

Gender differences in patients with acute ST-elevation myocardial infarction complicated by cardiogenic shock

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Abstract

Introduction The aim of our analysis is to assess gender differences in baseline characteristics, acute therapies, and clinical outcome in patients with acute ST-elevation myocardial infarction (STEMI) complicated by cardiogenic shock.

Methods The Maximal Individual Therapy of Acute Myocardial Infarction PLUS registry (MITRA PLUS) is a German prospective, multicenter, observational data pool of current treatment of STEMI.

Results STEMI was more often ($P < 0.0001$) complicated by cardiogenic shock in female patients (12.9%) when compared to male patients (9.3%). This was still true after adjusting for confounding variables (OR 1.19, 95% CI 1.09–1.30). Women with STEMI admitted in a cardiogenic shock were older ($P < 0.0001$) and had more often concomitant diseases ($P < 0.0001$). There was no differences in rates of reperfusion therapy (OR 0.92, 95% CI 0.77–1.09). Hospital mortality was 67.7% in female patients,

when compared to 57.2% in male patients ($P < 0.0001$). After adjusting for confounding variables in the multivariate analysis hospital mortality did not differ between men and women (OR 1.16, 95% CI 0.98–1.38). Early reperfusion therapy was associated with a significant reduction of hospital mortality in female patients with STEMI complicated by cardiogenic shock (OR 0.68, 95% CI 0.52–0.90) with primary PCI being more effective than thrombolytic therapy (OR 0.46, 95% CI 0.31–0.68).

Conclusion In women, STEMI was more often complicated by cardiogenic shock when compared to men. However, the use of early reperfusion therapy did not differ between the sexes. Primary PCI was associated with the best outcome in female patients with STEMI complicated by cardiogenic shock and is therefore the therapy of choice.

Keywords ST-elevation myocardial infarction · Gender differences · Female gender · Early reperfusion therapy · Primary percutaneous coronary intervention

This study is conducted for the Maximal Individual Therapy In Acute Myocardial Infarction Plus (MITRA Plus) Study group.

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Introduction

Coronary heart disease is the leading cause of morbidity and mortality in women and in men. Coronary heart disease occurs about 10 years later in women than in men [1, 2]. Numerous studies consistently demonstrated that unadjusted rates of mortality during hospitalization or during the first 30 days after ST-elevation myocardial infarction (STEMI) are higher in women [3–5]. However, there are conflicting data about gender differences of mortality after adjusting for confounding variables [6–9]. In addition, some studies found a lower use of an invasive strategy in women than in men [10–12], whereas others

found no evidence for sex-related differences in the use of early reperfusion therapy [13, 14]. Cardiogenic shock is the major cause of death in female and male patients with STEMI [15–17]. Little is known about the impact of gender on outcome of cardiogenic shock. Early reperfusion therapy has improved survival of patients with STEMI [18–20] complicated by cardiogenic shock markedly and is therefore recommended by the European Society of Cardiology [21], the American College of Cardiology, and the American Heart Association [22]. The aim of this study is to assess gender differences in baseline characteristics and clinical outcome in patients with acute STEMI complicated by cardiogenic shock. In addition we aimed to investigate the clinical benefit of early reperfusion therapy in those patients.

Methods

MITRA Plus registry

The MITRA Plus registry is a German prospective, multicenter, observational data pool of current treatment of patients with STEMI. From 1992 to 2002, 36,643 consecutive patients with STEMI were included in the MITRA Plus registry. The MITRA Plus registry consists of four consecutive sub-registries that have been previously described: 60 min Myocardial Infarction Project (60 min MIP) [23], Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) [24], the Myocardial Infarction Registry (MIR) [25], and the Acute Coronary Syndromes (ACOS) registry [26].

The present investigation is an analysis of consecutive patients with STEMI < 24 h complicated by cardiogenic shock. Patients were recruited from 217 hospitals in Germany, mainly community hospitals.

Definitions

STEMI was diagnosed in the presence of the two following criteria: (1) persistent angina pectoris for ≥ 20 min and ST-segment elevation of ≥ 1 mm in ≥ 2 standard leads or ≥ 2 mm in ≥ 2 contiguous pre-cordial leads, or (2) persistent angina pectoris for ≥ 20 min and the presence of a left bundle branch block. ST-elevation AMI was later confirmed by an increase in cardiac enzymes to more than twice the upper limit of normal. Mortality, non-fatal re-infarction and non-fatal stroke were defined as major adverse cardiac and cerebrovascular events (MACCE).

The diagnosis of cardiogenic shock was made by the treating physicians in patients with hypotension (<100 mmHg), heart rate >100/bpm, dyspnoea and

reduction in urine output. In addition we included patients needing catecholamine support.

Data collection and statistical analysis

Data concerning the early intra-hospital period (first 48 h) were collected by use of a record form within the first 2–3 days at the intensive care unit. Clinical events after the initial period until hospital discharge were registered on a separate record form. All data sheets were sent to the central data center (Institut für Herzinfarktforschung, Ludwigshafen, Germany) for uniform monitoring, registration, and data processing.

Absolute numbers, percentages, medians, and quartiles were computed to describe the patient population. Categorical variables were compared by using Chi-square or Fisher's exact test and calculating the odds ratio (OR) and the 95% confidence intervals (CI). Multiple logistic regression was used to evaluate clinical outcomes (hospital mortality and hospital mortality/re-infarction/stroke [MACCE]). In the multivariate analysis the following variables were included: age, previous myocardial infarction, previous stroke, diabetes mellitus, arterial hypertension, impaired renal function, and prehospital delay.

Results

For this study, we evaluated 36,643 patients with STEMI of the MITRA Plus registry. 24,471 (66.8%) of those patients were male and 12,172 (33.2%) were female. STEMI was more often ($P < 0.0001$) complicated by cardiogenic shock in female patients (12.9%) when compared to male patients (9.3%). This was still true after adjusting for confounding variables (OR 1.19, 95% CI 1.09–1.30).

Clinical characteristics and adjunctive medication:

Baseline characteristics and adjunctive medication of female and male patients with STEMI and cardiogenic shock are shown in Tables 1 and 2. The baseline characteristics of the two groups differed markedly.

Female patients were older ($P < 0.0001$), had more often a history of systemic hypertension ($P < 0.0001$), diabetes mellitus ($P < 0.0001$), and prior stroke ($P < 0.01$). In addition women had more often a prehospital delay of more than 3 h. On the other hand, female patients had less often a history of myocardial infarction ($P < 0.0001$) and percutaneous coronary intervention, or coronary artery bypass graft ($P < 0.001$). There was no difference in concomitant medical treatment with aspirin, clopidogrel, and statins.

Table 1 Baseline characteristics

	Women <i>n</i> = 1574	Men <i>n</i> = 2283	<i>P</i> value
Age (in years)	76.3	68.0	<0.0001
Diabetes mellitus	39.1%	25.2%	<0.0001
Hypercholesterolemia	51.5%	53.0%	0.60
Smoker	17.9%	36.0%	<0.0001
Hypertension	45.3%	37.0%	<0.0001
Prior myocardial infarction	19.9%	25.6%	<0.0001
Prior PCI or coronary artery bypass graft	6.7%	13.2%	<0.001
Prior stroke	5.9%	3.9%	<0.01
Renal insufficiency	8.9%	7.7%	0.18
Anterior myocardial infarction	53.3%	54.1%	0.63
Prehospital delay > 3 h	62.3%	47.8%	<0.0001
Door to balloon time (in min)	90.0	84.0	0.19

Table 2 Acute (<48 h) medical treatment

	Women <i>n</i> = 1,574 (%)	Men <i>n</i> = 2,283 (%)	<i>P</i> value
Aspirin	81.9	82.9	0.41
Clopidogrel	28.9	33.6	0.08
Statins	30.9	33.3	0.31

Reperfusion therapy

49.9% of the female and 62.7% of the male patients (*P* < 0.0001) received early reperfusion therapy within 48 h (Fig. 1). Gender differences in use of early reperfusion therapy disappeared after adjustment for confounding variables (OR 0.92, 95% CI 0.77–1.09).

Clinical events

Hospital mortality was 67.7% in female patients, when compared to 57.5% in male (<0.0001). There was no difference (*P* = 0.24) in re-infarction (6.7% female/5.2% male patients) and stroke (2.8% female/3.7% male patients; *P* = 0.34), whereas a significantly lower (*P* < 0.0001) combined endpoint (hospital mortality/re-infarction and

stroke [MACCE]) was seen in male patients (Table 3). After adjusting for confounding variables the multivariate analysis showed (Table 4) that hospital mortality in female patients did not differ significantly from male patients (OR 1.16, 95% CI 0.98–1.38). Hospital mortality and combined endpoint (hospital mortality/re-infarction/stroke [MACCE]) were lower in female patients with STEMI complicated by cardiogenic shock undergoing reperfusion therapy when compared to female patients not receiving early reperfusion therapy (Table 5). This was still true after adjusting hospital mortality for confounding variables (OR 0.68, 95% CI 0.52–0.90). Hospital mortality was lower in female patients receiving primary PCI when compared to patients receiving no reperfusion therapy (OR 0.40, 95% CI 0.27–0.59), whereas no difference was seen between women receiving thrombolysis and women not receiving early reperfusion therapy (OR 0.83, 95% CI 0.61–1.12). Primary PCI was more effective than thrombolysis in female patients with STEMI complicated by cardiogenic shock (OR 0.46, 95% CI 0.31–0.68).

Discussion

Cardiogenic shock occurs in about 3% of patients with unstable angina and in about 2% with non-STEMI [15, 27]. STEMI is complicated by cardiogenic shock in about 4–7% [15]. In our study, STEMI was complicated by cardiogenic shock in 10.5%. The higher rate of cardiogenic shock in our study may reflect variability in the interpretation of the definition of shock. Commonly, the cutoff point for systolic blood pressure is less than 90 mmHg [16, 28], or less than 80 mmHg [15]. For our study, the diagnoses of cardiogenic shock were made by the treating physicians in patients showing the clinical picture of cardiogenic shock including hypotension (<100 mmHg), heart rate >100/bpm, dyspnoea, reduction in urine output, and basilar pulmonary

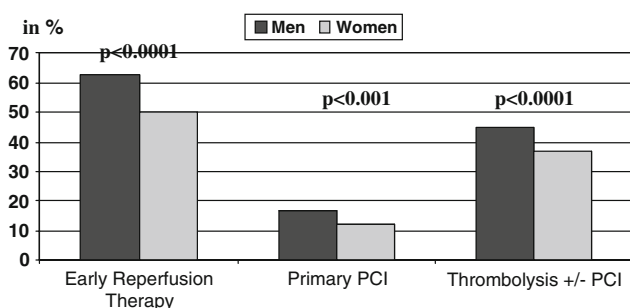


Fig. 1 Rates of early reperfusion therapy

Table 3 Clinical events

	Women <i>n</i> = 1,574 (%)	Men <i>n</i> = 2,283 (%)	<i>P</i> value
Hospital mortality	67.7	57.5	<0.0001
Non-fatal re-infarction	6.7	5.2	0.24
Non fatal stroke	2.8	3.7	0.34
Hospital mortality/Re-infarction/Stroke	70.7	61.1	<0.0001

Table 4 Adjusted and non adjusted hospital mortality in women versus men with STEMI complicated by cardiogenic shock

Hospital mortality in women versus men	OR (95% CI)
Hospital mortality (non-adjusted)	1.55 (1.36–1.78)
Hospital mortality (adjusted for age, previous myocardial infarction, previous stroke, diabetes mellitus, arterial hypertension and impaired renal function and prehospital delay)	1.16 (0.98–1.38)
Hospital mortality (adjusted for primary percutaneous intervention)	1.49 (1.29–1.71)
Hospital mortality (adjusted for age, previous myocardial infarction, previous stroke, diabetes mellitus, arterial hypertension and impaired renal function, prehospital delay and primary percutaneous intervention)	1.17 (0.98–1.39)

Table 5 Clinical events of female patients with STEMI complicated by cardiogenic shock

	Female patients receiving primary PCI <i>n</i> = 193 (%)	Female patients not receiving early reperfusion therapy <i>n</i> = 764 (%)	<i>P</i> value
Hospital mortality	42.5	75.3	<0.0001
Non-fatal re-infarction	4.5	6.1	0.57
Non fatal stroke	5.4	2.6	0.22
Hospital mortality/re-infarction/stroke	48.2	77.4	<0.0001

rales. In addition we included patients needing catecholamine support.

STEMI was more often complicated by cardiogenic shock in female patients (12.9%) when compared to male patients (9.3%). This was still true after adjusting for confounding variables. Women and men were different in their risk profiles: female patients were older by an average of 8 years, had more often concomitant diseases and had more often a prehospital delay of more than 3 h, but were less likely to have a history of myocardial infarction. These results are in line with numerous previous studies [3, 4, 9].

49.9% of the female and 62.7% of the male patients in our study received early reperfusion therapy (thrombolysis and/or percutaneous coronary intervention) within 48 h. However, gender differences in use of early reperfusion therapy disappeared after adjustment for confounding variables. In other studies gender differences in use of early reperfusion therapy also disappeared after adjustment for confounding variables [29, 30]. Adjusted lower rates of early reperfusion therapy in female patients have been reported by other investigators [31, 32]. However, the GUSTO-I trial showed that re-vascularization in shock patients was associated with improved survival [33, 34].

The benefit was independent of several baseline variables, which were generally less favorable in patients with cardiogenic shock who did not undergo re-vascularization. Result of the SHOCK trial registry [35] showed that patients with cardiogenic shock complicating acute myocardial infarction who underwent PCI had lower in-hospital mortality rates than patients treated medically (46.4 vs. 78.0%, $P < 0.001$). This was still true after adjustment for patient differences. These results are in line with our results: early reperfusion therapy was associated with a significant reduction of hospital mortality in female with STEMI complicated by cardiogenic shock, with primary PCI being more effective than thrombolytic therapy.

Despite early reperfusion therapy and supportive medication, hospital mortality in patients with cardiogenic shock is still extraordinarily high. In GUSTO III midterm mortality of patients with STEMI and cardiogenic shock treated with alteplase or reteplase and cardiogenic shock was about 60%. Hasdai et al. [17] reported that in-hospital death rate among patients with cardiogenic shock was greater than 70% from 1975 to 1990, but declined to 59% in 1997.

Consistent with most previous study [3–5] unadjusted rates of hospital mortality after STEMI were higher in

women when compared to men. However, after adjusting for confounding variables the multivariate analysis showed that hospital mortality in female patients with STEMI complicated by cardiogenic shock did not differ from male patients. No gender differences in adjusted mortality after STEMI have already been reported by other investigators [5, 6], whereas the GUSTO-I angiographic study [36] found gender to be an independent predictor of 30-day mortality.

In summary, primary early reperfusion therapy is associated with a significant reduction in hospital mortality in female patients complicated by cardiogenic shock. Primary PCI is the therapy of first choice in those patients. Therefore, efforts should be made to establish a network between hospitals with and without angioplasty facilities to improve hospital and transportation logistics to keep the time loss from admission to primary PCI as short as possible.

Limitations

In the MITRA Plus registry treatment was left to the discretion of the physicians. This could result in selection bias, which cannot be fully eliminated by multivariate analysis.

Conclusion

In women, STEMI was more often complicated by cardiogenic shock when compared to men. However, the use of early reperfusion therapy did not differ between the sexes. Primary PCI was associated with the best outcome in female patients with STEMI complicated by cardiogenic shock and is therefore the therapy of choice.

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