

Research Paper

Gender Related Survival Differences in ST-Elevation Myocardial Infarction Patients Treated with Primary PCI

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Abstract

Background: Data about gender as an independent risk factor for death in ST-elevation myocardial infarction (STEMI) patients is still contrasting. Aim was to assess how gender influences in-hospital and long-term all-cause mortality in STEMI patients with primary percutaneous coronary intervention (PCI) in our region.

Methods: We analysed data from 2069 STEMI patients undergoing primary PCI in our institution from January 2009–December 2014, of whom 28.9% were women. In-hospital and long-term mortality were observed in women and men. The effect of gender on in-hospital mortality was assessed by binary logistic regression modelling and by Cox regression analysis for long-term mortality.

Results: Women were older (68.3±61.8 vs 61.8±12.0 years; $p<0.0001$), with a higher prevalence of diabetes (13.7% vs 9.9%; $p=0.013$) and tend to be more frequently admitted in cardiogenic shock (8.4% vs 6.3%; $p=0.085$). They were less frequently treated with bivalirudin (15.9% vs 20.3%; $p=0.022$).

In-hospital mortality was higher among women (14.2% vs 7.8%; $p<0.0001$). After adjustment, age (adjusted OR: 1.05; 95% CI: 1.03 to 1.08; $p < 0.001$) and cardiogenic shock at admission (adjusted OR: 24.56; 95% CI: 11.98 to 50.35; $p < 0.001$), but not sex (adjusted OR: 1.47; 95% CI: 0.80 to 2.71) were identified as prognostic factors of in-hospital mortality.

During the median follow-up of 27 months (25th, 75th percentile: 9, 48) the mortality rate (23.6% vs 15.1%; $p<0.0001$) was significantly higher in women.

The multivariate adjusted Cox regression model identified age (HR 1.05; 95% CI 1.04–1.07; $p<0.0001$), cardiogenic shock at admission (HR 6.09; 95% CI 3.78–9.81; $p<0.0001$), hypertension (HR 1.49; 95% CI 1.02–2.18; $p<0.046$), but not sex (HR 1.04; 95% CI 0.74–1.47) as independent prognostic factors of follow-up mortality.

Conclusion: Older age and worse clinical presentation rather than gender may explain the higher mortality rate in women with STEMI undergoing primary PCI.

Key words: ST-elevation myocardial infarction, percutaneous coronary intervention, mortality, gender.

Introduction

Higher mortality rates were observed among women admitted with ST-elevation myocardial infarction (STEMI) in comparison to men (1-12). Data about gender as an independent prognostic factor for death is conflicting (1-3,5,10,12-15). Underuse of evidence based treatment and delayed reperfusion are

noticed in women (16-18). Women often delay seeking medical care compared with men probably because they experience more often atypical symptoms (16-18). Only a limited number of studies reported results about medium or long term mortality in women with STEMI receiving modern treatment

(1,15,19-21). Changes in percutaneous coronary intervention (PCI) practice and quality initiatives aimed at reducing door-to-balloon times may have influenced these sex-related differences over time (1,16). The aim of our study was to assess sex differences in in-hospital and follow-up outcomes in a retrospective cohort of STEMI patients undergoing primary PCI.

Materials and methods

The present study is a retrospective single-centre analysis of consecutive 2069 STEMI patients treated in our hospital from January 2009 to December 2014. Patients were treated according to the current guidelines for STEMI management (22). Angioplasty strategy, PCI of other coronary arteries and concomitant medication were at the discretion of the operator. Median follow-up time was 27 months (25th, 75th percentile: 9, 48). The study was approved by the local ethical committee.

Definitions

To assess baseline clinical characteristics of the study cohort, we collected data concerning gender, diabetes, hypertension, dyslipidemia, all performed interventions, stents, lesions, interventions, TIMI grade flow before and after procedure and outcome. Data on dates of death were provided by Slovenian National Cause of Death Registry.

AMI definition was based on the current Guidelines (22,23). Thrombolysis in Myocardial Infarction (TIMI) flow grades were used for coronary flow assessment (24). Unsuccessful PCI was defined as PCI with TIMI grade flow 0/1 after PCI.

Pain-to-first medical contact (FMC) time was defined as the time from symptom onset to FMC. FMC-to-cathlab time was the time from FMC to arrival in catheterization laboratory; FMC-to-balloon time was the time from FMC to balloon inflation (not wire passage). Cathlab-to-balloon time was the time from arrival in the cathlab to balloon inflation. Pain-to-balloon time was the time from symptom onset to balloon inflation.

Outcomes

The end points were all-cause in-hospital and follow-up mortality in male and female patients.

Statistical methods

Univariate logistic regression modelling was used to calculate adjusted odds of in-hospital mortality. Kaplan-Meier mortality curves for men and women were constructed. Cox proportional hazards regression was used to compute hazard ratios (HRs) as estimates for follow-up mortality.

Distributions of continuous variables in the two groups were compared with either the 2-sample t-test or the Mann-Whitney test according to whether data followed the normal distribution. Distributions of categorical variables were compared to the chi-square test. Data was analysed with the SPSS 21.0 software for Windows (SPSS, Inc., Chicago, Illinois). All p-values were two-sided; values less than 0.05 were considered statistically significant.

Results

Descriptive data for patients

Out of 2069 STEMI patients 597 (28.9%) were female. Women were in average almost 7 years older (61.8 ± 12.0 vs 68.3 ± 12.6 ; $p < 0.0001$) and almost 40% of them were older than 75 years ($p < 0.0001$). Significantly more women had diabetes (9.9% vs 13.7; $p = 0.013$) and were less frequently treated with bivalirudin (20.3% vs 15.9; $p = 0.022$). They tend to present themselves more often in cardiogenic shock (6.3% vs 8.4%; $p = 0.085$) Basic clinical and angiographic characteristics are shown in Table 1.

Table 1. Basic patients' clinical and angiographic characteristics.

	MEN N = 1472 (71.1%)	WOMEN N = 597 (28.9%)	All patients N = 2069 (100%)	p
Age, years [∞]	61.8 ± 12.0	68.3 ± 12.6	63.7 ± 12.5	<0.0001
Age >75, N (%) [*]	246 (16.7)	231 (38.7)	477 (23.1)	<0.0001
Cardiogenic shock at admission, N (%) [*]	92 (6.3)	50 (8.4)	142 (6.9)	0.085
Diabetes, N (%) [*]	146 (9.9)	82 (13.7)	228 (11.0)	0.013
Hypertension, N (%) [*]	547 (37.2)	234 (39.2)	781 (37.7)	0.395
Dyslipidemia, N (%) [*]	472 (32.1)	179 (30.0)	651 (31.5)	0.375
Bivalirudin, N (%) [*]	289 (20.3)	95 (15.9)	384 (19.0)	0.022
GPIIb/IIIa, N (%) [*]	803 (54.6)	325 (54.4)	1128 (54.5)	1.000
PCI LMCA, N (%) [*]	45 (3.1)	23 (3.9)	68 (3.3)	0.344
PCI LAD, N (%) [*]	652 (44.3)	270 (45.2)	922 (44.6)	0.733
PCI LCX, N (%) [*]	274 (18.8)	90 (15.1)	364 (17.6)	0.056
PCI RCA, N (%) [*]	518 (35.2)	230 (38.5)	748 (36.2)	0.158
Unsuccessful PCI, N (%) [*]	54 (3.7)	31 (5.2)	85 (4.1)	0.114
Multivessel PCI, N (%) [*]	181 (12.3)	66 (11.1)	247 (11.9)	0.455
Radial, N (%) [*]	156 (10.6)	54 (9.0)	210 (10.0)	0.335
IABP, N (%) [*]	35 (2.4)	22 (3.7)	57 (2.8)	0.104
DES, N (%) [*]	526 (35.7)	216 (36.2)	742 (35.9)	0.879
TIMI 3 at admission, N (%) [*]	63 (4.3)	30 (5.0)	93 (5.0)	0.483
TIMI3 after PCI, N (%) [*]	1172 (79.6)	485 (81.2)	2069 (100)	0.430

[∞] Mean (standard deviation); comparison made using the t-test.; ^{*} Comparison made using the chi-square test;

DES = drug eluting stent; GPI = GPIIb-IIIa receptor inhibitors; IABP = intra-aortic balloon pump insertion; LAD = left anterior descending artery; LCX = circumflex artery; LMCA = left main coronary artery; Multivessel PCI = PCI of more than one major coronary artery; PCI = percutaneous coronary intervention; Radial = radial approach; RCA = right coronary artery; TIMI3 after PCI = TIMI 3 grade flow after procedure; TIMI 3 at admission = TIMI grade flow before procedure; Unsuccessful PCI = TIMI grade flow after PCI = 0/1.

Time to treatment

Median pain-to-FMC time (110min in men vs 133min in women) and cathlab-to-balloon time (24min vs 25min) were similar in both groups (Table 2).

The time from FMC-to-cathlab (73min vs 82min; p=0.009), the time from FMC-to-balloon (100min vs 107min; p=0.004) and the pain-to-balloon time (225min vs 244min; p=0.042) were longer in women (Table 2).

Mortality

In-hospital mortality

Women had a significantly higher in-hospital mortality [115 men (7.8%) died vs 85 women (14.2%); p<0.0001] (Table 3). Unadjusted women-to-men odds ratio for mortality was 1.96 (95% confidence interval 1.45 to 2.64; p<0.0001). The difference was no longer significant after multivariate analysis (adjusted OR: 1.47; 95% CI: 0.80 to 2.71). Age (adjusted OR: 1.05; 95% CI: 1.03 to 1.08; p < 0.001) and cardiogenic shock (adjusted OR: 24.56; 95% CI: 11.98 to 50.35; p < 0.001) at presentation were identified as independent prognostic factors of increased in-hospital overall mortality.

Follow-up mortality

Women had a significantly higher follow-up mortality during the observation period; logRank<0.0001 (Table 3, Figure 1).

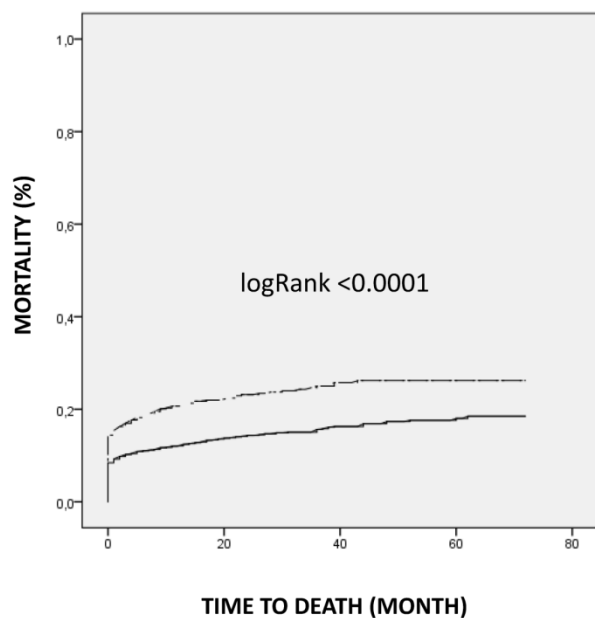


Figure 1. Follow-up mortality in STEMI patients among men and women. Women = dashed line; Men = solid line.

The multivariate Cox regression analysis identified age (HR 1.05; 95% CI 1.04–1.07; p<0.0001), cardiogenic shock (HR 6.09; 95% CI 3.78–9.81; p<0.0001), hypertension (HR 1.49; 95% CI 1.02–2.18; p<0.046) but not gender (HR 1.04; 95% CI 0.74–1.47) as independent prognostic factors of increased long-term mortality.

Quality of care

Women were brought to hospital with a delay [FMC-catheterization laboratory time was longer for women (73min vs 82min; p=0.009)] and less often received bivalirudin. Otherwise they were treated as aggressive as men but with the median time delay of 19 minutes (Table 1,2).

Table 2. Time to treatment among men and women.

	MEN (N = 1472)	WOMEN (N =597)	ALL PATIENTS (N =2069)	P
Pain-to-FMC, (min) [‡]	110 (50, 250)	133 (53, 261)	117 (50, 251)	0.140
FMC-to-cathlab (min) [‡]	73 (50, 107)	82 (57, 123)	75 (52, 112)	0.009
FMC-to-balloon, (min) [‡]	100 (75, 135)	107 (82, 158)	103 (77, 142)	0.004
Cathlab-to-balloon, (min) [‡]	24 (18, 30)	25 (17, 34)	24 (18, 31)	0.146
Pain-to-balloon, (min) [‡]	225 (148, 387)	244 (160, 446)	230 (150, 397)	0.042

[‡] Median (25th, 75th percentile); comparison made using the Mann-Whitney test; Balloon = time of first inflation of balloon; cathlab = time when patient entered catheterization laboratory; FMC = first medical contact; min = minutes, pain = start of symptoms.

Table 3. Mortality in men in women after STEMI.

MORTALITY	MEN (N =1472)	WOMEN (N =597)	ALL PATIENTS (N=2069)	P
In-hospital, N (%) [*]	115 (7,8)	85 (14,2)	200 (9.7)	<0.0001
Follow-up mortality, N (%) [*]	222 (15,1)	141 (23,6)	363 (17.5)	<0.0001

^{*} Comparison made using the chi-square test.

Discussion

The key findings of our analysis were:

- women were older, with higher prevalence of diabetes and a higher occurrence of severe hemodynamic impairment;
- higher in-hospital and follow-up mortality were observed among women, however the difference disappeared after age adjustment and gender was not independently associated with in-hospital and long-term mortality;
- the quality of care was similar as far as it concerns door-to-balloon time and procedural success, but women were treated with a time delay and received less bivalirudin.

Women were almost 7 years older than men, had

more comorbidities and tend to have more hemodynamic impairment which is in accordance to previous observations (1-4,6,7,9,10,13,14,25-28).

Higher unadjusted women's in-hospital mortality in STEMI patients undergoing primary PCI was also previously described (1,3,8,9,11,15). However data about gender as an independent prognostic factor for death is still conflicting (1,10,12-14). In-hospital mortality was not independently linked to female gender after adjustment for age, comorbidities and clinical picture at admission in most studies (1-4,6,15,20,29), but some had noticed that female sex was linked with a higher mortality (9-12).

The same is true for long-term mortality. The majority of studies show a gender difference in long-term mortality rates (10,15,30), but some showed no gender difference (6,9,20,27). Differences in the mortality rate after adjustments persisted only in one study and only in patients younger than 65 years (30).

In our study gender was not an independent predictor neither for in-hospital nor for long-term mortality after adjustments for confounders.

Data about longer ischemic time in women is still contrasting (12,13,29). Women in our study had a longer total ischemic time compared to men as it was seen before (6,10,12,13,15,31). Any delay in restoring reperfusion results in a larger infarct and thus may contribute to the poorer outcomes (13-32). The delay in presentation to hospital may be due to atypical symptoms and the underestimation of the prevalence of coronary heart disease amongst women within the community (13). Welders et al. found that every 10 minutes longer ischemic time results in additional 1% higher 7-day-mortality. The median difference in ischemic time in our study was 19 minutes. However in contrast to the mentioned study the observed difference in ischemic time was not the predictor for in-hospital or follow-up mortality after adjustments.

The results of our study may influence the daily clinical practice. Particular attention should be paid to women. They experience more often atypical symptoms (nausea, shortness of breath, back, neck and yaw pain, indigestion, palpitations, dizziness, fatigue, loss of appetite, and syncope) (13,17). Even after STEMI is recognized, the "sense of urgency" may be lost by the triage personnel resulting in a less urgent triage classification and subsequent delay (13). This may explain longer FMC-catheterization laboratory time in our study.

Limitations

There are limitations of this study that merit being mentioned. Firstly this was an observational and a single-centre study. Secondly our data

encompassed all-cause mortality only which is certainly considered to be a limitation of the study. Finally, data about bleeding and smoking were not collected.

Conclusion

Our study showed that gender was not a predictor for a higher mortality in STEMI patients. In order to achieve a better survival-rate of women with STEMI, they should be treated as aggressive and fast as men. Furthermore women should be informed about the atypical presentation of STEMI and the importance of an immediate medical contact after the start of symptoms.

Competing Interests

The authors have declared that no competing interest exists.

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