ST-Elevation Myocardial Infarction in Patients ≤35 Years of Age

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ST-elevation myocardial infarction (STEMI) in very young patients is an uncommon entity but with significant clinical meaning for the patient. These individuals may have different risk profiles and prognosis. Few reports have described epidemiology, clinical features, and long-term outcomes of these patients in the era of percutaneous coronary intervention, particularly of those ≤35.

This observational study evaluates the clinical characteristics of patients <35 years with STEMI between January 2004 and September 2016 in 3 different centers. We gathered data and follow-up from the prospective database of the interventional cardiology department, medical history, and phone interviews.

Over a total of 3,883 STEMI, we retrieved 61 patients ≤35. They were mainly male (88%), smokers (80%), and overweight (67%). Twenty-six percent were drug consumers. Only 2 patients (3%) were free of conventional risk factors. In-hospital mortality was 5% (3 deaths). They were followed-up for 5.9 ± 4.2 years with a total survival of 96.6% (2 deaths). Major adverse cardiovascular events incidence at the end of follow-up was only 17.2% (10 patients).

STEMI in the young is a rare condition. These patients have several modifiable predisposing factors, a low clinical risk profile, and excellent short- and long-term prognosis with state-of-the-art treatment. **(Am J Cardiol 2019;123:889−893)**

Coronary artery disease (CAD) is a prevalent condition occurring primarily over the age of 45, and carrying significant morbimortality.[1] Younger individuals can be affected, constituting an important problem for patients and physicians because of the devastating effect of this disease on the quality of life of young patients. It has been suggested that etiopathogenic and prognostic characteristics of acute myocardial infarction (AMI) in young patients may differ from those in older patients.[2,3] Different reports have estimated that young patients make up between 2% and 10% of all AMIs[3] but information about clinical patterns and prognosis of MI in younger subjects is very limited. Most studies are based on data from years from prereperfusion era[4] or have used an age cutoff of 40 to 55 years to define youth.[5] Few reports have described AMI in very young patients, particularly those ≤35 years old.[6] Our goal was to review the clinical profile of patients with a very premature (35 years old or less) ST-elevation myocardial infarction (STEMI) as well as its short- and long-term prognosis.

Methods

We evaluated clinical characteristics of all patients aged ≤35 with STEMI admitted from January 2004 to September 2016 in 3 different hospitals belonging to an interventional cardiology network.[7] All hospitals had access to 24/7 percutaneous coronary intervention (PCI). The participating centers shared a prospectively updated interventional cardiology database containing epidemiological, clinical, and angiographic fields.

The diagnosis of STEMI was established according to the Third Universal Definition of myocardial infarction,[8] concretely to the type I AMI presenting with ST elevation in the first ECG. Consequently, all the patients included presented with symptoms suggesting AMI, new ST elevation at the J point in 2 contiguous leads and angiographic demonstration of atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in 1 or more of the coronary arteries. The management was decided by the attending physician according to current practice guidelines.[9,10] Risk factors and acute event data were extracted from the prospective database. Follow-up and missed baseline characteristics data were collected from medical charts, in-office and telephone interviews performed by trained personnel.

In order to establish the clinical profile of patients with a very premature STEMI, we performed a comprehensive assessment of epidemiologic and clinical characteristics including conventional and nonconventional risk factors, associated related conditions and acute event clinical variables.

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Demographic variables included age and gender, body mass index, known dyslipidemia, diabetes mellitus, hypertension, as well as smoking and family history of CAD. We compared the prevalence of modifiable classic cardiovascular risk factors (hypertension, diabetes, smoking, dyslipidemia, and overweight) in our cohort with a reference cohort from the general population in a similar age group.[11] Other associated conditions like drug consumption, active neoplasm, or hypercoagulable states were assessed. We defined hypercoagulable state as diagnosed rheumatoid disease, known coagulation abnormality or hormonal contraceptive treatment. Traditional risk factor definitions were based on those recommended by the European Society of Cardiology standards.[12]

Acute event data included in-hospital mortality, Killip-Kimball class and ischemic mortality and hemorrhagic risk at presentation, left ventricular ejection fraction on admission, culprit artery, fibrinolytic pretreatment, interventional procedure variables like thrombus aspiration, stent implantation and type, and infarct size estimated by peak of troponin I. Ischemic and hemorrhagic risk were calculated using the validated GRACE[13] and CRUSADE[14] scores, respectively. In-hospital mortality risk was considered as high (GRACE >140 points), intermediate (GRACE 109 to 110) or low (GRACE ≤108). Hemorrhagic risk was considered by CRUSADE[14] score as very low (≤20), low (21 to 30), moderate (31 to 40), high (41 to 50), and very high (>50).

Long-term follow-up data of survivors were reviewed. Major adverse cardiovascular event (MACE) was defined as composite end point of all-cause death, AMI, heart transplant, and stroke or systemic embolism. In order to perform a detailed prognosis profile, we collected as well all severe cardiovascular and hemorrhagic events since the index event. These include MACE plus need for coronary revascularization, pulmonary embolism, hemorrhage, ventricular arrhythmia, and hospitalization due to heart failure. We defined hemorrhage as bleeding requiring medical intervention. Patients were also asked about functional class, smoking cessation, coagulation disorders workup or malignancy.

Categorical variables are presented as numbers (proportion), and continuous variables are presented as average (± standard deviation). Given the high dispersion of the variable, troponin I was expressed as median and interquartile range. Follow-up was censored at the date of last contact. Cumulative survival and event rates were assessed using Kaplan-Meier curves. All analyses were performed using IBM SPSS Statistics, version 20.0 (Chicago, IL).

Results

Between January 2004 and September 2016, 3,883 patients with STEMI were admitted in the participating centers. From those, 61 (1.6%) were ≤35. Mean age was 32 years. Most of them were men, smokers, and overweight. Only 2 (3%) of young patients were free of conventional risk factors. All clinical findings are shown in Table 1.

We compared the observed prevalence of classic modifiable cardiovascular risk factors with a reference cohort from general population ≤45 in Spain.[11] We found that the group of young patients with STEMI had significantly more diabetes, dyslipidemia, overweight, and smoking compared with a similarly aged general population (Table 2).

Table 1
Demographic characteristics and risk factors in patients ≤35 of age

Description	Patients n = 61
Age (years)	32±3
Male vs. female	54 (88%) vs. 7 (12%)
BMI (Kg/m^2)	27±5
Hypertension	10 (16%)
Diabetes mellitus	9 (15%)
Smoker	49 (80%)
Current smoker	46 (75%)
Former smoker	3 (5%)
Dyslipidemia*	20 (32%)
BMI >25 Kg/m^2	41 (67%)
BMI >30 Kg/m^2	15 (24%)
Prior AMI	1 (1.5%)
Family history of CAD	12 (20%)
HIV	2 (3%)
Drugs	16 (26%)
Hypercoagulable states†	8 (13%)
Active neoplasm	1 (1.5%)
Familial hypercholesterolemia	3 (5%)

AMI = acute myocardial infarction; BMI = body mass index; CAD = coronary artery disease; HIV = human immunodeficiency virus.
* Known hypercholesterolemia or hypertriglyceridemia.
† Rheumatoid disease, coagulation abnormalities, or hormonal contraceptives.

Clinical patterns of the acute event are detailed in Table 3. Most patients (55, 90%) presented with acute chest pain, 4 (6.5%) with cardiogenic shock, and 1 (1.5%) with cardiac arrest. GRACE and CRUSADE scores show respectively an intermediate mean in-hospital mortality risk and a very low mean bleeding risk. These scores could not be calculated in 3 patients due to lack of reliable information about some of the items required.

All patients underwent cardiac catheterization during their hospitalization and eventual PCI according to attending physician decision. Most of them underwent primary PCI, only 8 (13%) received out-of-hospital fibrinolytic agents before PCI.

The total number rate of death was 5 (8%). Three patients died in the primary event. One patient passed away due encephalic death. Two patients died because of cardiogenic shock shortly after admission. Complications during admission were infrequent (Table 3).

Table 2
Prevalence of modifiable cardiovascular risk factors in the study cohort compared with a general similar aged population

Description	Patients aged ≤35 (n = 61)	Reference population (n = 5,148)	p Value
Hypertension	10 (16%)	830 (16%)	0.95
Diabetes mellitus	9 (15%)	85 (2%)	<0.001
BMI>25 Kg/m^2	41 (67%)	748 (15%)	<0.001
Current smoking	46 (75%)	2406 (47%)	<0.001
Dyslipidemia*	20 (32%)	171 (3%)	<0.001

BMI = body mass index.
* Known hypercholesterolemia or hypertriglyceridemia.

Table 3
Index event clinical patterns

Description		Value
GRACE ischemic risk score		107±30
CRUSADE bleeding risk score		12±10
Fibrinolytic treatment before angiography		8 (13%)
Killip class on admission	I	52 (85%)
	II	5 (8%)
	III	0
	IV	4 (7%)
PCI procedure	Vascular access	
	Radial	18 (29%)
	Femoral	42 (69%)
	Others	1 (1,5%)
	Initial TIMI flow (0/1/2/3)	40/3/5/13
	Intracoronary imaging (OCT/IVUS)	11 (18%)
	Stent implantation (total)	51 (84%)
	DES	37 (73%)
	BMS	14 (27%)
	Stent size (mm)	3.29+0.5
	Stent length (mm)	22.3+10.1
	Thrombus aspiration	17 (28%)
	Anti IIbIIIa	42 (70%)
Culprit coronary artery	Left main coronary	0
	Left anterior descending	40 (67%)
	Right coronary artery	15 (25%)
	Circumflex coronary artery	5 (8%)
	Other	1 (1.5%)
Coronary artery occlusion mechanism	Aterothrombotic	61 (100%)
	Spontaneous coronary artery dissection	0
	Embolic	0
Peak troponin I, ng/dl*		49 (24-158)
LVEF (%)	Mean	51±14
	>50	34 (56%)
	35-50	20 (33%)
	<35	7 (11%)
Complications	Death	3 (5%)
	Heart failure or cardiogenic shock	10 (16%)
	In-hospital cardiac arrest	3 (5%)
	Stroke	1 (1.5%)
	Complete AV block	1 (1.5%)
	Post MI pericarditis	1 (1.5%)
	Renal failure	1 (1.5%)
	Vascular access	0

AV = atrioventricular; BMS = bare metal stent; DES = drug-eluting stent; LVEF = left ventricular ejection fraction; MI = myocardial infarction; OCT/IVUS = optical coherence tomography/intravascular ultrasound; PCI = percutaneous coronary intervention.

* Normal value <0.05 ng/dl.

Patients who survived the index event were followed up for 5.9 ± 4.2 years (maximum 13.4), with a survival rate of 96.6% (2 deaths). Patients alive at the end of follow-up had a good functional class. MACE incidence at the end of follow-up is 17.2% (n = 10), and severe event incidence is 20.7% (n = 12). Survival curves for all-cause mortality, MACE, and severe events are depicted in Figure 1. Patients who suffered MACE were 6 AMI, 2 sudden cardiac deaths, 1 retinal embolism, and 1 heart transplant. One patient suffered pulmonary embolism and another underwent PCI for unstable angina.

Subsequent diagnostic workup revealed 2 antiphospholipid syndromes and 1 protein C deficit, but coagulation disorders were searched in only 7 patients, upon clinician suspicion. We did not find any diagnosis of malignancy during the follow-up period. Regarding secondary prevention, 27 (58%) active smokers stated smoking cessation after STEMI. Only 27 patients (44%) attended a cardiac rehabilitation program.

Discussion

The present study makes a comprehensive description of the demographic, clinical, and long-term outcomes of patients ≤35 with STEMI. These patterns are gathered only in a few published studies[2,15] mostly previous to the implementation of current STEMI management, with different age groups or including other clinical entities like non-STEMI or MI with normal coronary arteries.

In our study, ≤35-year-old patients comprise 1.6% of all patients from the participating centers. In accordance with previous studies, this series is predominantly composed by male smoker patients. Smoking and dyslipidemia have been reported as the most important risk factors of this population.[4] In a registry study of 6,892 patients with acute STEMI treated by primary PCI from 1998 to 2010, 78% of patients ≤35 were smokers, compared with a 23% in the same aged general population, and smoking rates decreased with increasing age.[16] In our cohort of 61 patients, smoking and obesity were the most prevalent conditions (Table 1). Diabetes mellitus and hypertension appear to be less common in young patients with CAD than in older patients.[17] Our observations are consistent with this, with 10% of diabetes and 9% of hypertension. Cohorts of the similarly aged patients reported analogous rates of smoking, overweight, hypertension, and diabetes.[18] As we showed in Table 2, when we compare the prevalence of modifiable conventional risk factors in our cohort with a big sample of same aged population,[11] we find a significantly higher prevalence. This observation points to the important role of classical risk factors in the development of premature STEMI.

We found a low rate of family history of CAD, compared with other studies.[17] This is possibly a consequence of the limited sample size. A quarter of patients had a regular consumption of cocaine and/or cannabis. Both are related with multiple cardiovascular deleterious effects. Its use is present in 10% of patients with AMI at age ≤50 and is associated with worse prognosis. These findings reinforce current recommendations for substance use screening in young adults with an AMI, and the need for counseling to prevent future events.[19]

Premature cardiovascular disease and MI have been associated with many patterns different from conventional cardiovascular risk factors, such as some polymorphisms,[20]

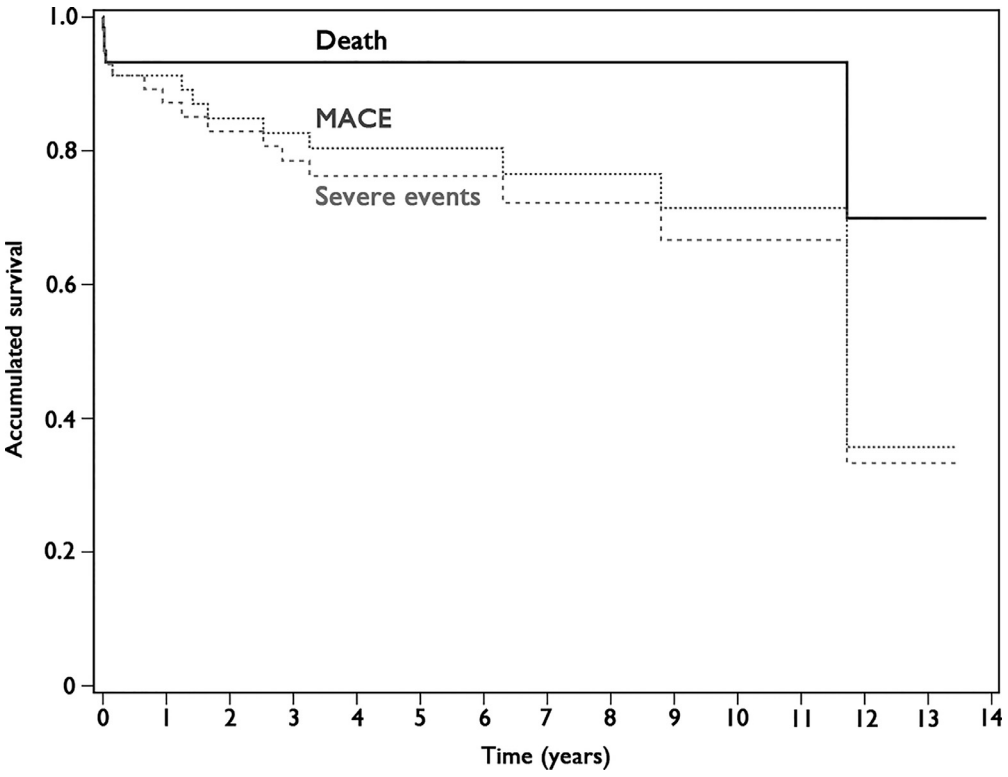

Figure 1. Accumulated survival curves (in years) for overall mortality (solid black line), MACE (dotted line), and severe events (dashed line).

high levels of lipoprotein(a),[21] thrombophilia,[22] or previous diseases like Kawasaki.[23] These conditions could be more relevant for young patients presenting with MI with normal coronary arteries (MINOCA), nonrepresented in the present study. A distinct risk factor profile in patients with MINOCA has been reported, suggesting different pathophysiological mechanisms for the genesis of STEMI than for those with atherosclerotic disease.[15] Cases related with a mix of predisposing conditions could be more frequent.

In the present series, there were 9 patients with a known diagnosis of a procoagulant condition (Table 1) and 3 thrombophilic disorders were found in posterior workups.

Given the high prevalence observed, conventional and modifiable lifestyle risk factors seem to be more attractive and an affordable intervention target for early cardiovascular disease prevention. Young adults are less aware of cardiovascular risk but the most beneficiated group of primary preventive care; subsequently, primary prevention of smoking, dyslipidemia, and overweight should be more aggressively promoted in adolescence in order to decrease the incidence of premature MI. Moreover, though available data about secondary prevention are very limited in our cohort, the low rate of smoking cessation (58%) and cardiac rehabilitation attendance (44%) after the event deserves a thought about how we perform secondary intervention.

Our in-hospital treatment for STEMI was consistent with then in-force guidelines of the American and European Society of Cardiology[9,10] advising revascularization therapy regardless of age. Most of patients underwent PCI and drug-eluting stent implantation. Radial access use varies over time, increasing and becoming predominant in the last years. This is an expected finding since femoral access was the most frequent until recently.

Reported in-hospital and long-term outcomes are both good in young patients, and better than in elder patients.[4,24] We observed a similar rate of in-hospital (5%) and long-term (4.4%) mortality to these series.

The present study of ≤35 aged patients with STEMI complements the scarce literature focusing on very young patients with MI. Our series lies in a very young population, not mixed with "not so young adults," with a particular condition and specific management within the spectrum of CAD. Moreover, this series was treated according to the current recommendations for early PCI in STEMI interventional management, updating data derived from observations before PCI implementation. Given the lack of data about this population, prospective larger studies are warranted in order to clarify the specific profile of these patients.

There are some limitations in our analysis that need to be mentioned. First, issues involve the collection of some retrospective data despite having been collected by trained personnel. Second, the sample was taken out from a homogeneous Mediterranean and Caucasian population with a common genetic and environmental background that may hamper generalization to other groups. We do not have objective, reliable data about diet, physical activity or treatment adherence, which could be important modifying agents.

In conclusion, STEMI in very young patients is an uncommon but significant entity given the risk or morbidity and potential life lost. Our results translate a high incidence of modifiable cardiovascular risk factors and a good short- and long-term prognosis after treatment following current recommendations.

Conflicts of Interest

The authors declare no conflicts of interest.

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