

Acute myocardial infarction due to left main coronary artery disease: A large multicenter national registry

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Abstract

Background: *Optimal management of patients with acute myocardial infarction (MI) due to critical stenosis of an unprotected left main coronary artery (ULMCA) is not established. However, data from observational studies and registries encourage to perform percutaneous coronary intervention (PCI) in high risk patients. We investigated gender-related discrepancies, clinical course and prognosis in patients with acute MI and ULMCA as an infarct-related artery.*

Methods: *A total of 643 consecutive patients (184 [28.6%] females and 459 [71.4%] males) with acute MI due to critical ULMCA stenosis were selected from the population of 121,526 patients hospitalized due to acute coronary syndromes between 2003 and 2006. The primary endpoints were in-hospital, 30-day, 6-month and 12-month mortality.*

Results: *Women were older than men with significantly higher proportion of women older than 65 and with unfavorable risk profile. The management in men and women was similar. There was no significant gender-related differences in mortality in all follow-up periods. In multivariate analysis cardiogenic shock, pulmonary edema, ST elevation myocardial infarction (STEMI) and advanced age significantly increased mortality, whereas successful PCI decreased mortality.*

Conclusions: *No significant differences in clinical course, treatment and prognosis between men and women were noted. Mortality remained very high in both genders. The most unfavorable prognostic factors were cardiogenic shock, pulmonary edema, STEMI and advanced age. Percutaneous coronary angioplasty is feasible and offers high success rate in this subset of patients. (Cardiol J 2013; 20, 2: 190–196)*

Key words: acute coronary syndrome, left main coronary artery, mortality, therapeutic strategy, gender

Introduction

Since analysis of data from the CASS registry [1] critical stenosis of unprotected left main coronary artery (ULMCA) has become a classic indication

for coronary artery bypass grafting (CABG) in patients with stable angina pectoris. Effective and safe percutaneous coronary intervention (PCI) in ULMCA stenosis in stable patients is technically feasible, and long-term outcomes are highly sati-

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Received: 14.10.2012

Accepted: 15.11.2012

satisfactory when drug-eluting stents are used [2, 3]. Patients at particularly high risk are those with acute myocardial infarction (MI) and ULMCA as an infarct-related artery. Optimal method for coronary revascularization in this population has not been assessed in randomized studies, however observational data and registries [4] encourage the use of percutaneous coronary intervention (PCI) in these highest-risk patients.

Because of the emphasis on studying gender-related differences in the prevalence and treatment of cardiovascular disease, unfavorable clinical characteristics and suboptimal treatment of women with acute coronary syndromes have been documented in Poland [5, 6].

In the present study a unique attempt was made to assess clinical course, treatment and prognosis in men and women with MI due to critical stenosis of the left main coronary artery.

Methods

Of 121,526 patients with acute coronary syndromes consecutively hospitalized between 2003 and 2006 a group of 643 (1.9%) patients was identified in whom coronary angiography confirmed critical stenosis of ULMCA which was responsible for the development of ST-segment elevation myocardial infarction (STEMI) or non ST-segment elevation myocardial infarction (NSTEMI). The study group consisted of 184 (28.6%) women and 459 (71.4%) men. Data of hospitalized patients were obtained from the Polish Registry of Acute Coronary Syndromes (PL-ACS). Data on post-discharge events were obtained from the National Health Fund and data regarding mortality from the Vital Statistics Office. In order to identify gender-related differences in the course of ULMCA lesions and treatment women and men in the present study were compared with respect to medical history, clinical symptoms, strategy of treatment, pharmacotherapy during in-hospital stay and medication prescribed at discharge. Study end-points were defined as in-hospital death, mortality at 30 days, 6 and 12 months. Multivariate analysis included such factors as age, gender, presence of arterial hypertension, diabetes mellitus, smoking, obesity, previous MI, TIMI-3 flow prior to intervention, effective PCI (TIMI-3 flow post intervention), use of intraaortic counterpulsation and CABG.

Statistical analysis

Continuous variables, depending on the distribution type, were presented as means \pm standard

deviation (SD) or median and interquartile range. The significance of differences between the two means was tested using Student's t-test or Mann-Whitney U-test. If the data were non-normally distributed the Kruskal-Wallis one-way analysis of variance by ranks or the Mann-Whitney U-test was performed. Homogeneity of variances was checked by means of the F test. Qualitative variables were tested using the χ^2 test. One year mortality was analyzed using the Kaplan-Meier method, and the significance of differences between the groups was tested using the log-rank test. Multivariate analysis of in-hospital and 12-month mortality was performed using multiple logistic regression. Results were presented as odds ratio (OR) and relative risk with 95% confidence interval (95% CI). A p value ≤ 0.05 was considered to be significant.

Results

There were 643 consecutive patients with acute MI due to critical stenosis or acute occlusion of ULMCA, STEMI — 47.4%, NSTEMI — 52.6%. Women more frequently presented later than 2 h after symptom onset and were older than men. There was higher proportion of women over 65 and with arterial hypertension, diabetes and obesity. Cardiac arrest before hospitalization was more frequent in men (Table 1). There was a similar percentage of women in STEMI and NSTEMI group (28.9% vs. 28.5%; $p = 0.94$). Isolated ULMCA disease was more frequent in STEMI group (30.6% vs. 16.0%; $p < 0.0001$) in contrast to NSTEMI group where multivessel disease was dominant (45.1% vs. 66.0%; $p < 0.0001$). In general, there were no significant differences in the treatment strategy (Table 2) and pharmacotherapy between men and women except of more frequent use of diuretics (41.8% vs. 32.2%; $p = 0.021$) and insulin (22.3% vs. 14.2%; $p = 0.012$) in women. In women and men who underwent PCI there were different treatment options: plain old balloon angioplasty (10.7% vs. 10.5%; $p = \text{NS}$), bare metal stent (BMS, 27.0% vs. 73.0%; $p = 0.0005$) and drug-eluting stent (DES, 50% vs. 50%). There were no differences in mortality between genders in all follow-up periods (Table 3). However, when considering STEMI and NSTEMI subgroups there was a clear difference in mortality in favor of NSTEMI both in in-hospital (27.2% vs. 10.4%; $p < 0.0001$) and in 12-month follow-up (38.4% vs. 24.6%; $p < 0.0001$). In patients treated with DES in-hospital (9.0% vs. 24.1%; $p = 0.08$) and 12-month (20.0% vs. 33.2%; $p = 0.05$) there was a tendency towards lower mortality with borderline

Table 1. Basic clinical characteristics.

		Women, n = 184 (28.6%)	Men, n = 459 (71.4%)	P
Age		69.0±12.3	64.5±11.0	< 0.0001
Age ≥ 65		128 (69.6%)	235 (51.2%)	< 0.0001
Arterial hypertension		136 (73.9%)	295 (64.3%)	0.019
Diabetes		59 (32.1%)	100 (21.8%)	0.0063
Hypercholesterolemia		93 (50.5%)	201 (43.8%)	0.12
Smoking		35 (19%)	179 (39%)	< 0.0001
Obesity (BMI > 30 kg/m ²)		50 (27.2%)	49 (10.7%)	< 0.0001
Prior MI		40 (21.7%)	127 (27.7%)	0.12
Prior PCI		8 (4.3%)	18 (3.9%)	0.80
Prior CABG		11 (6%)	32 (7%)	0.65
Symptom onset — admission time	0–2 h	15 (8.2%)	64 (13.9%)	0.043
	2–6 h	77 (41.8%)	162 (35.3%)	0.12
	6–12 h	30 (16.3%)	64 (13.9%)	0.44
	> 12 h	40 (21.7%)	110 (24%)	0.55
Killip class	4	30 (16.3%)	73 (15.9%)	0.90
	3	14 (7.6%)	24 (5.2%)	0.25
	1 and 2	140 (76.1%)	362 (78.9%)	0.44
CK-MB [U/L]	Max. activity	57 (24-186)	62 (28-232)	0.25
	> 50%	38 (27.9%)	63 (20%)	0.063
EF	30–50%	78 (57.4%)	188 (59.7%)	0.64
	< 30%	20 (14.7%)	64 (20.3%)	0.16
Number of arteries diseased	LM only	46 (25.1%)	101 (22%)	0.39
	LM + 1	33 (18%)	94 (20.5%)	0.48
	LM + ≥ 2	102 (55.7%)	258 (56.2%)	0.91

BMI — body mass index; MI — myocardial infarction; PCI — percutaneous coronary intervention; CABG — coronary artery by-pass grafting; CK-MB — creatine phosphokinase-myocardial isoenzyme; EF — ejection fraction; LM — left main

significance. Complication rate (reinfarction, stroke, bleeding, target vessel revascularization) was relatively low and there were no significant differences between genders both in general population (Table 2) and in STEMI/NSTEMI subgroups (data not shown). In multivariable analysis cardiogenic shock, pulmonary edema, STEMI and advanced age significantly increased in-hospital and 1-year mortality. Female sex did not influence mortality. Successful PCI assessed as post-procedural TIMI 3 flow significantly improved prognosis (Table 4).

Discussion

Critical ULMCA stenosis is rare (5–7% of patients undergoing coronary angiography), it is however associated with serious prognosis. European guidelines allow for PCI of the ULMCA in patients with single vessels disease and the lesion

not extending to the bifurcation (Class IIa recommendation), in more complex cases PCI is upgraded to a Class IIb recommendation, whereas in patients with multiple vessel disease or SYNTAX Score ≥ 33 PCI of the ULMCA is contraindicated [7]. American guidelines say that PCI of the ULMCA can be considered in select patients (Class IIb recommendation) [8]. MI due to acute total occlusion of ULMCA, if not leading almost immediately to death, usually is complicated by severe ventricular arrhythmia and acute left ventricular failure as evidenced by pulmonary edema or shock with in-hospital and long-term mortality being very high. In stable patients CABG is the recommended modality offering good long-term outcomes. However, in patients with the ULMCA as the infarct-related artery optimal revascularization strategy is not obvious. Primary PCI in these patients is feasible and restores blood flow in a shorter time

Table 2. Treatment strategy.

		Women, n = 184 (28.6%)	Men, n = 459 (71.4%)	P
Conservative		55 (29.9%)	141 (30.7%)	0.84
Fibrinolysis		2 (1.1%)	12 (2.6%)	0.37
Invasive	PCI	120 (65.2%)	279 (60.8%)	0.30
	CABG	8 (4.3%)	29 (6.3%)	0.33
	PCI + CABG	1 (0.5%)	7 (1.5%)	0.53
STEMI symptoms-to-balloon time	0–2 h	5 (6.8%)	17 (9.8%)	0.44
	2–6 h	20 (27%)	58 (33.3%)	0.33
	6–12 h	15 (20.3%)	22 (12.6%)	0.12
	> 12 h	34 (45.9%)	77 (44.3%)	0.81
Stenting		108 (89.3%)	256 (89.5%)	0.94
IABP		25 (13.6%)	49 (10.7%)	0.30
GP IIb/IIIa antagonist		45 (24.5%)	112 (24.4%)	0.99
TIMI flow before PCI	0	45 (37.5%)	128 (45.1%)	0.16
	1	26 (21.7%)	46 (16.2%)	0.19
	2	18 (15.0%)	52 (18.3%)	0.42
	3	31 (25.8%)	58 (20.4%)	0.23
Post-procedural TIMI flow	0	5 (4.1%)	16 (5.6%)	0.54
	1	3 (2.5%)	13 (4.6%)	0.48
	2	7 (5.8%)	22 (7.7%)	0.49
	3	106 (87.6%)	234 (82.1%)	0.17
In-hospital complications	STEMI	4 (2.2%)	7 (1.5%)	0.81
	NSTEMI/UA	9 (4.9%)	21 (4.6%)	0.86
	Stroke	0 (0%)	4 (0.9%)	0.47
	Bleeding	6 (3.3%)	10 (2.2%)	0.61
	Re-PCI	3 (1.6%)	6 (1.3%)	0.96

CABG — coronary artery by-pass grafting; PCI — percutaneous coronary intervention; IABP — intraaortic balloon pump; GP — glycoprotein; N/STEMI — non/ST-segment elevation myocardial infarction; UA — unstable angina, Re-PCI — target vessel revascularization

Table 3. Mortality.

	Women, n = 184 (28.6%)	Men, n = 459 (71.4%)	P <
In-hospital	38 (20.7%)	80 (17.4%)	0.34
30-day	45 (24.5%)	100 (21.8%)	0.46
6-month	58 (31.5%)	127 (27.7%)	0.33
12-month	60 (32.6%)	140 (30.5%)	0.60

than CABG. Short- and long-term outcomes and lower periprocedural risk of stroke, even with a higher rate of repeat revascularization within the treated vessel, offer a favorable alternative to surgical treatment [9]. There is increasing evidence showing that outcomes after PCI of the ULMCA in

stable patients does not differ from that after CABG with respect to the rate of post-procedural death or MI. For this reason there is growing interest in angioplasty procedures in highest risk patients in whom the fastest reperfusion (TIMI grade 3 flow) is closely associated with better prognosis [10, 11].

Because of the frequently described differences in the course of MI between men and women we analyzed a number of factors that might have an impact on the clinical manifestations of acute coronary syndromes caused by critical ULMCA stenosis in both sexes. Women were decidedly in the minority, they were older than men by 4.5 years on average and they were diagnosed significantly more frequently with arterial hypertension, diabetes mellitus and obesity, and what's perhaps most important time from the onset of pain to admission was longer than that for men. Most stu-

Table 4. Multivariate analysis — in-hospital and 12-month mortality.

	In-hospital OR (95% CI)	P	12-month RR (95% CI)	P
Age (per 10 years more)	1.40 (1.03–1.90)	0.030	1.35 (1.13–1.61)	0.0010
Female gender	1.24 (0.61–2.52)	0.55	1.03 (0.7–1.52)	0.88
Arterial hypertension	0.58 (0.29–1.15)	0.12	0.9 (0.62–1.31)	0.59
Diabetes	1.29 (0.60–2.77)	0.51	1.09 (0.72–1.65)	0.67
Smoking	0.61 (0.28–1.33)	0.22	0.64 (0.4–1.01)	0.053
Obesity	1.03 (0.40–2.65)	0.95	0.89 (0.51–1.53)	0.67
Prior MI	1.05 (0.47–2.37)	0.90	1.88 (1.22–2.9)	0.0041
Prior revascularization	0.71 (0.22–2.33)	0.57	0.54 (0.28–1.04)	0.066
Heart rate \geq 100/min	0.76 (0.32–1.83)	0.54	1.05 (0.67–1.65)	0.83
Pulmonary edema	3.66 (1.16–11.59)	0.027	4.29 (2.4–7.66)	< 0.0001
Cardiogenic shock	10.15 (4.94–20.87)	< 0.0001	3.78 (2.45–5.84)	< 0.0001
STEMI (vs. NSTEMI)	2.37 (1.14–4.91)	0.020	1.52 (1.01–2.27)	0.045
LM + 1 vessel	1.20 (0.48–2.98)	0.70	1.4 (0.83–2.37)	0.21
LM + 2 or more vessels	1.58 (0.71–3.52)	0.26	1.43 (0.91–2.27)	0.12
TIMI 3 flow before PCI	0.56 (0.22–1.46)	0.24	0.68 (0.41–1.15)	0.15
Post-procedural TIMI 3 flow	0.10 (0.05–0.23)	< 0.0001	0.2 (0.13–0.3)	< 0.0001
IABP	1.96 (0.87–4.41)	0.10	1.34 (0.88–2.04)	0.17
CABG	0.99 (0.09–10.97)	0.99	1.33 (0.45–3.94)	0.60

MI — myocardial infarction; PCI — percutaneous coronary intervention; CABG — coronary artery by-pass grafting; LM — left main; IABP — intraaortic balloon pump; N/STEMI — non/ST-segment elevation myocardial infarction

dies comparing cardiovascular risk factors in men and women confirm such risk distribution among patients admitted for MI [12]. It is noteworthy that the number of risk factors increases significantly with age, however in those both below and over 65 years of age there are still more women with arterial hypertension, diabetes mellitus and obesity whereas more smokers are encountered among men. In a large database of patients with acute coronary syndromes admitted to hospitals in 2001–2004 cardiovascular risk factors in men and women had similar rates of occurrence. Women made up about 30% of the study population, they were older than men by 6 years on average and had arterial hypertension (66.4% vs. 56.8%; $p = 0.001$) and diabetes (30.8% vs. 18.6%; $p < 0.001$), whereas there were more smokers among men (66.2% vs. 6.6%; $p < 0.001$) [13]. Although the statistics regarding patients with MI due to total occlusion of the left main coronary artery are limited, it seems that the distribution of major cardiovascular risk factors is similar to that in the population of MI patients in general. According to one of the few reports on patients undergoing angioplasty of the unprotected left main coronary artery stenosis women representing 27.8% of the study population were older and had been more frequently diagnosed with arterial hypertension and

diabetes [14]. Significantly less women were found to be admitted to hospital within 2 h after the onset of chest pain (8.2% vs. 13.9%; $p = 0.043$). Delay to treatment in MI frequently occurs in women. This fact is believed to be caused by differences in the clinical manifestations of acute coronary syndromes between men and women. One study evaluating the symptoms of acute MI in females demonstrated that chest pain was absent in almost 50% of women, and shortness of breath (58%), weakness (55%) and fatigue (43%) were found instead [15]. Moreover, women's low awareness of coronary risk not infrequently was the reason for ignoring the symptoms and not seeking medical care. Therefore, women even with typical symptoms of MI were admitted to emergency departments later than men [16, 17].

Mortality after elective PCI with DES in low risk patients with ULMCA (good left ventricular ejection fraction, favorable anatomy of the left main bifurcation) is low [18, 19] as compared with very high (exceeding often 40%) mortality in MI due to ULMCA stenosis [20–23]. These reports are rare because of the short time elapsed from the introduction of PCI in these patients. In the present study in-hospital and annual mortality is high but relatively low as compared with other studies. Most investigators emphasize poorer pro-

gnosis in females, however these differences are increasingly frequently interpreted as a result of age and a larger number of risk factors. Analysis of a large database of patients admitted to hospital due to MI confirmed higher in-hospital and early post discharge mortality among women and equalization of survival in both genders over longer follow-up. Investigators emphasize probable effects of the sex-specific clinical characteristics on these statistics, and they also agree that reliable evaluation is difficult because of the nonhomogeneity of the studies. It is however suggested that higher early post MI mortality among women may be associated with less frequent use of an invasive management strategy and delayed admission to hospital [24].

Several investigations show better survival in women which is related to progress in reperfusion therapy. A population of patients admitted to hospital due to MI was analyzed in three series: group I: 1981–1988 (fibrinolysis), group II: 1989–1995 (balloon angioplasty), group III: 1996–2001 (PCI with stenting). Mortality over 3-year follow-up was higher in women in the first two groups, whereas in group III there were no differences in mortality between men and women (12% vs. 10%; $p = 0.66$). The investigators emphasize that the number of men and women selected for reperfusion therapy was similar in all groups [25]. Analysis of patients undergoing angioplasty of the ULMCA generated similar results. Although over 18-months follow-up there was higher risk of cardiac death, MI and total mortality among women, in multivariate analysis female gender did not affect negatively the survival [14]. In the present study there were no significant differences in mortality between men and women in general group and within STEMI/NSTEMI and DES/BMS subgroups.

Chieffo et al. [3] compared stenting on the left main bifurcation performed with two types of stents. In their study 45% of patients received DES and 34% — BMS. Serious complications developed in 15.8% of DES patients vs. 45.4% of BMS patients. Cardiac deaths were also more frequent in BMS patients (22.7%) than in DES patients (5.2%). In the present study there was a tendency towards lower mortality in patients with DES. Nevertheless the small sample size does not permit definitive conclusions or extrapolation to the general population.

Multivariate analysis provided extremely interesting results in an attempt to answer a question which factors have the most important effect on in-hospital and long-term mortality. Of all factors age and symptoms of acute left ventricular failure

were the most important predictors of mortality. Cardiogenic shock is a real killer and treatment of this dangerous complication should be instituted in the first place in MI even if it is caused by occlusion of the ULMCA. Undoubtedly treating the underlying cause is important. Rapid restoration of coronary blood flow also at the microcirculatory level is the best treatment strategy. In the present study TIMI grade 3 flow resulted in a 5-fold decrease of annual mortality. Increasing evidence suggests that both treatment modalities (CABG and PCI) may be accepted as equivalent or complementary in patients with critical lesions in the left main coronary artery, because once a patient with MI has stabilized and the acute phase has passed, complete revascularization with CABG after PCI of the left main is still possible.

Limitations of the study

Despite our study presents important data, it has several limitations. First, its retrospective nature biases the conclusions. Second, the choice of treatment strategy was operator dependent. Third, small number of DES used resulted in insignificant differences in outcomes what is known to be false. Finally, we have no data on lesion location (ostial vs. bifurcation of the ULMCA) and manual thrombectomy prior to PCI which also have significant impact on mortality.

Conclusions

No significant differences in clinical course, treatment and prognosis between men and women were noted, although women were older and had more concomitant risk factors. Mortality remained very high in both genders. The most unfavorable prognostic factors were cardiogenic shock, pulmonary edema, STEMI and advanced age. Percutaneous coronary angioplasty is feasible and offers high success rate in this subset of patients.

Conflict of interest: none declared

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