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Gender-Related Differences in Risk Profile in Young Patients with St-Elevation Myocardial Infarction a 7-Year Single Centre Experience

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Abstract

Few studies have focused on acute ST-elevation myocardial infarction (STEMI) in young patients. We aimed to analyze the incidence, risk factors, management, and prognosis of STEMI in 182 consecutive young patients (age </= 50 years) (2004 to 2012), focusing on gender-related differences.

Males (87.4%) showed higher BMI values (p=0.004), a higher incidence of overweight and obesity (p=0.016). Diabetes was more frequent in females (p=0.02).

The main findings of your investigation are as follows: a) over the 7 year-study period the percentage of young STEMI patients did not change; b) the risk profile of males was different from that of females who showed a higher incidence of diabetes, while the frequency of smoking and hypertension was comparable between the two subgroups; c) no gender-related difference was detectable in management also in regard to medical therapy at discharge; d) young STEMI patients showed a good prognosis at short and long term.

Keywords

Young STEMI; Gender; BMI; Diabetes; Obesity

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Introduction

On currently available evidence, young patients represent 0.4%-19% of all acute coronary syndrome (ACS) cases, depending on the cut-off age used [1-12].

Few studies have focused on acute ST-elevation myocardial infarction (STEMI) in young patients but, despite the fact that young patients are a relatively small proportion of those having STEMI, it is important to recognize these patients for the purpose of risk factor modification and secondary prevention in younger patients.

The present investigation was aimed to analyze the incidence, risk factors, management, and prognosis of STEMI in young patients (age </= 50 years) consecutively admitted to our Intensive Cardiac Unit from 2004 to 2012, focusing on gender-related differences.

Methods

From 1st January 2004 to 31th December 2012, 1724 consecutive patients with STEMI (within 12 hours from symptoms' onset) were admitted to our ICCU [13], after primary percutaneous coronary intervention (PCI) [13,14]. In our hospital, in Florence, the reperfusion strategy of STEMI patients is represented by primary PCI [15-18]. STEMI patients are first evaluated by the medical emergency system staff in the prehospital setting and then directly admitted to the catheterization laboratory or transferred to it after rapid stabilization in the emergency department. After primary PCI, patients are admitted to our ICCU.

Among the 1724 STEMI patients, 182 (11.8%) were aged </= 50 years and constituted the population of the present investigation.

The presence of comorbidities was determined by taking the patients' history directly.

On ICCU admission, after PCI, in a fasting blood sample the following parameters were measured: glucose (mg/dl), insulin (mUI/l), glycated hemoglobin (%), troponin I (Tn I, ng/ml), uric acid (mg/dl) , NT-pro Brain Natriuretic Peptide (NT-BNP) (pg/ml) (20), total cholesterol (mg/dl), triglycerides (mg/dl), fibrinogen (mg/dl), leukocytes count (*10^3/µl), erythrocyte sedimentation rate (ESR) and C-Reactive Protein (CRP, mg/dl), fibrinogen (mg/dl), total cholesterol (mg/dl) HDL (mg/dl), triglycerides (mg/dl). Admission creatinine (mg/dl) was measured in order to calculate admission glomerular filtration rate (ml/min/1.73 m2) [19] . Glucose, creatinine and Tn I were measured three times a day during ICCU stay and peak values for each variable were considered. Acute insulin resistance was defined according to the Homeostatic Model Assessment index, as previously described. Subjects whose values exceeded the sex-specific 75th percentile (i.e. 1.80 for women and 2.12 for men) were considered to have insulin resistance (HOMA-IR) [15,16].

Transthoracic 2-dimensional echo-cardiography was performed in order to measure left ventricular ejection fraction (LVEF) on admission and at discharge.

Worsening creatinine was calculated as the difference between the patient's admission creatinine and peak creatinine during hospitalization. Worsening in renal function (WRF) was defined as an increased in creatinine ≥ 0.3 mg/dl, as previously described [20,21].

Ventilatory support, renal replacement therapy (continous venous-venous ultrafiltration - CVVHDF) and intra-aortic balloon pump were used, when need [14,22].

The primary endpoint was all-cause death at follow-up.

The study protocol was in accordance with the Declaration of Helsinki and approved by the local Ethics Committee. Informed consent was obtained in all patients before enrollment.

Statistical Analysis

Statistical analysis has been conducted with IBM-SPSS Statistics 20.0 for Windows software (SPSS Inc, Chicago, IL). In all cases, a two-tailed p-value <0.05 has been considered statistically significant. Continuous variables have been reported as median (interquartile range: "IR"); categorical variables are depicted as frequency (percentage). Comparisons were made with Mann-Whitney U test and chi-square or Fisher's exact test, as needed. Trends through years 2004-2012 have been investigated by means of linear regression analysis. Several logistic regression models were constructed to investigate whether age (1 year step), gender (male vs. female), body mass index (BMI, 1 Kg/m^2 step), known diabetes mellitus, left ventricle ejection fraction (LVEF) at admission (1% step), serum glucose at admission (1 g/dL step) and estimated glomerular filtration rate (eGFR, calculated by MDRD formula, 1 ml/min/1.73m^2 step) at admission were related to total death (both in-ICCU death and at long term follow-up); only unadjusted odds ratios have been reported due to the small number (seven) of events recorded.

Results

Table 1 shows the differences in risk factors between elderly and young patients. Among elderly patients, a higher percentage of females was detectable (p<0.001) as well as a higher incidence of diabetes mellitus (p=0.004) COPD (p=0.002), previous PCI (p=0.041), previous MI (p=0.019) and hypertension (p<0.001). The incidence of overweight (BMI >25 to ≤30) and obese (BMI > 30) was comparable between the two subgroups.

	All patients n=1542	Young </= 50 years n=182 (11.8%)	Elderly > 50 years n=1360 (88.2%)	p value
Age (yrs), median (IR)	67 (58-77)	47 (44-49)	70 (61-78)	<0.001
M/F	1127/415 (73.1/26.9)	159/23 (87.4/12.6)	968/392 (71.2/28.8)	<0.001
BMI (Kg/m^2) , median (IR)	26.1 (23.9-27.9)	26.3 (24.7-28.6)	26.0 (23.8-27.8)	0.023
BMI (Kg/m^2), frequency (%)				0.151
≤25	556 (36.2)	56 (30.8)	503 (37.0)	
>25 to ≤30	771 (50.3)	95 (52.2)	680 (50.0)	
>30	207 (13.5)	31 (17.0)	177 (13.0)	
History of, frequency (%)				
Diabetes mellitus	362 (23.5)	27 (14.8)	339 (24.9)	0.004
Smoking	940 (61.0)	152 (83.5)	788 (57.9)	<0.001
COPD	137 (8.9)	5 (2.7)	132 (9.7)	0.002
Previous PCI	211 (13.7)	16 (8.8)	195 (14.3)	0.041
Previous MI	214 (13.9)	15 (8.2)	199 (14.6)	0.019
Hypertension	820 (53.2)	60 (33.0)	760 (55.9)	<0.001

BMI: body mass index; COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention; MI: myocardial infarction

Table 1 . Differences in risk factors between elderly and young patients

Our population comprises 182 patients. The percentage of young STEMI patients (aged </= 50 years) observed each year is depicted in Figure 1: no difference was detectable in the incidence of young STEMI through the study period (Chi-square 4.9, p=0.773).

As shown in Table 2, in our series, 159 patients (87.4%) were males who showed higher BMI values (p=0.004), a higher incidence of overweight and obesity (p=0.016). Diabetes was more frequent in females (p=0.02). Anterior myocardial infarction was more frequent in females (p=0.011). No difference was observed in mortality rates during ICCU stay and at follow-up between the two subgroups. Throughout the study period, the percentage of diabetic patients did not change [Figure 2] while the percentage of hypertensive patients progressively declined (R2=0.48, p=0.039). As depicted in Figure 4, the percentage of overweight patients declined (R2=0.45, p=0.047) while the incidence of obesity did not change (p=0.530) [Figure 4a and 4b respectively].

	All patients n=182	Males n=159 (87.4%)	Females n=23 (12.6%)	p value
Age (yrs), median (IR)	47 (44-49)	47 (44-49)	46 (44-48)	0.434
BMI (Kg/m^2), median (IR)	26.3 (24.7-28.6)	26.3 (24.9-28.7)	23.9 (22.7-26.7)	0.004
BMI (Kg/m^2), frequency (%)				0.016
≤25	56 (30.8)	43 (27.0)	13 (56.5)	
>25 to ≤30	95 (52.2)	87 (54.7)	8 (34.8)	
>30	31 (17.0)	29 (18.2)	2 (8.7)	
History of, frequency (%)				
Diabetes mellitus	27 (14.8)	20 (12.6)	7 (30.4)	0.024
Smoking	152 (83.5)	135 (84.9)	17 (73.9)	0.184
COPD	5 (2.7)	3 (1.9)	2 (8.7)	0.121*
Previous PCI	16 (8.8)	15 (9.4)	1 (4.3)	0.421
Previous MI	15 (8.2)	12 (7.5)	3 (13.0)	0.370
Hypertension	60 (33.0)	52 (32.7)	8 (34.8)	0.843
Symptom door-to-balloon time (minutes), median (IR)	195 (120 to 300)	195 (120 to 290)	195 (140 to 375)	0.263
Admission Systolic arterial pressure (mmHg), median (IR)	125 (110-140)	125 (110-140)	120 (110-130)	0.174
Admission heart rate (bpm), median (IR)	76 (67-89)	75 (66-89)	78 (71-88)	0.232
AMI location, frequency (%)				0.011
Anterior	98 (53.8)	79 (49.7)	19 (82.6)	
Inferior	72 (39.6)	68 (42.8)	4 (17.4)	
Other	12 (6.6)	12 (7.5)	0 (0.0)	
Coronary artery disease, frequency (%)				0.203
1-vessel	108 (59.3)	92 (57.9)	16 (69.6)	
2-vessel	42 (23.1)	36 (22.6)	6 (26.1)	
3-vessel	32 (17.6)	31 (19.5)	1 (4.3)	
PCI failure, frequency (%)	3 (1.7)	2 (1.3)	1 (4.5)	0.325*
Killip, frequency (%)				0.186
1-II	170 (93.4)	150 (94.3)	20 (87.8)	
III-IV	12 (6.6)	9 (5.7)	3 (13.0)	
Admission LVEF (%), median (IR)	45 (40-52)	45 (40-52)	45 (40-51)	0.695
Discharge LVEF (%), median (IR)	48 (43-54)	50 (44-55)	46 (42.5-50)	0.164
In-ICCU mortality, frequency (%)	4 (2.2)	3 (1.9)	1 (4.3)	0.420*
Total mortality, frequency (%)	$7/_{125}$ (5.6)	$5/_{111}$ (4.5)	$2/_{14}$ (14.3)	0.134
total follow-up (months), median (IR)	37 (15-63)	34 (14-62)	52 (32-65)	0.315

*Fisher's exact test

BMI: body mass index; COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention; MI: myocardial infarction; AMI: acute myocardial infarction; LVEF: left ventricular ejection fraction, ICCU: intensive cardiac care unit;

Table 2 Clinical and angiographic data of the study population

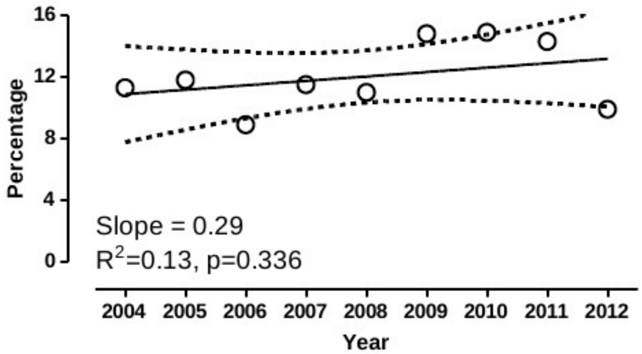


Figure 1 STEMI patients aged ≤ 50 years

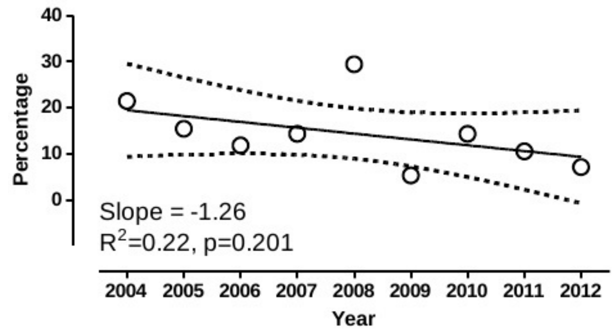


Figure 2 Diabetic STEMI patients aged ≤ 50 years

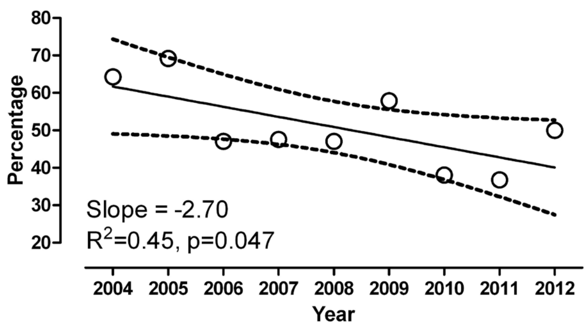
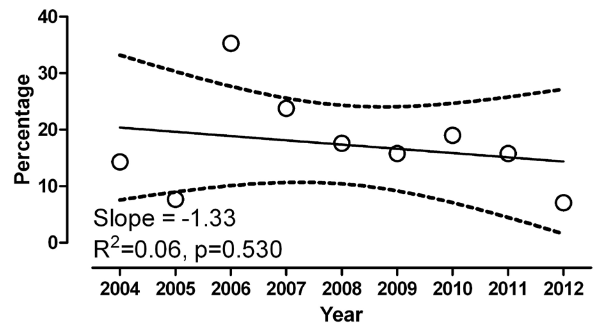


Figure 4a Overweight (BMI 25 to 30)



Fugure 4b Obese patients

Table 3 depicts bio-chemical data. In the comparison between males and females, no difference was detectable except for higher values of uric acid observed in males (p<0.001). The use of devices and well as the incidence of complications were comparable between males and females [Table 4]. During ICCU stay, males were more frequently administered ACE-inibitors/angiotensin receptor blockers (p=0.029), while no differences were observed in medications at discharge [Table 5].

At univariable regression analysis, admission glycemia and LVEF was associated with total mortality (p<0.001 and p<0.001, respectively) [Table 6].

	All patients n=182	Males n=159 (87.4%)	Females n=23 (12.6%)	p value
Admission Glucose (g/L)	1.12 (1.01-1.31)	1.11 (1.00-1.31)	1.20 (1.02-1.44)	0.460
Peak glucose (g/L)	1.27 (1.12-1.45)	1.26 (1.11-1.44)	1.33 (1.18-1.46)	0.406
Admission glycemia > 140 mg/dL, frequency (%)	36 (19.8)	30 (18.9)	6 (26.1)	0.417
Discharge glucose (g/L)	0.95 (0.86-1.13)	0.94 (0.86-1.11)	1.04 (0.84-1.31)	0.427
HbA1c > 6.5%, frequency (%)	21 (11.5)	18 (11.3)	3 (13.0)	0.809
Insulinemia (UI/L)	9.1 (5.2-17)	9.3 (5.0-16.8)	8.9 (6.2-15.8)	0.815
HOMA index high, frequency (%)	$10/_{105}$ (9.5)	$8/_{92}$ (8.7)	$2/_{13}$ (15.4)	0.442
Peak Tn I (ng/mL)	86.0 (41.8-179.0)	80.6 (41.9-180.1)	105.0 (41.9-105.0)	0.886
NT-proBNP (pg/mL)	544 (215-1087)	451 (214-1056)	587 (325-1559)	0.330
Uric acid (mg/dL)	5.5 (4.6-6.3)	5.6 (4.8-6.7)	4.2 (3.6-5.2)	<0.001
ESR (mm/h)	14 (6+26)	14 (6-25)	18 (6-38)	0.529
Leucocytes ($*10^3$/µL)	12.1 (9.4-15.2)	119 (9.4-15.1)	13.3 (10.4-15.6)	0.320
hs-CRP positivity, frequency (%)	$46/_{113}$ (40.7)	$41/_{99}$ (41.4)	$5/_{14}$ (35.7)	0.685
Fibrinogen (mg/dL)	360 (299-410)	362 (302-413)	334 (292-394)	0.327
Admission eGFR (ml/min/1.73m^2)	98.4 (84.9-116.0)	98.5 (85.3-116.2)	95.9 (83.6-111.0)	0.880
Nadir eGFR (ml/min/1.73m^2)	87.2 (75.7-103.5)	87.2 (75.7-96.8)	88.8 (82.2-97.8)	0.958
Total cholesterol (mg/dL)	197 (165-225)	194 (163-225)	181 (161-220)	0.341
HDL cholesterol (mg/dL)	40 (34-47)	39 (34-46)	41 (35-51)	0.180
Triglycerides (mg/dL)	123 (91-172)	123 (94-163)	103 (62-190)	0.154

All values are medians (IR) unless otherwise specified.

HOMA: homeostatic model assessment; NT-pro BNP: N terminal pro brain natriuretic peptide; ESR: erythrocyte sedimentation rate; CRP: C reactive protein; eGFR: estimated glomerular filtration rate.

Table 3 Laboratory data

	All patients n=182	Males n=159 (87.4%)	Females n=23 (12.6%)	p value
Mechanical ventilation	11 (6.0)	10 (6.3)	1 (4.3)	0.715
Non invasive ventilation	2 (1.1)	1 (0.6)	1 (4.3)	0.237*
CVVHDF	2 (1.1)	2 (1.3)	0 (0.0)	1*
IABP	31 (17.0)	27 (17.0)	4 (17.4)	0.961
Complications	26 (14.3)	21 (13.2)	5 (21.7)	0.274
WRF	8 (4.4)	6 (3.8)	2 (8.7)	0.282
transfusions	5 (2.7)	4 (2.5)	1 (4.3)	0.495*

All values are frequancies (%)

•Fisher's exact test

CVVHDF: continuous venous-venous ultradiafiltration; IABP: intra-aortic balloon pump; WRF: worsening renal failure.

Table 4 Devices and complications

	All patients n=182	Males n=159 (87.4%)	Females n=23 (12.6%)	p value
During ICCU				
β-blockers	169 (92.9)	147 (92.5)	22 (95.7)	0.578
ACEi - ARB	165 (90.7)	147 (92.5)	18 (78.3)	0.029
Calcium channel blockers	4 (2.2)	3 (1.9)	1 (4.3)	0.420*
Diuretics	106 (58.2)	91 (57.2)	15 (65.2)	0.468
ASA	182 (100)	159 (100)	23 (100)	1*
Clopidogrel	175 (96.2)	154 (96.9)	21 (91.3)	0.196
IIbIIIa GP inhibitors	159 (87.4)	140 (88.1)	19 (82.6)	0.463
Statin	177 (97.3)	156 (98.1)	21 (91.3)	0.121*
At discharge	**All patients n=178**	**Men n=156 (87.6%)**	**Women n=22 (12.4%)**	
β-blockers	162 (91.0)	140 (89.7)	22 (100)	0.115
ACEi - ARB	158 (88.8)	141 (90.4)	17 (77.3)	0.068
Ca channel blockers	3 (1.7)	2 (1.3)	1 (4.5)	0.328*
Diuretics	68 (38.2)	59 (37.8)	9 (40.9)	0.780
ASA	177 (99.4)	155 (99.4)	22 (100)	1*
Clopidogrel	154 (86.5)	136 (87.2)	18 (81.8)	0.491
Statins	173 (97.2)	152 (97.4)	21 (95.5)	0.487*

All values are frequancies (%)

*Fisher's exact test

ARB: angiotensin receptor blockers, IIbIIIa GP inhibitors: IIbIIIa glycoprotein inhibitors

Table 5 Medications

	Unadj.HR	95% CI	p value
Age (1 year step)	1.06	0.89-1.25	0.517
Admission LVEF (1% step)	0.88	0.82-0.95	<0.001
Gender (M vs. F)	0.30	0.06-1.52	0.145
Admission glycemia (1 g/dL step)	4.46	2.16-9.20	<0.001
Admission eGFR (1mL/min/1.73m^2 step)	0.99	0.96-1.02	0.405
Diabetes	2.16	0.42-11.15	0.357
BMI (1 Kg/m^2 step)	1.07	0.88-1.31	0.507

LVEF: left ventricular ejection fraction, eGFR: estimated glomerular filtration rate; BMI: body mass index.

Table 6 Univariable regression analysis

Discussion

The main findings of your investigation, performed in 182 consecutive STEMI patients aged </= 50 years submitted to primary PCI, are as follows: a) over the 7 year-study period the percentage of young STEMI patients did not change; b) the risk profile of males was different from that of females who showed a higher incidence of diabetes, while the frequency of smoking and hypertension was comparable between the two subgroups; c) no gender-related difference was detectable in management also in regard to medical therapy at discharge; d) young STEMI patients showed a good prognosis at short and long term.

In our series the incidence of young STEMI, which was comparable to that reported in previous studies [23,24], did not change over the 7 year study period, thus underlying the need of more efficacious policies for primary prevention in young subjects.

While smoking and hypertension were confirmed as a common risk factors [5,24-26], both in males and females, gender-related differences in risk profile were, for the first time, detectable in our series. Females showed a higher incidence of diabetes which remained unchanged over the study period. Our population comprised all Caucasian subjects with no significant differences in dietary habits since almost all subjects followed Mediterranean diet (3 patients were while the incidence of vegetarians), Our finding may be explained with the higher prevalence of overweight and obesity in males within our population, as recently reported [27], though, in our investigation, it showed a progressive reduction over time. Our findings suggest the need of different strategies for primary (and secondary) prevention according to gender.

In our population, while the incidence of hypertension and overweight decline throughout the study period, obesity and diabetes remained unchanged, thus suggesting that in recent years the occurence of STEMI in young patients was more frequently associated with diabetes and obesity. In a small subset of 36 young (< 45 years old) STEMI patients, Basoor et al. [28] reported a high incidence of obesity (78%), confirming previous data by Chau et al. [24] who documented that obesity was detectable I the 48% of patients (27/99 patients) and by Ueda et al. [10] reporting an incidence of obesity of 42% (28/66 patients). However, many investigations performed in young AMI patients mostly in the '80s and '90s, BMI and/or obesity were not considered as risk factors [1-4,29].

In our study, addressing for the first time gender-related differences in management in young STEMI, we observed that males and females were equally treated in terms of devices and medications (during ICCU stay and at discharge).

In agreement with previous reports [1-2,24,29], young STEMI patients exhibited a good prognosis at short and long terms. In our series, factors associated, at univarible regression analysis, with long term prognosis was represented by the extent of myocardial injury (as inferred by LVEF) and admission glycemia. These findings strongly suggest the need of a more intensive monitoring program in the subset of young STEMI patients presenting with larger infarct size and subsequent more severe metabolic derangement.

Overall, on a clinical ground, our data strongly suggest the need of efficacious primary and secondary prevention policies gender-tailored.

Conflict of Interest

No

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