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Gender Effects on Coronary Artery Flow and Left Ventricular Function in Patients with Acute Anterior ST Elevation Myocardial Infarction (STEMI) after Primary Coronary Angioplasty

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Abstract

Background: Coronary disease is the most frequent disease and cause of mortality in women. The aim of this study was to examine gender effects in acute anterior ST-elevation myocardial infarction (STEMI) and primary percutaneous intervention (PPCI) on coronary artery and myocardial perfusion and left ventricular systolic function.

Methods: 184 consecutive patients, 33 women, with acute anterior STEMI treated by PPCI were evaluated. TIMI flow, myocardial blush grade (MBG) in the left anterior descending (LAD) coronary artery, ST-Elevation resolution, LAD blood velocity parameters, diastolic deceleration time (DDT) and left ventricular systolic function parameters, early and late post-PPCI, were measured.

Results: Women were older (69 ± 11.9 vs. 58.2 ± 11.9, $p < 0.0001$), had lower weight (73.2 ± 14.1 vs. 85.2 ± 15.2 kg, $p < 0.005$), less smokers (61.9% vs. 84%, $p < 0.05$), less diabetics (28.6% vs. 42.7%, $p < 0.05$), but more hypertension (79.3% vs. 63%, p = < 0.05). Time intervals till PPCI were similar. TIMI grades before and after PPCI were similar. MBG > 1 before PPCI was found in 20% of women and 9.4% in men, $p < 0.05$; however after PPCI, MBG in men and women were similar. Women had larger extent of ST-elevation resolution 2.5 ± 2.12 mm while men had 1.375 ± 1.19 mm, $p < 0.05$. 71.4% of women had LAD-DDT > 600 msec, while only 43.3% of men, $p < 0.05$. Left ventricular systolic function parameters were similar in women and men.

Conclusions: Women with anterior STEMI treated by PPCI were older, had lower body weight, with less smoking and diabetes mellitus. Women had more ST-elevation resolution and higher rates of late LAD-DDT > 600 msec. Left ventricular systolic function in women was similar to that in men.

Keywords

Women, Acute myocardial infarction, Primary coronary angioplasty, Coronary flow

Introduction

Coronary artery atherosclerotic disease (CAD) is the most prevalent disease in industrialized countries [1]. In the United States of America more than 1 million patients every year are admitted to the coronary care unit with suspected acute myocardial infarction [2,3].

Survival of women with acute coronary syndrome is lower than that in men [4,5]. Women with acute coronary syndromes were treated less intensively than men [6,7], and reperfusion therapy is less frequently applied, which may explain the lower survival in women. Women with acute ST-elevation myocardial infarction (STEMI) treated by percutaneous coronary intervention (PPCI) had 2.3 fold higher risk compared to men after adjusting for age, associated diseases and time to

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treatment [8]. In addition, women had higher risk of bleeding compared to men [4-9]. Therefore, the present study was performed to test the hypothesis, that women with anterior STEMI develop suboptimal coronary and myocardial flow after PPCI, and subsequently have lower left ventricular systolic function.

Materials and Methods

Study participants

One hundred eight four consecutive patients, 33 women, with acute anterior STEMI and treated by PPCI were evaluated. All fulfilled the following criteria: 1) First anterior wall STEMI, 2) PPCI within 12 hours of the onset of symptoms, 3) Routine informed consent to perform PPCI. Anterior STEMI was defined as continuous chest pain for at least 30 minutes and ST elevation of at least 2.0 mm in ≥ 2 contiguous precordial ECG leads. Exclusion criteria included one of the following clinical or angiographic findings: Prior bypass surgery, previous anterior STEMI, significant left main artery disease, failed PPCI.

Primary PCI was performed in standard fashion. All subjects were treated with oral clopidogrel (600 mg) followed by 75 mg/d, or prasugrel loading dose of 60 mg followed by 10 mg/d in addition to aspirin (300 mg) in the emergency department. Before catheterization, patients were treated with an intravenous bolus injection of heparin (50-70 U/Kg) to achieve coagulation time of = 250 msec or with intravenous bivalirudin as a bolus of 0.75 mg/kg, and a maintenance infusion at a rate of 1.75 mg/kg/hour for 4 hours, and if clinically indicated 0.2 mg/kg/hour for additional 20 hours.

Coronary angiography and PPCI were performed subsequently. Bare metal stents were deployed by high-pressure implantation techniques. Low magnification angiogram at either the right 30° or 90° lateral projections with prolonged cine was performed to optimize myocardial blush grade (MBG) documentation at the end of the intervention as previously described [6]. All patients were treated with clopidogrel or prasugrel in addition to aspirin for 12 months after the procedure.

Fourteen-lead electrocardiograms were performed at admission and after PPCI. Measurement of ST-segment in mm was performed from the lead of highest elevation. The ratio of difference of ST-elevation before and after PPCI to ST elevation before PPCI was calculated. When the ration exceeded 70% ST-elevation resolution was considered complete, a ration between 30% and 70% was considered partial, and resolution of ST elevation was diagnosed when the ratio was less than 30%.

Siemens, Acuson Sequoia echocardiographic system, California, equipped with 3.5-7 MHZ transducers was used. All patients had complete Doppler echcardiographic studies, within the first 6 hours after PPCI and 5 days later.

Chamber diameters and usual measurements were performed according to recommendations of American Society of Echocardiography. Ejection fraction of LV (LVEF) was measured from biplane apical views.

For the calculation of wall motion score index

$$\text{LV-WMSI} = \frac{\sum \text{score of 16 segments}}{16} \quad (1)$$

assigning a value of 1 for normal LV wall motion, 2 for hypokinesis and 3 for akinesis. Using the same values of wall motion scores, LAD 9 segmental score index was calculated as:

$$\text{LAD-WMSI} = \frac{\sum \text{score of 9 segments}}{9} \quad (2)$$

In order to obtain LAD flows, the color Doppler Nyquist limit was set at 17 cm/sec. From low parasternal short axis view, search for diastolic color flow in the anterior interventricular groove followed by clockwise rotation was performed, while form apical foreshortened two chamber views LAD diastolic flow was located in the interventricular groove and the counter-clockwise rotation of the transducer was performed.

Parameters of LAD velocity patterns were averaged from 3 beats, all in sinus rhythm. Diastolic LAD deceleration Time (DDT) was measured as the time from peak diastolic velocity to the intercept of the tangent of the velocity envelope with baseline.

Statistical analysis

Statistical analysis was conducted using SPSS software version 13. All values were expressed as means and standard deviations. Chi-square test was used to examine differences in categorical parameters. Student t-test and analysis of covariance (ANCOVA) were used to examine differences in continuous variables, $p < 0.05$ was considered as statistically significant. Logistic regression models were performed, where TIMI grade and MBG equal to 3 post PPCI, LAD-DDT > 600 msec and LVEF < 50%, were defined as the dependent variable and adjusted to gender, age, body weight, and cardiovascular risk factors.

Results

Patient characteristics

The study population consisted of 184 consecutive patients, 33 (17.9%) of them were women. Characteristics of the patients are described in table 1. Women were significantly older than men, had lower body weight, higher prevalence of hypertension but lower prevalence of cigarette smoking, diabetes mellitus and family history of coronary artery disease (Table 1). The average Killip classification was similar in women and men, however, 9.8% of men were in Killip class III and IV, but none of the women (Table 1). No significant difference was found in time intervals from the onset of chest pain to hospital arrival and time to PPCI (Table 1). No significant differences were found in anticoagulant or anti-platelet treatments (Table 1).

Table 1: Baseline characteristics.

	Male (n = 151)	Female (n = 33)	P-value
Age (yrs.)	58.2 ± 11.9	69 ± 11.9	< 0.0001
Weight (Kg)	85.2 ± 15.2	73.2 ± 14.1	< 0.005
HTN (%)	67	79.3	< 0.05
HLP (%)	86.3	80.6	ns
DM (%)	42.7	28.6	< 0.05
Smoker (%)	84	61.9	< 0.05
Obesity (%)	51.6	40	ns
FH of CAD (%)	56.8	31.6	< 0.05
Killip class 1 (%)	85.2	93.1	ns
Killip class 2 (%)	4.9	6.9	ns
Killip class 3 (%)	7.4	-	
Killip class 4 (%)	2.4	-	
Killip class mean	1.27	1.07	ns
Pain to door (min)	127.14 ± 105.57	126.37 ± 95.69	ns
Door to balloon (min)	94.58 ± 118.45	114.61 ± 99.04	ns
Pain to balloon (min)	220.43 ± 172.45	244.48 ± 142.11	ns
Number of narrowed coronary arteries (%)			
1	59	63.6	ns
2	33.1	27	ns
3	7.9	9.4	ns
Proximal LAD (%)	43	51.5	ns
Mid LAD (%)	53	45.5	ns
Stent diameter	2.87 ± 0.33	2.83 ± 0.4	ns
Stent length	16.9 ± 5.9	14.3 ± 6.3	ns
Aspirin on arrival (%)	100	100	ns
Prasugrel on arrival (%)	34.45	33.38	ns
Clopidogrel on arrival (%)	65.55	66.62	ns
Heparin on arrival (%)	25.7	32.78	ns
Bivalirudin on arrival (%)	74.3	67.22	ns

DM: Diabetes Mellitus; FH OF CAD: Family History of Coronary Artery Disease; HTN: Hypertension; HLP: Hyperlipidemia.

Angiographic findings

The average of TIMI (Table 2) and MBG (Table 2) grades in the LAD were similar in both genders; however, more women (20% vs. 9.4%, p < 0.05) presented with MBG 2 or 3 before PPCI (Table 2).

Electrocardiographic findings

Higher prevalence of complete ST-elevation resolution was found in women (45.54 vs. 31.25%, p < 0.05), (Table 3) in addition, the extent of ST-elevation resolution was larger in women (2.5 ± 2.12 vs. 1.375 ± 1.19, p < 0.05), (Table 3).

Velocity parameters in the left anterior descending coronary artery

On early evaluation, women had higher systolic velocities in the LAD, however, a larger proportion of men had DDT > 600 msec (Table 4). Five days after PPCI, maximal diastolic and systolic velocities as well as velocity integrals in the LAD were similar (Table 4), however, DDT and P1/2T were larger in women (Table 4).

Left ventricular systolic function and myocardial biomarkers

Left ventricular systolic function parameters were similar in both groups, early on admission, and 5 days after PPCI (Table 5). Myocardial biomarkers, including troponin I blood levels and creatinine phosphokinase blood levels were also similar in women and men (Table 5).

The logistic multivariate analysis model did not reveal significant independent effect of gender or other variables on TIMI and MBG post PPCI, LAD-DDT and LVEF (Table 6).

Discussion

In this study, women with anterior STEMI treated by PPCI were older, with lower prevalence of diabetes mellitus and smoking and had lower body weight. More women presented with MBG grade > 1 before PPCI, but TIMI before and after PPCI as well as MBG after PPCI were similar in men and women. Women had more ST-elevation resolution after PPCI, and higher rates of LAD-DDT > 600 msec, however left ventricular systolic function parameters were similar to those in men.

In a previous study, women with STEMI treated by PPCI had 2.3 higher risk compared to men after adjusting for age, associated diseases and time to treatment [8]. Accordingly, the hypothesis of our study was that women fare worse than men when treated with PPCI in the setting of anterior STEMI. However, our findings showed that left ventricular systolic function parameters were similar to those in men. These findings are discordant with previous reports including thrombolysis studies, which showed higher mortality in women [7,10-17]. In these studies, gender differences between remained significant after adjustments to comorbidities in most of studies [7,10-16] but disappeared in another study [17].

The results of the present study may be attributed to differences in basic characteristics between women and men. Similar to other studies, in our study, women were older than men [10-15,18], however, contrary to other studies, we found that women had lower prevalence of diabetes mellitus, 10-16 in addition to lower prevalence of cigarette smoking [10-12,14,16,17]. These differences may contribute to better outcome in women.

Differences in pain to balloon time intervals and improvement in PPCI technique may also affect outcome in PPCI patients. Similar, to another study [14], we found that in women, the pain to balloon time was similar to that in men. However, this finding is contradictory to other studies which showed that men had earlier PPCI than women [10,16,17].

The aim of PPCI is re-establish flow in the obstructed infarct-related coronary artery and to achieve adequate myocardial reperfusion. Patients arriving with open infarct related artery and with better myocardial

Table 2: Coronary angiographic findings.

	Male	Female	P-value
TIMI pre PPCI			
TIMI 3 pre PPCI	11.38%	14.28%	ns
TIMI 2 pre PPCI	13.82%	14.28%	ns
TIMI 1 pre PPCI	4.88%	0%	ns
TIMI 0 pre PPCI	69.92%	71.43%	ns
TIMI ≤ 1 pre PPCI	74.80%	71.43%	ns
TIMI mean pre PPCI	0.67 ± 1.09	0.71 ± 1.18	ns
TIMI post PPCI			
TIMI 3 post PPCI	93.50%	89.28%	ns
TIMI 2 post PPCI	5.69%	7.14%	ns
TIMI 1 post PPCI	0%	0%	ns
TIMI 0 post PPCI	0.81%	3.57%	ns
TIMI ≥ 2 post PPCI	99.20%	96.43%	ns
TIMI mean post PPCI	2.92 ± 0.35	2.82 ± 0.61	ns
MBG pre PPCI			
MBG 3 pre PPCI	5.13%	8%	ns
MBG 2 pre PPCI	4.27%	12%	ns
MBG 1 pre PPCI	14.53%	4%	ns
MBG 0 pre PPCI	76.07%	76%	ns
MBG ≤ 1 pre PPCI	90.60%	80%	<0.05
MBG mean pre PPCI	0.38 ± 0.8	0.6 ± 1.04	ns
MBG post PPCI			
MBG 3 post PPCI	50.43%	48%	ns
MBG 2 post PPCI	47%	44%	ns
MBG 1 post PPCI	2.56%	8%	ns
MBG 0 post PPCI	0%	0%	ns
MBG ≥ 2 post PPCI	97.43%	92%	ns
MBG mean post PPCI	2.48 ± 0.55	2.4 ± 0.64	ns

MBG: Myocardial Blush Grade; PPCI: Primary Percutaneous Coronary Intervention; TIMI: Thrombolysis in Myocardial Infarction score.

Table 3: ST elevation resolution.

	Male	Female	All	P value
Complete STE resolution > 70%	31.25%	45.54%	33.90%	< 0.05
30% ≤ Partial STE resolution < 70%	56.25%	45.54%	54.24%	ns
Without resolution < 30%	12.50%	9.09%	11.86%	ns
Mean resolution (mm)	1.375 ± 1.19	2.5 ± 2.12	1.56 ± 1.07	< 0.05

STE: ST Elevation.

Table 4: Early and late LAD doppler velocities.

	Male	Female	P-value
Early			
LAD diam (mm)	2.45 ± 0.48	2.35 ± 0.51	ns
Diastolic velocity (cm/sec)	44 ± 15.46	46.31 ± 17.34	ns
Systolic velocity (cm/sec)	14.43 ± 11.17	19.61 ± 5.85	0.02
TVI diastole (cm)	12.08 ± 5.04	12.41 ± 4.78	ns
TVI systole (cm)	3.91 ± 9.5	3.88 ± 1.89	ns
PHT (msec)	152.8 ± 94.56	130.42 ± 63.01	ns
DDT (msec)	543.6 ± 329.8	436.75 ± 238.4	ns
DDT > 600 (msec)	43.33%	25%	< 0.05
HR (bpm)	77.2 ± 12.96	78.44 ± 12.04	ns
Late			
LAD diam (mm)	2.54 ± 0.33	2.51 ± 0.4	ns
Diastolic velocity (cm/sec)	42.12 ± 13.14	42.45 ± 15.62	ns
Systolic velocity (cm/sec)	16.98 ± 11.47	20.15 ± 8.24	ns
TVI diastole (cm)	13.7 ± 4.8	14.97 ± 3.61	ns
TVI systole (cm)	3.44 ± 2.31	4.25 ± 1.99	ns
PHT (msec)	167 ± 71.74	219.9 ± 68.84	0.003
DDT (msec)	563.33 ± 242.37	746.6 ± 236.37	0.004
DDT > 600 (msec)	53.03%	71.43%	< 0.05
HR (bpm)	70.1 ± 11.49	69 ± 13.14	ns

DDT: Diastolic Declaration Time; HR: Heart Rate; LAD: Left Anterior Descending Coronary Artery; PHT: Pressure Half Time; TVI: Time Velocity Integral.

perfusion in the infarct area have better outcome. In our study, higher rates of MBG II and III were found in women, however, after PPCI, TIMI grade and MBG in women were similar to those in men. In addition, in our study, adjunctive therapies to PPCI, were similar in men and women, while, previously it was reported that men were treated more intensively [10]. These findings demonstrating similar pain to balloon time, and similar adjunctive PPCI treatments between women and men may account for the better outcome in women compared to other studies.

It was reported, that the extent of myocardial damage evaluated by myocardial biomarkers and left ventricular systolic function correlated with electrocardiographic ST-elevation resolution [18]. In our study, a higher percentage of women had complete ST-elevation resolution and higher extent of resolution compared to men. These findings imply that in the present study, women had better myocardial perfusion after PPCI compared to men.

After PPCI, recovery of left ventricular systolic function is related to the flow in the infarct related artery as evaluated by transthoracic Doppler [19]. The velocity parameters needed to calculate flow in the LAD in the present study were similar in women and men. Therefore, it is expected that blood flow after PPCI in the infarct related artery in women and men were similar, and this may account for the absence of gender differences in LV systolic function. In addition, the coronary microcirculation after PPCI can be evaluated by transthoracic Doppler, and LAD-DDT > 600 msec predicted better outcome [20]. We reported that the function of the coronary microcirculation after PPCI is dynamic [21], and that serial evaluation of LAD-DDT predicted recovery of left ventricular systolic function [22]. Again, women had higher frequency of optimal function of the coronary microcirculation by Doppler, and contributing to better outcome than expected in women.

In our study, LV systolic function at all measurement occasions was similar in women and men. However, in a recent study which included patients with STEMI treated with PPCI, women had worse LV function compared to men despite receiving similar treatment [17]. The number of patients in both studies was similar. In current study all patients presented had anterior STEMI, however patients in the quoted study presented with STEMI with no regard to infarction location; only 43-49% of all patients presented with anterior STEMI [17]. Women were older than men in the quoted study, as in our study. Mean age in men was similar in both studies. However mean age in women in the current study was 7 years higher than in the other study. According to this difference in mean age it is expected to have worse results in women compared to men. There is fundamental difference between the studies; in the quoted study the echocardiography was done only once, till 3 days of admission. In our study echocardiography was done early and late after PPCI and comparison between them was done. Early LV function, represents the extent of jeopardized myocardium at presentation, while the late evaluation better represent LV functional recovery. Intermediate timing of evaluation as in the quoted study, neither represents the extent of myocardial jeopardy nor LV function recovery. In addition, in the present, study LV function was measured by several parameters: EF, LV-WMSI and LAD-WMSI early and late after PPCI. All these parameters behaved in the same manner, and

Table 5: Left ventricle systolic function.

	Male	Female	P value
EF early (%)	36.37 ± 6.4	38 ± 5.65	0.081
EF late (%)	42.54 ± 8.45	44.88 ± 7.89	0.078
ΔEF	6.38 ± 7.24	6.88 ± 6.59	ns
LV WMSI early	1.65 ± 0.24	1.51 ± 0.28	ns
LV WMSI late	1.49 ± 0.29	1.52 ± 0.37	ns
Δ LV WMSI	0.014 ± 0.277	0.057 ± 0.345	ns
LAD WMSI early	2.12 ± 0.38	1.96 ± 0.51	ns
LAD WMSI late	1.84 ± 0. 47	1.8 ± 0.51	ns
Δ LAD WMSI	0.27 ± 0.398	0.117 ± 0.535	ns
Max trop (ng/mL)	49.74 ± 47.25	52.24 ± 48.05	ns
Max CPK (U/L)	1636 ± 1391	1407.4 ± 1334.9	ns

CPK: Creatine Phosphokinase; EF: Ejection Fraction; LAD: Left Anterior Descending; LV: Left Ventricle; PPCI: Primary Percutaneous Coronary Intervention; TROP: Troponin; WMSI: Wall Motion Score Index.

Table 6: Logistic regression models.

Correlates	Model 1		Model 2		Model 3		Model 4	
	TIMI =3, post PPCI		BLUSH = 3, post PPCI		DDT > 600 (msec)		LVEF < 50% at discharge	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Gender	0.01 (0.003-0.05)	0.98	0.36 (0.045-15)	0.55	0.78 (0.0004-10)	0.78	0.96 (0.446-11.3)	0.33
Age	0.3 (0.022-2.005)	0.9	0.78 (0.6-1.2)	0.38	0.3 (0.008-12)	0.86	0.93 (0.94-1.03)	0.46
Weight	0. 1 (0.2-0.95)	0.99	0.096 (0.85-1.3)	0.76	0.24 (0.003-13)	0.63	1.99 (0.99-1.06)	0.16
HTN	0.041 (0.045-0.65)	0.99	0.022 (0.053-12.5)	0.88	0.036 (0.002-10)	0.85	0.42 (0.41-6)	0.52
HLP	0.001 (0.002-0.25)	0.97	0.003 (0.064-18.5)	0.95	0.082 (0.008-4)	0.76	3.2 (0.86-24.1)	0.07
DM	0.001(0.032-0.75)	0.98	0.039 (0.026-19.5)	0.84	0.4 (0.0006-4.4)	0.53	1.6 (0.068-1.8)	0.2
Smokers	0.001 (0.01-0.04)	0.99	0.001 (2.8-12)	0.9	0.001 (0.002-0.004)	0.9	1.4 (0.58-9.34)	0.23
Obesity	0.001 (0.002-0.005)	0.99	0.001 (3.6-36.2)	0.89	0.31 (0.009-12)	0.58	0.26 (0.34-6.3)	0.61
FH of CAD	0.001 (0.032-0.055)	0.88	0.58 (0.014-11)	0.58	0.3 (0.0002-13)	0.58	1.55 (0.09-1.7)	0.21
Previous CAD	0.001 (0.02-0.05)	0.9	0.0003 (0.44-0.9)	0.6	0.24 (0.0001-10)	0.63	0.085 (0.09-5.8)	0.77

DM: Diabetes Mellitus; FH OF CAD: Family History of Coronary Artery Disease; HTN: Hypertension; HLP: Hyperlipidemia.

thus support the findings of the current study. Moreover, myocardial bio- markers, CPK and troponin maximal levels were similar in both studies, supporting the current study findings.

Limitation

This study was single-center. The patient number included in this study is relatively small. In addition, the study results regards anterior STEMI, thus the study's findings to other coronary territories is not confirmed. There was no information regarding long-term follow-up including death or heart failure. Future studies, multi-center, long-term with larger patient number should be done to verify and to generalize current study results.

Conclusions

When women with acute STEMI are treated similar to men, current PPCI outcome is not affected by gender.

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