



Is NSTEMI different than STEMI in young patients?

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Abstract

The number of young patients diagnosed with non-ST elevation myocardial infarction (NSTEMI) is increasing and more focused research on their profile and outcome is needed. We analyzed and compared data from 173 patients younger than 45 years of age, 139 patients with STEMI and 34 with NSTEMI) admitted for AMI between January 2009 - December 2011; they were prospectively followed for up to 4 years (mean 3±1 years). NSTEMI patients were older (41±4 years vs 39±5, p=0.02) and had a higher prevalence of dyslipidemia (82% vs 60%, p=0.01) than the young STEMI patients who also had higher levels of troponin I (58±51 vs 11±9ng/ml, p<0.001) and a lower mean left ventricle ejection fraction (47±10% vs 54±95, p<0.001) than the NSTEMI young patients. The Killip class ≥ II (in 19% of STEMI vs 15% of NSTEMI patients, p=0.1) and the mean BNP at presentation (313±452 in STEMI vs 297±483pg/ml in NSTEMI patients, p=0.8) were similar. Multivessel atherosclerotic coronary disease (48% of the NSTEMI patients) and significant stenosis of the circumflex artery (56%) were more frequent in the young NSTEMI group. The PCI rate was significantly higher in the STEMI group (87% vs 68%, p<0.01). Young NSTEMI patients had the same inhospital complications rate (32% vs 31% of STEMI patients, p=0.9) and a similar 3-years survival without MACE (62% vs 74%) as the young STEMI group. In our cohort of young patients, those with NSTEMI have similar risk profile and outcome but are less likely to benefit from early revascularization procedures compared to the young STEMI group

Keywords: young, myocardial, infarction

Background

The leading cause of death in the world, coronary artery disease (CAD), is largely studied worldwide however literature focusing on premature CAD and

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especially myocardial infarction (MI) is modest (1). Consequences of this disease in young patients are of most importance not just for the individual but for the entire society. The current knowledge about MI in young population suggest different presentation, risk factors and management, better inhospital and short-term outcome than the older MI patients (1,2,3,4). However limited, age-specific long-term follow-up data show higher morbidity and mortality

in young AMI survivors than in general population (5,6). Regardless of age, there is no difference between the short outcome and longterm survival of patients with ST-elevation MI (STEMI) versus non-ST elevation type (NSTEMI) but the number of young patients diagnosed with non-ST elevation myocardial infarction (NSTEMI) is increasing and more focused research on their clinical profile and outcome is needed (2,3,7).

In our country, the registry RO-STEMI is providing information about profile, treatment and inhospital outcome of the patients with STEMI (8) but the data focusing on young patients and especially their mid and longterm outcome after an MI, including NSTEMI, is limited (9).

Purpose

Our study aim is to compare the clinical, biological, imagistic, therapeutic characteristics and the long term outcome in patients younger than 45 years of age with STEMI and NSTEMI.

Materials and Methods

Study group and data collection

Between 1 January 2009 and 31 December 2011, patients admitted in the two acute cardiac units of "Sf. Pantelimon" Emergency Hospital and Bucharest Emergency Hospital were screened and 173 consecutive patients met our study inclusion criteria: age less than 45 years old, residence in Romania, a diagnosis of acute myocardial infarction using the appropriate criteria established by the current European guidelines (10) and complete index event data. All of the studied patients provided an informed consent and agreed to participate in the follow-up. The study complied with the Declaration of Helsinki regarding investigations in humans and had the ethical approval of our hospitals.

Our retrospective-prospective cohort study consisted of two phases: the index event hospitalization and the post-discharge, yearly follow-up period. In order to minimize data collection biases, the initial AMI data were collected in a standardized form from the patient's original files:

- for biological profile of the patients, only blood samples collected immediately upon admission and in the first 24 hours after the AMI onset and determined in the certified laboratories of both hospitals; were appropriate, normalization of the results was done using the "location scale" formula (11);
- the electrocardiograms (ECG) were interpreted by the same physician and only validated recordings performed at admission (prior to any treatment), after the revascularization procedure and at discharged were used;
- echocardiographic parameters were measured before discharge, according to the specifications of the European Association of Cardiovascular Imaging (12);
- diagnostic and therapeutic coronarographic data were obtained from cath labs certified for primary angioplasty
- the index event treatment, inhospital death rate and complications (recurrent ischemia, arrhythmias, acute heart failure), the duration of hospitalization were also recorded

All discharged patients were followed up yearly, for 2 to 4 years, either by clinic visits or by phone/email. When patients were not accessible data were obtained from other medical resources or the National Medical Assurance Integrated Information System. The patients with unknown or incomplete outcome information were not included in the survival analysis.

The cohort of young patients with AMI was divided in two groups: patients that fulfilled the criteria for ST elevation MI (STEMI) and another group of patients diagnosed with non-ST elevation MI (NSTEMI).

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. 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. The survival without MACE was described using the Kaplan-Meyer survival function and the comparison between the two studied groups was done with log-rank test. P value of < 0.05 was considered significant.

Results

Between 2009 - 2011, 173 consecutive young patients admitted for AMI in the two selected

emergency hospitals were included in the study; 139 (80%) patients met the criteria for STEMI and 34 patients (20%) had NSTEMI. The baseline characteristics and the comparisons between the two studied groups are summarized in Table 1.

NSTEMI patients were older and had a significantly higher prevalence of dyslipidemia than the young STEMI patients. Female gender had the same incidence in both groups. Regarding past medical history of ischemic heart disease or peripheral arteriopathy, we found no difference between the two groups but the patients with NSTEMI reported a higher incidence of chronic kidney disease. Ischemic preconditioning has been demonstrated to influence the infarcted area and the degree of necrosis

Table 1. Comparison between baseline characteristics of young patients with STEMI versus NSTEMI

	STEMI (n=139)	NSTEMI (n=34)	p-value
Age (mean ± SD, years)	39±5	41±4	0.02
Male gender % (no)	91 (127)	91 (31)	0.5
Risk factors			
Family history of premature CVD % (no)	14 (20)	21 (7)	0.3
Hypertension	39 (54)	50 (17)	0.2
Dyslipidemia	60 (84)	82 (28)	0.01
Diabetes mellitus	13 (18)	15 (5)	0.5
Smoking % (no)	92 (128)	85 (29)	0.6
BMI \geq 30 kg/m2 % (no)	34 (47)	44 (15)	0.5
Medical history			
Ischemic Heart disease %	10	15	0.3
Peripheral Artery disease %	6	9	0.3
Chronic kidney disease %	3	12	0.04
Preinfarction angina % (no)	27 (38)	56 (19)	<0.01
Killip class ≥ 2	19%	15%	0.1
Systolic Blood Pressure on admission (mean±S-D,mmHg)	137±29	119±43	0.09
Diastolic Blood Pressure on admission (mean±SD,mmHg)	82±18	88±13	0.01

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 anticoagulant therapy (NSTEMI)

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(13); in our study, preinfarction angina (defined as the appearance or aggravation of angina-like thoracic pain in the last week prior to AMI onset) was present in more than half of the NSTEMI patients, significantly more frequent than in the STEMI group. Mean systolic blood pressure was similar between groups but diastolic BP was significantly lower in the STEMI group.

As expected, the young STEMI patients had higher levels of troponin I and a lower mean left ventricle ejection fraction than the NSTEMI young patients but the Killip class ≥ II and the mean BNP at presentation were similar. Elevated inflammatory markers are associated with rupture prone atherosclerotic plaques and our young patient with STEMI had higher levels of WBC and fibrinogen compared with the NSTEMI group; admittance glucose was also higher even though the glycemic status was similar between the two groups. NSTEMI patients were found to have a higher MPV which is a marker of increased platelet activation and adhesivity. Serum Uric Acid is considered to be an

independent prognostic marker of cardiovascular events and its level was also significantly higher in the NSTEMI young patients (Table 2).

Regarding percutaneous intervention, we found that the percentage of young patients with NSTEMI treated invasively was lower than in the STEMI group despite the fact that multivessel disease was significantly more often found in the young patients diagnosed with NSTEMI. There was a difference in the culprit artery as well: left anterior descending artery in the STEMI patients and circumflex artery in the NSTEMI group which may partly explain the lack of ST-elevation patterns in these patients (Table 3).

We found no difference between the in hospital event rates of the NSTEMI and STEMI young patients (32% vs 31% of STEMI patients, p=0.9) (Table 4).

After discharge, 80% of STEMI patients and 91% of the NSTEMI group were followed up for 3±1 years. Higher numbers of cardiovascular death, subsequent MI and CABG were registered in the NSTEMI group although the statistical significance

Table 2. Biological and imagistic profile of studied patients

	STEMI (n=139)	NSTEMI (n=34)	p-value
Lab findings			
Admission White Blood Cell count (mean±SD, / mm3)	12666±3988	10622±2973	<0.01
Mean Platelet Volume (mean±SD, fL)	7.3±1.8	8.1±1.7	0.01
Fibrinogen (mean±SD, mg/dl)	429±194	303±100	<0.01
Blood glucose at presentation (mean \pm SD, mg/dl)	147±74	119±43	<0.01
Fasting Blood glucose (mean \pm SD, mg/dl)	100±2.8	109±42	0.4
Serum Uric Acid (mean±SD, mg/dl)	6.1±1.5	9.6±2.4	<0.001
Maximum Troponin I (mean±SD, ng/ml)	58±51	11±9	<0.001
BNP (mean±SD, pg/ml)	313±452	297±483	0.8
Echocardiographic parameters			
LVEF (mean±SD, %)	47±10	54±9	<0.001
WMI (mean±SD)	1.5±0.4	1.2±0.3	<0.001
Mitral Regurgitation ≥ II/IV degree (%)	10	3	0.3

BNP=brain natriuretic peptide; LVEF=left ventricle ejection fraction; WMI=wall motion index

Table 3. PCI and coronary significant lesions* characteristics according to the type of AMI

	STEMI (n=139)	NSTEMI (n=34)	p-value
Any PCI % (no)	87 (121)	68 (23)	<0.01
Primary/early invasive PCI % (no)	47 (66)	3 (1)	< 0.0001
Delayed PCI % (no)	16 (22)	27 (9)	0.1
Elective PCI % (no)	24 (33)	38 (13)	0.08
Coronary anatomy			
No significant coronary lesions % (no)	9 (11)	13 (3)	0.5
Culprit artery % (no)			
Left main	1 (1)	0 (0)	0.7
Left anterior descending artery	57 (43)	22 (2)	0.04
Circumflex artery	19 (14)	56 (5)	0.01
Right coronary artery	23 (17)	22 (2)	0.9
Multivessel disease % (no)	30 (35)	48 (11)	0.03

^{*=} coronary stenosis > 50%; Any PCI =emergency and/or elective percutaneous coronary intervention for the initial AMI; Primary/early invasive PCI= performed in the first 24 hours after symptom's onset; Delayed PCI=PCI performed during the index hospitalization; Elective PCI=PCI performed after the index hospitalization

was not met possible due to the relative low overall event rates that we found in the studied cohort (Table 4).

Overall (inhospital + follow up) mortality was 9% in both AMI groups and there was a a similar 3-years survival without MACE (62% in the NSTEMI group vs 74% in the young STEMI patients) (Figure 1)

Discussion

Although youngs with AMI associate with greater social and economical burden than older patients there are few studies which analyze this population characteristics and fewer that provide follow-up data. Myocardial infarction in patients younger than 45 years of age accounts for less than 10 % of all hospitalized AMI worldwide (1,2,3,4); in Romania, 8.5% of STEMI patients are young and to the present there are no reported data regarding the incidence of young patients with NSTEMI in our country (9).

In our study, which triggered data from two important emergency hospital in our country's capital, one fifth of patients was diagnosed with NSTEMI, similar with the rates reported by other authors of

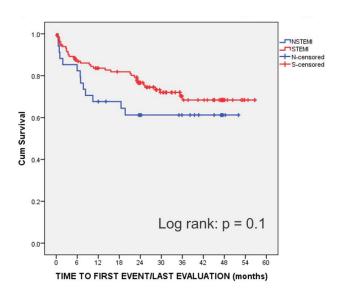


Figure 1: Survival without MACE according to AMI type

Table 4. Index hospitalization and follow-up MACE

	STEMI (n=139)	NSTEMI (n=34)	p-value
Index event hospitalization			
Death % (no)	4 (6)	0 (0)	0.2
Recurrent ischemia % (no)	12 (16)	15 (5)	0.6
Heart failure % (no)	16 (22)	12 (4)	0.5
Arrhythmias % (no)	11 (16)	12 (4)	0.9
Follow-up	n=111	n=31	
Cardiovascular Death % (no)	4 (4)	10 (3)	0.1
Subsequent AMI % (no)	6 (7)	10 (3)	0.5
New revascularization % (no)	15 (17)	16 (5)	0.9
PCI % (no)	12 (13)	7 (2)	0.4
CABG % (no)	4 (4)	10 (3)	0.1
Emergency cardiac readmissions % (no)	30 (33)	39 (12)	0.3
Overall mortality % (no)	9 (10)	9 (3)	0.7

MACE=major adverse cardiovascular events; PCI=percutaneous coronary intervention; CABG=coronary artery bypass grafting

approx. 25-30% (2,3,7). Most of the baseline characteristics between the two MI groups were similar, with male predominance and clustering of atherosclerotic risk factors. Our NSTEMI patients were older, more dyslipidemic and associated significant comorbidities, like high diastolic blood pressure and chronic kidney disease, which may explain also the higher prevalence of multivessel involvement found at PCI.

Compared with the data reported by other studies, our young patients with MI have similar rates for hypertension (40% Poland, 45% USA), diabetes (7% Poland, 19% USA) and obesity (21% Poland, 48% USA) but hyperlipidemia (56% USA, 33% Poland) and smoking (52% USA, 74%- Poland) are much more frequently in our patients (2,4), suggesting that targeted intervention to reduce smoking and dyslipidemia may be needed in our young population to prevent CAD.

The laboratory findings in our MI patients, with increased inflammatory and glycemic response in the acute phase in STEMI patients and high uric

acid and platelet activation in NSTEMI patients, sustain the hypothesis that there may be a different, unknown trigger for the rupture of atherosclerotic plaque and MI (14,15).

We found a significant disparity between the mean LVEF of STEMI (47%) and NSTEMI (54%) young patients, that is mild decline versus normal systolic function. The values are similar to those reported by other authors, regardless of the region or date of the study: 51% (Hoit, 1986), 47.6% (Doughty, 2002), 48.4% (Bangalore, 2012), 48% (Puricel, 2013), 52% (Jaquemin, 2010) (16,17,18,19, 20).

Regarding coronary catheterization and PCI, our study showed some important aspects; first, a definite, significant increase in the primary PCI in STEMI young patients compared with the data from RO-STEMI 1997-2009 (47% versus 7.37%, 9) but this value is still lower than the figures reported by USA (92%) and Poland (72%) (2,4). Other important finding is that the young patients with NSTEMI benefited much less of acute or elective PCI even though they have a more extensive and

severe coronary atherosclerotic disease. Our rate (68%) is much lower than that reported in other young NSTEMI cohorts (91%, 2) and may explain the MACE rate in short and longterm follow-up. There is an open debate on early invasive versus delayed PCI in young patients with NSTEMI who usually have low TIMI risk but are also under-represented in clinical trials, therefore TIMI-based approach may not be valid for these patients (1,2).

The inhospital mortality (0% and 4% for NSTEMI and STEMI group) is lower than that reported for older STEMI Romanian patients (13.39%) but similar to that reported for the young subset of patients in RO-STEMI (4.4%) and other studies (USA- 2.6% and 3.4% for NSTEMI and STEMI young patients, Poland- 1.6%, 3.7% - Spain) (21, 2,4,6)

There were no differences between the cumulative and singular MACE rate of young patients with NSTEMI compared with those with NSTEMI, finding analogous with other studies (2,3,4,7).

Prior studies of long-term follow-up of young MI patients demonstrated a higher mortality (25-30%) than the general population of the same age which was predicted by diabetes, smoking, LVEF less than 45% and the presence of peripheral artery disease (5,6).

In our study, after a mean 3 year follow up the death rate was 4% and 10% in STEMI and NSTEMI patients and the survival without MACE was also impaired (Figure 1), similar with Japanese and American reports (22,23).

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 location.

Also, we have demonstrated for the first time in Romania that despite different management, the inhospital and long-term prognosis of young NSTEMI patients is comparable to that of young STEMI patients, consistent with worldwide prior reports (2,3,4,22).

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 they didn't met 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. In conclusion we can not generalize our findings to the entire young Romanian AMI patients.

Conclusion

In our cohort of young patients, those with NSTEMI have similar risk profile, inhospital and long-term outcome but are less likely to benefit from early revascularization procedures compared to the young STEMI group

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Conflict of interest

The authors confirm that there are no conflicts of interest

References

- Shah N, Kelly AM, Cox N, Wong C, Soon K. Myocardial Infarction in the "Young": Risk Factors, Presentation, Management and Prognosis. Heart Lung Circ. 2016 Oct;25(10):955-60
- Tisminetzky M, Coukos JA, McManus DD et al. Decade-long trends in the magnitude, treatment, and outcomes of patients aged 30 to 54 years hospitalized with ST-segment elevation and non-ST-segment elevation myocardial infarction. Am J Cardiol. 2014 May 15;113(10):1606–10
- 3. McManus DD, Piacentine SM, Lessard D, Gore JM, Yarzebski J, Spencer FA, et al. Thirty-year (1975 to 2005) trends in the incidence rates, clinical features,

- treatment practices, and short-term outcomes of patients with STEMI and NSTEMI. Am J Med. 2011 Jan;124(1):40-7
- 4. Trzeciak P, Gierlotka M, Poloński L, Gąsior M. Treatment and outcomes of patients under 40 years of age with acute myocardial infarction in Poland in 2009-2013: an analysis from the PL-ACS registry. Pol Arch Intern Med. 2017 Oct 31;127(10):666–673
- Cole HJ, Miller III IJ, Laurence S. Sperling SL, Weintraub SW. Long-Term Follow-Up of Coronary Artery Disease Presenting in Young Adults. JACC Vol. 41, No. 4, 2003, February 19, 2003: 521–528
- Fournier JA, Cabezón S, Cayuela A, Ballesteros SM, Cortacero JA et al. Long-term prognosis of patients having acute myocardial infarction when <=40 years of age. Am J Cardiol. 2004 Oct 15;94(8):989–92
- 7. Puymirat E, Simon T, Cayla G, and FAST-MI investigators. Acute Myocardial Infarction: Changes in Patient Characteristics, Management, and 6-Month Outcomes Over a Period of 20 Years in the FAST-MI Program (French Registry of Acute ST-Elevation or Non-ST-Elevation Myocardial Infarction) 1995 to 2015. Circulation. 2017 Nov 14;136(20):1908–1919
- Tatu-Chitoiu G, Cinteza M, Dorobantu M, Udeanu M, Vintila M et al. In-hospital case fatality rates for acute myocardial infarction in Romania. CMAJ. 2009 Jun 9:180(12):1207–13
- Ţînţ D, Rădoi M, Dorobanţu M, Vinereanu D, Petriş A, Tatu-Chiţoiu et al. Vârsta, factorii de risc cardiovascular, terapia şi mortalitatea intraspitalicească la pacienţii cu infarct miocardic acut cu supradenivelare de segment ST. Un subraport al Registrului Român pentru infarctul miocardic acut cu supradenivelare de segment ST (RO-STEMI). Rom J Card. 2011: 26(1):4-13
- Thygesen K., Alpert J. S. and White H. D. on behalf of the Joint ESC/ACCF/AHA/WHF Task Force - Universal Definition of Myocardial Infarction. European Heart Journal (2007) 28, 2525–2538
- 11. Chuang-Stein C. Summarizing laboratory data with different reference ranges in multi-center clinical trials. Drug Information Journal 1992; 26(1): 77–84
- 12. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E at al. Recommendations for chamber quantification. Eur J Echocardiogr. 2006 Mar;7(2):79-108

- Kanitz MG, Giovannucci SJ, Jones JS, Mott M. Myocardial infarction in young adults: risk factors and clinical features. J Emerg Med. 1996 Mar-Apr;14(2):139-45
- 14. Ozkan B, Uysal OK, Duran M et al. Relationship Between Mean Platelet Volume and Atherosclerosis in Young Patients With ST Elevation Myocardial Infarction. Angiol. 2013;64:371-4
- 15. Tatli E, Aktoz M, Buyuklu M, Altun A. The relationship between coronary artery disease and uric acid levels in young patients with acute myocardial infarction. Cardiol J. 2008;15(1):21-5
- 16. Hoit BD, Gilpin EA, Henning H, Maisel AA, Dittrich H et al. Myocardial infarction in young patients: an analysis by age subsets. Circulation 1986;74;712-72
- 17. Doughty M, Mehta R, Bruckman D et al. Acute myocardial infarction in the young-The University of Michigan experience. Am Heart J 2002; 143:56
- 18. Bangalore S, Fonarow GC, Peterson ED et al: Get with the Guidelines Steering Committee and Investigators. Age and gender differences in quality of care and outcomes for patients with ST-segment elevation myocardial infarction. Am J Med. 2012 Oct;125(10):1000-9
- 19. Puricel S, Lehnerb C, Oberhänslia M et al. Acute coronary syndrome in patients younger than 30 years aetiologies, baseline characteristics and long-term clinical outcome. Swiss Med Wkly. 2013;143:w13816
- 20. Jacquemin L, Bourrelly N, Roth O et al. Acute myocardial infarction in young smokers treated by coronary angioplasty. In-hospital prognosis and long-term outcome in a consecutive series of 93 patients. Ann Cardiol Angeiol 2010 59(3):119-24
- 21. Benedek I, Gyongyosi M, Benedek T. A prospective regional registry of ST-elevation myocardial infarction in Central Romania: impact of the Stent for Life Initiative recommendations on patient outcomes. Am Heart J. 2013 Sep;166(3):457-65
- 22. Shiraishi J, Kohno Y, Yamaguchi S, Arihara M, Hadase M et al; AMI-Kyoto Multi-Center Risk Study Group. Medium-term prognosis of young Japanese adults having acute myocardial infarction. Circ J. 2006 May;70(5):518-24
- 23. Montalescot G, Dallongeville J, Van Belle E, et al. for the OPERA Investigators. STEMI and NSTEMI: are they so different? 1 year outcomes in acute myocardial infarction as defined by the ESC/ACC definition (the OPERA registry). Eur Heart J 2007;28:1409–17