

# Sex differences in case fatality before and after admission to hospital after acute cardiac events: analysis of community based coronary heart disease register

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## Abstract

**Objective**—To determine whether the reported higher case fatality in hospital after an acute cardiac event in women can be explained by sex differences in mortality before admission and in baseline risk factors.

**Design**—Analyses of data from a community based coronary heart disease register.

**Setting**—Auckland region, New Zealand.

**Subjects**—5106 patients aged 25–64 years with an acute cardiac event leading to coronary death or definite myocardial infarction within 28 days of onset, occurring between 1986 and 1992.

**Main outcome measures**—Case fatality before admission, 28 day case fatality for patients in hospital, and total case fatality after an acute cardiac event

**Results**—Despite a more unfavourable risk profile women tended to have lower case fatality before admission than men (crude odds ratio 0.88; 95% confidence interval 0.77 to 1.02). Adjustment for age, living arrangements, smoking, medical history, and treatment increased the effect of sex (0.72; 0.60 to 0.86). After admission to hospital, women had a higher case fatality than men (1.76; 1.43 to 2.17), but after adjustment for confounders this was reduced to 1.18 (0.89 to 1.58). Total case fatality 28 days after an acute cardiac event showed no significant difference between men and women (0.85; 0.70 to 1.02).

**Conclusions**—The higher case fatality after an acute cardiac event in women admitted to hospital is largely explained by differences in living status, history, and medical treatment and is balanced by a lower case fatality before admission.

## Introduction

Incidence rates of coronary heart disease in middle aged men are about three times higher than in women.<sup>1</sup> Conversely, after a myocardial infarction women have been reported to have a higher mortality in hospital, although the results of studies are inconsistent.<sup>2-7</sup> The combination of lower incidence rates and a higher case fatality is paradoxical. No previous study has examined differences in mortality before admission to hospital in detail as a possible explanation for the observed improved survival in men. We determined, firstly, whether the higher case fatality in women is restricted to patients in hospital, and, secondly, whether differences in case fatality before admission together with the adverse risk profile seen in women can explain the paradoxical findings.

## Patients and methods

Data for this study came from the New Zealand centre of the World Health Organisation MONICA (monitoring trends and determinants in cardiovascular disease) project,<sup>8</sup> a community based coronary heart disease register for the period between 1986 and 1992. The study population included all men and women aged 25–64 years who were resident in Auckland and increased from 420 234 in 1986 to 462 993 in 1992.

Auckland is served by four hospitals with coronary care units and a comprehensive emergency ambulance system. All major fatal and non-fatal cardiac events occurring in Auckland citizens were identified. Patients admitted to hospital were registered through active screening of hospital admissions ("hot pursuit" method). Results of tests for cardiac enzymes were extracted from hospital notes and electrocardiograms were copied and subsequently coded according to the Minnesota code.<sup>9</sup> Information on fatal episodes was collected from death certificates, postmortem records, and from relatives by using a questionnaire administered by an interviewer. Case fatality at 28 days for all registered cases was determined from hospital records or by telephone follow up and a review of Auckland death certificates.

The MONICA diagnostic algorithm uses data on symptoms, peak cardiac enzyme activities, electrocardiograms, history of coronary heart disease, and postmortem results to classify events into one of six outcome categories.<sup>8</sup> All events classified as definite acute myocardial infarction, possible fatal acute myocardial infarction, and fatal coronary events with insufficient information for further classification but with death certificate diagnosis of coronary heart disease were included in this study. Case fatality at 28 days was separated into two categories: fatality before admission and fatality within hospital.<sup>10</sup>

Patients were interviewed shortly after the event, usually in the coronary care unit. Relatives were interviewed at home, usually within six weeks of the event. Information on age, living arrangements (single or permanently living with others), history of myocardial infarction, and antecedent angina were recorded. Smoking was classified into three categories: current smokers, who smoked at least one cigarette a week at the onset of symptoms or gave up smoking less than one month before the index event; former smokers, who had abstained from smoking for at least one month before the onset of symptoms; and non-smokers who had never smoked. Patients who were regular cigar or pipe smokers were classified as non-smokers if they did not also report smoking cigarettes. Information on the use of diuretics, antiplatelets, and  $\beta$  blockers within four weeks before the event and administration of thrombolytic therapy in the coronary care unit was also collected. Deaths that occurred in the hospital emergency department were counted as deaths in hospital. Time from onset of symptoms until arrival in a coronary care unit was recorded for patients admitted to hospital.

## STATISTICAL METHODS

The levels of risk factors for both sexes were calculated and compared with the Mann-Whitney U test for continuous variables and the  $\chi^2$  test for categorical variables. The sex differences in case fatality were assessed with logistic regression to give crude odds ratios (95% confidence intervals) for case fatality before and after admission and in total for women versus men. All the risk factor variables were then included in the logistic regression model to assess the effect of sex after

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adjustment for potential confounders. Dummy variables representing the years of study were also included in the model to remove any effect of time. Adjusted odds ratios (95% confidence intervals) for case fatality before and after admission and in total for women versus men were obtained from this model.

A considerable amount of data from before admission was missing for people who died before admission compared with those subsequently admitted to hospital. To assess the effect of this missing data the analyses first used cases with full data on all potential confounding variables; the analyses were repeated after the removal of variables with considerable missing information. A two tailed P value of 0.05 was considered to indicate significance, and all analyses were performed by using SAS version 6.10 for Windows.<sup>11</sup>

## Results

Between 1 January 1986 and 31 December 1992, 7104 patients aged 25-64 years were identified with a suspected acute coronary event. Of these, 5106 met the MONICA project definition for definite myocardial infarction or coronary death; 4028 were men and 1078 women. Univariate analyses of baseline characteristics showed women to have a less favourable risk profile when compared with men (table 1). Within this age restricted group women tended to be older than men. Women were more often living on their own and were

more likely to have a history of angina and to use diuretic drugs within four weeks before the event but less likely to receive thrombolytic therapy. Men were more likely to have suffered a previous myocardial infarction. A higher proportion of women than men were current smokers, although the difference was not significant, whereas more men than women had given up smoking. No substantial differences were observed in the use of  $\beta$  blockers and antiplatelets. The time from onset of symptoms until arrival in a coronary care unit was similar for men and women. Of the fatal cases, significantly ( $P < 0.001$ ) more women (44.4%) than men (32.1%) survived one hour after the onset of their event.

Crude odds ratios (95% confidence intervals) were calculated for both definitions of case fatality (before and after admission) and the two groups combined (total case fatality). These findings were then adjusted by using the available potential confounding variables—age, living arrangement, history of myocardial infarction, history of angina, current and past smoking, use of diuretics,  $\beta$  blockers, and antiplatelets, and the administration of thrombolytic therapy (used only in the assessment of data after admission as it is given only on admission to hospital) (table 2). Women tended to have a lower crude case fatality before admission (odds ratio 0.88; 95% confidence interval 0.77 to 1.02). Adjustment for their unfavourable risk profile, however, increased the effect of sex (0.72; 0.60 to 0.86). After admission to hospital women fared worse than men (1.76; 1.43 to 2.17). Adjustment for potential confounding factors reduced the effect, there being an 18% (0.89 to 1.58) increase in the odds of dying of an acute coronary event remaining after correction for confounding. Total case fatality—that is, the proportion of all patients who died either before or after admission to hospital—tended to be lower in women (multivariate adjusted odds ratio 0.85; 0.70 to 1.02). The dummy variables for year indicated some different levels of effect for some years, but there was no pattern to this effect.

Several analyses were performed to account for the effects of missing values in some variables. For the patients who died before admission to hospital information on use of diuretics,  $\beta$  blockers, and antiplatelets was unknown in over 20% and past and present smoking status was unknown in over 12%. History of myocardial infarction was unknown in 5%. The revised model without these variables gained another 665 cases, leaving only 123 (2.4%) patients with missing data, and gave a sex odds ratio of 0.77 (0.66 to 0.89) (table 2). The analysis of data after admission was not so affected with 204 (6.5%) patients not having complete data. When the variable indicating whether the patient was a former smoker was removed, 88 more patients were included in the analysis, but this changed the results very little. The analysis of total case fatality was affected by missing data similarly to the analysis of data from before admission; the result changed little when the variables given above were removed from the model.

## Discussion

This study found a higher case fatality in women compared with men after admission to hospital after acute cardiac events but a lower case fatality in women before admission. Differences in baseline characteristics largely explain the higher case fatality in women after admission.

This study used patients from a community based coronary heart disease register rather than data only on patients admitted to hospital; the register has been shown to be highly accurate and complete.<sup>1</sup> Although this enabled us to assess results for a wider range of patients and to compare results before and after admis-

**Table 1**—Distribution of baseline characteristics and variables related to infarction in patients with acute cardiac events from 1986 to 1992 by sex. Figures are numbers (percentages) of patients unless stated otherwise

Characteristic	Men (n = 4028)	Women (n = 1078)	P value
Mean (SD) age (years)	54.7 (7.7)	56.2 (7.5)	<0.001
Living alone	897 (22.5)	383 (35.9)	<0.001
Previous myocardial infarction	1091 (27.7)	223 (21.2)	<0.001
Previous angina	416 (10.5)	173 (16.4)	<0.001
Current smoker	1679 (43.5)	473 (46.7)	0.07
Former smoker	1353 (36.1)	257 (26.6)	<0.001
Drug treatment:			
$\beta$ Blockers	664 (18.2)	172 (18.0)	0.86
Antiplatelet drugs	487 (13.2)	126 (12.9)	0.80
Diuretics	601 (16.3)	297 (30.6)	<0.001
Admission to hospital	2446 (60.7)	686 (63.6)	0.08
Thrombolytic treatment	1073 (26.8)	229 (21.4)	<0.001
Median time (25th, 75th centile) to coronary care unit (h)	3.0 (1.8, 6.0)	3.1 (1.8, 5.9)	0.99

**Table 2**—Case fatality and crude and adjusted odds ratios (95% confidence intervals) by sex for acute cardiac events in patients aged 25-64 years, Auckland 1986-92

Detail	Men (n = 4028)	Women (n = 1078)
Before admission:		
Case fatality (%)	39.3	36.4
Crude odds ratio (n = 5106)		0.88 (0.77 to 1.02)
Adjusted odds ratio (n = 4318; 15.4% missing data)*		0.72 (0.60 to 0.86)
Adjusted odds ratio (n = 4983; 2.4% missing data)†		0.77 (0.66 to 0.89)
After admission:		
Case fatality (%)	14.9	22.5
Crude odds ratio (n = 3132)		1.76 (1.43 to 2.17)
Adjusted odds ratio (n = 2928; 6.5% missing data)‡		1.18 (0.89 to 1.58)
Adjusted odds ratio (n = 3016; 3.7% missing data)§		1.16 (0.88 to 1.53)
Total:		
Case fatality (%)	48.3	51.4
Crude odds ratio (n = 5106)		1.13 (0.99 to 1.29)
Adjusted odds ratio (n = 4298; 15.8% missing data)‡		0.85 (0.70 to 1.02)
Adjusted odds ratio (n = 4953; 3.0% missing data)†		0.85 (0.72 to 1.01)

\*Adjusted for age; living alone; history of myocardial infarction; history of angina; current and past smoking; use of diuretics,  $\beta$  blockers, and antiplatelet drugs; years of infarction.

†Adjusted for age; living alone; history of angina; years of infarction.

‡Adjusted for age; living alone; history of myocardial infarction; history of angina; current and past smoking; use of diuretics,  $\beta$  blockers, antiplatelet drugs, and thrombolytic treatment; years of infarction.

§Adjusted for age; living alone; history of myocardial infarction; history of angina; current smoking; use of diuretics,  $\beta$  blockers, antiplatelet drugs, and thrombolytic treatment; years of infarction.

### Key messages

- Women have been reported to have higher case fatality after admission to hospital after myocardial infarction
- Data from a community based coronary heart disease register were used to examine sex differences in case fatality before and after admission
- Women had a higher case fatality after admission but a lower case fatality before admission
- Total case fatality 28 days after an acute cardiac event showed no significant difference between men and women
- The higher case fatality after an acute cardiac event in women admitted to hospital is largely explained by confounding

sion, little angiographic information was available, and previously postulated theories which associated the extent and severity of infarcts to sex related differences in mortality were not assessed.<sup>5</sup> Furthermore, as information on deaths before admission was gathered from relatives, these data were not as complete or possibly as accurate as they were for those admitted to hospital. There is, however, no reason to believe that these missing data were associated with sex and therefore it is unlikely that they will bias the results. The addition of patients with missing data on medical treatment to the analysis made little change to the case fatality ratio, although this analysis required the removal of some variables from the model.

No previous study has examined in detail the relation between sex and mortality before admission to hospital after an acute coronary event. Brett and Madans included deaths before admission in their long term survival study but did not perform separate analyses on this subgroup of patients.<sup>7</sup> Our study shows that women, despite a less favourable risk profile, have a lower case fatality before admission to hospital and therefore an increased chance of arriving in a coronary care unit. This may be explained by more men experiencing a sudden or early death leading to a lower risk cohort arriving in hospital. It has been suggested, however, that women have a longer delay in seeking treatment,<sup>12</sup> resulting in more preventable deaths and a reduced survival before admission. The delay has been associated with women's lower awareness of the risk of coronary heart disease, their less specific symptoms of myocardial infarction,<sup>13</sup> and the higher proportion of women living alone.<sup>14</sup> These factors could adversely influence the outcome in women, and this is supported by the present study as correction for living

arrangements increased the sex difference in survival before admission. Among patients in hospital, however, no difference between sexes was observed in time from onset of symptoms until arrival in coronary care unit, which suggests that the delay in seeking treatment is likely to be fatal before arrival in hospital. Previous studies on patients in hospital revealed a higher crude case fatality among women, and this is supported by our results.<sup>2-6</sup> Adjustment for age and a wide range of different covariates reduced the sex difference in some studies and completely explained it in others.

The observed paradox of a lower incidence of acute myocardial infarction in women and a higher case fatality in hospital is complex. This study shows that the higher case fatality in women after admission to hospital is balanced by their higher survival before admission and is largely explained by their unfavourable risk profile.

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Conflict of interest: None.

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## What information is available on request from drug advertisers in India?

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Drug advertisements rarely give complete information on the product, but advertisers usually offer to give more information on request. We studied how often this request is met and the quality of the information given.

### Methods and results

We studied 87 advertisements in a recent issue of the *Monthly Index of Medical Specialities (MIMS-India)*. Fifty five advertisements offered some more information; in 31 cases further information was offered, in 16 full prescribing information, in two complete

prescribing information, in one detailed prescribing information, and in five further details. We posted a standard letter demanding the offered information to the given address of the 26 pharmaceutical companies that had placed the 55 advertisements for 58 products. Non-responders were reminded in a letter with a certificate of posting after six weeks. Information for 31 products was received after the first letter within three to 35 days (average 20). For a further 13 products a reply was obtained after the reminder letter within four to 89 days (average 21). Information was not made available for the remaining 14 products.

For 13 of the 44 products with further details, the information was in the form of promotional pamphlets with or without the prescribing details; for 11 it was the therapeutic index of the company (a list with some description of all products), for seven promotional booklets, for seven typed or printed text such as a statement of claims, for four package inserts, and for two a newsletter or trial report. We read and evaluated the information against standard,

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