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Original Paper

Acute Myocardial Infarction in Youngs: Presentation, Treatment and Outcome

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REZUMAT

Infarctul miocardic acut la tineri: prezentare, tratament și prognostic

Obiective: Despre infarctul miocardic acut (IMA) la tinerii români există puține date publicate. În acest studiu s-a urmărit identificarea profilului clinic, biologic, imagistic si terapeutic, a evoluției intraspitalicești și a prognosticului pe termen mediu postIMA la pacienții români cu vârsta sub 45 de ani.

Metode: Au fost luați în studiu 173 de adulți români (vârstă medie 39 ± 5 ani, între 19 și 45 ani) internați pentru IMA în două unități de terapie intensivă coronariană din Ianuarie 2009 până în Decembrie 2011. Particularitățile inițiale, investigațiile și tratamentul au fost înregistrate la momentul evenimentului index. Pacienții au fost urmăriți ulterior pe o perioadă de până la 4 ani (în medie 3 ± 1 an). Obiectivul principal a fost totalitatea evenimentelor cardiovasculare majore: deces de cauză cardiovasculară, reinfarctizare, revascularizare ulterioară și reinternare de urgență de cauză cardiovasculară.

Rezultate: Majoritatea pacienților au fost bărbați (91.3%). Fumatul (90.8%), dislipidemia (64.7%) și hipertensiunea (41%) au fost cei mai frecvenți factori de risc asociați; în 2.9% din pacienți nu s-a identificat niciun factor de risc. IMA cu supradenivelare de segment ST (STEMI) a fost diagnosticat la 80.3% din pacienți iar 19.7% au suferit un IMA fără supradenivelare de ST (NSTEMI). Aproximativ 2/3 din pacienții cu STEMI (71.9%) au beneficiat de terapie de reperfuzie: angioplastie primară (PTCA) în 43.9% din cazuri, tromboliză (23.7%) și angioplastie coronariană facilitată la 4.3% din pacienți. Mediana timpului de la debutul simptomatologiei până la tromboliză a fost de 168 minute (120-225 min) iar mediana timpului de la debutul simptomatologiei până la angioplastie a fost de 310 minute (210-540 min) ($p<0.01$). Boală coronariană obstructivă a fost diagnosticată la 90.3% din pacienți coronarografiați: leziune unicoronariană în 58.3% și stenoze semnificative plurivasculare în 31.9% din cazuri. La externare, Fracția de ejecție a ventriculului stâng a fost în medie 49 ± 11%. Cele mai frecvente complicații intraspitalicești: insuficiență cardiacă la 15%, ischemie recurentă la 12.1% și aritmii la 10.4% din pacienți. Mortalitatea intraspitalicească a fost de 3.5% (6 decese). Prognosticul pe termen mediu la această cohortă de pacienți tineri a fost rezervat: 33.8% din cei 142 de pacienți urmăriți au suferit cel puțin un eveniment cardiovascular major după IMA inițial.

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Concluzii. Tineri pacienți români cu IMA au o mare încărcare aterosclerotică. Chiar dacă beneficiază într-un număr ridicat de terapie de reperfuzie precoce și rata lor de supraviețuire este mare, prognosticul pe termen lung este complicat de evenimente cardiovasculare majore la 1 din 3 pacienți tineri cu IMA. Cercetări orientate asupra factorilor care influențează prognosticul și intervenții individualizate se impun la acest subgrup distinct si vulnerabil de pacienți cu IMA

Cuvinte cheie: infarct miocardic acut, tineri, factori risc, tratament, prognostic

ABSTRACT

Objectives: Few data regarding acute myocardial infarction (AMI) in young Romanian adults are published. The present study aims to identify the clinical, biological, imagistic, therapeutic profile and the inhospital and mid-term outcomes of the myocardial infarction in a Romanian population younger than 45 years.
Methods: The studied population consisted of 173 Romanian adults (mean age 39 ± 5 years, range 19 to 45 years) admitted for AMI in two acute cardiac care units between January 2009 and December 2011. The baseline characteristics, procedures and treatment were collected at the time of the index event. The patients were followed-up for up to 4 years (mean 3 ± 1 years). The primary endpoint was a composite of major adverse cardiac events (MACE): cardiovascular death, new myocardial infarction, subsequent revascularization and emergency cardiac readmissions.
Results: The majority of patients were male (91.3%). Smoking (90.8%), dyslipidemia (64.7%) and hypertension (41%) were the most prevalent risk factors and in 2.9% of patients no apparent risk factor was identified. ST-elevation acute myocardial infarction (STEMI) was diagnosed in 80.3% of patients and 19.7% had a non-ST elevation acute myocardial infarction (NSTEMI). Almost 2/3 of the STEMI patients (71.9%) received reperfusion therapy: primary angioplasty (PTCA) in 43.9% of cases, thrombolysis (23.7%) and facilitated PTCA in 4.3% of patients. The median ”symptom onset-to-needle” time was 168 (120-225) minutes while median ”symptom onset-to-balloon” time was 310 (210-540) minutes ($p<0.01$). Obstructive coronary artery disease was diagnosed in 90.3% of the patients who underwent coronary angiography: single vessel disease in 58.3% and significant multivessel stenosis in 31.9% of patients. Mean left ventricle ejection fraction at discharge was 49 ± 11%. The most frequent acute complications were: heart failure in 15%, recurrent ischaemia in 12.1%, and arrhythmias in 10.4% of patients. The in-hospital mortality was 3.5% (6 deaths). The long term outcome in this cohort of young patients was poor: 33.8% of 142 followed-up patients had at least 1 recurrent MACE after the initial AMI.
Conclusion: The young Romanian patients with AMI have a high atherosclerotic burden. Even though they benefit in a large proportion of timely reperfusion therapy and the survival rate is high, the long term outcome is impaired by major cardiovascular complications in 1 of 3 young patients with AMI. Focused research on the factors that influence the outcome and targeted interventions are needed in this distinct and vulnerable subgroup of AMI patients.

Key words: acute myocardial infarction, youngs, risk factors, therapy, outcome

BACKGROUND

Coronary Artery Disease (CAD), the world’s leading cause of death and morbidity, it is not anymore an attribute of old age (1). The increase prevalence of atherosclerotic risk factors among the young and very young population is responsible for more premature CAD cases (2). Prior studies highlighted that AMI in young’s is associated with different clinical features and has a better short-term outcome than in older population (3,4,5). However, long-term follow-up revealed a higher mortality and morbidity in young AMI survivors than in general population (6,7). Also, the conclusion of several studies and “real-world” registries was that patients with STEMI and NSTEMI, regardless of age and despite different management, have similar inhospital outcome and longterm survival (8,9).

In our country, RO-STEMI registry is providing the most extensive information on the profile, treatment and inhospital outcome of the STEMI Romanian patients (10) but only few reports about mid and long-term follow up of young Romanian patients with AMI, especially in case of NSTEMI, are available (11,12,13).

Objectives

The primary objectives of our study are to asses the clinical, biological, imagistic and angiographic characteristics of the young Romanian patients with AMI, to provide insights on their current management and inhospital evolution and to establish their mid-term clinical outcome. Another objective of our study is to make an extensive comparison between young STEMI and NSTEMI Romanian patients both in terms of initial profile, management and outcome.

MATERIALS AND METHODS

Study population and data collection

The study group consisted of 173 patients admitted in the two cardiology clinics of Bucharest Emergency Hospital and "Sf. Pantelimon" Emergency Hospital between 1 January 2009 and 31 December 2011. The inclusion criteria were: age less than 45 years old at the hospitalization, a diagnosis of Acute Myocardial Infarction with or without ST elevation (STEMI and NSTEMI), using the ESC criteria established in 2007 (14), and willingness to provide informed consent and to participate in follow-up. Patients with incomplete index event data, residents of foreign countries, who died before admittance and with peri-procedural AMI, were excluded. The study complied with the Declaration of Helsinki regarding investigations in humans and was approved by the Ethics Committee of both hospitals. This was a retrospective-prospective cohort survey. The initial AMI data were collected in a standardized form from the patient's original files (Table 1). For establishing the biological profile of the patients, only the blood samples that fulfilled the following requirements were used in the analysis: collection in the first 24-48 hours after the AMI onset, fasting or late postprandial withdrawal, rapid (one hour) processing of the blood samples in the certified laboratories of both hospitals. Were appropriate, normalization of the results using the "location scale" formula was used (15).

The electrocardiograms (ECG) evaluation was

Tabel 1. Baseline characteristics of young patients with AMI

	Overall (n=173)	STEMI (n=139)	NSTEMI (n=34)	p-value
Age (mean ± SD, years)	38.9±4.7	38.5±4.8	40.5±3.74	**0.0190**
Male gender % (no)	91.3 (158)	91.4 (127)	91.2 (31)	0.5975
Risk factors				
Family history of premature CVD % (no)	15.6 (27)	14.4 (20)	20.6 (7)	0.3719
Hypertension	41 (71)	38.8 (54)	50 (17)	0.2360
Dyslipidemia	64.7 (112)	60.4 (84)	82.4 (28)	**0.0164**
Diabetes mellitus	13.3 (23)	12.9 (18)	14.7 (5)	0.4872
Smoking (current+former) % (no)	90.8 (157)	92.1 (128)	85.2 (29)	0.6065
BMI ≥ 30 kg/m² % (no)	35.8 (62)	33.8 (47)	44.1 (15)	0.4773
Transportation to hospital % (no)				
EMS transportation	64.7 (112)	70.5 (98)	41.2 (14)	**0.0041**
Self-transportation	35.3 (61)	29.5 (41)	58.8 (20)	
"Pain-to-FMC" time (minutes) median (IQR)	130 (67-350)	130 (73-360)	131.5 (67-300)	0.6347
"Pain-to-treatment*" time (minutes) median (IQR)	257 (150-520)	270 (165-540)	231 (120-378)	0.5454
Chest pain % (no)	92.5 (160)	93.5 (130)	88.2 (30)	0.3757
Preinfarction angina % (no)	33 (57)	27.4 (38)	55.9 (19)	**0.0049**
Killip class I	82.1 (142)	81.3 (113)	85.3 (29)	0.1219
Killip class II	13.9 (24)	15.1 (21)	8.8 (3)	
Killip class III	1.7 (3)	0.7 (1)	5.9 (2)	
Killip class IV	2.3 (4)	2.9 (4)	0 (0)	
Blood glucose at presentation (mean ± SD, mg/dl)	141±70	147±74	119±43	**0.0083**
Total cholesterol (mean ± SD, mg/dl)	215±55	212±54	228±59	0.1506
Maximum CK-MB (mean ± SD, UI/l)	229±206	265±209	60±49	**<0.0001**

SD=standard deviation; no=number; CVD=cardiovascular diseases; BMI=body mass index; EMS=emergency medical system; FMC=first medical contact (initial medical evaluation); IQR=interquartile range; *treatment=ballon/needle (STEMI) and antiplatelet therapy (NSTEMI)

also standardized: only 12 leads, good quality, validated recordings performed at admission (prior to any treatment), after the revascularization procedure, 24hours afterwards and at the discharge were used. The interpretation of all the recordings was performed by the same trained physician.

Standard cardiac ultrasound was performed after the revascularization therapy and before discharge, by skilled echocardiographists on GE VIVID 7 (Emergency hospital) or PHILIPS iE33 ("Sf. Pantelimon" hospital), according to the specifications of the European Association of Cardiovascular Imaging (16). Diagnostic and therapeutic coronarographic data were obtained from the cath labs (certified for primary angioplasty) of: Bucharest Clinical Emergency Hospital, "C.C. Iliescu" Institute for Emergency in Cardiovascular Diseases and University Emergency Hospital of Bucharest. The index event treatment was also reviewed. Inhospital death rate and cause, recurrent ischemia, arrhythmias, acute heart failure and the duration of hospitalization were used for assessing short-term outcome of young AMI patients. All eligible patients were followed-up for up to 4 years (minimum 2 years). A specially designed protocol was performed either at clinic visits or by telephone interviews at 30 days, 6 month and then yearly after the initial AMI. When the patient was not accessible, data were retrieved from the general physician, hospitals electronic databases or the Integrated Information System ("SIUI"). The primary clinical endpoint pursued was a composite of major cardiovascular adverse events (MACE): cardiovascular death, subsequent myocardial infarction, and revascularization (percutaneous coronary intervention - PCI or coronary artery bypass grafting – CABG) and emergency cardiac readmissions.

Statistical analysis

The Microsoft Excel and SPSS software (Chicago, Illinois; Version 18.0) were used for all statistical analyses. Continuous variables are presented as means ± standard deviation or medians with interquartile range (IQR). Categorical variables are presented as percentages and counts. P value of < 0.05 was considered significant. For continuous variables the unpaired t-test or the Mann-Whitney u test were employed according to their distribution. The likehood ratio, chi-square and the Fisher's exact tests were used to account for differences between categorical variables.

RESULTS

Between 2009-2011, 173 young patients admitted for AMI in the two selected emergency hospitals met the inclusion criteria of the current study. Mean age of the patients was 39 (±5 years standard deviation SD); 158 (91.3%) were male and only 15 (8.7%) were female. The majority of patients have an urban provenance (74.6%). The baseline characteristics of the young patients with AMI are summarized in **Table 1**.

Major cardiovascular risk factors

In the studied patients, smoking (90.8%), dyslipidemia (64.7%) and hypertension (41%) had the higher prevalence. The young's with AMI are high risk patients with more than 1 cardiovascular risk factor: 30.6% of patients had 2 risk factors, 25.4% had 3 risk factors and in 25.5% of patients ≥4 major CAD risk factors were identified. A positive family history of premature cardiovascular disease was reported in 13.9% of male patients and 33.3% of women with AMI (p=0493). There were also differences in the risk profile of men versus women; in case of the first category smoking and lipid abnormalities were most prevalent while hypertension (in 73.3% of cases), smoking (73.3%) and dyslipidemia (66.7%) were the most frequent risk factors in case of young women with AMI.

Non-atherosclerotic risk factors

From the 23 patients who were screened for coagulopathies only 8 patients (2 females and 6 males) were diagnosed with a coagulation disorder: C protein deficiency (2 patients), S protein deficiency (2 patients), C and S proteins deficiency (1 patient), antiphospholipid antibody syndrome (2 patients) and factor V Leiden mutation (1 female patient). No drug usage/abuse or malformations of the culprit coronary artery was identified among the studied young patients.

In 2.9% no risk factor (including non-atherosclerotic etiology) was able to be identified. Prior MI was present in 12.7% of patients; 8 (4.6%) of the studied patients had a history of revascularization procedure (stenting in 5 cases and CABG in 1). Other significant concomitant medical conditions were: peripheral artery disease in 11 patients (6.3%), 7 patients with heart failure (4%), chronic kidney disease in 8 patients (4.6%), venous thrombosis and pulmonary embolism in 3 patients (1.7%) and

ischemic stroke in 2 patients (1%). There were also 3 patients with autoimmune disease (lupus and rheumatoid arthritis).

Electrocardiographic findings

According to the initial Ecg, 139 (80.3%) of the patients had a STEMI and 34 (19.7%) patients had a NSTEMI. Anterior location was diagnosed in 46% of the STEMI Ecg, inferior location in 31% and in 23% of the STEMI cases there was a lateral involvement. Prolonged QRS (>90msec) was previously associated with poor short and long term outcome post-MI (17); in our study, mean QRS duration on the admission Ecg was 93.4 msec, without significant statistical difference between STEMI and NSTEMI patients. LBBB was diagnosed in 2.3% of the initial Ecg, while RBBB was found in 3.5% of patients. Another Ecg finding that influences outcome in STEMI is the reduction of ST-segment elevation after revascularization procedures: in our study, 23% of STEMI patients had partial (< 50%) or no (<30%) resolution of ST – elevation on their discharge Ecg. Almost half (47.1%) of the patients diagnosed with NSTEMI had significant ST-depression on their admission Ecg.

Angiographic parameters (including normal coronary)

In the studied group, 83.2% of the patients had a coronary angiography: 67.6% of the NSTEMI patients and 87.1% of the STEMI group (p=0.0208). Normal coronary arteries were found in just 8.3% of patients while more than 90% of the young AMI patients included in the study had severe and extensive coronary arteries stenosis. Involvement of the Left anterior descending artery was significantly more diagnosed in STEMI patients while Circumflex artery lesions were more frequent in NSTEMI patients. No statistical difference regarding the extension and the severity of the coronary lesions were found between STEMI and NSTEMI patients (Table 2).

Echocardiographic findings

Complete and validated echocardiographic data were available in 168 of the studied patients (134 STEMI and the 34 NSTEMI patients). The mean left ventricle ejection fraction (LVEF), calculated using the modified biplane Simpson's method (16), was 49% ± 11%; there was a significant difference (p=0.0004) between mean LVEF of STEMI patients (47%±10%) and that found in NSTEMI patients (54%±10%). The same difference was present in the mean wall motion score index: 1.2 ± 0.3 (NSTEMI) and 1.5 ± 0.4 in STEMI patients (p=0.0001). Right ventricle dysfunction was diagnosed in 7 patients (4.2%). Other complications: 14 patients (8.3%) with ischemic mitral regurgitation's degree greater than II (13 STEMI and 1 NSTEMI); left ventricle aneurisms were identified in 8 STEMI patients (5 of anterior location and 3 inferior aneurisms) and in 4.2% of the patients left ventricle thrombosis was identified.

Management of acute myocardial infarction

Timely reperfusion therapy was performed in 71.9% of young STEMI patients: primary angioplasty (PTCA) in 43.9% of cases, thrombolysis (23.7%) and facilitated PTCA in 4.3% of patients. The reasons for not performing prompt reperfusion procedures were: late presentation (13.7% of patients), clinical and Ecg criteria of spontaneous reperfusion (7.9% of patients) and other causes (6.5% of patients). Early PCI was performed in only 1 young NSTEMI patient and there were also significantly less PCI in the NSTEMI group

Table 2. Distribution of significant* coronary lesions

	Overall (n=144)	STEMI (n=121)	NSTEMI (n=23)	p-value
No significant coronar y lesions % (no)	9.7 (14)	9.1 (11)	13 (3)	0.5637
Single-vessel disease % (no)	58.3 (84)	62 (75)	39.1 (9)	0.0430
Left anterior descending artery	53.6 (45)	57.3 (43)	22.2 (2)	0.0494
Right coronary artery	22.6 (19)	22.7 (17)	22.2 (2)	0.9731
Circumflex artery	22.6 (19)	18.7 (14)	55.6 (5)	0.0145
Left main artery	1.2 (1)	1.3 (1)	0 (0)	0.7317
Two-vessel disease % (no)	22.2 (32)	20.7(25)	30.4 (7)	0.3070
Triple-vessel disease % (no)	9.7 (14)	8.3 (10)	17.4 (4)	0.1797
Extensive coronary lesions (>1 obstructive stenosis) % (no)	39.6 (57)	36.4 (44)	56.5 (13)	0.0729

Significant = angiographic coronary stenosis > 50%

Table 3. Results of coronary interventions

	Overall (n=173)	STEMI (n=139)	NSTEMI (n=34)	p-value
Thrombolysis % (no)	NA	23.7 (33)	NA	
Any PCI % (no)	83.2 (144)	87.1 (121)	67.7 (23)	0.0072
Primary/early invasive PCI % (no)	35.8 (62)	43.9 (61)	2.9 (1)	<0.0001
Facilitated PCI % (no)	NA	4.3 (6)	NA	
Delayed PCI % (no)	33 (57)	29.5 (41)	47.1 (16)	0.0520
Type of PCI procedure	n=144	n=121	n=23	
Ballon PTCA % (no)	3. 5 (5)	3.3 (4)	4.4 (1)	0.7922
Ballon PTCA + stenting % (no)	51. 4 (74)	56.2 (68)	26.1 (6)	0.0090
Direct Stenting % (no)	18.8 (27)	18.2 (22)	21.7 (5)	0.6941
Drug-eluting stent % (no)	11.1 (16)	9.9 (12)	17.4 (4)	0.2956
Thromboaspiration % (no)	12.5 (18)	14.5 (18)	0	0.0533
No coronary procedure % (no)	18.8 (27)	15.7 (19)	34.8 (8)	0.0331

Any PCI =emergency and/or elective PCI for the initial AMI; Primary/early invasive PCI= percutaneous coronary intervention performed in the first 24 hours after symptom's onset; Facilitated PCI=PCI after thrombolysis performed in the first 24 hours of the AMI; Delayed PCI=PCI performed during the index hospitalisation; NA=not applicable

compared to the STEMI group (**Table 3**). Both AMI groups received in high percentages evidenced-based adjuvant therapy for AMI (**Fig. 1**).

In-hospital clinical outcome

Signs and symptoms suggestive for Killip class higher than 1 were found at presentation in 31 patients (18%) with 4 cases of cardiogenic shock. Resuscitated cardiac arrest at admission was encountered in 8 patients (4.6%). The length of hospital stay was 8.8±2.5 days with no statistical difference between STEMI and NSTEMI. Inhospital mortality was 3.5%; the cause of death was cardiac in all 6 cases. The most frequent acute complications were: heart failure in 15%, recurrent ischaemia in 12.1%, and ventricular and supra-ventricular arrhythmias in 11.6% of patients (**Table 4**). Other complications found in STEMI patients: 5 cases of reinfarctization, 3 early stent thrombosis (1 acute and 2 subacute), 3 patients with complete atroventricular block that required permanent (1) or temporary pacemaker, 1 case of free left ventricle wall rupture 4 hours after successful PTCA, 1 cardioembolic stroke and 1 case of upper digestive bleeding.

Follow-up

Of the 167 initial AMI survivors, 25 patients were

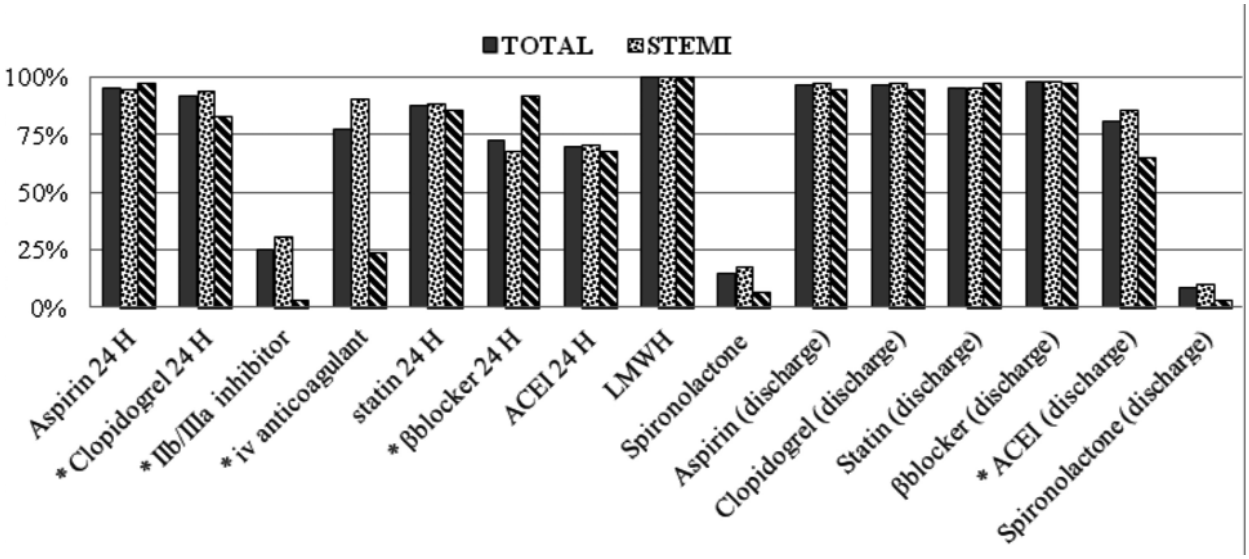

Figure 1. Inhospital and discharge therapy of AMI patients
IIb/IIIa inhib.= glycoprotein IIb/IIIa inhibitor; ACEI=angiotensin converting enzyme inhibitors;
LMWH=low molecular weight heparins; iv=intravenous; 24 H=administrated in the first 24 H after AMI; * = p < 0.05

Table 4. Inhospital and 3-year clinical outcomes

	Overall (n=173)	STEMI (n=139)	NSTEMI (n=34)	p-value
Inhospital death % (no)	3.5 (6)	4.3 (6)	0 (0)	0.2202
Inhospital Reinfarctization % (no)	2.9 (5)	3.6 (5)	0 (0)	0.2631
Inhospital recurrent ischemia % (no)	12.1 (21)	11.5 (16)	14.7 (5)	0.6091
Inhospital heart failure % (no)	15 (26)	15.8 (22)	11.8 (4)	0.5502
Inhospital arrhythmias % (no)	11.6 (20)	11.5 (16)	11.8 (4)	0.9609
Not-sustained ventricular tachycardia % (no)	7.5 (13)	8.6 (12)	2.9 (1)	0.2590
Ventricular fibrillation % (no)	2.3 (4)	2.2 (3)	2.9 (1)	0.8090
Atrial fibrillation % (no)	1.7 (3)	0.7 (1)	5.9 (2)	0.0382
Length of hospital stay (mean±SD, days)	8.8±2.5	8.7±2.6	9.1±2.2	0.2740
3-year follow-up	n=142	n=111	n=31	
3-year MACE % (no)	33.8 (48)	31.5 (35)	42 (13)	0.2764
3-year cardiovascular death % (no)	4.9 (7)	3.6 (4)	9.7 (3)	0.1677
3-year subsequent AMI % (no)	7 (10)	6.3 (7)	9.7 (3)	0.5141
3-year new revascularization % (no)	15.5 (22)	15.3 (17)	16.1 (5)	0.9134
3-year PCI % (no)	10.6 (15)	11.7 (13)	6.5 (2)	0.4064
3-year CABG % (no)	5 (7)	3.6 (4)	9.7 (3)	0.1677
3-year emergency cardiac readmissions % (no)	31.7 (45)	29.7 (33)	38.7 (12)	0.3425
≥ 2 MACE/pacient	60.4 (29)	62.9 (22)	53.8 (7)	0.5695
Overall mortality % (no)	7.5 (13)	9 (10)	8.8 (3)	0.7515

MACE=major adverse cardiac events; AMI=acute myocardial infarction; PCI=percutaneous coronary intervention; CABG=coronary artery bypass grafting; NA=not applicable

not available for complete evaluation during the follow up period. However, survival status was obtained for all the 167 patients. Median follow up duration was 2.9 years (IQR 2-3.9 years). Overall, the MACE rate was found to be 33.8%. Seven young patients (4.9%) died within 4 years succeeding the AMI. The cause of all deaths was due to a cardiovascular complication. There were also a high rate of emergency cardiac readmissions (31.7%) and more than half of the followed patients (60.4%) had at least 2 different MACE. In our study, there was no statistical difference between the inhospital and 3-year follow up clinical outcome of the NSTEMI patiens compared with that of STEMI patients (Table 4).

DISCUSSION

Myocardial infarction in young patients accounts for 2 to 10% of all hospitalized AMI (18,19); in Romania, 8.5% of STEMI patients are younger than 45 years old (12) and the incidence of NSTEMI in young patients is not currently known.

Prior studies (2,5,12,19) have shown that AMI in young population has a male predominance that was also found in our studied group: only 8.7% of patients were women.

Even if a different risk profile was found in young patients compared with older (2,3), no prior study identified other significant etiology than atherosclerotic coronary disease in young patients (4,5,18-22). In our study, the atherosclerotic burden was high with more than 80% of patients having at least 2 major CAD factors; smoking was the most prevalent factor in this young cohort, finding consistent with prior reports (18-22). The relative low and steady incidence of AMI amongst young smoker population (18) and the high aggregation of risk factors in the young AMI population may suggest that smoking is not the only precipitating factor and maybe its association with lipid abnormalities (22) and other not yet identified factors is the trigger for AMI.

Regarding the risk profile, there were some distinct findings in our study: no history of illicit drug usage (cocaine abuse was previously reported (23) as high as 5% in young AMI patients) and a relative low prevalence of positive family history of premature cardiovascular disease (ranging from 14 to 69% in prior studies (18)). The role of coagulation disorders is still understudied in the young AMI patients even though it has an important impact on treatment; only 13.3% of our studied patients were investigated with just 3.5% of them being diagnosed with a coagulopathy.

The majority of patients included in our study had a STEMI; however there were only few significant differences in the baseline characteristics between the two subsets. NSTEMI patients were older, with higher prevalence of dyslipidemia and prior preinfarction angina, lower glycemia level

at presentation and better left ventricle systolic function than STEMI patients.

There are discrepancies in published data regarding the most frequent AMI location in young patients; in VALIANT, a randomized trial of high-risk AMI, anterior location was present in 69.7% of patients under 45 years (24) while in Spanish PRIM-VAC registry, 53.4% of young patients had an inferior location of the AMI (5). In our study, anterior STEMI was the most frequent and it correlates with the moderate impairment of LVEF, also reported by other studies of young AMI patients (7,19,25).

About revascularization therapy, in RO-STEMI, between 1997-2009, the rate of thrombolysis was 77.75% while primary PCI was performed in only 7,37% of patients younger than 45 years (12); in our study, started in 2009, the rate of thrombolysis was 23.7% while primary PCI increased to 44%. Still, a 72% rate of reperfusion therapy in young AMI patients is less than that recently reported by American [78.6% (24), 81.3 (26)], Japanese (90.5% (21)) and European [88.6% (27), 79.1% (23)]. Surprisingly, in the 803 young patients included in VALIANT, the rate of reperfusion therapy was 65.7 % (24). In our study, the median "pain-to-treatment" time did not vary significantly between STEMI and NSTEMI patients but was longer than the median time reported by the Euro Heart Survey 2009 Snapshot (176/244 minutes in STEMI, 192 minutes in NSTEMI) (13); possible reasons for the delay: late presentation of the patients, prolonged transfer to primary PCI center.

The angiographic studies revealed that the Romanian young AMI patients have mostly single-vessel atherosclerotic coronary lesions in 58.3% of patients, similar to prior reported rates (39% (3) to 76.9% (21)). The rate of AMI with normal coronary arteries was 14% consistent with other studies (3,18,21). Another important finding of our study is that the young NSTEMI patients benefited much less than STEMI patients of acute or elective PCI even though they have a more extensive and severe coronary artery disease.

The low rate of revascularization procedures, especially in the early phase of AMI, may explain why there were no statistical differences between the inhospital and late outcome of the STEMI and NSTEMI patients.

In RO-STEMI, the inhospital mortality was 4.4% in the young subset of patients; other studies reported an early mortality ranging from 0% (21,27) to 3.7% (7). In our study, inhospital mortality was 3.5%; anterior STEMI, delay to reperfusion, early reinfarctization, subacute stent thrombosis and severe irreversible left ventricle failure were factors contributing to the early deaths.

The prior assumption that AMI in young population has a good long-term outcome when compared to older counterparts was contradicted by other studies with 10 to 15-years follow up. They demonstrated a significantly higher mortality (25-30%) of young patients with AMI compared to those without the disease, predicted by prior MI, diabetes, peripheral arterial disease, continuation of smoking and LVEF less than 45% (6,7);

The mid-term outcome of our young cohort of AMI patients was also not benign; we report a 3-years MACE rate of 33.8% and an overall mortality of 4.9%, similar with the Japanese and American reports (8,21).

Our study is a retrospective-prospective, observational analysis of the baseline characteristics, management and medium-term outcome of a cohort of young Romanian patients with AMI. The results are comparable with those already published worldwide, suggesting that AMI in young population has the similar features regardless of race or place of birth.

Also, we have demonstrated for the first time that despite different management, the inhospital and medium-term prognosis of young NSTEMI patients is comparable to that of young STEMI patients, consistent with prior reports (8,9). Even if young NSTEMI patients are initially considered low-risk patients the severity of their coronary artery disease suggests that they may benefit from a more early invasive approach (6) than that currently recommended by the guidelines.

There are several limitations of our study. We included a relative small number of patients (especially young women), but comparable to that of other similar studies. The patients were collected from only two emergency hospitals in the same city even though they attend a larger array of population. Some patients were transferred from other hospitals so admission data were lacking or it did not meet the protocol criteria. Because of the observational character of this survey some parameters regarding the underlying etiology, metabolic and rheological profile of young patients were not available. So generalizations of our findings to the entire young Romanian AMI patients may not be possible.

CONCLUSION.

The young Romanian patients with AMI have a high atherosclerotic profile. Even though they benefit in large proportions of high standard quality-of-care and they have a low rate of inhospital complications the mid-term outcome is impaired in one third of the patients. There is no difference between the initial and mid-term outcome of the young STEMI and NSTEMI patients. Because of the multiple individual and general consequences of this disease in young Romanian population, further larger, controlled-case studies are needed in order to better identify the risk factors and individualize therapy in this distinct and vulnerable subset of AMI patients.

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