Originale article

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Myocardial infarction in young adults: risk factors, clinical characteristics and prognosis according to our experience

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Abstract

Objectives. Myocardial infarction is a relatively unusual phenomenon in young subjects. The aim if this work is to characterize the risk profile and factors influencing outcomes of these patients since it makes possible to manage prevention interventions.

Patients and Methods. We examined cardiovascular risk factors, clinical presentation, angiographic picture and outcome of a group of young patients hospitalized for a myocardial infarction. We enrolled 121 young patients consecutively admitted to our hospital for a myocardial infarction and examined them not only at the initial stage, but also after 3 months and one year; finally a long-term telephonic follow up was performed, when possible.

Results. We found some peculiarity making these patients quite different from the older ones who develop a myocardial infarction: cigarettes smoking, family history of ischemic heart disease and hyperlipidemia were the most frequent cardiovascular risk factors, while diabetes and hypertension were less represented; moreover coronary angiography showed more frequently a less extensive coronary atherosclerosis. Patients who developed a cardiovascular event at follow-up presented a significantly higher prevalence of hypertension and obesity and a significantly lower frequency of healthy coronary arteries and of previous revascularization.

Conclusions. Myocardial infarction in young adults presents several peculiarities, represented not only by the risk profile, but also by the angiographic picture and the prognosis. Considering the long life expectancy of the involved population, the essential role of preventive interventions should be strongly underlined. ***Clin Ter 2013; 164(2):e77-82.*** **doi: 10.7417/CT.2013.1535**

Key words: *cardiovascular prevention, cardiovascular risk factors, coronary artery disease, ischemic heart disease, myocardial infarction, young adults*

Introduction

Myocardial infarction is an uncommon disease in young adults and its incidence varies between 2% and 10%, according to different surveys (1-4). In most of published studies, the definition of young patients included individuals aged less than 45. Although these patients account for only a minor proportion of all patients with acute coronary syndromes, this population is of particular interest because of the long life expectancy.

In the past, it has been demonstrated that young subjects who develop a myocardial infarction present peculiar genetic (5-7) and laboratory characteristics (8-14).

In this paper we focused our attention on risk factors, clinical presentation, angiographic characteristics and outcome of a group of young patients admitted to the emergency department for an acute myocardial infarction.

Materials and Methods

We performed a prospective study enrolling young adults (aged less than 45 years) with ST elevation acute myocardial infarction (STEMI) or non-ST elevation acute myocardial infarction (NSTEMI). Patients were admitted either from the emergency department of our hospital or were transferred from other hospitals of Western Sicily. We enrolled all consecutive patients who were diagnosed with an acute myocardial infarction (AMI), according to the World Health Organization criteria (15). Demographic characteristics included age and sex. The risk profile of each patient was investigated. Family history of coronary heart disease was defined as any first-degree relative younger than 55 years who was affected by ischemic heart disease. Each person who smoked at least one cigarette/day was defined smoker. Overweight was defined by an increased BMI ranging from 25 to 29.9 kg/m^2 and obesity by ì BMI ≥30 Kg/m^2. Hypertension was defined as a systolic blood pressure > 140 mmHg and/or a diastolic blood pressure >90 mmHg and/or the use of anti-hypertensive drugs. Hyperlipidemia was defined as a total plasma cholesterol >220 mg/dl and/or the use of cholesterol-lowering agents. Diabetes was defined as a fasting glycaemia >126 mg/dl and/or the use of oral or insulin therapy. It was also investigated the personal history of ischemic heart disease. In females, the use of oral contraceptives was evaluated. Finally, the use of cocaine was considered.

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Concerning clinical presentation, patients were divided in two groups according to the type of myocardial infarction: STEMI and NSTEMI patients.

Angiographic characteristics were investigated and patients were divided in three different groups according to the angiographic picture: patients without significant coronary stenosis, patients with a single vessel disease (in which a >70% stenosis was present in one coronary artery) and patients with a multi vessel disease (in which a > 70% stenosis was present in at least two coronary arteries). Furthermore, in patients with significant coronary disease the occurrence of revascularization (PCI or CABG) was analyzed.

Ejection fraction was analyzed too. Finally, the discharge therapy was investigated.

Enrolled patients were examined three months and one year after the discharge, performing an ECG and a visit and it was evaluated the recurrence of ischemic events and the occurrence of heart failure. A long term telephonic follow-up was also performed. New episodes of angina or infarction were investigated as well as the presence of heart failure. Informed consent was obtained from participants in the study.

Concerning statistical analysis, continuous variables were expressed as mean ± SD and categorical variables as proportions. Summary measurements were compared between groups using *t* Student test, for unpaired data, and chi-square test or Fisher exact test, for frequencies. Statistical significance was set at the conventional $p \leq 0.05$ level.

Results

Demographic characteristics and cardiovascular risk factors are listed in Table 1. Since June 2001, 121 AMI patients were enrolled. The mean age was 39.7 ± 5.3. Among these patients, 110 (91%, mean age 39.6) were males and 11 patients (9%, mean age 40.6) were females. The most frequent risk factors were cigarettes smoking (74.4%), family history of ischemic heart disease (56.1%) and hyperlipidemia (47.1%). Among the 88 patients who smoked, the 75% used to smoke more than 20 cigarettes/day, 23% smoked 10-20 cigarettes/day and only 2% smoked less than 10 cigarettes/day. Dividing our population according to BMI, 25.1% were obese, 44.6% were in overweight and only 29.7% had a normal BMI. Hypertension and diabetes were less frequent risk factors (20.7% and 9.9%, respectively). A personal history of ischemic heart disease was present in 9% of our sample. Three patients admitted the use of cocaine. Among the 11 enrolled women, 5 (45.5%) took oral contraceptives. At the same time, these 5 women were smokers. Only 7 patients (3.3%) didn't present any of the studied cardiovascular risk factors.

Table 1. Demographic characteristics and cardiovascular risk factors (n=121).

Age (mean ± SD)	39.7 ± 5.3
Male n (%)	110 (91%)
Smoke habit n (%)	90 (74.4%)
Family history of ischemic heart disease n (%)	68 (56.1%)
Hyperlipidemia n (%)	57 (47.1%)
BMI >30 Kg/m^2 n (%)	31 (25.1%)
BMI 25-29.9 Kg/m^2 n (%)	54 (44.6%)
BMI <25 Kg/m^2 n (%)	36 (29.7%)
Diabetes mellitus n (%)	25 (20.7%)
Hypertension n (%)	12 (9.9%)
Women taking oral contraceptives n (%)	5 (45.5%)

Concerning clinical presentation, 86 patients (71%) were admitted with a STEMI, while 34 patients (28%) had a NSTEMI. In one case, it was not possible to obtain information about the clinical picture at the hospitalization. Localization of infarction was anterior in 60 subjects (49.6%), inferior in 60 subjects (49.6%) and indefinite in 1 subject (0.8%).

Angiographic picture was assessed in 114 patients; in 7 individuals coronary angiography was not performed for various reasons (it was refused by the patient or not recommended by the physician). Young patients were more likely to have a single-vessel disease (43% of the sample, n=49). A multi vessel disease was found in the 27% of patients (n=31), while the 25% (n=29) presented normal coronaries. In these latter patients an alternative diagnosis, such as myocarditis or pericarditis, was ruled out on the basis of the clinical, electrocardiographic and echocardiographic picture and of the laboratory data; STEMI was diagnosed in the 65.5% of these cases (n=19; 12 of them underwent fibrinolysis) while NSTEMI in the 34.5% (n=10).

Finally five patients showed a non-atherosclerotic origin of the myocardial infarction (coronary ectasia, coronary spasm, myocardial bridging).

Among the 114 patients who underwent coronary angiography, 80 presented a significant coronary stenosis. Among these 68 (85%) were subjected to a revascularization procedure: 60 underwent PCI and 8 CABG.

Echocardiographic data were available for 113 patients. The mean ejection fraction was 54.6% ± 7.8 (range 35-75%). A moderate left ventricular dysfunction (i.e., EF ≤45%) was present in 17 subjects (15%).

At discharge 55 patients (45.4%) took aspirin, 12 (9.9%) took aspirin and ticlopidin, 42 (34.7%) took aspirin and clopidogrel, 9 (7.4%) ticlopidin and 3 (2.5%) took anticoagulants. Beta-blokers were recommended to 80 patients (66%), statins to 92 (76%) and ACE-inhibitors to 64 (52.9%).

Three months follow up was obtained from 111 patients. In this period the 9% of patients (n=10) were admitted to the emergency department for an ischemic event and the 8% (n=9) developed heart failure. Statistical analysis showed that the only risk factor significantly associated with a new event at short term follow up was hypertension; a trend towards statistical significance is also present in the distribution of diabetes (Table 2).

Moreover, the absence of coronary stenosis and previous revascularization interventions (performed in the acute or subacute phase of myocardial infarction) were significantly associated with the absence of events while the localization of the culprit lesion in left anterior descending artery was significantly associated with the recurrence of ischemic events (Table 3).

Table 2. New ischemic events at three months follow-up and cardiovascular risk factors (n=111).

		New event		
	All	**Yes n=10**	**No n=101**	**p**
Age (mean ± SD)	39.8 ± 5.4	42.1 ± 2,6	39.6 ± 5.6	0.2
Male n (%)	101(91%)	8 (80%)	93 (92%)	0.2
Smoke habit n (%)	83 (74.8%)	7 (70%)	76 (75%)	0.4
Family history of ischemic heart disease n (%)	62 (55.9%)	7 (70%)	55 (54%)	0.2
Hyperlipidemia n (%)	53 (47.7%)	5 (50%)	48 (47%)	0.5
BMI > 30 Kg/m^2 n (%)	26 (25.0%)	4 (40%)	22 (23%)	0.2
BMI (mean ± SD)	29.8 ± 4.35	32.7 ± 7.5	28.7 ± 3.8	0.1
Diabetes mellitus n (%)	12 (10.9%)	3 (30%)	9 (9%)	0.07
Hypertension n (%)	26 (23.4%)	5 (50%)	21 (21%)	0.05*
Absence of cardiovascular risk factors n (%)	6 (5.4%)	0	6 (6%)	0.5

*Fisher exact test

Table 3. New ischemic events at three months follow-up and angiographic and echocardiographic picture (n=111).

		New event		
	All	**Yes n=10**	**No n=101**	**p**
STEMI n (%)	80 (72.7%)	6 (60%)	74 (74%)	0.2
Anterior infarction n (%)	56 (50.5%)	7 (70%)	49 (48%)	0.16
Healthy coronaries n (%)	28 (27.7%)	0 (0%)	28 (30%)	0.04*
Involvement of ADA n (%)	46 (52.9%)	8 (89%)	38 (49%)	0.02*
EF <45% n (%)	15 (14.6%)	2 (22%)	13 (14%)	0,38
Previous revascularization	63 (78.8%)	5 (50%)	58 (83%)	0.03*

*Fisher exact test

Data about one year follow-up are available from 95 patients: 13.5% (n=13) of them were hospitalized for a new ischemic event and the 2.1% (n=2) developed new heart failure. In this subgroup age, hypertension and obesity were associated with a new episode of angina or infarction and a trend towards significance is present in the distribution of diabetes (Table 4).

Data about one year follow-up confirm the trend of the short term follow-up being the absence of coronary stenosis and previous revascularization interventions significantly associated with the absence of new events (Table 5).

Finally, long term follow-up (4.9±1.6 years) was completed in 69 patients: 20.2% (n=14) developed a new ischemic event and 4.3% (n=3) developed new heart failure. No cardiovascular risk factor was significantly associated with new events. A trend towards statistical significance could be noted in the frequency of diabetes, hypertension and obesity, being these risk factors more frequent in the subgroup of patients who develop a new ischemic episode (Table 6).

The only characteristic significantly associated with a better prognosis was the presence of healthy coronaries while the presence of an EF <45% was significantly associated with the recurrence of events (Table 7).

Discussion

The study of ischemic heart disease in young individuals is important in the era of preventive cardiology. Data from literature indicate that nearly the 10% of all patients hospitalized for AMI are <45 year old (3, 16-21). Thus, taking into account that the early onset of ischemic heart disease is not so rare, the evaluation of its risk profile, clinical features and prognosis may have a relevant clinical impact for risk factors modification and for the improvement of primary and secondary prevention.

Previous studies suggested that myocardial infarction is predominantly a disease of male (21, 22). Overall, 91%

Table 4. New ischemic events at one year follow-up and cardiovascular risk factors (n=95).

		New event		
	All	**Yes n=13**	**No n=82**	**p**
Age (mean ± SD)	39.9 ± 5.6	43 ± 1.9	39.4 ± 5.8	0.01#
Male n (%)	86 (90.5%)	12 (92%)	74 (90%)	0.6
Smoke habit n (%)	71 (74.7%)	10 (76%)	61 (74%)	0.4
Family history of ischemic heart disease n (%)	52 (54.7%)	10 (77%)	42 (51%)	0.07
Hyperlipidemia n (%)	48 (50.5%)	8 (61%)	40 (49%)	0.2
BMI > 30 Kg/m^2 n (%)	23 (25.6%)	5 (42%)	18 (23%)	0.1
BMI (mean ± SD)	28.9 ± 4.3	32.4 ± 6.6	28.4 ± 3.5	005#
Diabetes mellitus n (%)	10 (10.6%)	3 (23%)	7 (9%)	0.1
Hypertension n (%)	21 (22.1%)	6 (46%)	15 (18%)	0.03*
Absence of cardiovascular risk factors n (%)	5 (5.3%)	1 (8%)	4 (5%)	0.5

Table 5. New ischemic events at one year follow-up and angiographic and echocardiographic picture (n=95).

		New event		
	All	**Yes n=13**	**No n=82**	**p**
STEMI n (%)	68 (72.3%)	8 (61%)	60 (74%)	0.2
Anterior infarction n (%)	48 (50.5%)	7 (54%)	41 (50%)	0.5
Healthy coronaries n (%)	26 (29.9%)	1 (8%)	25 (34%)	0.05*
Involvement of ADA n (%)	40 (54.1%)	7 (58%)	33 (53%)	0.4
EF <45% n (%)	11 (12.5%)	3 (27%)	8 (10%)	0.13
Previous revascularization	54 (81.8%)	5 (45%)	49 (89%)	0.002*

* Fisher exact test

Table 6. New ischemic events at long-time follow-up and cardiovascular risk factors (n=69).

		New event		
	All	**Yes n=14**	**No n=55**	**p**
Age (mean ± SD)	41.0 ± 3.8	42.1 ± 2.6	40.8 ± 4.1	0.2
Male n (%)	63 (91.3%)	13 (93%)	50 (91%)	0.6
Smoke habit n (%)	50 (72.5%)	10 (71%)	40 (73%)	0.5
Family history of ischemic heart disease n (%)	40 (58.0%)	8 (57%)	32 (58%)	0.5
Hyperlipidemia n (%)	37 (53.6%)	8 (57%)	29 (53%)	0.5
BMI > 30 Kg/m^2 n (%)	17 (25.8%)	5 (38%)	12 (23%)	0.2
BMI (mean ± SD)	28.9 ± 4.3	30.6 ± 3.4	28.6 ± 3.8	0.1
Diabetes mellitus n (%)	8 (11.6%)	3 (21%)	5 (9%)	0.1
Hypertension n (%)	19 (27.5%)	6 (43%)	13 (24%)	0.1
Absence of cardiovascular risk factors n (%)	4 (5.8%)	1 (7%)	3 (5%)	0.6

Table 7. New ischemic events at long-time follow-up and angiographic and echocardiographic picture (n=69).

		New event		
	All	**Yes n=14**	**No n=55**	**p**
STEMI n (%)	49 (71.0%)	10 (71%)	39 (71%)	0.6
Anterior infarction n (%)	33 (47.8%)	9 (64%)	24 (43%)	0.1
Healthy coronaries n (%)	20 (31.3%)	1 (8%)	19 (37%)	0.03*
Involvement of ADA n (%)	26 (50.0%)	8 (61%)	18 (46%)	0.2
EF <45% n (%)	8 (12.5%)	4 (33%)	4 (8%)	0.03*
Previous revascularization	40 (83.3%)	9 (69%)	31 (89%)	0.12

*Fisher exact test

of our patients were male, confirming literature data. Epidemiologic differences related to sex become less evident when older individuals are examined (21).

A peculiarity of populations composed of young patients with AMI is represented by the risk profile. Cigarette smoking is uniformly the most common risk factor in many surveys, with an incidence ranging from 70% to more than 90% (1, 2, 21, 23-25). The current study confirms that a preponderance of young patients with AMI reported using tobacco at the time of the event. Many mechanisms are hypothesized to explain the role of smoking in the development of coronary heart disease: it plays, in fact, a role, not only in atherogenesis, but also in thrombogenesis, as well as in the development of endothelial dysfunction, favoring coronary spasm. These characteristics may help to explain the frequent found of healthy coronaries or of a non critical coronary atherosclerosis.

A family history of coronary heart disease is considered one of the most relevant risk factors for the early onset of AMI (1, 2, 21). Mechanisms regulating the heredity of the predisposition to develop atherosclerosis and its complications are not fully explained, but recently it has been widely demonstrated that genetic background may play a role in the risk of ischemic heart disease (26-28).

Finally, hypertension and diabetes mellitus, well established cardiovascular risk factors, are not as prevalent in younger age groups as they are in older ones. This observation is consistent with several studies (2, 3, 16, 21, 23, 29).

The low incidence of AMI in women limited the possibility to investigate adequately their risk profile. In this small sub-population oral contraceptives are an additive risk factor: approximately 40% of the female patients were taking oral contraceptives. Moreover all of them were smokers, confirming the synergic prothrombotic action of cigarettes and contraceptives.

Regarding the extent of coronary atherosclerosis, young patients generally show a less evolved disease. Coronary angiography demonstrated, in fact, an absence of significant coronary stenosis in the 25% of our patients and the presence of a single-vessel disease in the 43% of them. In these cases, myocardial infarction might be interpreted as the consequence of an acute thrombotic event, even on healthy or not critically stenosed coronaries. These data confirm previous literature observations (2, 16, 21, 30). Moreover in young patients it is less rare to find a non atherosclerotic mechanism of the ischemia: coronary ectasia, coronary spasm, coronary inflammation or coronary bridging.

Discharge therapy in our population of young AMI patients was in agreement with currently recommended treatment: 97.5% was taking an anti-platelet agent, 76% statin and 66% beta-blocker. Nearly the 45% of our patients were discharged with double-antiaggregation. This fact might be explained taking into account that the enrollment started on 2001 and the use of a second antiplatelet agent in acute myocardial infarction was not common at that time.

Follow up data show an increase in rates of new ischemic events during the studied period. Unfortunately just approximately half of our patients were available for a long term follow-up and this is a limitation of this study. In fact we are not able to estimate the real mortality of this group of patients. The reason of this lack of patients should be found in the distance between our center and the site of provenience of some of them.

Short and medium time follow up events showed that patients who developed a new cardiovascular event were more likely hypertensive and obese, with a trend towards the statistic significance for diabetes. At long term follow-up no cardiovascular risk factor resulted significantly associated with a recurrent event. This datum could be explained as a consequence of the small sample size. Interestingly, risk factors more often associated with coronary artery disease in older patients (i.e. hypertension and diabetes) were less frequent in this young population, but they showed a relevant prognostic role.

Prognosis seemed to be also affected by angiographic picture and by the occurrence of revascularization. In fact, both at the early and at the medium time follow up, the absence of significant coronary stenosis was associated with a better prognosis as it was also a previous revascularization (PCI or CABG).

The presence of healthy coronary arteries has a positive prognostic impact also at long time follow-up, while a decreased ejection fraction is associated with the recurrence of events. These data confirm the poor published data about prognosis of young patients with myocardial infarction (31, 32).

In conclusion, despite partial information about the long-term follow-up of this group of young subjects with AMI, we retain of particular interest the description of risk factors and of clinical and angiographic picture that seem to affect prognosis.

Risk profile in these subjects is quite different from the one of older populations, as it is angiographic picture. Nevertheless a deep impact on prognosis seems to be played by those risk factors which are more frequent in older patients.

Considering the long life expectancy of these patients and their peculiarities, we believe that the study of their characteristics deserves a deep attention that needs further investigation especially enlarging the record of cases.

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