

GENDER DIFFERENCES IN THE TREATMENT OF PATIENTS WITH ACUTE MYOCARDIAL ISCHEMIA AND INFARCTION IN ENGLAND

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Abstract

We conducted a retrospective cohort study based on a case note review to determine whether there are differences in the treatment pathways followed for men and women admitted with acute myocardial ischemia and infarction after adjusting for differences in case mix. Women were as likely as men to receive thrombolysis, but were less likely subsequently to undergo exercise testing (adjusted odds ratio, 0.58; 95% CI, 0.40–0.84) or angiography (adjusted odds ratio, 0.62; 95% CI, 0.39–0.99). Coronary anatomy was the strongest predictor of revascularization regardless of sex. Women with diagnosed cardiac pain are less likely than men to be placed on the investigative pathways that lead to revascularization. Those women who are investigated are as likely as men to undergo revascularization. These findings are independent of the effects of age, angina grade, comorbidity, or cardiac risk factors. Clinicians' and patients' beliefs and preferences about treatment require investigation.

Keywords: Women; Cardiology; Health Services Accessibility

Coronary heart disease (CHD) is the most common cause of death in the United Kingdom (27), killing one in three men and one in four women (6). Many studies have found gender-related differences in the clinical management of CHD

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(3;8;13;14;25;29), both in the United Kingdom and abroad. Women in the United Kingdom are less likely than men to receive medical treatment (7) or to be referred for diagnostic investigations such as exercise testing (15;21). They are also less likely than men to undergo revascularization either by percutaneous transluminal coronary angioplasty (PTCA) or by coronary artery bypass grafting (CABG) (5;19).

There may be many reasons for these gender differences. Most research has included patients with chronic chest pain. The greater frequency of normal epicardial arteries in women with chest pain compared with men, and the lower specificity of electrocardiographic exercise testing (23), may motivate clinicians to attribute anginal symptoms in women to non-cardiac causes and to administer fewer cardiological investigations. In addition, women present with symptomatic coronary disease at a later age than men (16) and may have more associated diseases, making surgery more risky. Finally, coronary anatomy in women may be less suitable for intervention (19). It might be expected that gender differences would diminish in patients admitted to hospitals with acute chest pain thought to be of cardiac origin. In this situation, the immediate risks to the patient are high and treatment strategies are well defined (24).

Previous studies have investigated discrete portions of the clinical pathway in isolation, and so have been unable to provide a comprehensive overview of the points in the pathway at which differences in the management of male and female patients occur. In order to clarify this issue, it is necessary to study the progress of patients from their admission with acute chest pain through potential revascularization.

On admission to hospital with cardiac chest pain, eligible patients should receive thrombolysis (30). Their subsequent treatment depends on the characteristics of their chest pain (10;18;32). Patients who have sustained an uncomplicated myocardial infarction or who have suffered a discrete episode of atypical chest pain and are considered to be at low risk of coronary heart disease tend to be initially investigated with exercise electrocardiograph (ECG) testing (10;32). Echocardiography and isotope scanning increase the accuracy of the results. If investigation confirms the presence of coronary ischemia, then patients undergo angiography to determine the pattern and extent of coronary stenosis. Patients who have had a non-Q-wave myocardial infarction, severe unstable angina, or continuing pain forego exercise testing, but have the other investigations described (18). The decision to refer a patient for subsequent revascularization depends on the result of the angiogram as well as the patient's age, comorbidity, and symptom severity (14).

We therefore compared the treatment of men and women receiving the same working diagnosis who were admitted to five hospitals with acute chest pain between 1993 and 1994.

PATIENTS AND METHODS

Study Group

Patients were identified from routinely available hospital discharge data and their case notes were retrieved from the five hospital medical record departments. The inclusion criteria were that the patient had to be a resident of the local health district (identified by postal code), and admitted as an emergency with a primary discharge diagnosis of acute myocardial infarction or other subacute and chronic ischemic heart disease, including angina and old myocardial infarction (ICD 9 410-414), between April 1, 1993 and March 31, 1994.

Table 1. Information collected

Sociodemographic ^a	Sex, age, date of birth, marital status
Chest pain history ^a	“Typical presentation” was defined as chest pain recorded as typical of ischemia in the case notes. Patients reported grade of angina.
Relevant comorbidity and other risk factors ^a	Congestive cardiac/left ventricular heart failure; chronic obstructive airways disease, past history of stroke, renal failure, diabetes, hyperlipidemia, hypertension, smoking, family history of CHD, history of previous myocardial infarction.
Investigations performed on admission ^a	Cardiac enzymes, ECG
Medical treatment received on admission ^{a,b}	Thrombolysis and/or aspirin
Working and discharge diagnosis ^a	Myocardial infarction, angina, unspecified chest pain, or other. Working diagnosis made on the basis of the history, initial examination, cardiac enzyme levels, and resting ECG performed on admission.
Presence of further pain during admission ^a	Present/absent
Administration ^c and results of investigations ^a	Exercise ECG, echocardiogram, isotope scan, angiography
Occurrence of revascularisation ^c	
Vital status	Alive/dead 12 months after admission

^a Explanatory variable.

^b Response variable.

^c Thrombolysis was both a response and explanatory variable.

Data Collection

A data extraction form was developed by two of the authors (RR and JC) using information from the literature (2;11;12;26;28;31) and published treatment guidelines for angina and myocardial infarction (10;18;29;30;32). It was piloted on 30 sets of case notes. The form was designed to collect information on sociodemographic characteristics, recent and past medical history, and clinical treatment for 12 months after emergency admission (Table 1).

Data were extracted by one of the authors (KLC). It was not feasible to blind her to the patients' sex. The patient's clinical status and the results of investigations were recorded as described in the notes. Relevant normal biochemical values at each hospital were noted. Intra-observer variation was assessed by the data extractor examining the same sets of 20 notes on two occasions 2 weeks apart. For those patients whose case notes could not be found, their age, sex, vital status on discharge, and whether revascularization was performed were extracted from regional flat file data.

Sample Size and Analytical Techniques

Data were coded either as present or absent (absent in the notes, not applicable, not mentioned in the notes, or the result of an investigation was not recorded). Odds ratios were strictly defined as the odds of the known presence of a factor versus “all other” status.

The required sample size was based on the assumption that men would be about one and a half times as likely to receive revascularization (15) as women.

Preliminary data from the regional flat files suggested that there would be about twice as many men in the sample as women. We set the following parameters when performing the power calculation to compare the proportion of men receiving revascularization with the proportion of women in the study: a 90% probability of detecting a significant treatment difference where one really existed and a 5% chance of detecting a difference where there was in fact none. Approximately 510 patients were required. Having found about 1,000 patients from the regional flat files who met our study inclusion criteria, and being uncertain of the detection rate for their case notes, we decided to include all of these patients in the study.

The kappa statistic was used to assess intra-observer reliability for completing the case-note questionnaire on the same records and the χ^2 test was used to compare the distribution of categorical variables in the men and women studied.

Backwards stepwise logistic regression was used to identify any possible independent effect of gender after controlling for other factors (Table 1) associated with clinical investigation and revascularization. These explanatory factors (footnote "a" in Table 1) were derived from the literature (2;10;11;12;18;28;29;30;31). Initially, the statistically independent effects of the variables on the patients' management, excluding the effect that the results of one investigation may have had on the decision to perform another, were studied. This was done because patients may receive various combinations of investigations depending on their mode of presentation. Subsequent analysis took account of the fact that investigations might have been linked clinically, and included the independent effect that the results of investigations performed may have had on patients' treatment. The effects of different combinations of investigations were analyzed in order to reflect alternative treatment pathways.

RESULTS

Data Completeness and Response Bias

Routine data sources identified 1,083 patients eligible for inclusion. Of this number, there were 715 (66%) patients for whom notes had been correctly coded and could be retrieved. Patients whose notes were missing were less likely to have undergone revascularization ($p < .001$) and to be alive at discharge ($p < .001$) (Table 2). The missing female patients were older than those women whose case notes were studied (12 [7.6%] over 90 years compared with six [2.3%] female patients studied, $p < .02$).

Intra-rater Reliability of Form

The intra-observer reliability of extracting information from the case notes was measured on 10 pairs of variables. Complete agreement (kappa = 1) was obtained for six pairs of variables, and kappa ranged from 0.57 to 0.90 for the remaining four pairs of variables.

Characteristics of Patients

Table 3 shows the characteristics of the patients studied. Women tended to be older than men (59% were over 70 years, compared with 37% of men, $p = .001$). Other significant differences between sexes were confined to a higher prevalence of hypertension recorded in women (41% of women compared with 34% of men, $p = .05$), and of smoking recorded in men (77% of men compared with 50% of women, $p = .001$). However, a significantly greater percentage of men (89%) were alive 12 months after admission compared with women (80%) ($p = .001$).

Table 2. Comparison of Characteristics of Eligible Patients Whose Notes Were Studied with Eligible Patients Whose Notes Were Missing^a

	Men studied (n = 456)	Missing men (n = 210)	p-Value	Women studied (n = 259)	Missing women (n = 158)	p-Value
Age, yrs						
30-49	47 (10.3)	9 (4.3)	.02	9 (3.5)	3 (1.9)	NS
50-69	230 (50.4)	108 (51.4)	NS	91 (35.1)	39 (24.7)	<.05
70-89	168 (36.8)	87 (41.4)	NS	153 (59.1)	104 (65.8)	NS
> 90	11 (2.4)	6 (2.9)	NS	5 (2.3)	12 (7.6)	<.02
Intervention performed						
PTCA/CABG	117 (25.7)	19 (9)	<.001	46 (17.8)	7 (4.4)	<.001
Alive at discharge	406 (89)	147 (70)	<.001	208 (80.3)	85 (53.8)	<.001

^a Values are numbers of patients.

Table 3. Patients Admitted as Emergencies with Chest Pain (ICD9 410-414)

	Men (n = 456) (64)	Women (n = 259) (36)	Significance χ^2	df	p-Value
Presentation					
Typical chest pain history	370 (81.1) _b	208 (80.3) _b	0.07	1	.79
Reported grade of angina			11.6	1	.07
Working clinical diagnosis: myocardial infarction	318 (69.7)	171 (66.0)	1.05	1	.31
Working clinical diagnosis: angina	109 (23.9)	69 (26.6)	0.66	1	.42
Working clinical diagnosis: chest pain	7 (1.5)	5 (1.9)	0.16	1	.69
Age, yrs:					
30-49	47 (10.3)	9 (3.5)	10.68	1	.001
50-69	230 (50.4)	91 (35.1)	15.64	1	.001
70-89	168 (36.8)	153 (59.1)	32.99	1	.001
Comorbidity and coronary risk factors					
Heart failure	146 (32.0)	95 (36.7)	1.607	1	.205
Diabetes	8 (1.8)	8 (3.1)	1.34	1	.25
Hypertension	155 (33.9)	107 (41.3)	3.81	1	.05
Chronic obstructive airways disease	92 (20.2)	41 (15.8)	2.06	1	.15
Stroke	46 (10.1)	27 (10.4)	0.02	1	.89
Smoking	352 (77.2)	131 (50.6)	53.38	1	.001
Hyperlipidemia	57 (12.5)	33 (12.7)	0.01	1	.93
Previous myocardial infarction	134 (29.4)	65 (25.1)	1.51	1	.22
Treatment and outcome					
Further chest pain in hospital	88 (19.3)	63 (24.3)	2.5	1	.11
PTCA done	53 (11.6)	31 (12.0)	0.02	1	.89
CABG done	64 (14.0)	15 (5.8)	11.4	1	.001
Alive 12 months after admission	406 (89.0)	208 (80.3)	10.4	1	.001

^a Values are numbers of patients; n = 715.

^b Severity of pain was coded on a standard six-point scale and analyzed using χ^2 test for trend.

Table 4. Adjusted Odds Ratios for the Treatment of Patients Admitted with Chest Pain after Controlling for Clinical and Demographic Variables Described

Procedure	Subsetting	Adjusted effect of sex ^a (odds ratio, 95% confidence interval)	N
Streptokinase given		1.203 (0.75–1.93)	715
Exercise test		0.58 (0.40–0.84)	715
Isotope scan		1.07 (0.62–1.84)	715
Echocardiography		0.82 (0.57–1.19)	715
Angiography		0.77 (0.44–1.33)	715
Angiography	Excluding exercise ECG as an explanatory variable	0.62 (0.39–0.99)	715
Angiography or exercise ECG		0.63 (0.40–0.99)	715
PTCA alone		2.29 (1.26–4.18)	695
CABG alone		0.68 (0.30–1.55)	695
PTCA or CABG		0.68 (0.30–1.56)	695
PTCA or CABG	Only patients with +ve exercise ECG and angiogram	0.99 (0.13–1.99)	75
PTCA or CABG	Only patients with +ve angiogram	0.73 (0.18–3.01)	169

^a The table given the odds ratio for women compared to men, where the male odds of undergoing a procedure = 1. These odds ratios have been adjusted for the explanatory variables shown in Table 1, including age, characteristics of pain, comorbidity, and other risk factors. Abbreviation: N = number of patients.

Predictors of Treatment

Multiple logistic regression was used to analyze the effect of gender on the treatment of patients, after controlling for the possible explanatory variables (Table 4). Logistic regression models were constructed for each of several possible outcomes along the diagnostic pathway. A total of 12 logistic regression models were therefore constructed, and in each model the backwards stepwise technique allowed non-significant explanatory variables ($p > .05$) to be dropped one at a time from the model.

On admission, the administration of thrombolysis to 315 (44%) patients was given on the basis of characteristic presentation rather than on the basis of gender (adjusted odds ratio nonsignificant) (Table 4) (e.g., cardiac enzymes more than twice the upper limit of normal: adjusted odds ratio, 3.49; 95% confidence interval (CI), 2.33–5.23; characteristic ECG: adjusted odds ratio, 2.35; 95% confidence interval 1.26–4.37).

Subsequent treatment varied according to the patient's sex.

Exercise Testing. Two hundred forty-eight men (54%) and 84 women (32%) underwent exercise testing. After controlling for the possible explanatory variables (noted in Table 1), the adjusted odds ratio for women was 0.58 (95% CI, 0.40–0.84), i.e., women were 42% less likely to undergo exercise testing than men. A typical history of chest pain did not significantly predict the use of exercise testing, nor did the working diagnosis (myocardial infarction, angina, unspecified chest pain). The other factor that independently predicted the administration of exercise testing was a young age (30–49 years: adjusted odds ratio, 3.40; 95% CI, 1.00–15.98; 50–69 years: adjusted odds ratio, 4.35, 95% CI, 1.26–15.04) compared with age 70 or more.

Perfusion Scans and Echocardiography. Fifty-eight (13%) men and 31(12%) women had a nuclear perfusion scan and 192 (42%) men and 96 (37%) women underwent echocardiography. After controlling for explanatory variables, the effect of gender was found to be nonsignificant. However, our model could only explain about 7–10% of the variation in the likelihood of undergoing these tests.

Angiography. One hundred eighty (40%) men and 71 (27%) women underwent angiography. The most important predictive factor for angiography was a positive exercise ECG (adjusted odds ratio, 8.01; 95% CI, 4.41–14.55). The likelihood of having an exercise test had already been shown to be gender-dependent. In order to examine the possibility of persistent gender bias affecting the decision to perform angiography, exercise testing as an explanatory variable was excluded from the logistic regression. Women were still found to be nearly 40% less likely to undergo angiography (adjusted odds ratio, 0.62; 95% CI, 0.39–0.99), regardless of whether the patient had a working diagnosis of acute myocardial infarction, angina or unspecified chest pain. When a woman did undergo exercise testing, sex-related differences in her subsequent treatment did not occur and the decision to go on to angiography was again mainly influenced by the results of the exercise test (positive exercise ECG, adjusted odds ratio, 7.59, $p = .04$).

Finally, variations in the treatment pathways leading to angiography were accounted for. The characteristics of the patients' presentation may determine the clinical decision to refer a patient for an exercise test first, or directly for angiography. Female patients with a working diagnosis of cardiac pain were nearly 40% less likely to be placed on either of these pathways (adjusted odds ratio for angiography or exercise ECG, 0.63; 95% CI, 0.40–0.99).

Revascularization. For patients who passed along the treatment pathways, whether via exercise testing and angiography or via angiography only, it was the results of angiography that influenced the decision to undergo revascularization and not gender. Patients were, for example, nearly seven times more likely to undergo revascularization if angiography revealed that there was a greater than 70% stenosis of the left anterior descending (LAD) artery (e.g., adjusted odds ratio of LAD occlusion proximal to the first diagonal 6.97, $p < .001$), and 10 times more likely to receive revascularization if there was disease of the circumflex coronary artery (adjusted odds ratio, 10.26, $p < .001$). Women were more than twice as likely as men to undergo PTCA (adjusted odds ratio, 2.29; 95% CI, 1.26–4.18), but were less likely to receive CABG (adjusted odds ratio, 0.68; 95% CI, 0.30–1.55), although this was not statistically significant ($p = .36$).

DISCUSSION

We have shown that women admitted with acute myocardial ischemia or infarction were less likely than men to undergo investigation. This gender difference affected both noninvasive and invasive investigations. Those women who were investigated were as likely as men subsequently to undergo revascularization. Therefore, the women in our sample did not have access to the investigations that determined the decision to revascularize. These findings were independent of the effects of comorbidity, characteristics of the pain, or coronary risk factors. They were also independent of the effects of smoking. In view of the social class gradient found for smoking status (4), this is a useful proxy for social class in the absence of the availability of accurate and completely collected direct measures such as occupation.

The findings were also independent of age, in contrast to previous results (1). Younger patients in our study were more likely to undergo exercise testing, but the effects of gender remained after adjusting for the effects of age.

We have confirmed previous U.K. findings that sex did not determine thrombolysis administration (31), and U.S. results showing that once women are referred for exercise testing (17) or angiography (22), they are as likely as men to be referred for revascularization. The advantage of our study over previous research is that we have been able to provide a comprehensive clinical picture of current long-term treatment, rather than just a snapshot of isolated stages in the clinical pathway.

Clinicians may assume that the female patients studied were less likely to have chest pain of cardiac origin, which could have resulted in under-recording of their cardiac risk in the case notes. As in any retrospective study, we have relied on the information actually recorded; we have assumed that the variables were recorded in a complete and standardized fashion. We do not know whether clinicians were more easily satisfied by negative answers about cardiac risk factors when interviewing female patients. The effect on our findings can only be assessed in a prospective study.

We were unable to retrieve the notes of nearly 38% of the female patients and nearly 32% of the male patients who fulfilled the study criteria. The information recorded could be biased because the sample studied was systematically different from the missing patients. However, the study sample was younger, significantly more likely to have revascularization, and less likely to die. It is therefore expected to reflect active treatment for both men and women reliably, and so it was justifiable to make comparisons between the treatment of men and women from the study sample.

Our study addressed some of the possible reasons for the gender differences observed in the management of female cardiac patients. One was that women were less likely to undergo exercise testing because it is less specific in women than in men. If this were true, then it might be expected that women would be more likely to undergo perfusion imaging and possibly stress echocardiography in order to retain predictive accuracy (29), or to proceed directly to angiography. However, this was not the case. The second possibility was that clinicians may be reluctant to investigate female patients who are too sick to undergo revascularization. However, the women in our sample did not appear to suffer from greater comorbidity than the men, although they were slightly older.

It may be that the differential treatment is born out of the beliefs and preferences of the clinician or the patient. Clinicians may view coronary heart disease as more severe or coronary surgery as more efficacious in men, even though neither can be shown to be the case (9;23;29). Patients may display sex-related differences in their perception of the severity of their coronary heart disease or in the benefits and risks of treatment (9). Prospective qualitative data collection is necessary to investigate these possibilities.

The treatment pathways for acute chest pain are clearly defined. The results of this study suggest that there is inequitable care for women even with proven myocardial infarction or chest pain thought to be of cardiac origin. We recommend confirmation of our findings by prospective methods.

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