Comparison of management and 30-day mortality of acute myocardial infarction in men versus women in Estonia

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Objective — There is conflicting information about gender differences in clinical features, management and outcome after acute myocardial infarction (AMI). The objective of the study was to compare the baseline characteristics, management and 30-day mortality of AMI in men and women in Estonia.

Methods — This study included consecutive unselected patients from the Myocardial Infarction Registry (MIR) in Estonia, who were admitted to a university hospital between January 2001 and February 2002. Logistic regression analysis was used to estimate crude and adjusted odds ratios (OR) with 95 percent confidence intervals (95% CI).

Results — The study included 228 men and 167 women. Women were older than men (73.49 ± 10.95 vs. 65.63 ± 12.60, p < 0.000), and had more comorbidities. After age-adjustment, the higher prevalence of comorbidities, like diabetes (age-adjusted odds ratio [OR] 2.48, 95% confidence intervals [CI] 1.45-4.24), hypertension (OR 1.78, 95% CI 1.15-2.76) and history of congestive heart failure (OR 2.14, 95% CI 1.32-3.46) in women was preserved. Women were more frequently treated with diuretics (OR 2.68, 95% CI 1.69-4.25) and less frequently with statins (OR 0.61, 95% CI 0.39-0.96), after age-adjustment. Although thrombolytic therapy, coronary angiography and angioplasty were performed less frequently in women, these differences disappeared after age-adjustment. Female gender was not an independent predictor of 30-day mortality after AMI, crude OR was 1.39, 95% CI 0.80 to 2.41, adjustment for age and other covariates reduced OR to 0.98, 95% CI 0.44 to 2.20.

Conclusions — Among AMI-patients, age but not gender is an important determinant of care and early mortality. (Acta Cardiol 2004; 59(3): 275-281)

Keywords: acute myocardial infarction – gender – mortality – management.

Introduction

In Estonia, as in most countries, cardiovascular diseases are the leading cause of death in men, as well as in women.

There is conflicting information about gender differences in clinical features, management and outcome after acute myocardial infarction (AMI) in the era of thrombolytic therapy. Some studies have found less frequent use of thrombolysis and invasive procedures in women than in men1-6, whereas other studies found that treatment selection and referral patterns are influenced by age7,8. The prognosis of women with myocardial infarction has been much discussed over the last few years. Generally women are considered to have a worse prognosis early after AMI3,6,9. Recent data has shown that only women at younger ages have higher short-term mortality than men of the same age7,10-12. There is no such data available in Estonia. This study assessed gender differences in baseline characteristics, management and 30-day mortality of AMI among unselected consecutive patients admitted to a university hospital in Estonia.
Materials and methods

PATIENT SELECTION

This study included consecutive unselected patients from the Myocardial Infarction Registry (MIR) in Estonia, who were admitted to the Tartu University Clinics (referral centre of tertiary care) between January 2001 and February 2002. The MIR is an Internet-based secure database for the collection of data on patients with AMI who have been treated in the hospital. The registry was initiated in January 2001 in the university hospital. This is a hospital with 50 wards and 1053 beds. Exclusion criteria for this study included transfer from another hospital (to avoid tertiary referral bias) and development of AMI after coronary bypass grafting or invasive cardiac procedures.

DEFINITIONS

The criteria for the AMI diagnosis were based on a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. AMI criteria were typical rise and fall of biochemical markers (troponin T, CK-MB mass) and one of the following: a) ischaemic symptoms; b) development of pathologic Q waves; c) ECG changes indicative of ischaemia (ST-segment elevation or depression, T-wave inversion). 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.

DATA COLLECTION

Information on a prespecified form that comprises 78 variables with definitions was completed by physicians at discharge or, if the patient died, on the day of death. The form comprises personal identification data, risk factors, symptoms, ECG description, complications during the hospital stay, pharmacological treatment, interventional procedures, peak of biochemical markers, cholesterol values, discharge diagnosis according to International Classification of Diseases Tenth Revision (ICD-10), mortality, date of admission and discharge. The data completeness in myocardial infarction registry 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.

MORTALITY FOLLOW-UP

Mortality rates at 30 days were assessed by matching the personal identification number of patients with the Estonian Population Registry, which includes the vital status of the population of Estonia.

STATISTICAL METHODS

The continuous variables are presented in tables as mean ± SD. Differences between categorical variables were tested by Pearson chi-square statistic; continuous variables were compared by t test. Logistic regression analysis was used to estimate crude and adjusted odds ratios (OR) with 95 percent confidence intervals (95% CI).

Baseline characteristics and in-hospital complications in women and men were compared first without adjustment, and then with adjustment for age.

In-hospital management was compared between women and men, first without adjustment, then with adjustment for age and finally with adjustment for age and other covariates.

Thirty-day mortality in women and men was first compared without adjustment, then with adjustment for age alone, and finally with adjustment for age and other covariates with and without the addition of medications. P ≤ 0.05 was considered statistically significant. All analyses were performed with the STATA programme.

Results

BASELINE CHARACTERISTICS

Baseline characteristics are shown in Table 1. Of 395 patients, 167 were women (42.3%). As expected, women were significantly older than men (mean age, 73.5 years vs. 65.6 years p < 0.000). Women had more comorbidity. After adjustment for age, what remained significant was the prevalence of diabetes, hypertension and history of congestive heart failure. The initial cholesterol values were higher in women. Women had a longer delay from pain to admission (within 4 hours of pain onset, 50% of men were admitted vs. 38.3% of women p = 0.024). Also the mean time from pain onset to thrombolysis was slightly longer in women than in men (4.32 hours vs. 3.46 hours, p = 0.09).

IN-HOSPITAL COMPLICATIONS

The rate of in-hospital complications (Table 2) was similar in both genders, except for cardiogenic oedema.
After adjustment for age the difference disappeared, only reinfarction tended to be more frequent in men than in women (OR 0.30, 95% CI 0.08-1.15, p = 0.08).

IN-HOSPITAL MANAGEMENT

The ORs of in-hospital management are shown in Table 3. Women were less often treated with clopidogrel, glycoproteins IIb/IIIa inhibitors, and statins but more often treated with digitalis and diuretics. After age-adjustment, the difference that remained, was that women were treated more often with diuretics and less often with statins. The other medication used was similar for both sexes. Further adjustment for age and other covariates did not significantly change these ORs. Thrombolytic therapy was less frequently used in women than in men, a difference that already disappeared after age-adjustment.

Coronary angiography and percutaneous transluminal coronary angioplasty (PTCA) were performed less frequently in women than in men, these differences were lost after adjustment for age alone. Performance of coronary artery bypass graft surgery (CABG)
was infrequent for both sexes. Primary PTCA was rarely performed (4.8% of men and 0.6% of women, p = 0.002). Insertion of a permanent pacemaker (4.8% versus 1.2% in men and women, respectively, p = 0.031) was infrequent in both sexes.

MORTALITY

Thirty-day mortality was 13.2% in men and 17.4% in women (p = NS), unadjusted odds ratio in women compared with men was 1.39 (95% CI, 0.80 to 2.41). Adjustment for age reduced odds ratio to 1.03 (Table 4). Further adjustment for age and other covariates further reduced the odds ratio. Additional adjustment for other covariates of treatment (thrombolysis, PTCA, beta-blockers, aspirin and ACE inhibitors) revealed similar results (data not tabulated). When patients were examined by age group, women younger than 65 years of age tended to have a higher mortality than men (Fig. 1).

DISCUSSION

Baseline characteristics and in-hospital management

Results of our study are in accordance with previous studies which have shown that women and men were different in their risk profiles: women were older, had a higher prevalence of hypertension, diabetes mellitus, history of congestive heart failure, and higher cholesterol values. Some of the cholesterol measurements might have been done after 24 hours of hospitalization, making the results less reliable.
The treatment of AMI should be the same in women and men because multiple trials have shown equal benefits for both sexes. However, some studies have found a management bias — women were less likely to be treated with aspirin, beta-blockers, but more likely with digitalis. Many reports have shown medical management similarity for both sex groups after age or covariates adjustment. In the present study, after adjustment for age we found no evidence for differences in the use of treatments for AMI, except diuretics and statins. Diuretics were used significantly more frequently in women than in men, probably due to a greater prevalence of congestive heart failure and cardiogenic oedema in women. The reason why women were treated less with statins is unclear. After further adjustment for age and covariates, it was not significant. At the same time, the initial cholesterol values were higher in women. It may be that in younger women, not older ones, have a real gender gap.

With regard to thrombolysis treatment, our findings produced the same results as previous studies. Differences disappeared after adjustment for age and clinical variables. Several studies have shown that women were less likely to receive thrombolysis even after adjustment for ineligibility due to higher age, comorbid conditions, and late arrival. The more significant presence of atypical symptoms, a recognized feature of AMI in women, may have lowered the initial index of suspicion and therefore the use of thrombolysis. In this study the time from pain onset to arrival was longer in women, but there were no differences in the presence of typical symptoms (83.3% in men vs. 78.4% in women, p = 0.19).

Women had undergone less coronary angiography and revascularization than men. These differences disappeared after age adjustment. Our findings are in accordance with studies reporting similar rates of these procedures in men and women, but differ in this regard from others.

IN-HOSPITAL COMPLICATIONS AND 30-DAY MORTALITY

Mahon et al. reported higher complication rates in women including left ventricular failure, reinfarction, and atrial fibrillation after adjustment for age. Others have also found more in-hospital complications in women. In our study, both groups had the same rate of in-hospital complications. Men tended to have more reinfarction, after age-adjustment. This may be due to more frequent intra-arterial manipulations. Eight out of 10 reinfarctions in men were connected with angiography or PTCA. It should be noted that the occurrence of cardiogenic shock in our population was more frequent than the other studies have shown. The reasons for these differences are not clear. One explanation might be the high percentage of prior heart failure in this unselected study group.

Another consideration could be that an emergency medical aid system in this area is well organized, so that the patients who would usually die outside of the hospital or in the emergency room reach the intensive care or coronary care unit in time. Unfortunately, there is a lack of data to support this idea.

Based on the Tallinn Acute Myocardial Infarction Registry data collected according to the MONICA protocol, there was no in-hospital mortality difference between men and women aged 25-64 years for the period 1991-94 (11.9% in men vs. 12.6% in women). Among unselected consecutive patients with AMI, our study showed similar 30-day mortality rates in men and women before adjustment. There was slightly higher mortality in women, but this was insignificant. Female gender was not an independent predictor of mortality after age and covariates adjustment. There is conflicting data about gender differences in early mortality of AMI patients after adjustment for age and other prognostic factors. Some studies have found a similar outcome in men and women after such adjustment, whereas others failed to show the impact of age and risk factors on the higher mortality rates in women. In this study, women under the age of 65 years had a mortality rate that was almost twice as high as that of men (12.9% vs. 6.0%, respectively). This result did not reach statistical significance probably due to the small sample size. It is supposed that the reason lies in a higher rate of comorbid conditions in younger women compared with men. In the present study, women under the age of 65 years had a mortality rate that was almost twice as high as that of men (12.9% vs. 6.0%, respectively). This result did not reach statistical significance probably due to the small sample size. It is supposed that the reason lies in a higher rate of comorbid conditions in younger women compared with men. For example, diabetes has been found to negate the protective effect of female sex against coronary heart disease and death from cardiovascular disease and to be a stronger prognostic factor after MI in women than in men. One explanation is that acute coronary ischaemia is less typical in women than in men, especially at younger ages, and
it is possible that milder cases of MI are more often missed in women\textsuperscript{7,10}. A recent population-based study has suggested that the age-gender mortality interaction among patients with AMI may be attributable to selection bias or a survivor effect arising from gender differences in the rates of out-of-hospital deaths before AMI presentations\textsuperscript{30}. Studies from the Scottish and Glasgow MONICA project have found that higher in-hospital mortality among younger women may be due to a difference in pre-hospital mortality between younger men and women, with more women dying after hospital arrival\textsuperscript{31,32}.

Vaccarino et al.\textsuperscript{26} suspected that conflicting information between results of different studies may be explained by differences in patient selection, study design, and methods used.

### Study Limitations

First, the present study was observational and included only patients with AMI who were hospitalised for AMI. All patients who died before reaching the hospital were not included. Secondly, single-centre data was used, for reliable representation we need replication from other centres. Thirdly, a relative small sample size reduced the power of the subset analysis and precluded the investigation of potentially important interactions.

### Conclusions

There are gender differences in risk profiles among AMI-patients. Our study suggests that age is a more important determinant of the management and outcomes in patients with AMI than gender. Treatment differences in men and women largely reflect an issue of “age bias” rather than “gender bias”. The female gender is not an independent predictor of early mortality after AMI.

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