Gender differences in the treatment of patients with ST-elevation myocardial infarction: implication for the re-evaluation of revascularisation strategies in elderly females

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Summary

There is scarce information about gender differences in clinical characteristics and the treatment of patients with ST-elevation myocardial infarction (STEMI).

Objectives: The aim of this study was to assess gender differences regarding risk factors and hospital treatment of STEMI patients in different age groups.

Design and Methods: This study included 655 consecutive unselected patients with STEMI from Estonian Myocardial Infarction Registry, who were admitted to the Tartu University Clinics between January 1, 2001 and December 31, 2003. Patients transferred from other hospitals were excluded. The patients were stratified into two age groups: <75 years and ≥75 years.

Results: In comparison with male patients, female patients presented diabetes, hypertension and prior chronic heart failure more often ($p < 0.05$). There was no gender difference in the usage of evidence-based medications in both age groups, except for ACE-inhibitors. More frequent treatment with ACE-inhibitors in females ($p < 0.05$) might mainly be explained by a particular risk profile in this group. Older female patients were less frequently treated with thrombolysis than older male patients and no primary percutaneous coronary intervention (PCI) was performed for revascularization in this group either.

Conclusion: This study points towards the need to re-estimate reperfusion therapy of elderly females ≥75 years old with STEMI in our hospital. Most probably, primary PCI as an effective and safe strategy of revascularisation could be proposed for elderly females who have frequently elevated blood pressure and, therefore, are more prone to intracranial haemorrhage related to thrombolysis.

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In Estonia, cardiovascular disease (CVD), including acute myocardial infarction (AMI), is the main cause of death, accounting for more than 50% of all causes of death [1]. Developed countries have shown marked decline in coronary artery disease during the past three decades [2,3], but Estonia has not [4]. At least partly, this change is explained by growing effectiveness of the treatment of AMI [3,5]. In the Estonian health care service, regular evaluation of treatment modalities and outcomes, and subsequent use of this as a basis for systematic improvement efforts, has not previously been a standard procedure. To get precise information about every-day clinical practice, to achieve a systematic approach in the management of patients with AMI, and to improve treatment quality, the Estonian Myocardial Infarction Registry (MIR) has been created in the year 2001. MIR is a prospective multicentre Estonian Internet-based secure registry investigating the current treatment of AMI in the hospitals.

Gender differences in the management and outcome of patients with AMI have been investigated in a numerous epidemiological and clinical studies, but the results have been inconsistent [6–10]. Also, the existence of gender bias in the delivery of cardiac care is controversial [8]. Some studies have demonstrated that women are less likely to be given thrombolysis and to un-

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dergo invasive coronary interventions than men [11–14], whereas others have found that treatment selection and referral patterns are remarkably influenced by age [15,16]. However, little attention has been given to gender differences in risk profile and treatment strategies of patients with ST-elevation myocardial infarction (STEMI).

This retrospective descriptive analysis within 2001–2003 was undertaken in two age groups (<75 and ≥75 years old) to estimate gender differences in baseline characteristics and management of patients admitted to the Tartu University Clinics with STEMI, based on MIR data.

Design and Methods

Patient selection

This study included 655 consecutive unselected patients with STEMI from the MIR in Estonia, who were admitted to the Tartu University Clinics (the referral centre of tertiary care) between January 1, 2001 and December 31, 2003. The Tartu University Clinics is a hospital with 49 wards and 1030 beds, and with the resources for angiography and revascularization during working hours 5 days a week. The registry was initiated in January 2001 in the University hospital. For this study, patients transferred from other hospitals were excluded. The patients were stratified into two age groups: <75 years and ≥75 years.

Diagnostic criteria

The criteria for the AMI diagnosis in the MIR are based on a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction [17]. AMI criteria are typical rise and fall of biochemical markers (troponin T, CK-MB mass) and one of the following: (a) ischemic symptoms; (b) development of pathologic Q waves; (c) ECG changes indicative of ischemia. In addition, for patients who died and for whom no cardiac markers were obtained or cardiac marker(s) were negative because of the short time of attack onset, the presence of new ST-segment elevation and new chest pain were considered to meet the criteria for AMI. STEMI was defined for this study if on admission ECG ST-segment elevation of ≥1 mm in 2 or more contiguous leads, or a new left bundle branch block presented. The onset of chest pain or the latest intensified or prolonged discomfort sensation that led to the consultation of medical services was defined as the onset of STEMI. Prehospital delay was defined as the time interval between the onset of STEMI and hospital arrival. Chronic heart failure was defined as New York Heart Association class heart failure II to IV.

Data collection

Information on a prespecified form that comprised 78 variables with definitions was completed by physicians at discharge or, if a patient died, on the day of death. The form comprised personal identification data, risk factors, symptoms, ECG description, complications during the hospital stay, pharmacological treatment, interventional procedures, a peak of biochemical markers, cholesterol values, discharge diagnosis according to International Classification of Diseases Tenth Revision (ICD-10) [18], mortality, the date of admission and discharge. The data completeness in the MIR was ascertained by regular review of the discharge lists of the hospital. Records of patients with ICD-10 codes of I21-22, present on the list of discharge but not in the registry, were checked and evaluated for registration.

Statistical analysis

Data are expressed as mean ± SD, or median for continuous variable, and as percentages for categorical variables. Comparisons between the study groups were performed using a *t*-test or the Mann–Whitney *U*-test for continuous variables and the chi-square test for categorical variable. *P*-values <0.05 were considered significant. These statistical analyses were done utilizing the Statistica 6 program.

The study was conducted according to the principles of the Declaration of Helsinki.

Results

Baseline characteristics

From 655 patients 60% were men, and 40% – women. The mean age was 63.6 ± 12.5 years for men and 74.2 ± 10.6 years for women ($p < 0.05$). Among <75 year-old patients, 73% were men, and 27% – women. Among ≥75 year-old patients, 35% were men, and 65% – women.

Women in both age groups were more often diabetic when compared to men, and the difference between the age groups was strikingly high (35.0% in women and 5.2% in men, $p < 0.05$) (Table 1). Hypertension, another risk factor of coronary artery disease, was more prevalent in women as well ($p < 0.05$ for both age groups).

In comparison with male patients, hyperlipidemia was more often present in female patients <75 years old ($p < 0.05$). In comparison to men, smoking was less prevalent among women, and this difference reached statistical significance in younger patients (12.9% *versus* 42.3% in the

Table 1.
Baseline characteristics of STEMI patients

	<75 y			≥75 y			Men <75 y vs men ≥75 y	Women <75 y vs women ≥75 y
	Men N = 319 (%)	Women N = 116 (%)	P	Men N = 77 (%)	Women N = 143 (%)	P	P	P
Smoking	42.3	12.9	<0.05	5.2	3.5	NS	<0.05	<0.05
Diabetes	14.4	27.6	<0.05	5.2	35.0	<0.05	<0.05	NS
Hypertension	43.2	59.5	<0.05	41.6	66.6	<0.05	NS	NS
Hyperlipidemia	56.1	68.1	<0.05	37.7	45.5	NS	<0.05	<0.05
Prior MI	24.7	24.1	NS	35.1	44.1	NS	NS	<0.05
Prior chronic heart failure	17.5	33.6	<0.05	44.1	60.8	<0.05	<0.05	<0.05
Typical symptoms	88.7	81.9	NS	89.6	81.8	NS	NS	NS
Anterior MI	46.4	45.7	NS	44.2	54.5	NS	NS	NS
Q-wave MI	74.9	65.5	NS	70.1	67.8	NS	NS	NS

y – years; MI – myocardial infarction.

groups <75 years old, $p < 0.05$) (Table 1). Also, female patients had more often chronic heart failure when compared to male patients in both age groups.

There was a slight trend towards the more frequent presence of atypical symptoms in women but this did not reach statistical significance in either age groups. There was no significant delay in women compared to men in seeking medical care after the onset of symptoms (data not tabulated). No difference between the anterior location of AMI was detected in both age groups.

Reperfusion treatment

In the age group <75 years, the usage of thrombolysis was equal in female and male patients (38.8% and 35.7%, respectively). Thrombolysis was somewhat less used in elderly men (28.6% *versus* 35.7%, p = NS), but significantly less in older women when compared to those <75 years of age (in 16.8% *versus* in 38.8%, respectively, $p < 0.05$). Primary precutaneous coronary intervention (PCI) was less frequently performed in older males and females when compared to those <75 years of age ($p < 0.05$). There was a slight trend towards less utilization of primary PCI in younger women as compared to men of the same age. While there was a lower reperfusion rate with primary intervention in elderly men (1.3% and 15.7% in <75 years of age, $p < 0.05$), no patient in the older female group was treated by PCI. Altogether, the percentage of patients who received reperfusion therapy was higher in elderly men when compared to women of the same age (29.9% *versus* 16.8%, respectively, $p < 0.05$). In the age group <75 years, reperfusion therapy was performed in 51.4% of men and 47.4% of women ($p > 0.05$). In general, reperfusion therapy was less frequently used in elderly patients (Table 2).

Concomitant medical treatment

ACE-inhibitors was the only group of drugs during hospitalization which was more often prescribed for women irrespective of their age: in the female group <75 years of age 80.2% received ACE-inhibitors (in comparison to 70.1% of men), and in the group ≥75 years of age 75.5% were treated with ACE-inhibitors, as compared to 62.3% in the male group ($p < 0.05$ for both age groups).

Although statins were significantly less often used in both elderly groups when compared to younger patients ($p < 0.05$), no gender differences in the treatment with aspirin, anticoagulants, beta-blocking agents, or Ca-antagonists were revealed (Table 2).

In-hospital mortality

Although there was a tendency towards higher mortality of older women and men when compared to the younger age groups, in-hospital mortality demonstrated no significant differences between the study groups (Table 2).

Discussion

In accordance with previous studies, our study also shows that women and men suffering from STEMI are different in their risk profiles: women were older than men; women in general had a higher prevalence of systemic hypertension, diabetes mellitus and chronic heart failure [14,16, 19,20]. Consistent with most previous investigations, the prevalence of cigarette smoking was more common in men [13,16,19]. More frequent treatment with ACE-inhibitors in women ($p <$ 0.05) is apparently explained by higher prevalence of systemic hypertension and pre-existing

Table 2.
In-hospital treatment, procedures and mortality of STEMI patients

	<75 y			≥75 y			Men <75 y vs men ≥75 y	Women <75 y vs women ≥75 y
	Men $N = 319$ (%)	Women $N = 116$ (%)	P	Men $N = 77$ (%)	Women $N = 143$ (%)	P	P	P
Aspirin	94.4	94.0	NS	92.2	93.0	NS	NS	NS
Anticoagulants	93.4	92.2	NS	91.0	92.3	NS	NS	NS
β-blockers	73.7	71.6	NS	63.6	67.8	NS	NS	NS
Ca-antagonists	19.7	27.6	NS	22.1	22.4	NS	NS	NS
ACE-inhibitors	70.1	80.2	<0.05	62.3	75.5	<0.05	NS	NS
Statins	58.3	56.0	NS	27.3	21.7	NS	<0.05	<0.05
Thrombolysis	35.7	38.8	NS	28.6	16.8	<0.05	NS	<0.05
Primary PCI	15.7	8.6	NS	1.3	—	NS	<0.05	<0.05
Coronarography	58.6	49.1	NS	22.1	7.7	<0.05	<0.05	<0.05
PCI	43.6	29.3	<0.05	14.3	4.2	<0.05	<0.05	<0.05
Echocardiography	87.1	86.2	NS	85.7	73.4	<0.05	NS	<0.05
In-hospital mortality	8.2	12.9	NS	14.3	21.7	NS	NS	NS

y – years; PCI – percutaneous coronary intervention.

chronic heart failure in this group. The concomitant medical treatment was not underused in women of any age. As there is no evidence that women obtain less benefit from long-term usage of evidence-based medications than men after AMI, these medications should be applied equally in men and women. In this respect, medical management of AMI-patients in our hospital followed the treatment guidelines of STEMI patients [21].

Despite these baseline differences, clinical manifestations of STEMI in women did not differ from those in men. Although women presented somewhat more frequently with atypical symptoms in the early phase of STEMI, there was no significant delay in comparison with men in seeking emergency attention. In this study, we did not attempt to identify a subgroup of ideal candidates for thrombolysis and primary PCI, and all patients with suspected STEMI were considered to be equally eligible for reperfusion therapy. Despite this, women ≥75 years old were only about half as likely as men to receive thrombolysis. The reasons for the lower rate of thrombolysis are unclear. It does not reflect increased use of primary PCI among elderly women because there was no use of this therapy during the study period at all. From the previous experience, it is clear that women with AMI benefit from thrombolysis [22, 23]. However, advanced age, female gender, prior hypertension, systolic and diastolic hypertension on admission are known to be significant predictors of intracerebral hemorrhage [24–26], and therefore significant concern remains worldwide in the usage of thrombolysis in elderly hypertensive women. Regarding the presenting symptom complex, the presence of atypical symptoms, a recognized feature of AMI in women [27], may have lowered the initial of suspicion, and therefore, the use of thrombolysis. However, elderly women in this study were not to receive emergent PCI during the early phase of STEMI, as well. There was also a tendency to lower the usage of primary PCI for revascularization in younger women compared to men. This relatively less frequent utilization of primary PCI in women may have stemmed from gender bias, or from their other features that rendered emergency intervention in women less compelling. It should be noted that no gender-related disadvantage has been demonstrated in women treated with primary PCI [28,29]. Similar hospital mortality has been demonstrated in women and men who underwent PCI for AMI, though it was higher in patients aged over 75 years than in patients aged under 75 years [28]. The GUSTO II-B PCI substudy have demonstrated that women (mean age 68.6 ± 11 years) derived a greater absolute benefit from direct PCI than men. Thus, it has been concluded that in institutions where PCI is readily available, women with STEMI who are at higher risk for intracerebral hemorrhage following thrombolytic therapy should be referred for direct PCI [29]. Summarizing revascularization issues, even when considering physicians' concern about safety issues while initiating thrombolysis in the elderly (and frequently hypertensive females) in this study, underutilization of any strategy of revascularization in this group of patients has no clinical explanation and may eventually be a contributor to the worse prognosis in women ≥75 years.

Study limitations

As single-centre data were used, our data might not be representative not only of other countries, but of other centres in Estonia as well. Also, a relatively small sample size reduced the power of subset analysis and precluded the investigation of potentially important interactions. Finally, because the assessment of risk factors was not exhaustive and no adjustment for risk factors was performed, this study might give only a partial insight into the multitude of variables that influence how, when and why patients with STEMI are treated and subsequently managed.

Conclusion

It is still a major problem in Estonia that the administration of thrombolytics and primary precutaneous coronary intervention (PCI) are reduced in elderly patients, and particularly in elderly women. Patients admitted to the hospital with ST-elevation myocardial infarction should be offered optimal treatment, irrespective of age and sex. Most probably, primary PCI as effective and safe strategy of revascularisation could be proposed for elderly women who have frequently elevated blood pressure and, therefore, are more prone to intracranial haemorrhage related to thrombolysis.

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