Clinical Manifestations and Outcome of Acute Myocardial Infarction in Very Young Patients

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Abstract

Background: Acute myocardial infarction is rare in people under the age of 30.

Objective: To determine the clinical features and outcome in young patients presenting with AMI.

Methods: All patients aged 30 years and younger hospitalized with AMI during a period of 8 years (1993–2000) were evaluated for clinical features and outcome.

Results: Of the 3,758 patients with AMI, 15 were 30 years old or younger (0.4%). The mean age was 28 (range 21–30 years) and all were male. Eight had normal coronary arteries on angiogram; seven had obstructive coronary artery disease. Patients with OCA had more classical risk factors for coronary disease. A complete diagnostic work-up was abnormal in four patients with NCA: thrombophilia in two patients, spasm due to alcohol withdrawal and hyperthyroidism in one patient each. All patients presented with typical new-onset chest pain. None had a previous history of angina. All patients with OCA received reperfusion therapy as compared to one patient with NCA. Peak creatine phosphokinase in NCA and OCA was 504 $\pm$ 547 and 1,328 $\pm$ 440 respectively ($P < 0.01$). All patients with NCA had good left ventricular function on follow-up echocardiography, compared to only three in the OCA group ($P = 0.02$). There was one death due to cardiogenic shock in a patient with OCA. Follow-up of 4 $\pm$ 2 years demonstrated recurrent acute coronary syndromes in four of seven patients with OCA versus none in the NCA patients ($P = 0.02$).

Conclusions: AMI is rare in very young patients, and more than half have NCA. A thrombophilic tendency or spasm should be considered. Young patients with NCA have an excellent prognosis.

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Acute myocardial infarction is rare before the age of 30. Most of these patients do not have classical risk factors for ischemic heart disease excluding smoking, and a large proportion has normal coronary arteries. Non-classical risk factors such as vasospastic tendencies and thrombophilic conditions, which have been reported to be prevalent in this group, are rarely investigated. We sought to evaluate the clinical manifestation of AMI in a very young population and, more importantly, the classical and non-classical predisposing risk factors. In addition, we evaluated the prognosis of these patients by clinical follow-up.

Patients and Methods

All patients between 20 and 30 years of age with a diagnosis of AMI admitted to Hadassah University Hospital, Jerusalem, Israel during the 8 year period 1993–2000 were included in this study. A diagnosis of AMI was based on three criteria consistent with AMI: chest pain, electrocardiographic changes, and typical time-related pattern of elevated cardiac enzymes (CK-MB). In order to support the diagnosis (and to exclude myocarditis), we included echocardiography data that suggested AMI, i.e., regional wall abnormalities during the acute syndrome. Only patients with these criteria were included in the study. All patients were evaluated for risk factors, clinical and laboratory findings, and coronary artery anatomy. Obstructive coronary disease and vessel disease was defined as >50% reduction in the internal diameter of the coronary arteries on standard diagnostic angiography. The patients underwent an extensive evaluation for non-classical risk factors that included hypercoagulable states, resistance to activated protein C, a carrier of factor V Leiden or factor II mutant, antithrombin III deficiency, protein C or S deficiency, antibodies to cardiolipin or beta-2 glycoprotein or positive lupus anticoagulant. Serum homocysteine and other medical conditions that may have influenced the acute event were also evaluated.

All patients were followed by a clinic visit or telephone interview for outcome, which included further acute coronary events, the need for revascularization, and mortality until the end of the study (1 January 2002).

The data were compared and analyzed statistically using the Fisher exact test for categorical variables and the Student *t*-test for continuous variables. A *P* value of less than 0.05 was considered to indicate a statistically significant difference.

Results

Fifteen of 3,758 patients admitted to our hospital due to AMI were aged 30 or younger (0.4%). All were men with a mean age of 28 (range 21–30 years). All underwent a diagnostic coronary angiogram. Eight had normal coronary arteries on angiogram, and seven had obstructive coronary artery disease. Clinical details of the patients with or without NCA are shown in Table 1.

Risk factors

Classical risk factors for IHD were more common in patients with OCA as compared to patients with NCA [Table 1]. Six of the seven patients with OCA had at least two risk factors for IHD as compared to only one patient with NCA ($P = 0.04$). Smoking was equally common in each group: 6/7 (86%) in OCA vs. 7/8 (87%) in NCA.

AMI = acute myorcardial infarction
OCA = obstructive coronary artery disease
NCA = normal coronary arteries

CK = creatine kinase
IHD = ischemic heart disease

However, hyperlipidemia (serum low density lipoprotein levels >160 mg/ml) was more common in the OCA patients: 4/7 (57%) vs. 2/8 (25%), and a family history and hypertension were present only in OCA patients: 3/7 (43%) and 1/7 (14%). None of the patients had diabetes. A complete diagnostic work-up was abnormal in four patients with NCA (50%) as compared to none of the patients with OCA ($P = 0.05$): thrombophilia in two patients, possible spasm due to alcohol withdrawal in one, and hyperthyroidism in one [Table 2].

Clinical features

All patients presented with typical new-onset chest pain. None had a previous history of angina. All patients had stable hemodynamics on admission except for one patient with OCA in cardiogenic shock. ECG findings included ST elevation in leads corresponding to the infarct in all patients with OCA but only in 50% of patients with NCA ($P = 0.05$). Five patients had an anterior infarct, six had an inferior infarct, three had a lateral infarct, and one had a posterior infarct. All patients with OCA received reperfusion therapy: five with thrombolysis and two with primary angioplasty. Two patients needed rescue angioplasty. One patient with NCA underwent thrombolysis, the others were treated conservatively due to clinical or ECG improvement prior to treatment. Peak CPK in NCA and OCA was 504 $\pm$ 547 and 1,328 $\pm$ 440 respectively ($P < 0.01$). Five of seven patients with OCA (71%) had single vessel disease, two (29%) had double vessel disease; none had triple vessel disease. All underwent a percutaneous intervention including angioplasty with or without stent implantation.

Outcome

All patients with NCA had good left ventricular function on follow-up echocardiography, compared to only three in the OCA group ($P = 0.02$). There was one death due to cardiogenic shock in a patient with OCA. Follow-up of 4 $\pm$ 2 years demonstrated recurrent acute coronary syndromes in four of the seven patients with OCA, one suffering a myocardial infarction [Table 3]. None of the NCA patients suffered from recurrent episodes ($P = 0.02$).

Discussion

Acute myocardial infarction is a potentially dangerous syndrome caused by acute obstruction of coronary flow. Narrowing of the coronary artery lumen due to atherosclerosis and subsequent rupture of an unstable plaque with thrombosis causes acute obstruction and infarction [1]. Classical risk factors for atherosclerosis and the subsequent development of IHD are well known and include hypercholesterolemia, hypertension, smoking, diabetes mellitus, and a positive family history. This is the classical profile of older patients suffering a myocardial infarct. Younger patients who develop myocardial infarction have a completely different profile. Few of these patients have classical risk factors and most are heavy smokers [2–5]. This was the case in our patients. In addition, a significant proportion of young patients (up to 20%) have coronary arteries that appear normal or near normal without significant obstruction on coronary angiogram [2–4]. In the present study 53% had normal coronary arteries. This large proportion could be due to the small sample size, leading to an overestimation. However, it is

Table 1. Clinical characteristics of patients with myocardial infarction and normal and obstructive coronary arteries

	All patients (n=15)	Normal coronary arteries (n=8)	Obstructive coronary arteries (n=7)	*P* value*
Age (yrs)				
Mean	27.5	27.5	28	
Range	21–30	21–30	25–30	0.4
Risk factors				
Smoking	13	7	6	1
Hyperlipidemia	6	2	4	0.3
Family history	3	–	3	0.07
Hypertension	1	–	1	0.4
Diabetes	–	–	–	–
Patients with more than one risk factor	7	1	6	0.04
Typical chest pain	14	8	6	–
ECG changes				
ST elevation	11	4	7	0.05
T wave changes	4	4	–	
Type of infarct				
Anterior	5	2	3	
Lateral	3	2	1	–
Inferior	6	3	3	
Posterior	1	1	–	
Peak CPK (units)	779 $\pm$ 547	504 $\pm$ 359	1,328 $\pm$ 440	0.005
Acute treatment				
Thrombolysis	6	1	5	
Primary PTCA	2	–	2	0.04
Rescue PTCA	2	–	2	
Final treatment				
PTCA	7	–	7	–
Stent implantation	2		2	
Obstructive CAD				
Single vessel		–	5	–
Double vessel			2	
Triple vessel			0	

* *P* value refers to patients with normal coronary arteries compared to patients with obstructive coronary arteries.
PTCA = percutaneous transluminal coronary angioplasty
CAD = coronary artery disease

Table 2. Non-classical risk factors and specific etiologies for myocardial infarction with normal and obstructive coronary arteries

Specific etiologies	Normal coronary arteries (n=8)	Obstructive coronary arteries (n=7)	*P* value
Thrombophilia	Anticardiolipin syndrome (n=1)	None	0.05
Other	Heterozygote for factor V Leiden (n=1)		
	Alcohol withdrawal (n=1)		
	Hyperthyroidism (n=1)		

Table 3. Outcome of patients with myocardial infarction with normal and obstructive coronary arteries

	Normal coronary arteries (n=8)	Obstructive coronary arteries (n=7)	*P* value
Left ventricular function (per echocardiogram)			
Good	8	3	
Mild	–	–	0.02
Moderate	–	2	
Severe	–	2	
In-hospital mortality	0	1	0.4
Congestive heart failure	0	1	0.4
Recurrence			
Acute coronary syndrome	0	4	0.02
Revascularization	0	2	0.2

possible that this is an accurate estimation in very young patients, and the higher proportion stems from the patient selection in this analysis. We included only a very young cohort (below 30 years of age) as compared to other studies that include patients aged up to 35 or 40 years old. In patients with AMI the probability of obstructive disease rises significantly with increasing age [2–4].

The possibility that a number of these patients had myocarditis cannot be ruled out completely. Myocarditis may mimic AMI, especially in young patients with normal coronary arteries [6]. The diagnosis is not always simple; for this reason we included in our study only patients who, in addition to the standard criteria of AMI, were required to have a typical time-related elevation of cardiac enzymes and regional motion abnormalities on echocardiography as further evidence of AMI.

The cause of the acute obstruction in patients without significant obstruction is still not completely clear; coronary spasm or thrombosis with reperfusion have been suggested as possible causes. Although the coronary angiogram does not demonstrate significant obstruction in these patients, this does not always exclude atherosclerosis with positive remodeling of the artery. Rupture of an insignificant plaque causing temporary obstruction by a clot may cause an infarct. Subsequent lysis is possible and may leave the lumen intact. Intravascular ultrasound of the coronary arteries, which provides a tomographic view of the arterial wall (not only the lumen), may reveal coronary artery disease despite an apparent normal coronary angiogram. However, this is not undertaken routinely in our laboratory. Moreover, an endothelium overlying an atherosclerotic plaque is more sensitive to spasm or thrombosis. Smoking is very common in these patients and is known to predispose to vasospasm, perhaps due to impaired endothelial vasodilator dysfunction [7]. Specific vasospastic substances such as cocaine have also been reported to cause acute obstruction due to vasospasm and should be sought as a possible cause. In our cohort, two patients with NCA had a possible spastic predisposition: alcohol withdrawal, which has been reported to cause an AMI due to sympathetic hyperactivity with coronary spasm [8], and hyperthyroidism. Thrombosis is the other probable cause of acute obstruction. Hypercoagulable states may play a significant role in acute occlusions of pathologically normal coronary arteries. A recent study [9] showed that patients with myocardial infarction and NCA had fewer risk factors for coronary artery disease and a higher prevalence of thrombophilia and a tendency for vasospasm. In another study [10], coronary spasm was verified in 40% of patients with NCA when provoked by ergonovine, and thrombophilia in 36% when a full diagnostic work-up was conducted. However, in a larger study [11] of 91 patients, coronary spasm was found in only 15% of patients and thrombophilia in 12%. It is important to emphasize that these studies included patients of all ages and not specifically young patients, among whom these features could be more common. In the present study we found that a large proportion of young patients with NCA had non-classical risk factors including a suspected vasospastic tendency or thrombophilia. Due to the small patient size in our study it is hard to draw definite conclusions. However, based on our study and other studies in the literature it is our feeling that these risk factors should be sought in the young population with NCA.

Young patients with an AMI have a better prognosis than older patients (after stratification for other prognostic variables) [2–4], although their life expectancy is unknown and may be shorter. In addition, patients with NCA have a more favorable prognosis than patients with obstructive disease [11,12]. The combination of young age and NCA should be good. Indeed, our study supports that young patients with NCA had an excellent prognosis, with no recurrent ischemic events at follow-up.

In conclusion, AMI is rare in young patients and smoking is the most important risk factor. More than half have NCA. In these patients, thrombophilia or vasospasm is common and these causes should be considered. Young patients with NCA have an excellent prognosis.

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