Acute myocardial infarction due to left main coronary artery disease in men and women: does ST-segment elevation matter?

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Abstract

Introduction: Gender-specific issues regarding ST-segment elevation (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI) due to unprotected left main coronary artery (ULMCA) disease were not sufficiently studied. We assessed the value of STEMI/NSTEMI initial classification on the management of men and women with acute MI due to critical stenosis or occlusion of the ULMCA.

Material and methods: The study group consisted of 643 consecutive patients with acute MI with the ULMCA as the infarct-related artery. Data derive from an ongoing, nationwide, multicenter, prospective, observational registry.

Results: Isolated ULMCA disease was more frequent in women and multivessel disease was more frequent in men in the NSTEMI group. The incidence of cardiogenic shock or pulmonary edema and cardiac arrest was higher in the STEMI group. Totally occluded ULMCA was more frequent in the STEMI group. Although the majority of patients underwent percutaneous coronary intervention (PCI), it was less frequently used in NSTEMI women and NSTEMI men. Although in-hospital and long-term mortality rates were higher in the STEMI group, there were no gender-related differences within groups. The initial ST-segment elevation was an independent predictor of in-hospital (OR = 2.37, 95% CI: 1.14–4.91, $p = 0.02$) and 12-month (OR = 1.52, 95% CI: 1.01–2.27, $p = 0.045$) mortality.

Conclusions: There were no gender-related differences in the management within the STEMI or NSTEMI group. Although acute myocardial infarction due to ULMCA disease is associated with high mortality in both genders, STEMI was a negative prognostic factor of in-hospital and 12-month mortality. Despite poor baseline characteristics and clinical presentation in women, female gender itself did not influence mortality.

Key words: myocardial infarction, ST-segment, left main, gender, women.

Introduction

The unprotected left main coronary artery (ULMCA) supplies up to 75–100% of left ventricular mass depending on the dominance type [1]. For that reason acute non-ST-segment elevation (NSTEMI) or ST-seg-

ment elevation (STEMI) myocardial infarction due to critical stenosis or abrupt occlusion of the ULMCA is a catastrophic situation with a very high in-hospital and long-term mortality [2]. Many cases are never reported because of pre-hospital death. Although coronary artery bypass grafting (CABG) remains a class I recommendation for LM revascularization in European and American guidelines, percutaneous coronary intervention (PCI) is becoming an attractive option in patients with acute myocardial infarction and ULMCA as an infarct-related artery, especially when in cardiogenic shock [3, 4]. Advances in devices and adjunctive pharmacotherapy make PCI of the ULMCA feasible and with at least non-inferior results to CABG [5–7]. Although electrocardiography is not a highly specific method for the diagnosis of myocardial infarction due to ULMCA disease, the primary results of our registry suggest that STEMI (vs. NSTEMI) remains an independent predictor of in-hospital and 12-month mortality [8]. Several lines of evidence indicate that not all patients with severe ULMCA disease develop ECG changes before a hemodynamic collapse. In those who present with ST-segment abnormalities an aVR lead is one of high specificity and sensitivity for ULMCA disease, especially when ST-elevation is higher than in the V1 lead, which correlates with mortality and hemodynamic deterioration [9, 10]. Mahajan *et al.* reported that differences in ST-segment deviations in the V1 and V6 leads are even more specific for predicting ULMCA disease than the aVR lead itself [11].

An initial diagnosis of STEMI or NSTEMI is crucial for determining the patients' flow and further management. Gender-specific issues were precisely analyzed in our country both for STEMI and NSTEMI patients [12, 13], but data on the patients' management in acute MI and the ULMCA as an infarct-related artery are scarce. The aim of our study was to assess whether the initial classification of STEMI vs. NSTEMI and the classification-related therapeutic approach influence mortality in men and women with acute myocardial infarction due to critical stenosis or occlusion of the ULMCA.

Material and methods

The principles of our registry (PL-ACS) have been reported elsewhere [14]. Briefly, this is an ongoing, nationwide, multicenter, prospective, observational mandatory registry of all consecutive acute coronary syndrome (ACS) cases in Poland. So far, there are over 500 000 cases recorded. The study group consisted of 643 consecutive patients hospitalized during three years (from October 2003 to August 2006) with acute MI with ULMCA as the infarct-related artery (IRA) defined as stenosis over 50% or total occlusion. Cases with IRA other than ULMCA but with significant ULMCA disease were excluded from the analysis. Basic clinical characteristics, treatment strategy and prognosis for the entire population with ULMCA-related MI were reported previously [8]. Subjects were divided into STEMI and NSTEMI groups and into females and males within each group. Data analyzed included information from patients' history, coronary risk factor profile, clinical presentation, therapeutic approach and adjunctive treatment. The primary end-points were in-hospital, 30-day, 6-month and 12-month mortality. Mortality data were obtained for all subjects included from the governments' official mortality records.

Statistical analysis

Variables were expressed as mean ± standard deviation, counts and percentages or median and interquartile ranges as appropriate. The significance between groups was tested using Student's *t*-test, the Mann-Whitney *U* test or Kruskal-Wallis ANOVA test depending on normality as well as homogeneity of variances tested by the *F* test. Categorical variables were tested by the χ^2 test. Follow-up mortality was analyzed using the Kaplan-Meier method for multiple-group comparisons. A two-sided p-value ≤ 0.05 was considered significant. For all calculations, Statistica 7.1 software (StatSoft, Inc., Tulsa, OK, USA) was used.

Results

ST-segment elevation myocardial infarction patients were on average 4 years younger than NSTEMI patients ($p < 0.0001$) and less frequently developed arterial hypertension (60.0% vs. 73.4%; $p < 0.0003$). Women with STEMI more often were smokers than women with NSTEMI, whereas NSTEMI men more often than STEMI men had a previous myocardial infarction (Table I). While there was no difference between genders in the extent of the disease in the STEMI group, an isolated ULMCA disease was more frequent in women and multivessel disease was more frequent in men in the NSTEMI group. The incidence of cardiogenic shock or pulmonary edema, activity of myocardial isoenzyme of creatine phosphokinase, cardiac arrest and larger extent of the coronary artery disease were higher in the STEMI group (Table II).

There were no differences in medication between STEMI men and women. The NSTEMI women slightly less frequently received nitrates as compared with NSTEMI men (47.9% vs. 60.3%; $p < 0.038$). ST-segment elevation myocardial infarction patients, both men and women, as compared with NSTEMI patients significantly less frequently received low molecular weight heparins,

β-blockers, calcium channel antagonists, angiotensin-converting enzyme inhibitors and statins (data not shown).

Both males and females in the STEMI group presented more frequently with totally occluded ULMCA. Although the majority of patients underwent PCI, it was less frequently used in NSTEMI women and NSTEMI men. Similarly, the use of glycoprotein IIb/IIIa inhibitors in the NSTEMI subgroups was lower (Table III).

The complication rate was very low. Only repeat NSTEMI and unstable angina were more frequent in the NSTEMI group, both in females and in males (Table IV). Treatment outcomes were similar for both genders, with a high rate of post-procedural TIMI 3 flow (Table IV). In-hospital and long-term mortality rates were higher in the STEMI vs. NSTEMI group (in-hospital: 27.2% vs. 10.4%, $p < 0.0001$; 12-month: 38.4% vs. 24.6%, $p < 0.0001$) [8]. There were no differences in mortality between genders within the STEMI and NSTEMI groups in all patients and subgroups treated medically and invasively. However, in patients who underwent a conservative strategy and in those treated invasively significant differences were noticeable in favor of NSTEMI (Table V). As we have previously reported [8], together with cardiogenic shock, pulmonary edema and advanced age, initial ST-elevation on ECG was an independent predictor of in-hospital (OR = 2.37, 95% CI: 1.14–4.91, $p = 0.02$) and 12-month (OR = 1.52, 95% CI: 1.01–2.27, $p = 0.045$) mortality.

Discussion

Despite the increasing number of reports on primary angioplasty in the unprotected left main coronary artery, CABG remains the preferred treatment option for patients with this localization of the lesion. Both American and European cardiac societies recommend the quickest possible recanalization of acutely occluded vessels in patients with acute MI (level IA recommendation). It is interesting that most clinical trials evaluating outcomes of left main coronary artery angioplasty as compared with other therapies exclude patients with acute coronary syndromes. Only large registries such as GRACE [15], the meta-analysis by Lee *et al.* [16] and the present study have taken into account the physician's approach to a serious medical condition such as acute coronary syndrome due to significant left main coronary artery stenosis. Even in one of the recent large randomized studies, the SYNTAX trial comparing coronary angioplasty and coronary artery bypass grafting in patients with triple vessel disease or left main coronary artery disease, myocardial infarction was an exclusion criterion [17]. This may cause unnecessary hesitation when an interventional cardiolo-

Table I. Risk factor profile

Variable	STEMI, *n* (%)			NSTEMI, *n* (%)			Value of *p*		
	Female	Male	Value of *p*	Female	Male	Value of *p*	Female	Male	All
N (%)	88 (28.9)	217 (71.2)		96 (28.4)	242 (71.6)				
Age [years]	67.4 ±13.3	62.2 ±10.2	0.0003	70.4 ±11.2	66.5 ±11.4	0.0038	0.068	0.0001	0.0001
Age ≥ 65 years	58 (65.9)	91 (41.9)	0.0002	70 (72.9)	144 (59.5)	0.021	0.30	0.0002	0.0002
Arterial hypertension	61 (69.3)	122 (56.2)	0.034	75 (78.1)	173 (71.5)	0.21	0.17	0.0007	0.0003
Diabetes	28 (31.8)	53 (24.4)	0.19	31 (32.3)	47 (19.4)	0.011	0.95	0.19	0.31
Hypercholesterolemia	45 (51.1)	88 (40.6)	0.091	48 (50)	113 (46.7)	0.58	0.88	0.19	0.31
Smoking	22 (25)	90 (41.5)	0.0069	13 (13.5)	89 (36.8)	0.0001	0.048	0.30	0.079
BMI > 30 kg/m^2	23 (26.1)	21 (9.7)	0.0002	27 (28.1)	28 (11.6)	0.0002	0.76	0.51	0.51
Prior MI	15 (17)	46 (21.2)	0.41	25 (26)	81 (33.5)	0.18	0.14	0.0033	0.001
Prior PCI	1 (1.1)	6 (2.8)	0.66	7 (7.3)	12 (5)	0.40	0.092	0.23	0.053
Prior CABG	4 (4.5)	11 (5.1)	0.92	7 (7.3)	21 (8.7)	0.68	0.43	0.13	0.088

Resulted presented as n (%) or mean ± SD. BMI – Body mass index, MI – myocardial infarction, PCI – percutaneous coronary intervention, CABG – coronary artery bypass grafting.

Table II. Clinical presentation

Variable	STEMI, *n* (%)			NSTEMI, *n* (%)			Value of *p*		
	Female	Male	Value of *p*	Female	Male	Value of *p*	Female	Male	All
Onset-to-door time [h]:									
0–2	9 (10.2)	38 (17.5)	0.11	6 (6.3)	26 (10.7)	0.32	0.043	0.037	0.022
2–6	51 (57.9)	98 (45.2)	0.043	26 (27.1)	64 (26.4)	0.90	0.0001	0.0001	0.0001
6–12	14 (15.9)	31 (14.3)	0.72	16 (16.7)	33 (13.6)	0.89	0.44	0.84	0.93
> 12	11 (12.5)	37 (17.1)	0.32	29 (30.2)	73 (30.2)	0.0036	0.55	0.0010	0.0001
Cardiac arrest:									
Prior to admission	3 (3.4)	21 (9.7)	0.065	0 (0)	7 (2.9)	0.21	0.017	0.0024	0.0006
In-hospital	22 (25)	43 (19.8)	0.32	12 (12.5)	25 (10.3)	0.029	0.25	0.0043	0.0003
Killip class:									
4	25 (28.4)	57 (26.3)	0.70	5 (5.2)	16 (6.6)	0.0002	0.90	0.0001	0.0001
3	8 (9.1)	10 (4.6)	0.13	6 (6.3)	14 (5.8)	0.47	0.25	0.57	0.99
1 or 2	55 (62.5)	150 (69.1)	0.26	85 (88.5)	212 (87.6)	0.0001	0.44	0.0001	0.0001
CK-MB	128 (51–303)	127 (39–327)	0.67	28 (21–117)	45 (21–125)	0.019	0.25	0.0001	0.0001
Left ventricular ejection fraction (%):									
> 50	12 (19.4)	20 (14.2)	0.35	26 (35.1)	43 (24.7)	0.041	0.063	0.020	0.0022
30–50	40 (64.5)	87 (61.7)	0.70	38 (51.4)	101 (58)	0.12	0.64	0.51	0.16
< 30	10 (16.1)	34 (24.1)	0.20	10 (13.5)	30 (17.2)	0.67	0.16	0.13	0.13
Extent of the disease:									
LM	28 (32.2)	65 (30)	0.70	18 (18.8)	36 (14.9)	0.036	0.39	0.0001	0.0001
LM +1	17 (19.5)	52 (24)	0.41	16 (16.7)	42 (17.4)	0.61	0.48	0.080	0.078
LM +2	41 (47.1)	96 (44.2)	0.65	61 (63.5)	162 (66.9)	0.026	0.91	0.0001	0.0001

CK-MB – Creatinine phosphokinase maximum activity presented as median and interquartile range U/l, LM – left main, other abbreviations as in Table I.

Table III. Treatment strategy

Variable	STEMI, *n* (%)			NSTEMI, *n* (%)			Value of *p*		
	Female	Male	Value of *p*	Female	Male	Value of *p*	Female	Male	All
Medical	11 (12.5)	36 (16.6)	0.37	44 (45.8)	105 (43.4)	0.68	0.0001	0.0001	0.0001
Fibrinolysis	2 (2.3)	10 (4.6)	0.53	0 (0)	2 (0.8)	0.91	0.44	0.025	0.0037
Invasive	77 (87.5)	178 (82)	0.24	52 (54.2)	137 (56.6)	0.68	0.0001	0.0001	0.0001
PCI	74 (84.1)	166 (76.5)	0.14	46 (47.9)	113 (46.7)	0.84	0.0001	0.0001	0.0001
Stenting*	69 (93.2)	156 (92.3)	0.80	39 (83)	100 (85.5)	0.69	0.076	0.064	0.012
CABG	3 (3.4)	12 (5.5)	0.98	6 (6.2)	24 (9.9)	0.33	0.81	0.070	0.059
IABP	17 (19.3)	28 (12.9)	0.15	8 (8.3)	21 (8.7)	0.92	0.030	0.14	0.014
GP IIb/IIIa	35 (39.8)	74 (34.1)	0.35	10 (10.4)	38 (15.7)	0.21	0.0001	0.0001	0.0001
Initial TIMI flow:									
0	33 (44.6)	98 (58)	0.054	12 (26.1)	30 (26.1)	1.0	0.042	0.0001	0.0001
1	17 (23)	26 (15.4)	0.15	9 (19.6)	20 (17.4)	0.75	0.66	0.65	0.94
2	9 (12.2)	24 (14.2)	0.67	9 (19.6)	28 (24.3)	0.51	0.27	0.030	0.014
3	15 (20.3)	21 (12.4)	0.11	16 (34.8)	37 (32.2)	0.75	0.077	0.0001	0.0001

*PCI – Percutaneous coronary intervention, CABG – coronary artery bypass grafting, IABP – intraaortic balloon pump, GP IIb/IIIa – glycoprotein IIb/IIIa inhibitor, other abbreviations as in Table I. *Number (percentage) of patients treated by PCI who received one or more stents.*

Table IV. Post-procedural TIMI flow and in-hospital complications

Variable	STEMI, *n* (%)			NSTEMI, *n* (%)			Value of *p*		
	Female	Male	Value of *p*	Female	Male	Value of *p*	Female	Male	All
0	3 (4.1)	10 (6)	0.77	2 (4.3)	6 (5.1)	0.87	0.68	0.77	0.82
1	2 (2.7)	9 (5.4)	0.56	1 (2.1)	4 (3.4)	0.94	0.69	0.44	0.45
2	5 (6.8)	17 (10.1)	0.40	2 (4.3)	5 (4.3)	0.67	0.86	0.069	0.064
3	64 (86.5)	132 (78.6)	0.20	42 (89.4)	102 (87.2)	0.70	0.64	0.062	0.068
STEMI	2 (2.3)	5 (2.3)	0.69	2 (2.1)	2 (0.8)	0.68	0.68	0.36	0.28
NSTEMI	1 (1.1)	6 (2.8)	0.66	8 (8.3)	15 (6.2)	0.48	0.055	0.079	0.0068
Stroke	0 (0)	1 (0.5)	0.64	0 (0)	3 (1.2)	0.65	–	0.69	0.69
Bleeding	2 (2.3)	5 (2.3)	0.69	4 (4.2)	5 (2.1)	0.48	0.76	0.88	0.77
Re-PCI	2 (2.3)	4 (1.8)	0.83	1 (1)	2 (0.8)	0.65	0.94	0.59	0.41

STEMI – ST-segment elevation myocardial infarction, NSTEMI – non-ST-segment elevation myocardial infarction, re-PCI – target vessel revascularization, other abbreviations as in Table I.

Table V. Mortality in all patients and depending on treatment strategy

Variable	STEMI, *n* (%)				NSTEMI, *n* (%)				Value of *p*		
	Female	Male	All	Value of *p*	Female	Male	All	Value of *p*	Female	Male	All
All patients:											
In-hospital	27 (30.7)	56 (25.8)		0.39	11 (11.5)	24 (9.9)		0.67	0.0013	0.0001	0.0001
30-day	27 (30.7)	65 (30)		0.90	18 (18.8)	35 (14.5)		0.33	0.060	0.0001	0.0001
6-month	33 (37.5)	75 (34.6)		0.63	25 (26)	52 (21.5)		0.37	0.095	0.0018	0.0004
12-month	34 (38.6)	83 (38.2)		0.95	26 (27.1)	57 (23.6)		0.50	0.095	0.0006	0.0002
Medical treatment:											
In-hospital	2 (18.2)	5 (13.9)	(14.9)	0.89	4 (9.1)	6 (5.7)	(6.7)	0.45	0.75	0.22	0.082
30-day	2 (18.2)	8 (22.2)	(21.3)	0.89	7 (15.9)	10 (9.5)	(11.4)	0.26	0.78	0.093	0.087
6-month	4 (36.4)	12 (33.3)	(34.0)	0.86	10 (22.7)	20 (19.1)	(20.1)	0.61	0.59	0.078	0.050
12-month	4 (36.4)	15 (41.7)	(40.4)	0.97	10 (22.7)	22 (21.0)	(21.5)	0.81	0.59	0.015	0.0098
Invasive treatment:											
In-hospital	25 (32.5)	51 (28.6)	(29.8)	0.54	7 (13.5)	18 (13.1)	(13.2)	0.95	0.014	0.0010	0.0001
30-day	25 (32.5)	57 (32.0)	(32.6)	0.94	11 (21.1)	25 (18.2)	(19.0)	0.65	0.16	0.0057	0.0020
6-month	29 (37.7)	63 (35.4)	(36.1)	0.73	15 (28.8)	32 (23.4)	(24.9)	0.44	0.30	0.021	0.012
12-month	30 (39.0)	68 (38.2)	(38.4)	0.91	16 (30.8)	35 (25.5)	(26.9)	0.47	0.34	0.017	0.012

gist sees such a patient, being aware of increased risk for the patient on the one hand and bearing in mind mandatory guidelines on the other. Leaving the vessel occluded in patients evolving with cardiogenic shock is unlikely. However, it is a different situation when the patient is in a satisfactory clinical condition despite critical LM stenosis and manifestations of acute coronary syndrome. The commonly used scores such as EuroSCORE and Parsonnet evaluate cardiac operative risk and encourage interventional cardiologists to perform PCI – the higher the operative risk, the easier is the decision to perform coronary angioplasty. Other scores used in multicenter studies of acute coronary syndromes such as GRACE and the SYNTAX Score lead to similar decisions [15, 18, 19]. The higher the score, the higher is the operative risk and the more difficult it is to make a decision, both for interventional cardiologists and cardiac surgeons. Unfortunately, none of the scores include ST-segment deviation. Although the definition of myocardial infarction has been extended to include all patients who present with myocardial necrosis biomarkers, STEMI most frequently develops in subjects with total vessel occlusion with TIMI flow grade 0/1. The majority of these patients also have such complications as cardiogenic shock and/or cardiac arrest. The utility of initial classification of STEMI vs. NSTEMI in the context of ULMCA disease has been thoroughly studied in terms of both clinical outcomes [20] and identifying the culprit lesion [21]. In our study it was clearly demonstrated that patients presenting with the STEMI pattern have shorter onset-to-door times and are more frequently treated invasively (both PCI and/or CABG). However, treatment allocation (PCI vs. CABG) is often based on the TIMI flow grade, and STEMI patients have a better chance for immediate revascularization regardless of their condition [22]. Furthermore, STEMI is associated with isolated LM stenosis in contrast to NSTEMI, which occurs in patients with multivessel disease. Another interesting fact about the present study is age. Patients with STEMI were younger than those with NSTEMI. In general, STEMI patients had fewer comorbidities than NSTEMI subjects. The reasons for this difference can be related to factors initiating the development of collaterals, allowing quick opening of coronary collaterals and protection of blood flow beyond the occluded segment. Available registries reflect this approach. Most STEMI patients were treated by means of coronary angioplasty. Montalescot *et al.* analyzed data from the GRACE registry and made interesting observations. During the data collection period from 2000 to 2007 there was a shift from coronary artery bypass grafting towards coronary angioplasty performed in patients with acute coronary syndrome caused by critical LM stenosis (in 2004/2005) [23]. Most investigators emphasize the fact of quick and total restoration of blood flow after LM stenting. Also in the present study TIMI flow grade 2 and 3 was achieved in over 90% of patients undergoing PCI, which was performed in almost 80% of STEMI and in 47% of NSTEMI patients, in contrast to CABG performed in 3.9% and 7.4% of patients, respectively. Time to flow restoration depended largely on time to admission. In our study, STEMI patients were admitted earlier than their NSTEMI counterparts. The selection process for CABG is different. Analysis of the GRACE registry showed that PCI was performed on the day of admission and the time to recanalization did not exceed 24 h, whereas the mean selection time for CABG was 4.5 days.

Despite well-documented female sex-related discrepancies in the presentation, management, clinical course and outcomes in patients with STEMI or NSTEMI in the general population [12, 13], in the elderly [24] and in the young [25], in the present study we did not find any significant male-favoring difference. This is a surprising finding, leading to the conclusion that the deleterious impact of the ULMCA-related myocardial infarction on mortality is the greatest of all known risk factors. Whereas gender-related differences did not matter in the present study, we were able to demonstrate that patients with STEMI had greater mortality regardless of the modality of treatment. Initial classification of STEMI vs. NSTEMI allowed us to identify patients at high risk.

Our database is not free of flaws typical for other registries. Although data collection and case reporting are mandatory, we had no impact on data integrity. Moreover, the discrimination of ULMCA stenosis severity and each therapeutic decision were operator-dependent. Our registry did not allow us to collect data on the lesion location and complexity (i.e. ostial vs. bifurcation) or stenting strategy. Neither vascular access site selection nor any sophisticated parameters were considered, although they are also known to impact the mortality, as it has been recently reported [26, 27]. Mortality data, although obtained for all cases included, did not distinguish between cardiovascular and all-cause mortality. No follow-up data regarding post-discharge patient compliance or repeat hospitalizations and revascularization are available. Therefore, extrapolation of our results must be done with caution.

In conclusion, there were no gender-related differences in the management within the STEMI or NSTEMI group. Although acute myocardial infarction due to ULMCA critical stenosis or occlusion is associated with high mortality in both genders, STEMI was a negative prognostic factor of in-hospital and 12-month mortality. In the STEMI group, mortality was greater regardless of treatment

strategy. Despite poor baseline characteristics and clinical presentation in women, female gender itself did not influence mortality.

Conflict of interest

The authors declare no conflict of interest.

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