

Clinical features, management and in-hospital outcome of ST elevation myocardial infarction (STEMI) in young adults under 40 years of age

Aspetti clinici, trattamento e prognosi ospedaliera di giovani adulti con STEMI e meno di 40 anni

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ABSTRACT: *Clinical features, management and in-hospital outcome of ST elevation myocardial infarction (STEMI) in young adults under 40 years of age. S.K. Hosseini, A. Soleimani, A.A. Karimi, S. Sadeghian, S. Darabian, S.H. Abbasi, S.H. Ahmadi, A. Zoroufian, M. Mahmoodian, A. Abbasi.*

Objectives: This study was designed to evaluate the demographic and clinical findings and in-hospital management and outcome in patients with an acute ST-segment elevation myocardial infarction (STEMI).

Material and methods: By review of the Cardiovascular Tehran Heart Center Registry (CVDTHCR), 2028 patients were found to have the acute STEMI. We compared the patients' characteristics in 109 (5.4%) subjects ≤ 40 and 1919 subjects > 40 years old.

Results: The young patients had less diabetes, hypertension, dyslipidemia and history of MI or prior revascularization, and were more likely to be male (92.7% vs. 74%),

smoker (58.7% vs. 31.7%) and have family history of CVD (50.5% vs. 23.4%). The young patients had higher prevalence of angiographically normal coronary artery (13.7% vs. 0.9%; $p < 0.001$). The young patients were more likely to undergo percutaneous coronary intervention (38.5% vs. 18.6%), whereas coronary artery bypass grafting was more common in the old ones ($p < 0.001$). In-hospital death was markedly different among young and old patients (0.9% and 6.1%, respectively; $p < 0.01$).

Conclusion: In STEMI population, the risk profile, clinical findings and severity of coronary disease of the young differ substantially from the elderly counterparts. Young patients with STEMI have a favorable outcome compared with that in older patients.

Keywords: *ST-segment elevation, myocardial infarction, risk factors, young, coronary artery disease.*

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Introduction

Over the past three decades, mortality and morbidity attributable to cardiovascular diseases (CVD) have declined in several developed countries, whereas they appear to have increased substantially in many developing countries [1, 2]. ST-segment elevation myocardial infarction (STEMI) is one of the common causes of cardiac consultation and admission at emergency departments and currently accounts for the high burden on health care services. The mortality, incidence, and clinical presentation of CVD tend to vary greatly over the time. During recent years, the mean age of CVD has decreased, but its prevalence has increased in Iran. Also, several studies have shown significant differences in the risk factors profile and prognosis of MI between different age groups [3-7].

There is a paucity of data in the existing literature on young Iranian patients with STEMI. In an attempt to characterize the acute STEMI patients ≤ 40 years of age and older at our institution, we reviewed the Tehran Heart Center Cardiovascular Disease Registry (THCCVDR) and compared the demographics, clinical findings, and in-hospital outcome of these two groups of patients.

Methods

A total of 14848 patients who were admitted to our institution and had identification data in the THCCVDR between July 2003 and August 2007 were reviewed. Our study population was consisted of 2028 patients with STEMI from the THCCVDR. The THCCVDR contains patient data collected by

cardiologists and trained general practitioners. The validity of all the data is checked by reabstracting 10% of the patients' entries and by reentering 5% of the patients' records. The study protocol was approved by the institutional Review Board, overseeing the participation of human subjects in research at Tehran University of Medical Sciences. This study conforms to the principles outlined in the Declaration of Helsinki.

The validation of AMI was based on information on medical history, symptoms, electrocardiograms, and cardiac enzymes. STEMI was diagnosed by a cardiologist when new or presumed new ST-segment elevation ≥ 1 mm (≥ 2 mm in V1 to V3) was seen in any location in two or more contiguous leads or new left bundle branch block was found on the index or qualifying electrocardiograms with ≥ 1 positive cardiac biochemical marker of necrosis, including CK-MB or cardiac troponin-I measurements. To characterize the young patients, 2028 patients with STEMI were classified into two groups of 109 subjects ≤ 40 (young patients) and 1919 subjects > 40 years old. The following data were included for analysis: demographic data, namely age and gender, and CVD risk factors profile, comprised of current cigarette smoking history (patient regularly smokes a tobacco product/products one or more times per day or has smoked in the 30 days prior to admission), dyslipidemia (total cholesterol ≥ 5.0 , HDL-cholesterol ≤ 1.0 in men or ≤ 1.1 in women, triglycerides ≥ 2.0 mmol/l), family history of CVD (first-degree relatives before the age of 55 in men and 65 years in women), hypertension (systolic blood pressure ≥ 140 and/or diastolic ≥ 90 mmHg and/or on anti-hypertensive treatment), diabetes mellitus (symptoms of diabetes and plasma glucose concentration ≥ 200 mg/dl

(11.1 mmol/l), or fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/l) or 2-hp ≥ 200 mg/dl (11.1 mmol/l)), and opium consumption [8]. The cardiac status of the patients, namely acute coronary symptoms, clinical manifestations, MI location based on electrocardiographic findings, cardiac enzyme profile, left ventricular ejection fraction (LVEF), angiographic findings, and management and in-hospital outcomes were reported. In the patients who underwent a coronary angiography at the time of hospitalization, significant coronary artery disease (CAD) was defined as a diameter stenosis $> 50\%$ in each major epicardial artery. A narrowing of $< 50\%$ was considered mild CAD. Normal vessels were defined as the complete absence of any disease, including lack of even mild luminal irregularities, which were considered as evidence of early atherosclerosis.

The results were reported as mean \pm standard deviation (SD) or median with 1st and 3rd quartiles (whenever the data did not appear to have normal distribution) for the quantitative variables, and the categorized variables were summarized as frequencies and percentages. The groups were compared using the Student's t-test or Mann-Whitney U for the continuous variables, and the χ^2 test for the dichotomous variables. This study was done with the power of 90%. P values of 0.05 or less were considered statistically significant. All the statistical analyses were carried out via Statistical Package for Social Sciences version 16 (SPSS Inc, Chicago, Illinois, USA).

Results

The demographic and historical characteristics of the study population are listed in Table 1. The mean patient age was 60.6 ± 12.5 [20-112] years, and

Table 1. - Demographic and historical characteristics of patients with STEMI (n=2028)

	Pts ≤ 40 years (n=109)	Pts > 40 years (n=1919)	All pts (n=2028)	p Value
Age (years)	35.6 \pm 4.9	62.0 \pm 11.3	60.6 \pm 12.5	<0.001
Male gender	101 (92.7)	1421 (74)	1522 (75)	<0.001
Marital Status				
Married	86 (78.9)	1558 (81.2)	1644 (81.1)	
Single	12 (11)	15 (0.8)	27 (1.3)	
Divorced	1 (0.9)	10 (0.5)	11 (0.5)	
Widowed	0	183 (9.5)	183 (9.0)	<0.001
Family history of CVD	55 (50.5)	450 (23.4)	505 (24.9)	<0.001
Hypertension	20 (18.3)	848 (44.2)	868 (42.8)	<0.001
Diabetes mellitus	11 (10.1)	645 (33.6)	656 (32.3)	<0.001
Active cigarette Smoking	64 (58.7)	609 (31.7)	673 (33.2)	<0.001
Dyslipidemia	36 (33)	911 (47.5)	947 (46.7)	0.003
BMI	26.6 \pm 4.2	26.5 \pm 4.3	26.5 \pm 4.3	0.759
Opium use	16 (14.7)	197 (10.3)	213 (10.5)	0.144
Prior MI	2 (1.8)	90 (4.7)	92 (4.5)	0.504
Prior catheterization	9 (8.3)	284 (14.8)	293 (14.4)	0.135
Normal prior angiogram	2 (1.8)	4 (0.2)	6 (0.3)	0.133
Prior PCI	3 (2.8)	62 (3.2)	65 (3.2)	0.375
Prior CABG	0	48 (2.5)	48 (2.5)	0.154
Prior heart failure	0	12 (0.6)	12 (0.6)	0.258
Prior CVA	0	71 (3.7)	71 (3.5)	0.053

CVD, cardiovascular disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CVA, cerebrovascular accident; MI, myocardial infarction

75% of the patients were male. Risk factors included smoking in 33.2% of the cases, dyslipidemia in 46.7%, diabetes in 32.3%, and hypertension in 42.8% with an average body mass index (BMI) of 26.5±4.3 in this population. Family history of CVD was reported in 24.9%. Use of opium as a novel CVD risk factor [8] was found in 10.5%.

The frequency of the atherosclerotic risk factors and demographic and clinical characteristics for the patients ≤ 40 and > 40 years old was compared. Among the young patients, the frequency of the males, family history of CVD, and smoking was significantly more prevalent than that of the others (P<0.001). The old patients were more likely to have diabetes mellitus (P<0.001), hypertension (P<0.001), and dyslipidemia (P=0.003). In contrast, there was no significant statistical difference in BMI and opium use between the two groups.

The acute coronary symptoms, the chief complaints, Killip Class, and MI locations were similar between the young and old patients. In echocardiography, the young patients had a significantly higher

LVEF in comparison with the old ones (48.6±10.6 vs. 42.5±12.6; P<0.001). The arrhythmias were found more prevalent in the old patients; they were not, however, significantly different from the young patients. The serum level of the cardiac biochemical markers of necrosis was higher in the young patients (Table 2).

Coronary angiography was performed for 960 (43.3%) patients; the young patients were more likely to undergo a coronary angiography (67% vs. 46.2%; P<0.001). Significant coronary artery lesions were found in 688 patients (74.8%), mostly presented as multi-vessel disease (71.7%). The prevalence of significant left main coronary artery (LMCA) disease was low among all the patients (2.3%). The significant coronary lesions mainly affected the left anterior descending (LAD) coronary artery (823 patients, 87.1%). There was a statistically higher prevalence in coronary atherosclerotic vessels, for the multi-vessel, LAD, right coronary artery (RCA), and left circumflex artery (LCx) in the old patients. The young patients had a higher prevalence

Table 2. - Clinical, laboratory, and angiographic characteristics of patients with STEMI (n=2028)

	Pts≤ 40 years (n=109)	Pts> 40 years (n=1919)	All pts (n=2028)	p Value
Chest discomfort	106 (97.2)	1831 (95.4)	1937 (95.7)	0.483
Typical chest pain	77 (70.6)	1407 (73.3)	1484 (73.2)	
Atypical chest pain	27 (24.8)	369 (19.2)	396 (19.5)	
Without chest pain	5 (4.6)	143 (7.5)	148 (7.2)	0.244
Pain duration				
≤30 min	36 (33)	716 (37.3)	752 (37.1)	
>30 min	73 (67)	1203 (62.7)	1276 (62.9)	0.540
Dyspnea	17 (15.6)	357 (18.6)	374 (18.5)	0.425
Palpitation	5 (4.6)	60 (3.1)	65 (3.2)	0.402
Chest pain still present	70 (64.3)	1112 (57.9)	1937 (95.7)	0.185
Killip class				
I	55 (93.2)	916 (82)	971 (82.6)	
II	4 (6.8)	148 (13.2)	152 (12.9)	
III	0	23 (2.1)	23 (2)	
IV	0	30 (2.7)	30 (2.6)	0.224
CK-MB level (IU/L)	104 (55, 180.7)	78.5 (38, 161)	80 (39, 161.2)	0.019
Troponin I level (µg/L)	8.2 (2.4, 24.7)	5.1 (1.6, 16)	5.2 (1.7, 16.5)	0.031
LVEF in echocardiography	48.6±10.6	42.5±12.6	42.8±12.5	<0.001
Anterior MI	33 (30.3)	544 (28.3)	577 (28.5)	0.836
Inferior MI	49 (45)	697 (36.3)	746 (36.8)	0.252
Lateral MI	8 (7.3)	83 (4.3)	91 (4.5)	0.414
Anteroseptal MI	10 (9.2)	289 (15.1)	299 (14.7)	0.331
Angiography	73 (67)	887 (46.2)	960 (47.3)	<0.001
Normal coronary angiogram	11 (13.7)	8 (0.9)	18 (1.9)	<0.001
Mild coronary disease	1 (1.4)	20 (2.3)	21 (2.2)	
Single-vessel disease	29 (39.7)	204 (33)	233 (24.3)	
Multi- vessel disease	33 (45.2)	655 (73.8)	519 (54.1)	<0.001
LMCA disease				
≤50%	1 (1.4)	59 (6.7)	60 (6.2)	
>50%	0	23 (2.6)	23 (2.4)	0.073
LAD disease	50 (68.5)	773 (87.1)	823 (85.7)	<0.001
LCx disease	26 (35.6)	538 (60.7)	564 (56.8)	<0.001
RCA disease	36 (49.3)	588 (66.3)	624 (65)	0.003

CVD, cardiovascular disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CVA, cerebrovascular accident; MI, myocardial infarction; LMCA, left main coronary artery; LAD, left anterior descending; LCx, left circumflex; RCA, right coronary artery

of angiographically normal coronary artery (13.7% vs. 0.9%; $P<0.001$) (Table 2).

Percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) of the infarct-related lesions were performed in 398 (19.6%) and 433 (21.4%) patients, respectively. There was an age-related difference for revascularization options. The young patients were more likely to undergo PCI (38.5% vs. 18.6%; $P<0.001$), whereas CABG was more common in the old ones (22.1% vs. 18.6%; $P<0.001$). The others were put on a medical treatment. The length of stay in hospital was significantly shorter for the young patients ($p<0.001$). There was no cerebrovascular accident or recurrent major adverse coronary events in the young patients. In-hospital mortality occurred more frequently in the elderly patients compared with the young ones (6.1% vs. 0.9; $P<0.01$) (Table 3).

Discussion

The THCCVDR has been established as a prospective registry that describes the epidemiology, management practices, and in-hospital outcome of patients with the entire spectrum of ACSs or suspected to have an ACS. The proportion of acute STEMI amounted to 13.6% of all the Registry population during the four-year period. In real-life, there are substantial differences between patient populations and clinical trial patient populations. In addition, there is considerable heterogeneity in patient management practices [9-11]. Therefore, the large-scale observational data sets are important to complement the information obtained via randomized clinical trials. The current study showed a significantly different clinical, angiographic, and biochemical profile in younger patients with coronary artery disease undergoing coronary angiography compared with older patients. However, it should be noted that these findings were based on the epidemiology of CVD, health care facilities and services in our region.

The STEMI in young adults may have different atherosclerotic risk factors profile. Our results revealed that the male gender, smoking, and family history of CVD were more common in the younger patients. The present data are consistent with an overwhelming body of evidence that the atherosclerotic process starts in adolescence or early adulthood, insidiously progressing under the influence of various risk factors. As in the present study, in which about 60% of the patients were smokers, prior observations documented active tobacco abuse in 65-92% of young patients with MI [6, 12-26]. Concordantly, almost all the previous studies have mentioned that male patients and those with a family history of CVD have the propensity to earlier ACSs [19-23].

As expected, there was a lower incidence of hypertension, dyslipidemia, and diabetes in our younger patients, which is in agreement with previous studies [12-14, 20, 21, 27]. It is related to the long-term role of these metabolic and endocrine disorders in the atherosclerosis process and ACSs, whereas cigarette smoking may be associated with thrombogenicity and spasm of the coronary arteries [28, 29]. In our young patients, interactions between gender, family history, and smoking and metabolic syndrome [30] were tested, but no significant effect modification was found. Prescott *et al.* [31] also found no interaction between smoking and other MI risk factors on MI risk. Most of our young patients were male, smokers, or who had a family history of CVD. These findings suggest that coronary disease may have different predisposing conditions in this population. It seems to be concordant with the predominant role of men in the socioeconomic activities of Iranian families in comparison with women. The difficult and time-consuming financial commitments of males (e.g., males who work two or more shifts) can be assumed to be the culprit for an earlier development of CVD earlier. Further investigation needs to evaluate the effect of socioeconomic status and psychological stress of the society on young patients. Early lifestyle modifications and

Table 3. - Treatment and outcome of patients with STEMI (n=2028)

	Pts≤ 40 years (n=109)	Pts> 40 years (n=1909)	All pts (n=2028)	p Value
LOS in hospital (days)	6.2±3.4 (1-17)	8.1±5 (1-37)	8±4.9 (1-37)	0.031
Atrial fibrillation	0	33 (1.7)	33 (1.6)	0.257
Ventricular tachycardia	0	5 (0.3)	5 (0.2)	0.486
Ventricular fibrillation	0	15 (0.8)	15 (0.7)	0.435
RBBB	1 (0.9)	31 (1.6)	32 (1.6)	0.724
LBBB	1 (0.9)	38 (2.0)	39 (1.9)	0.720
AV block	0	27 (1.4)	27 (1.3)	0.397
PVC	2 (1.8)	24 (1.3)	26 (1.3)	0.647
Acute MR	5 (4.6)	143 (7.5)	148 (7.3)	0.519
CVA	0	6 (0.3)	6 (0.3)	0.053
Heart failure	2 (1.8)	109 (5.7)	111 (5.5)	0.258
Ventricular aneurysm	0	11 (0.6)	11 (0.5)	0.677
PCI	42 (38.5)	356 (18.6)	398 (19.6)	<0.001
CABG	9 (8.3)	424 (22.1)	433 (21.4)	<0.001
Death	1 (0.9)	117 (6.1)	118 (5.8)	0.010

LOS, length of stay; RBBB, right bundle branch block; LBBB, left bundle branch block, AV, atrioventricular; PVC, premature ventricular contraction; MR, mitral replacement; CVA, cerebrovascular accident; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting

pharmacological interventions should take into account smoking, dyslipidemia, and body weight control, particularly in men. It should be noted that hypertension and diabetes were less frequent at the age of our cohort. A general notion has evolved that the intensity of preventive efforts should be adjusted to a patient's risk for developing CVD, i.e., the higher the risk, the more aggressive the intervention should be.

Our findings that a normal coronary angiogram was more frequent in the young patients and that the young patients had a higher frequency of single-vessel disease as compared to the old patients are consistent with previous reports [6, 12, 13, 32, 33]. There is an overwhelming body of evidence that the atherosclerotic process starts in adolescence or early adulthood, insidiously progressing under the influence of various risk factors. Autopsy observations have shown that the occurrence of MI in young people with cardiovascular risk factors could be the expression of a premature and severe atherosclerotic process [34].

Not surprisingly, we observed that the rate of adverse outcomes (i.e., dysrhythmia, cerebrovascular accident, heart failure, and death) was lower in the younger patients, although we could not determine the relative contribution of younger age versus the more aggressive diagnostic procedures that younger patients received. The young patients in our study were more likely to have PCI as their coronary revascularization, whereas CABG was the more common revascularization option in the elderly patients. Importantly, the relative proportion of in-hospital mortality was significantly lower in the young age group (0.9% vs. 6.1%). In contrast to their younger counterparts, the elderly patients often presented with a more complex cardiovascular risk profile and prior events. Our young patients were less likely to have had a history of MI and prior revascularization, whereas the old patients had lower LVEF in comparison with the younger ones. In the present study, the rate of overall in-hospital mortality was 5.8%, which is comparable with the 15.1% mortality rate from the academic center in Tehran, Iran [3]. The previous reports from developed countries were 7% for STEMI and 6% for non-STEMI patients in the Global Registry of Acute Coronary Events (GRACE) Registry [35] and 7.4% in a study in the USA by Gheorghide *et al.* [36]. In the The Polish Registry of Acute Coronary Syndromes, the non-STEMI patients had lower mortality (6.6 vs. 9.3%, $p < 0.0001$) compared with the STEMI patients [37]. In the PRIAMHO II study, the outcome was better in the younger group, with a lower mortality rate at 28 days (3.7%), demonstrating that age < 45 years was an independent protective factor for mortality of AMI [38]. In a very recent study by Anderson *et al.*, the VALIANT trial [39], outcomes of the young patients with AMI was substantively better than their older counterparts.

The current analysis is strengthened by the diversity and size of the population studied; be that as it may, a number of limitations should be noted. Although patients ≤ 40 years of age comprised just 5.4% of the total STEMI population in the THCCVDR, this analysis of 2028 patients of STEMI represents one of the largest studies to focus on patients

after infarction. As this study population represented a relatively high-risk cohort of patients with MI, we remain cautious in generalizing these results to a broader group of lower risk, post-MI patients. Furthermore, our patients had been followed prospectively through other registries (i.e., Angiography, Angioplasty, and CABG); nevertheless, the present study, being a single-center survey may have lost some data of the patients who were not admitted. In other words, the majority of findings were related to local epidemiology of CVD, management habits, and facilities of our center. Some long-term follow-up events, particularly death and stroke, were not verified by checking the subjects' hospital records; and in these circumstances, the patients' declarations (or statements of their relatives) were accepted as true. Accordingly, the present analysis cannot claim to represent the findings for all patients early after MI.

In conclusion, we found that cigarette smoking, male gender, and a family history of cardiovascular diseases were more prevalent in young patients with STEMI, whereas the elderly patients were more likely to have dyslipidemia, hypertension, and diabetes. Although the young patients had less complex clinical profiles and more favorable outcome; given the progressive nature of atherosclerosis, further efforts at minimizing modifiable risk factors in young patients at risk for and after acute MI, especially males, are needed. The possible role of the other factors including socioeconomic and psychological status may be considered in further investigations in relation with the acute coronary syndromes.

Riassunto

Vengono descritte le caratteristiche cliniche, i trattamenti e la prognosi ospedaliera di una popolazione di 2028 pazienti con STEMI, tratti dal Registro Cardiovascolare del Tehran Heart Center, confrontando un gruppo di 109 pazienti di età inferiore a 40 anni con un gruppo di 1919 pazienti di età superiore a 40 anni.

Il profilo di rischio, le caratteristiche clinico-angiografiche ed i trattamenti differivano sostanzialmente nei due gruppi. In particolare il gruppo più giovane presentava una migliore prognosi ospedaliera rispetto ai pazienti più anziani con STEMI.

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