

Demographics and Angiographic Findings in Patients under 35 Years of Age with Acute ST Elevation Myocardial Infarction

Seyed Kianoosh Hosseini, MD¹, Abbas Soleimani, MD¹, Mojtaba Salarifar, MD^{1*}, Hamidreza Pourhoseini, MD¹, Ebrahim Nematipoor, MD¹, Seyed Hesameddin Abbasi, MD^{1,2}, Ali Abbasi, MD³

¹Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran.

²Family Health Research Center, Iranian Petroleum Industry Health Research Institute, Tehran, Iran.

³University Medical Center Groningen, Groningen, the Netherlands.

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Abstract

Background: ST-elevation myocardial infarction (STEMI) is a major cause of cardiovascular mortality worldwide. There are differences between very young patients with STEMI and their older counterparts. This study investigates the demographics and clinical findings in very young patients with STEMI.

Methods: Through a review of the angiography registry, 108 patients aged ≤ 35 years (Group I) were compared with 5544 patients aged > 35 years (Group II) who underwent coronary angiography after STEMI.

Results: Group I patients were more likely to be male (92.6%), smokers, and have a family history of cardiovascular diseases (34.6%). The prevalence of diabetes, dyslipidemia, and hypertension was higher in the old patients. Triglyceride and hemoglobin were significantly higher in Group I. Normal coronary angiogram was reported in 18.5% of the young patients, and in 2.1% of the older patients. The prevalence of single-vessel and multi-vessel coronary artery disease was similar in the two groups (34.3% vs. 35.2%). The younger subjects were more commonly candidates for medical treatment and percutaneous coronary intervention (PCI) (84.2%), while coronary artery bypass grafting (CABG) was considered for the 39.5% of their older counterparts.

Conclusion: In the young adults with STEMI, male gender, smoking, family history, and high triglyceride level were more often observed. A considerable proportion of the young patients presented with multi-vessel coronary disease. PCI or medical treatment was the preferred treatment in the younger patients; in contrast to their older counterparts, in whom CABG was more commonly chosen for revascularization.

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*Corresponding Author: Mojtaba Salarifar, Assistant Professor of Interventional Cardiology, Cardiology Department, Tehran Heart Center, North Kargar Street, Tehran, Iran. 1411713138. Tel: +98 21 88029257. Fax: +98 21 88029256. E-mail: salarifar@tehranheartcenter.org.



Introduction

ST-segment elevation myocardial infarction (STEMI) is one of the most common causes of emergency department admissions and cardiovascular mortalities and thus currently accounts for a high burden on health care services in the world. Although STEMI is an uncommon entity in young patients, it has always attracted special attention because of its unusual features and devastating effect on their more active lifestyle.¹⁻⁵

In recent years, whereas the mean age of coronary artery disease (CAD) has decreased, its prevalence seems to have been on the increase.⁴ A number of studies, including our previous report, have shown significant differences in the risk factor profile and coronary angiographic patterns between young and older patients with acute STEMI.^{1-3, 6-8} Traditional risk factors of CAD are prevalent in young patients with acute STEMI but with a different pattern compared to their older counterparts; these differences may cause different treatment strategies and outcome among these patients.^{3, 5, 9} There is evidence that a concentration of the novel risk factors of CAD such as LP (a) may be higher than normal in the offspring of patients with a history of premature MI.¹⁰

There is a dearth of available data on very young adults with STEMI, as a life-threatening cardiac emergency condition. In an attempt to characterize patients 35 years of age or younger suffering STEMI, we reviewed the Tehran Heart Center Angiography Registry (THCAR) and compared the demographics and clinical findings of these patients to those older than 35 years of age.

Methods

From all the patients admitted by cardiologists between January 2000 and March 2008 to the Angiography Department affiliated with the Academic Tehran Heart Center, we identified 5652 patients with a history of STEMI. The databank contains patients' data collected by cardiologists and trained general practitioners, and the validity of all the data is checked by reabstracting 10% of the patients' entries and by reentering 5% of the patients' records. The investigation 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 acute myocardial infarction (AMI) events was based on information on medical history, symptoms, electrocardiogram, and cardiac enzymes. STEMI was diagnosed when new or presumed new ST-segment elevation ≥ 1 mm (≥ 2 mm in V_1 to V_3) was seen in any location in two or more contiguous leads or new left bundle branch block was found on the index or qualifying electrocardiogram with ≥ 1 positive cardiac biochemical marker of necrosis

(including CKMB-mass or quantitative cardiac troponin measurements). The cardiologist who performed the coronary angiography documented and recorded STEMI diagnosis in the datasheets. Coronary angiography was performed in almost all the patients as part of the pharmacoinvasive strategy or as the primary treatment option (primary percutaneous coronary intervention [PCI]) based on the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the management of patients with STEMI.¹¹ To characterize the young patients, the patients were divided into 2 subgroups of ≤ 35 years (Group I, $n = 108$) and those older than 35 years (Group II, $n = 5544$). The following data were included for analysis: demographic data (i.e. age and gender) and CAD risk factor 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), hyperlipidemia (total cholesterol ≥ 5.0 , HDL-cholesterol ≤ 1.0 in men or ≤ 1.1 in women, and triglycerides ≥ 2.0 mmol/l), family history of CAD (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 blood sugar (FBS) ≥ 126 mg/dl (7.0 mmol/l) or 2-hp ≥ 200 mg/dl (11.1 mmol/l)), and opium consumption.¹²

Clinical manifestations, left ventricular ejection fraction (LVEF), hematologic indices, coronary angiographic findings, and treatment strategy were reported. Selective coronary arteriography was performed using standard technique in all the patients. Significant 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 in the left main coronary artery (LMCA), left anterior descending (LAD), right coronary artery (RCA), and left circumflex (LCx) as well as in their main branches (diagonal, obtuse marginal, ramus intermedius, posterior descending artery, and posterolateral branch). Even mild luminal irregularities were regarded as evidence of atherosclerosis.

The results were reported as mean \pm standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student t-test for the continuous variables and the Chi-square 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, IL, Chicago Inc., USA).

Results

The demographic and historical characteristics of the study

population are listed in Table 1. The mean patient age was 56.7 ± 10.8 (Range: 17-95) years. The male patients accounted for 79.8% of the total study population. The risk factors included smoking in 30.8% of the cases, hyperlipidemia in 59.4%, diabetes in 27.4%, and hypertension in 40.8% with an average body mass index (BMI) of 27.6 ± 4.4 kg/m² in this population. A family history of CAD was reported in 24.2% of the patients. Use of opium as a risk factor¹² was found in 16.6% of 3716 patients who had information of opium use in the registry.

The frequencies of the atherosclerotic risk factors, demographic, and clinical characteristics of the patients ≤ 35 and > 35 years old were compared. In Group I, the frequency of the male gender, current smoking, and a family history of CAD was significantly more common than that of Group II (p value < 0.001). The patients above 35 years were more likely to have diabetes mellitus (p value < 0.001), hypertension (p value < 0.001), and hyperlipidemia (p value = 0.009). Although the mean total cholesterol and high density lipoprotein levels were similar between two groups, the older patients had significantly higher low density lipoprotein and

FBS and lower triglyceride levels in comparison with Group I. There was no significant statistical difference in the BMI (27.7 ± 4.2 vs. 27.0 ± 4.1 in Group I vs. II, respectively; p value = 0.111) and opium use between the two groups.

There were 5527 (107 from Group I and 5420 from Group II) patients with STEMI, in whom baseline hemoglobin data were available. According to the World Health Organization definition (hemoglobin < 13 g/dL and < 12 g/dL for the male and female, respectively), 15.7% of the patients (867 of 5420) presented with anemia. The mean hemoglobin level of Group II was lower than that of Group I (14.2 ± 1.8 vs. 14.5 ± 1.5 g/dL, p value < 0.001); the young patients were less likely to be anemic compared with Group II (8.4% vs. 15.8%, p value = 0.037). There were 989 (18%) patients with elevated serum creatinine (> 1.4 mg/dl). Group II patients were more likely to have impaired renal function in comparison with Group I (18.1% vs. 9.4%, p value = 0.037). There was no significant difference in the LVEF measured by echocardiography or left ventriculography between the two groups (Table 2).

Significant coronary artery lesions were found in 5356

Table 1. Demographic and historical characteristics of the patients*

	≤ 35 years (n=108)	> 35 years (n=5544)	p value
Male gender	100 (92.6)	4412 (79.6)	< 0.001
Family history	36 (34.6)	1302 (24)	0.012
Hypertension	15 (13.9)	2283 (41.4)	< 0.001
Diabetes mellitus	11 (10.3)	1533 (27.7)	< 0.001
FBS (mg/dl)	106.7 ± 42.5	122.2 ± 53.7	0.004
Current Smoking	43 (39.8)	1689 (30.6)	0.037
Current Opium use	22 (20.4)	916 (16.5)	0.287
Dyslipidemia	51 (47.2)	3291 (59.7)	0.009
Total cholesterol (mg/dl)	186.9 ± 54.7	185.4 ± 45.6	0.740
LDL (mg/dl)	100.4 ± 32.7	109.6 ± 38	0.021
HDL (mg/dl)	39.1 ± 7.7	41 ± 9.9	0.066
Triglyceride (mg/dl)	218.6 ± 162.3	179 ± 108.2	< 0.001
BMI (kg/m ²)	27.7 ± 4.3	27.2 ± 4.3	0.111
WBC (cells/ μ l)	9241.1 ± 3233.1	8693.2 ± 2910.3	0.077
Hemoglobin (g/dl)	14.9 ± 1.5	14.2 ± 1.8	< 0.001
Platelet (10^6 /l)	237933.3 ± 70905.5	224838 ± 75648.3	0.103
Anemia	9 (8.4)	858 (15.8)	0.037
Prior catheterization	10 (9.3)	1104 (19.4)	0.006
Prior PCI	4 (3.7)	308 (5.6)	0.188
Prior CABG	1 (0.9)	140 (2.5)	0.285
Prior heart failure	2 (1.9)	184 (3.3)	0.683
Prior renal failure	0	79 (1.4)	0.215
Serum Cr (mg/l)	1.1 ± 0.2	1.2 ± 0.4	0.074
Prior CVA	1 (0.9)	129 (2.3)	0.336

*Data are presented as mean \pm SD or n (%)

FBS, Fasting blood sugar; LDL, Low density lipoprotein; HDL, High density lipoprotein; BMI, Body mass index; WBC, White blood count; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting; Cr, Creatinine; CVA, Cerebrovascular accident



Table 2. Investigation findings and treatment strategy of the patients*

	≤ 35 years (n=108)	> 35 years (n=5544)	p value
Echocardiography LVEF (%)	46.3±10.4	44.5±11.5	0.134
RWMA	64 (68.8)	3470 (69.2)	0.931
Catheterization LVEF (%)	46.6±10.5	44.3±11.6	0.051
Coronary artery dominance			
Right	86 (79.6)	4627 (83.4)	0.343
Left	12 (11.1)	587 (10.6)	
Codominant	10 (9.3)	330 (5.9)	
Normal coronary angiogram	20 (18.5)	116 (2.1)	<0.001
Minimal coronary disease	13 (12)	147 (2.7)	<0.001
Single-vessel disease	37 (34.3)	1355 (24.4)	0.019
Multi-vessel disease	38 (35.2)	3922 (70.8)	<0.001
LMCA disease			
<50%	0	428 (7.7)	<0.001
≥50%	1 (0.9)	194 (3.5)	
LAD disease	60 (55.6)	4735 (85.4)	<0.001
LCx disease	27 (25)	3215 (58)	<0.001
RCA disease	42 (38.9)	3637 (65.6)	<0.001
Recommended treatment strategy			
Medical follow-up or PCI	89 (82.4)	3356(60.5)	<0.001
CABG	13 (12.7)	2136 (39.5)	<0.001
Undetermined	6 (5.5)	52 (0.9)	

*Data are presented as mean±SD or n (%)

LVEF, Left ventricular ejection fraction; RWMA, Regional wall motion abnormality; LMCA, Left main coronary artery; LAD, Left anterior descending; LCx, Left circumflex; RCA, Right coronary artery; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting

(94.8%) patients, and they mostly presented as multi-vessel disease (70.1%). The prevalence of significant left main CAD was low among the patients (3.5%). The significant coronary lesions mainly affected the LAD coronary artery (4795 patients, 84.8%). There was a statistically higher prevalence in atherosclerotic involvement of the LAD, RCA, and LCx in Group II; whereas Group I patients were more likely to have angiographically normal epicardial coronary arteries (18.5% vs. 2.1%, p value < 0.001). A significant difference was found in prior catheterization (19.4 vs. 9.5%, respectively; p value = 0.006) between the two groups.

Medical treatment, PCI, and coronary artery bypass grafting (CABG) were recommended as the treatment strategy in the two patient groups. Group I subjects were more likely to be referred for PCI or continue medical treatment (82.4% vs. 60.5%, p value < 0.001), whereas CABG was more commonly considered in the older patients (12.7% vs. 39.5%, p value < 0.001). In Group I, only one case of LMCA disease was found, which was referred for CABG. From 194 patients older than 35 years who had LMCA with or without other epicardial disease, CABG was indicated for 83.3% of the cases.

Discussion

The THCAR has been established as a prospective registry that describes the epidemiology, angiography, and laboratory data of patients suspected to have the entire spectrum of CAD. The proportion of STEMI amounted to 21.6% 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.¹³⁻¹⁵ Therefore, large-scale observational data sets are important to complement the information obtained via randomized clinical trials. Our study showed a significantly different clinical, angiographic, and biochemical profile in the very young patients with CAD undergoing coronary angiography compared with older patients.

The prevalence of premature coronary disease is 2-11% of all the hospitalized myocardial infarcts. An increase in the incidence owing to earlier exposure to some risk factors such as smoking, life style, hyperlipidemia, and stress has been recognized.² Our results revealed that the male gender, current smoking, and family history of CAD were more common in the patients at or younger than 35 years. Concordantly, almost all the previous studies have mentioned that male

patients, smokers, and those with a family history of CAD have the propensity to earlier acute coronary syndromes (ACSs).¹⁶⁻¹⁸ In the Sozzi et al. study,¹⁸ the men developed AMI approximately 10 times more frequently than did the women, and also smoking and a family history were heavily present among the young patients. Zimmerman et al.¹ showed that a family history of premature CAD was more common in the young men with MI. A family history of premature MI has been considered as an independent risk factor for the development of cardiovascular events, particularly in young patients.¹⁹⁻²²

The role of positive family history of premature CAD will be completed by many reports about the role of genetic factors in the development of atherosclerosis and occurrence of STEMI in young patients. According to recent published studies, there may be polymorphisms in genes such as methylene tetrahydrofolate reductase,²³ Platelet receptors,²⁴ and plasminogen activator inhibitor 1 (PAI1),²⁵ which predispose the patients to STEMI. In contrast, there is at least one report about the polymorphism in beta fibrinogen gene and its protective effect against the incidence of premature STEMI.²⁶ Whether or not such findings could have therapeutic impacts needs to be illuminated in the future.

As was expected, there was a lower incidence of hypertension, dyslipidemia, and diabetes in our younger patients, which is in agreement with previous studies.^{17, 27, 28} It is related to the long-term role of these metabolic and endocrine disorders in the atherosclerosis process and ACS. However, it is deserving of note that our young patients had higher levels of serum triglyceride. These findings suggest that coronary disease may have different predisposing conditions in this population. Early lifestyle modifications and pharmacological interventions should take into account smoking, dyslipidemia, and body weight control. It should be noted that hypertension and diabetes were less frequent at the young age. A general notion has evolved that the intensity of preventive efforts should be adjusted to a patient's risk for developing CAD.

Our findings that a normal coronary angiogram was more frequent in the young patients and that they had a higher frequency of single-vessel disease as compared to the older patients are consistent with previous reports.^{1, 3, 29} Our older patients were more commonly diagnosed as multi-vessel disease in the coronary angiogram. It seems that younger patients who present with STEMI have lower atherosclerotic burden but higher propensity to thrombus formation. 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.³⁰ Not surprisingly, we observed that the young patients were less likely to have prior catheterization and to refer for CABG as their treatment strategy for coronary revascularization.

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. Patients ≤ 35 years of age comprised just 1.9% of the total STEMI population in the angiography registry, but this analysis of 5652 patients of STEMI represents one of the largest studies to focus on patients after infarction. As this study population represented relatively high-risk 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. Angioplasty and CABG); nevertheless, the present study, being a single-center survey may have lost some data of the patients who were not admitted. Some long-term follow-up events, particularly death and stroke, were not determined in this study. Accordingly, the present analysis cannot claim to represent the findings for all patients early after MI.

Conclusion

In conclusion, we found that the male gender, smoking, family history of cardiovascular diseases, and hypertriglyceridemia were more prevalent in the STEMI patients ≤ 35 years, whereas the elderly patients were more likely to have dyslipidemia, hypertension, and diabetes. Medical treatment or PCI were the preferred therapeutic strategy recommended to the younger patients in contrast to their older counterparts, in whom CABG was more commonly recommended. Further studies about the impact of genetic factors in the development of STEMI in young patients are needed.

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