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ORIGINAL ARTICLE

**JOURNAL of  
CARDIOLOGY**

Official Journal of the Japanese College of Cardiology

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# Trends in gender difference in mortality after acute myocardial infarction<sup>☆</sup>

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Received 17 May 2008; received in revised form 5 July 2008; accepted 8 July 2008

Available online 16 September 2008

## KEYWORDS

Myocardial infarction;  
Treatment;  
Prognosis;  
Reperfusion;  
Stent

## Summary

**Background:** Progress in management of acute myocardial infarction (AMI) might have changed the effect of gender on mortality.

**Methods:** From May 1981 to November 2002, 1984 consecutive patients with AMI underwent emergency coronary angiography. They were divided into three groups in chronological order: group I (1981–1988,  $n = 564$ ); group II (1989–1995,  $n = 678$ ); and group III (1997–2002,  $n = 742$ ). Multi-variable analysis was performed using Cox's proportional hazard regression, adjusting baseline clinical and angiographical variables.

**Results:** There were 405 women (20%). Thrombolysis was most frequently performed in group I (50%), balloon angioplasty in group II (71%), and stent in group III (66%), with no difference in the allocation of reperfusion therapy between men and women. Three-year mortality was significantly higher in women than in men in group I (27% vs 18%,  $p = 0.03$ ) and group II (23% vs 15%,  $p = 0.048$ ). In group III, there was no significant difference in 3-year mortality (12% vs 10%,  $p = 0.66$ ) between women and men. Women were associated with higher age, more diabetes, more hypertension, fewer current smokers, and less previous infarction than men. Multi-variable analysis showed that sex was not an independent predictor of 3-year mortality in the three groups.

**Conclusions:** Women with AMI who were treated mostly with primary intervention using stent in the contemporary era had similar mortality to men.

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<sup>☆</sup> There is no financial support for this study.

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## Introduction

Acute myocardial infarction (AMI) is a leading cause of mortality in women as well as men in developed countries. Since the introduction of reperfusion therapy, several studies have demonstrated beneficial effects of thrombolysis [1]. Primary balloon angioplasty, as compared with thrombolysis, has been shown to decrease mortality after AMI [2]. Outcome after AMI has further improved with contemporary management, including stent implantation and ancillary medications [3]. During recent decades, many studies have reported that women have higher mortality after AMI than men [4–7]. Recently, some studies have reported that benefits from coronary intervention are larger in women than men, and that gender is not a predictor of mortality in patients undergoing primary coronary intervention [8,9]. However, no previous study compared gender difference in mortality after AMI between the thrombolysis era, the balloon angioplasty era, and the stent era. In this study, we investigated the temporal trends in mortality of women and men with AMI.

## Methods

From May 1981 to November 2002, 1984 patients with AMI who underwent coronary angiography within 24 h after the onset of symptoms at Hiroshima City Hospital, a tertiary referral institution, were prospectively registered. AMI was diagnosed by chest pain consistent with ongoing myocardial ischemia persisting longer than 30 min and concomitant electrocardiographic changes. Serum creatine kinase was measured every 3 h for at least 24 h, and peak creatine kinase value had to be more than twice the normal upper limit. They were divided into three groups in chronological order: group I (thrombolysis era: 1981–1988,  $n=564$ ); group II (balloon angioplasty era: 1989–1995,  $n=551$ ); and group III (stent era: 1997–2002,  $n=869$ ).

Emergency coronary angiography was performed in a manner as previously reported [10]. Selective coronary angiography was performed in multiple projections before the initiation of reperfusion therapy. Immediately after diagnostic angiography, reperfusion therapy was performed with coronary thrombolysis or coronary intervention, if appropriate. Not only primary coronary intervention, but also coronary intervention following thrombolytic therapy was categorized as coronary intervention. Coronary intervention was classified into con-

ventional balloon angioplasty and coronary stent implantation. The allocation of thrombolysis or coronary intervention was not randomized and was based on the physician's decision.

All coronary angiograms were reviewed by two angiographers without knowledge of the clinical variables. The perfusion status of the infarct related artery was determined in accordance with the thrombolysis in myocardial infarction (TIMI) study classification [11]. An initially occluded artery was defined as TIMI-0 or TIMI-1 flow before the initiation of reperfusion therapy. Successful reperfusion was defined as TIMI-3 flow on the final shot of the angiography. Multi-vessel coronary disease was defined as  $\geq 75\%$  stenosis in one or more vessels remote from the infarct artery. Collateral circulation was considered to be present if partial or complete filling of the infarct artery distal to the infarct lesion was present.

## Statistical analysis

Categorical data are reported as proportions and continuous data as mean values with standard deviations. Statistical analysis was performed with the chi-square test for categorical variables. The  $t$  test and ANOVA were used for continuous variables. Kaplan–Meier estimates were used to construct a long-term survival curve. Follow-up was achieved for up to 3 years by reviewing a clinical record or a form mailed to the patients or families, determining the vital status of the patients. Differences in 3-year mortality were assessed with the generalized Wilcoxon test. Cox proportional hazards regression was used to obtain odds ratio (OR) and 95% confidence interval (CI) for 3-year mortality. Multi-variable analysis was performed to obtain OR and 95% CI of women for 3-year mortality, adjusting age (model 1) or age, hypertension, diabetes mellitus, current smoking, Killip class, time to angiography, infarct location, initial occlusion of the infarct artery, collateral circulation, multi-vessel disease, and final reperfusion (model 2). We used the JMP statistical package (version 5.0.1 J). A significance level of 0.05 was used and two-tailed tests were applied.

## Results

There were 405 women (20%) and 1579 men (80%). Baseline clinical and angiographic characteristics of women and men in group I, group II, and group III are shown in Table 1. Thrombolysis was most frequently performed in group I (50%), balloon angioplasty in group II (71%), and stent in group III (66%). On the

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