarction) study show that patients from the Middle East with their first AMI are on average 10–12 years younger than in Western countries [4]. The Middle Eastern Gulf region is known to have alarming high rates of cardiovascular risk factors early in life [5]. Yet, very little is known about the risk profile of young patients with AMI in this region. Moreover, the extent to which young age influences the clinical presentation, and outcomes from AMI is unclear [6–8].

Using data from 4 Middle Eastern Gulf countries enrolled in the Gulf locals with acute coronary syndrome events (Gulf COAST) registry, the aim of this study was to: (1) determine the prevalence of modifiable ASCVD risk factors in young patients with no established ASCVD who present with their first AMI, (2) explore how

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young and older patients differ by clinical presentation, disease severity and in-hospital treatment patterns, and (3) examine how in-hospital outcomes and long term post-discharge mortality differ by age. The Gulf COAST registry offers a unique opportunity to address these aims using data from a relatively homogenous cohort of patients with similar lifestyles and access to free medical care.

2. Methods

2.1. Study design

We examined a subset of patients enrolled in the Gulf COAST registry with no established cardiovascular disease presenting with their index AMI. Details on the Gulf COAST registry have been previously published [9]. In brief, Gulf COAST is a prospective, multicenter, multi-national cohort-based registry of consecutive patients admitted with a diagnosis of acute coronary syndrome (ACS) from January 2012 to January 2013. Twenty-nine hospitals from 4 Gulf countries, namely, Bahrain, Kuwait, Oman, and the United Arab Emirates, were included. Participants signed an informed consent prior to study enrolment. Kuwait University provided oversight of the Gulf COAST registry under project code XX02/11. The Gulf COAST registry received the approval of the ethics committees of each participating institution or country and conforms to the ethical guidelines of the 1975 Declaration of Helsinki. The authors of this manuscript have certified that they comply with the principles of Ethical publishing in the *International Journal of Cardiology Heart and Vasculature*.

2.2. Study participants

We included individuals enrolled in Gulf COAST with no prior history of clinical ASCVD who presented with acute coronary syndrome and carried the diagnosis of AMI as their admission event. Acute myocardial infarction was defined as a rise or fall in cardiac biomarkers with at least one value above the 99th percentile of the upper reference limit of the assay with evidence of myocardial ischemia including any of the following: ischemic symptoms, ischemic changes on electrocardiography, evidence of loss of viable myocardium on imaging, or angiographic evidence of coronary atherothrombosis. We excluded patients with prior percutaneous coronary interventions (PCI), coronary artery bypass surgery, prior history of transient ischemic attack or stroke, renal dysfunction requiring dialysis, or patients presenting with concomitant stroke or severe bleeding. We also excluded patients with a primary presenting diagnosis of severe (i.e. requiring intubation) chronic obstructive pulmonary disease exacerbation, or pneumonia; this was to avoid confounding patient prognosis and obscuring concomitant acute clinical heart failure.

2.3. In-hospital data collection

Patients were followed prospectively for the duration of their admission. A case report form was used to collect data and included data elements in accordance with the American College of Cardiology key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndrome [10]. The form included data on demographics, medical history, home medications, early symptoms, clinical management, in-hospital course, and discharge data. A research associate conducted a random source verification of 10% of case report forms in all participating hospitals to ensure data validation.

2.4. Cardiovascular risk factors

Data on modifiable ASCVD risk factors (including hypertension, dyslipidemia, diabetes, smoking, obesity and central adiposity) and non-modifiable ASCVD risk factors (including sex or family history of premature coronary artery disease) were obtained at the time of presentation. Hypertension was defined as a documented diagnosis of hypertension treated with medications or lifestyle changes. Hyperlipidemia was defined as a documented diagnosis of hyperlipidemia requiring lipid-lowering therapy. Diabetes was defined as a documented history of diabetes regardless of duration of disease, requiring antidiabetic agents or a fasting blood glucose greater than 126 mg/dL. Participants' body mass index (BMI) was calculated as the weight in kilograms divided by the height squared. Obesity was defined as a BMI of ≥ 30 kg/m². Central adiposity was defined as a waist circumference ≥ 102 cm in males and ≥ 88 cm in females. Family history of premature coronary artery disease was defined as the presence of any direct blood relatives (parents, siblings, and children) who suffered stable or unstable angina, myocardial infarction, or sudden cardiac death without an obvious cause before the age of 55 years.

2.5. Cardiovascular therapies

Therapies administered within the first 24 h were recorded. This included the use of aspirin, clopidogrel, prasugrel, ticagrelor, β -blockers, statins and primary reperfusion therapy. Primary reperfusion therapy included either primary coronary intervention (PCI) or primary fibrinolytic therapy. The proportion of those receiving primary reperfusion therapy was calculated as the percent of patients eligible for primary reperfusion who received it during admission. At the time of the study, eligibility for primary reperfusion therapy was assessed based on the 2013 American College of Cardiology/American Heart Association guidelines on management of acute coronary syndrome and included patients presenting with ST-elevation myocardial infarction (STEMI), new or presumed new left bundle branch block in the setting of clinical suspicion of AMI, or isolated posterior AMI [11]. Reasons for not receiving primary reperfusion therapy in those eligible was also recorded.

2.6. Cardiovascular outcomes

In-hospital outcomes were ascertained prospectively during the period of admission. We report on the development of 6 major in-hospital adverse cardiovascular events (MACE), namely reinfarction, heart failure, cardiogenic shock, cardiac arrest, stroke, and in hospital death. Cardiogenic shock was defined as the development of hypotension with a systolic blood pressure < 90 mm Hg for at least 30 min associated with end-organ hypoperfusion or a cardiac index ≤ 2.2 L/min/m² and a pulmonary capillary wedge pressures of ≥ 15 mm Hg. The diagnosis of in-hospital heart failure was at the physician discretion. Stroke was defined as the loss of neurological function caused by ischemic or hemorrhagic events with residual symptoms lasting ≥ 24 h after onset or leading to death. After discharge, clinic visits or phone calls were planned at 1, 6, and 12 months from the date of admission to ascertain survival data.

2.7. Statistical analysis

Patients were categorized into two age groups based on age at the time of hospital presentation: young (≤ 50 years of age) or older (> 50 years of age). Baseline characteristics were compared in the two age groups. Categorical variables were summarized using frequencies and proportions and compared using a Chi-square test or

Fisher's exact where appropriate. Continuous variables were summarized using means, standard deviations, medians, interquartile ranges and compared using a *t*-test for parametric variables or a Mann-Whitney-*U* test for non-parametric variables.

A composite outcome of in-hospital MACE (yes/no) was calculated based on the presence of any of the following in-hospital events (each coded as yes/no): re-infarction, heart failure, cardiogenic shock, cardiac arrest, stroke, and in-hospital death. The cumulative number of patients suffering death was calculated at the end of hospitalization, 1, 6, and 12-month follow-up. Cumulative death was compared between age groups. Because the incidence of events was low in the study, the association between the patient's age group (young vs. older) and in-hospital events (yes/no) or cumulative death during follow-up (yes/no) were estimated using logistic regression and summarized using odds ratios and 95% confidence intervals.

Regression models were used to adjust for sex, obesity, history of hypertension, diabetes, smoking status on presentation, use of lipid lowering or antihypertensive therapy, presenting heart rate, systolic blood pressure, blood creatinine value, presence of ST-segment deviation on the presenting electrocardiogram, cardiac arrest on presentation, elevated cardiac enzymes on initial labs, Killip class on presentation, the use of clopidogrel and β -blockers within the first 24 h of presentation, and receiving primary reperfusion therapy. The regression models' goodness-of-fit was tested using the Hosmer-Lemeshow goodness-of-fit test. All analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY). A two-sided *P*-value of <0.05 was considered statistically significant.

3. Results

Among the 4044 participants in Gulf-COAST with complete data, a total of 1562 patients with first AMI met the inclusion criteria for this analysis. Among patients presenting with first AMI, 407 (26.1%) were young (≤ 50 years of age) with a mean \pm SD age of 42.9 ± 5.9 years and 1155 (73.9%) were older adults (> 50 years of age) with a mean age of 64.7 ± 9.5 years. At the time of admission, a total of 216 (53.1%) of young and 434 (37.6%) of older patients were diagnosed with STEMI, 191 (46.9%) of the young and 698 (60.4%) of the older patients were diagnosed with non-STEMI, and 0 (0%) of the young and 23 (2.0%) of older patients had a new or presumed new left bundle branch block AMI. [Table 1](#) shows baseline characteristics according to age category.

The prevalence of modifiable and non-modifiable ASCVD risk factors was high at the time of presentation in both young and older patients ([Fig. 1](#)). Hypertension, dyslipidemia, diabetes, obesity and central adiposity were each present in more than one third and significant family history of premature coronary artery disease was present in one fifth of young adults. Compared with older patients, hypertension (59.3% vs. 35.1%), dyslipidemia (44.9% vs. 33.2%), and diabetes (51.2% vs 36.6%) were less prevalent in young patients ($P < 0.001$ for all). However, young patients were more likely to have family history of premature coronary artery disease (21.4% vs 10.4%), be current smokers (49.9% vs 19.0%), obese (38.3% vs 28.0%) and be currently working (73.7% vs. 18.2%) at the time of presentation ($P < 0.001$ for all). Central adiposity was prevalent in both young and older patients (46.9% vs 45.3%; $P = 0.566$)

Among those with a diagnosis of dyslipidemia prior to presentation, young patients were less likely to be on statin therapy at the time of presentation than older patients (56.3% vs 72.3%; $P < 0.001$). Similarly, among those with a diagnosis of hypertension at the time of presentation, young patients were less likely to be on antihypertensive medications than older patients (76.9% vs 84.8%; $P = 0.026$).

Details on the clinical presentation and lab values of young vs. older patients are shown in [Table 2](#). Although pain typical of ischemia was the commonest presenting symptom in the study sample (80.6%), pain typical of ischemia was more commonly experienced by young patients compared with older patients (88.9% vs 77.7%; $P < 0.001$). Cardiac arrest on presentation was more common in young compared to older patients (3.7% vs. 1.8%; $P = 0.031$). Having signs of heart failure on the presenting physical exam (i.e. Killip class > 1) was more common in the older group than in the young (21.2% vs 10.6%; $P < 0.001$). Compared with older patients, young patients had a more atherogenic lipid profile on presentation with higher levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol as well as lower levels of high-density lipoprotein cholesterol. There was no significant difference in the presenting troponin levels between young and older patients. However, young patients had a higher peak value of cardiac troponin than older patients (median 4.8 ng/mL vs. 3.5 ng/mL; $P = 0.018$).

There were significant differences in the initial treatment patterns in young vs. older patients presenting with first AMI as shown in [Table 3](#). The use of aspirin and statin therapy within the first 24 h was high and comparable in both groups. However, the use of adjuvant antiplatelet agents (82.6% vs 76.5%; $P = 0.011$) and beta-blockers (83.0% vs 74.4%; $P < 0.001$) was higher in the young compared with older patients. In patients with STEMI, new or presumed new left bundle branch block AMI, or isolated posterior AMI, young patients were more likely to be eligible for primary reperfusion therapy and more likely to receive emergent reperfusion therapy at the time of presentation compared to older patients ([Table 3](#)).

Fibrinolytic therapy was the commonest form of reperfusion therapy administered but had suboptimal rates of utilization in both groups. Primary angiography or PCI was performed in only 8.6% of the young and 3.9% of older patients who are eligible. The most common reason for not receiving primary reperfusion therapy when indicated was late presentation with symptom onset > 12 h. One third of patients underwent cardiac catheterization prior to discharge and were more likely to be young patients. Further details on the initial treatment patterns by AMI type are shown in [Supplemental Table 2](#).

We next compared in-hospital outcomes in the young vs. older patients with first AMI. [Fig. 2](#) (numbers shown in [Supplemental Table 3](#)) shows the prevalence of each of the in-hospital MACE events by age. In an unadjusted logistic regression model, young patients had a significant 62% lower odds for MACE (odds ratio [OR], 0.38; 95% CI, 0.26–0.55; $P < 0.001$), 63% lower odds of heart failure (OR, 0.33; 95% CI, 0.20–0.53; $P < 0.001$), 54% lower odds of cardiogenic shock (OR, 0.46; 95% CI, 0.25–0.84; $P = 0.011$), and 77% lower odds of in-hospital death (OR, 0.23; 95% CI, 0.11–0.51; $P < 0.001$) compared with older adults. With the exception of cardiogenic shock, these associations remained statistically significant after adjusting for patient demographics, comorbid conditions, clinical presentation factors and initial therapies received ([Table 4](#)). In both the young and older age groups, none of the modifiable risk factors on presentation were independent predictors of in-hospital mortality.

At 12-month follow-up, mortality data was available for 1505 (96.4%) of patients, indicating minimal loss to follow-up. The cumulative number of those who died (including those who died during hospitalization) was 108 (7.0%) at 1-month follow-up, 156 (10.7%) at 6-month follow-up, and 192 (12.8%) at 12-month follow-up. At 1-month follow up, there was a highly statistically significant 72% lower odds of cumulative death for younger adults compared with older adults (OR, 0.28; 95% CI, 0.14–0.53; $P < 0.001$). Similarly, statistically significant lower odds for cumulative death were observed at 6 months (OR, 0.24; 95% CI, 0.13–

Table 1
Baseline characteristics in young vs. older patients presenting with first AMI.

Characteristics	Total n = 1562		Young (≤50 years) n = 407		Older (>50 years) n = 1155		P-value*
	n	%	n	%	n	%	
Male sex	1105	70.7%	337	82.8%	768	66.5%	<0.001
Age; mean (SD)	59	(12.9)	42.9	(5.9)	64.7	(9.5)	<0.001
Body mass index; mean (SD)	28.4	(5.9)	29.4	(6.0)	28.0	(5.8)	<0.001
Waist circumference, mean (SD)	97.1	(17.0)	98.5	(16.2)	96.6	(17.2)	0.057
Work status at presentation							<0.001
Not working	1052	67.3%	107	26.3%	945	81.8%	
Working	510	32.7%	300	73.7%	210	18.2%	
Medication use Prior to Admission							
Aspirin	583	37.3%	88	21.6%	495	42.9%	<0.001
Statins	607	38.9%	101	24.8%	506	43.8%	<0.001
Any lipid lower therapy	612	39.2%	104	25.6%	508	44.0%	<0.001
Beta blocker	414	26.5%	60	14.7%	354	30.6%	<0.001
ACE-I	468	30.0%	86	21.1%	382	33.1%	<0.001
ARB	126	8.1%	15	3.7%	111	9.6%	<0.001
Calcium channel blocker	133	8.5%	13	3.2%	120	10.4%	<0.001
Diuretics	186	11.9%	15	3.7%	171	14.8%	<0.001
Warfarin	12	0.8%	2	0.5%	10	0.9%	0.457
Oral anticoagulant	7	0.4%	2	0.5%	5	0.4%	0.879
Treatment patterns prior to presentation							
Those with dyslipidemia on lipid lowering therapy	456	69.7%	79	58.5%	377	72.6%	0.002
Those with hypertension on anti-hypertensives	691	83.5%	110	76.9%	581	84.8%	0.026

Abbreviations: ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

* P-values compare young vs. older patient groups.

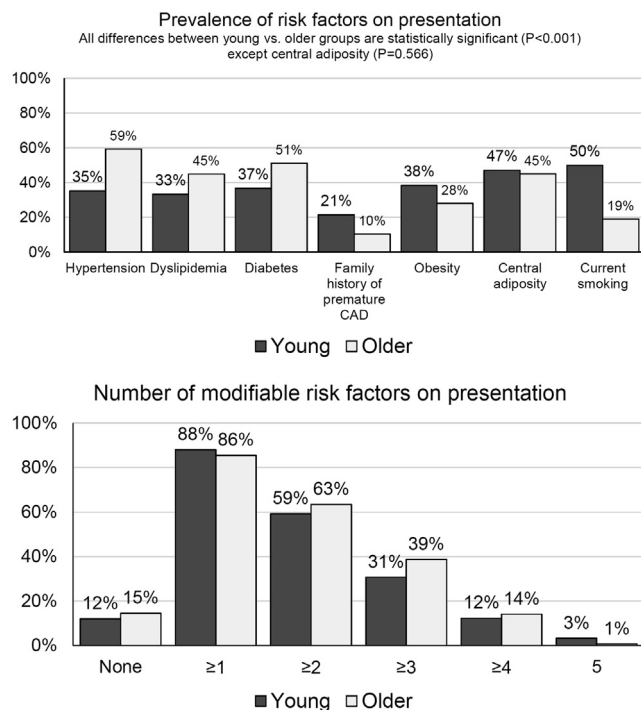


Fig. 1. The top panel shows the prevalence of modifiable and non-modifiable atherosclerotic cardiovascular disease risk factors by age group (young, ≤50 years; older, >50 years). The bottom panel shows the number of modifiable risk factors (hypertension, dyslipidemia, diabetes, obesity, and smoking) at the time of presentation by age group. Abbreviations: CAD, coronary artery disease.

0.42; P < 0.001) and 12 months (OR, 0.23; 95% CI, 0.14–0.39; P < 0.001). Compared with older adults, the lower odds of cumulative death at 1, 6, and 12 months for young adults remained highly statistically significant after adjusting for patient demographics, comorbid conditions, clinical presentation, and initial therapies received.

4. Discussion

In this analysis, we examined the prevalence of modifiable risk factors and clinical outcomes of young versus older patients with first AMI enrolled in the Gulf COAST registry. Young patients (≤50 years of age) comprised 26.1% of those presenting with first AMI and had an alarmingly high burden of ASCVD risk factors with 59% having at least 2 modifiable risk factors at the time of presentation. Compared with older patients, young patients were less likely to be on risk factor-modifying therapies such as statin therapy prior to their first AMI.

At the time of AMI, young patients were more likely to present with typical ischemic symptoms, less signs of heart failure on presentation, and receive guideline-proven therapies such as β-blockers, adjuvant antiplatelet therapy and primary reperfusion therapy when indicated. Young patients also had significantly lower likelihood of in-hospital death or any MACE and significantly lower likelihood of cumulative death up to 12-month post-discharge compared with older patients.

4.1. Modifiable risk factors are common in young adults at the time of first AMI

Our current study focused on patients presenting with AMI as their first ASCVD manifestation which allowed for identifying possible missed opportunities for primary AMI prevention. More than 8 out of 10 young patients had at least one known modifiable risk factor prior to their first AMI. Smoking was the leading modifiable risk factor in the young, and together with obesity and family history of premature coronary artery disease these risk factors were more prevalent in the young than in older patients. The prevalence of central adiposity was equally high in both young and older adults. Data from the INTERHEART study showed that dyslipidemia, smoking, psychosocial factors, and obesity have the highest population attributable risk for myocardial infarction in the Middle East region [4]. Therefore, the high prevalence of these risk factors in young Gulf locals is alarming. When taken together, our findings

Table 2
Clinical presentation and lab values in young vs. older patients.

	Total n = 1562		Young (≤50 years) n = 407		Older (>50 years) n = 1155		P-value*
Clinical presentation							
Presenting symptoms, n (%)							<0.001
No presenting symptoms	9	0.6%	2	0.5%	7	0.6%	
Pain typical of ischemia	1259	80.6%	362	88.9%	897	77.7%	
Pain atypical of ischemia	64	4.1%	16	3.9%	48	4.2%	
Shortness of breath	81	5.2%	6	1.5%	75	6.5%	
Shortness of breath AND ischemic pain	111	7.1%	16	3.9%	95	8.2%	
Other symptoms	38	2.4%	5	1.2%	33	2.9%	
Cardiac arrest on admission, n (%)	36	2.3%	15	3.7%	21	1.8%	0.031
Heart rate; mean (SD)	85	(20)	84	(19)	85	(21)	0.291
Systolic BP; mean (SD)	140	(28)	137	(26)	142	(28)	0.002
Diastolic BP; mean (SD)	82	(17)	83	(17)	81	(17)	0.031
Killip Class, n (%)							<0.001
I (No heart failure)	1274	81.6%	364	89.4%	910	78.8%	
II (rales)	170	10.9%	26	6.4%	144	12.5%	
III (Pulmonary edema)	99	6.3%	13	3.2%	86	7.4%	
IV (Cardiogenic shock)	19	1.2%	4	1.0%	15	1.3%	
Initial lab values, mean (SD)							
Hemoglobin, g/dL	13.58	(2.06)	14.5	(1.9)	13.3	(2.0)	<0.001
WBC, 10 ⁹ cell/L	9.73	(3.90)	10.4	(4.1)	9.5	(3.8)	<0.001
Platelets, 10 ⁹ cell/L	269.1	(85.1)	271.6	(82.2)	268.2	(86.2)	0.482
HbA1c, %	7.5	(2.31)	7.4	(2.5)	7.5	(2.2)	<0.001
Cholesterol, mmol/L	5.0	(1.36)	5.4	(1.4)	4.9	(1.3)	<0.001
Triglycerides, median [IQR], mmol/L	1.4	[1.0, 2.1]	1.7	[1.2, 2.5]	1.3	[0.9, 1.9]	<0.001
HDL-C, mmol/L	1.0	(0.3)	1.0	(0.3)	1.0	(0.3)	0.005
LDL-C, median [IQR], mmol/L	3.2	[2.5, 4.0]	3.5	[2.8, 4.3]	3.2	[2.4, 3.9]	<0.001
Creatinine, median [IQR], μmol/L	83.0	[69.0, 103.0]	79.4	[66.0, 93.0]	85.0	[70.0, 108.0]	<0.001
Troponin, median [IQR], ng/mL	0.3	[0.1, 2.2]	0.2	[0.0, 1.7]	0.3	[0.1, 2.5]	0.307

Abbreviations: BP, blood pressure; WBC, white blood cell count; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

* P-value compares young vs. older patients.

Table 3
Treatment patterns in young vs. older patients with first AMI.

	Total n = 1562		Young (≤50 years) n = 407		Older (>50 years) n = 1155		P-value*
	n	%	n	%	n	%	
Medications given within the first 24 h of presentation							
Aspirin	1547	99.0%	404	99.3%	1143	99.0%	0.591
Clopidogrel	1213	77.7%	335	82.3%	878	76.0%	0.009
Prasugrel	2	0.1%	0	0.0%	2	0.2%	0.401
Ticagrelor	4	0.3%	1	0.2%	3	0.3%	0.962
β-blockers	1197	76.6%	338	83.0%	859	74.4%	<0.001
Statins	1519	97.2%	391	96.1%	1128	97.7%	0.091
Reperfusion therapy (for new STEMI, new or presumed new LBBB, or isolated posterior AMI)							
Eligible for primary reperfusion therapy**	666	42.6%	215	52.8%	451	39.0%	<0.001
Received primary reperfusion therapy	525	78.8%	184	85.6%	341	75.6%	0.003
Fibrinolytic	427/666	64.1%	140/215	65.1%	287/451	63.6%	
Fibrinolytic in previous hospital	18/666	2.7%	9/215	4.2%	9/451	2.0%	
Primary angioplasty	80/666	12.0%	35/215	16.3%	45/451	10.0%	
Reason for not receiving primary reperfusion therapy							
Contraindication to fibrinolytic therapy	11	7.8%	3	9.7%	8	7.3%	0.551
Symptoms onset > 12 h	106	75.2%	21	67.7%	85	77.3%	
Other	24	17.0%	7	22.6%	17	15.5%	
Other therapies or tests							
Had cardiac catheterization during hospital stay	520	33.3%	161	39.6%	359	31.1%	0.002
Received PCI during hospital stay	134	8.6%	37	9.1%	97	8.4%	0.006
Echocardiogram during admission	1142	73.1%	292	71.7%	850	73.6%	0.469

Abbreviations: STEMI, ST-segment elevation myocardial infarction; LBBB, left bundle branch block; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention.

* P-value compares young vs. older adults.

** Eligible patients for primary reperfusion therapy include those with ST-elevation AMI, new or presumed new LBBB, isolated posterior AMI.

may help inform primary prevention initiatives that aim at reducing the burden of ASCVD in the region.

Uncontrolled early ASCVD risk factors significantly contribute to premature ASCVD [12,13]. In the current study, we show that

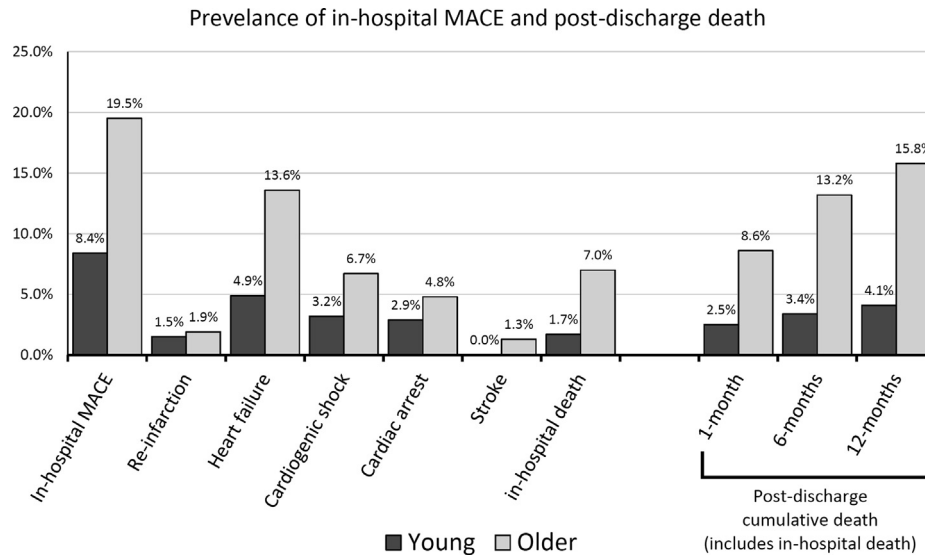


Fig. 2. Prevalence of in-hospital major adverse cardiovascular events (MACE) and cumulative post-discharge death by age group.

Table 4
In-hospital outcomes and cumulative death post-discharge in young vs. older (reference group) adults.

	Unadjusted model		Model 1		Model 2	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
In-hospital outcome						
Re-infarction	0.77 (0.31–1.91)	0.575	0.88 (0.33–2.38)	0.807	0.88 (0.32–2.46)	0.813
Heart failure	0.33 (0.20–0.53)	<0.001	0.46 (0.26–0.79)	0.005	0.50 (0.28–0.87)	0.015
Cardiogenic shock	0.46 (0.25–0.84)	0.011	0.53 (0.29–1.17)	0.129	0.67 (0.33–1.36)	0.265
Stroke	NA*	NA*	NA*	NA*	NA*	NA*
Cardiac arrest	0.60 (0.32–1.12)	0.110	0.72 (0.36–1.45)	0.353	0.87 (0.42–1.80)	0.869
In-Hospital death	0.23 (0.11–0.51)	<0.001	0.32 (0.14–0.73)	0.007	0.37 (0.16–0.86)	0.021
Any MACE**	0.38 (0.26–0.55)	<0.001	0.49 (0.31–0.76)	0.001	0.53 (0.34–0.83)	0.006
Cumulative death (including in-hospital death)						
Cumulative death at 1 month	0.28 (0.14–0.53)	<0.001	0.37 (0.18–0.76)	0.006	0.44 (0.21–0.90)	0.024
Cumulative death at 6 months	0.24 (0.13–0.42)	<0.001	0.31 (0.16–0.57)	<0.001	0.33 (0.18–0.61)	<0.001
Cumulative death at 12 months	0.23 (0.14–0.39)	<0.001	0.32 (0.18–0.56)	<0.001	0.34 (0.19–0.59)	<0.001

Abbreviations: MACE, major adverse cardiovascular event. Odds ratios were calculated with the older group as the reference group. Model 1 adjusted for sex, obesity, history of hypertension and diabetes, smoking status, use of lipid lowering and antihypertensive therapy, and the following variables on presentation: heart rate, systolic blood pressure, creatinine, presence of ST-segment deviation, cardiac arrest on presentation, elevated cardiac enzymes, Killip class on exam. Model 2 adjusted for the same variables in model 1 + use of clopidogrel, β-blockers, and primary reperfusion therapy. * Odds ratio and P-value cannot be estimated due to 0 stroke events in the young group. ** MACE defined as in-hospital: Reinfarction, Heart failure, cardiogenic shock, cardiac arrest, stroke, death.

young AMI patients with known dyslipidemia were less likely to be on statin or lipid lowering therapy prior to their presentation. This may explain why on average younger patients had a more atherogenic lipid profile than older patients. A potential explanation for the lower use of statin therapy in young patients may be that current guidelines use ASCVD risk estimates that are heavily influenced by age to determine statin eligibility [14,15]. As a result, most young patients would not meet treatment thresholds for statins prior to their AMI [16]. Recent reports have drawn attention to the higher prevalence of elevated lipoprotein (a) levels in young adults with AMI [17]. In the 2019 AHA/ACC Primary Prevention Guidelines, elevated lipoprotein (a) is considered a risk enhancer that favors intensifying risk lowering efforts to prevent future ASCVD [14]. In patients < 50 years of age with coronary artery disease or ACS treated with coronary stenting and on optimal lipid lowering therapy, elevated lipoprotein (a) levels remains a significant predictor of future ASCVD [18]. Therefore, recognizing lipoprotein (a) as a source of residual risk in young adults after their first AMI may be valuable in this high risk population. Taken together, these findings highlight important gaps in the primary

prevention of AMI in the young and call for future studies to identify alternative methods for determining eligibility for disease modifying therapies especially when ASCVD risk factors are present at a very young age [13].

4.2. Young patients are more likely to receive guideline-proven therapies for AMI

We observed significant differences in the clinical presentation and treatment patterns between young and older patients with first AMI. First, young patients presented with more straightforward symptoms typical of ischemia, while older patients were more likely to present with shortness of breath and signs of heart failure. This may have contributed to early AMI recognition and greater adherence to guideline-proven therapies in the young than in older adults. This presentation pattern compares favorably to other studies from the US and Europe [6,7]. Our finding of fewer heart failure symptoms at presentation in the young was in spite of a higher prevalence of STEMI and a higher peak value of troponin compared to older patients. Older patients have altered pain

thresholds [19], comorbid illnesses or socioeconomic factors such as limited access to transportation or medical insurance [20], which may contribute to a delay in presentation and higher likelihood of developing heart failure. In addition, prior studies suggest that patients with STEMI are more likely to present with symptoms typical of ischemia compared to NSTEMI, prompting an earlier visit to the hospital [21].

Second, while the utilization of aspirin and statins in the first 24 h of presentation was high in both age groups, the initial use of β -blockers and adjuvant antiplatelet agents were higher in the young patients; this may be because of higher confidence in the diagnosis of AMI on presentation and lower prevalence of heart failure signs compared with older adults. The use of adjuvant antiplatelet therapy is lower in the current study than in other studies of the same time period [22–24]. Clopidogrel was the most commonly prescribed adjuvant antiplatelet agent, while the use of other antiplatelet agents such as ticagrelor or prasugrel was extremely low. Cost considerations on patients are unlikely to explain higher clopidogrel use since health care is free in the countries included in Gulf COAST. Although there are no age-specific recommendations for adjuvant antiplatelet therapy in patients with AMI, older age is a significant predictor of bleeding risk and may have been a reason for withholding a second antiplatelet agent in the older group. Other studies have also reported similar findings [25–27].

Lastly, young patients were more likely to be eligible for primary reperfusion therapy than older patients. Among those eligible for primary reperfusion therapy, young patients were more likely to receive primary reperfusion therapy. This highlights an important treatment paradox, whereby older and perhaps sicker patients are less likely to receive potentially lifesaving therapies compared with young patients. Similar findings have been observed in other studies of myocardial infarction [28,29]. The current study extends these findings by demonstrating that late presentation is a major factor contributing to the undertreatment in the older population.

We also note the extremely low utilization of primary PCI among those eligible in both groups owing to low number of PCI capable hospitals at the time of the study. Since the time of this study, more hospitals have established onsite PCI capability. However, a recent report from The use of reperfusion in ST-elevation myocardial infarction in Kuwait (REPERFUSE Kuwait) prospective cohort showed that only 52.2% of STEMI patients received primary PCI as a primary reperfusion strategy and the majority of STEMI patients received either primary fibrinolytics or a pharmacoinvasive reperfusion strategy [24].

4.3. Young adults have lower in-hospital MACE and post-discharge mortality

Our current study is in line with prior reports showing better in-hospital outcomes for young patients with first AMI compared with older patients [21,30]. After adjusting for patient clinical presentation and comorbid conditions, young patients had significantly lower odds of any MACE including heart failure and stroke compared with older patients. The odds of cardiogenic shock was lower in the young in an unadjusted logistic regression model but was not significantly different from the odds of older adults in a fully adjusted model. This suggests that the observed difference in cardiogenic shock between the two age groups is mostly explained by measured differences in clinical presentation and comorbid conditions rather than age alone. We did not observe significant differences in re-infarction, cardiogenic shock, or in-hospital cardiac arrest between the two age groups; however, the low occurrence of these events may have limited the statistical power for this comparison by age.

Patients with first AMI have a high risk of death after their index event [31]. In the current study, 88 (5.6%) of AMI patients died during their index admission which represents 45% of all deaths observed in this study extending up to 12-month post-discharge. Young patients had significantly lower odds of death during hospitalization and up to 12-months of follow-up compared with older patients. These associations were independent of measured differences in baseline demographics, comorbid conditions, clinical presentation, and initial therapies. Our findings are in line with similar studies showing high risk of death after first AMI especially in older adults [32]. Several large observational studies show that the risk of death is highest in the first year after first AMI [32]. After the first year post-AMI, the risk of mortality remains substantially higher in AMI patients than in the general population [33]. These findings together with findings from the current study highlight the importance of establishing early and close post-discharge care with extended follow-up surveillance in patients with first AMI.

4.4. Strengths and limitations

Several strengths and limitations are worth highlighting. Gulf COAST enrolled only citizens of the 4 participating countries to ensure relative homogeneity of the patient cohort, as citizens of these countries receive free medical care and live a similar lifestyle. Hospitals participating in the Gulf COAST registry covered the majority of admissions for acute coronary syndrome in their respective countries. Therefore, the potential for selection bias is low and the generalizability of our findings to the Gulf population is strong. Gulf COAST is a prospective registry with limitations based on the inherent design of the study. The study only included patients presenting to the hospital with suspected acute coronary syndrome. Selection bias toward more severe symptoms or a sicker presentation may have enriched the prevalence of typical ischemic symptoms or STEMI in the young population. Data on the type of troponin assays used in each enrolling center were not collected. This may have resulted in varying sensitivities in detecting elevated troponin levels across centers. Last, although we report the use of primary reperfusion therapy by age category, the success rate of primary reperfusion therapy was not recorded in the current study. Therefore, whether some of the observed differences in outcomes by age may be due to unsuccessful reperfusion remains unclear.

5. Conclusion

This is the first report from the Middle East on the risk profile and clinical outcomes of adults without established ASCVD presenting with first AMI. Young patients with first AMI had a high burden of modifiable ASCVD risk factors and were more likely to be obese, smokers and have family history of premature coronary artery disease compared with older patients. We also observe an important treatment paradox, whereby older and perhaps sicker patients with AMI are less likely to receive potentially lifesaving interventions such as reperfusion therapy compared with younger patients. Factors contributing to age-related deficits in the care of patients with AMI such as perceived patient frailty or treatment futility in older adults should be investigated in future studies. Young patients had lower likelihood of suffering in-hospital MACE and significantly lower likelihood of cumulative death up to 12-month post-discharge. These observations suggest the need for implementing aggressive primary and secondary prevention strategies in both young and older Gulf-Arabs.

Funding and study registration

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcha.2020.100680>.

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