



Does the Patient's Sex Influence Cardiovascular Outcome After Acute Myocardial Infarction?

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■ **OBJECTIVES** To determine whether outcome differences based on the patient's sex occur after myocardial infarction (MI) at a large private hospital.

■ **STUDY DESIGN** We conducted a large cohort study.

■ **POPULATION** Inclusion required hospital admission between January 1, 1998, and June 30, 1999, and a diagnosis of acute MI or subendocardial infarction. The number of patients included in the study was 1669. Data were collected at discharge on age, sex, race, health insurance, hypercholesterolemia, diabetes, smoking, hypertension, and the extent of coronary artery disease.

■ **OUTCOMES MEASURED** The 8 outcomes analyzed were angiogram, angioplasty, stent placement, coronary artery bypass grafting (CABG), mortality, time in the intensive care unit, total length of stay, and combined catheterization procedures.

■ **RESULTS** After adjusting for 7 confounding variables, we found no significant differences between men and women for mortality, ICU time, total hospital time, stent placement, angiogram, angioplasty, or combined catheterization procedures. Men had significantly more CABG (relative risk [RR] 1.96, $P < .01$). Among patients who underwent CABG ($N = 204$), men had significantly more 3-vessel coronary disease (RR 1.44, $P < .01$) and left main coronary artery disease greater than 50% (RR 1.58, $P < .01$). Once we had controlled for the extent of coronary artery disease, we found no difference between the sexes for CABG.

■ **CONCLUSIONS** During hospitalization after an MI, most cardiovascular outcomes and process measures are the same for men and women. The greater frequency of CABG in men than in women is explained by men's greater frequency of 3-vessel and advanced left-main coronary disease.

■ **KEY WORDS** Cardiovascular; outcomes; sex; acute; myocardial infarction. (*J Fam Pract* 2002; 51:237-240)

KEY POINTS FOR CLINICIANS

- Unadjusted data reveal that in patients hospitalized for acute myocardial infarction, women experience higher mortality rates and undergo fewer procedures, particularly coronary artery bypass grafting, than men.
- Controlling for several comorbidities and the extent of coronary artery disease eliminates differences between the sexes in this context.

Recent studies have shown that women aged less than 75 years have a significantly higher rate of in-hospital mortality than men after acute myocardial infarction (MI).¹⁻³ A cohort study involving more than 384,000 patients admitted to the hospital for MI found that women aged 74 years or less had a higher mortality rate than men. The mortality rate in women aged less than 50 years was twice as high as that of men in the same age group.² The difference in mortality after an acute MI disappears at age 75 years.^{1,2,4}

Although women are as likely as men to have a positive stress electrocardiogram or stress thallium test after an acute MI, women are referred less often for additional noninvasive testing or cardiac catheterization.⁵ In a study of more than 12,000 patients with acute coronary syndromes, fewer women than men underwent cardiac catheterization.⁵ In hypothetical case studies, physicians shown videotapes of actors playing patients and given hypothetical case studies were less likely to say they would refer the women

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TABLE 1
CHARACTERISTICS OF THE STUDY POPULATION

	Men (N = 1038)	Women (N = 631)	P Value
Age	62.2 + 13.3	68.7 + 13.8	< .05
Race			< .05
White	789 (76%)	482 (76%)	
Black	62 (6%)	67 (11%)	
Asian	3 (0%)	1 (0%)	
Other	184 (18%)	82 (13%)	
Insurance			< .05
Medicaid	14 (1%)	25 (4%)	
Comorbidities			
Hypercholesterolemia	224 (22%)	108 (17%)	NS
Hypertension	444 (43%)	293 (46%)	NS
Smoking	411 (40%)	184 (29%)	< .01
Diabetes	267 (26%)	209 (33%)	< .01

for catheterization than the men. Black women were referred least.⁶

Men are also more likely than women to receive angioplasty or coronary artery bypass grafting (CABG) after acute MI.² Women undergoing CABG have significantly more comorbidities and less favorable patient characteristics preoperatively than do men.⁷ While women and men undergoing CABG have the same type and extent of symptoms overall, women are more likely to have preserved ventricular function and less likely to possess multivessel disease than are men.^{3,7,8}

The purpose of this study was to determine whether sex-related outcome differences existed after being treated for an MI at a large private hospital. We also evaluated how significantly any difference in the extent of coronary artery disease between the sexes would confound the rate of CABG performed after an acute MI.

METHODS

Study Design and Population

This is a hospitalization cohort study using data obtained from the Acute Myocardial Infarction Registry database at TriHealth hospitals in Cincinnati, Ohio. The TriHealth hospital system consists of 3 private hospitals in the greater Cincinnati area. Inclusion criteria for entering the cohort included admission to a TriHealth hospital during an 18-month period between January 1, 1998, and June 30, 1999, and a discharge diagnosis of acute MI or subendocardial infarction. Exclusion criteria included transfer to another local hospital for some of the patient's health care or more than 1 hospitalization for an MI during the cohort time period. Double admissions and transferred patients were rare (N = 7). Individuals were included in the cohort only dur-

ing their hospitalization for the acute MI. Patients exited the cohort at discharge.

Data Collection

Data were collected at hospital discharge on age, sex, race, insurance status, and various comorbidities, including smoking, hypercholesterolemia, diabetes, hypertension, and the extent of coronary artery disease. The 8 outcomes available for analysis included hospital mortality, time in the intensive-care unit, total length of stay, angiogram, angioplasty, stent placement, CABG, and the 3 catheterization procedures combined. For patients who underwent CABG, data were collected on the number of bypassed vessels and the presence of advanced left main coronary disease. Data on demographics, disposition, and length of stay were obtained by means of the hospital registry system. The comorbidity and cardiovascular data collection sheet was typically filled out at discharge, usually by the cardiologist and occasionally by a primary care physician. The presence or absence of comorbidities was determined by the physician who provided the patient data. Each comorbidity was listed on the data sheet with a "yes or no" option.

Analysis

Univariate analysis using chi-square and t-tests were performed that compared sex with mortality, with each procedure, and with each comorbidity. The relationship between the patient's sex and each of the 8 outcomes of interest (adjusted for age, race, insurance, smoking, hypertension, diabetes, and hypercholesterolemia) was investigated by logistic regression analysis for dichotomous variables and survival analysis for time to event variables. The significance of each analysis was set at $P = .01$, based on the Bonferroni adjustment⁹ for multiple comparisons and an overall $P = .05$. Analysis was performed using STATA (STATA

TABLE 2
UNADJUSTED OUTCOMES BY SEX

	Men (n = 1038)	Women (n = 631)	P Value
Hospital mortality	76 (7%)	70 (11%)	< .01
Mean time in ICU	2.1 days	1.9 days	NS
Mean length of stay	5.9 days	6.6 days	< .01
Angiogram	241 (23%)	139 (22%)	NS
Angioplasty	67 (6%)	38 (6%)	NS
Stent placement	346 (33%)	162 (26%)	< .01
CABG	157 (15%)	54 (9%)	< .01
3 catheterization procedures (angiogram, angioplasty, stent)	654 (63%)	339 (54%)	< .01

CABG denotes coronary artery bypass grafting; ICU, intensive-care unit.

TABLE 3
**ADJUSTED RELATIVE RISK
 FOR CARDIOVASCULAR OUTCOME**

Outcome	Relative Risk*
Hospital mortality	0.86 (0.6-1.23)
Time in ICU	0.95 (0.85-1.05)
Angiogram	1.02 (0.80-1.31)
Angioplasty	0.90 (0.59-1.39)
Stent placement	1.04 (0.82-1.32)
Coronary artery bypass graft	1.96 (1.41-2.76)†
Angiogram, angioplasty, or stent	1.04 (0.82-1.28)

* Men compared with women (ie, men who underwent coronary artery bypass grafting were more likely to have more extensive disease).
 † $P < .05$.
 ICU denotes intensive-care unit.

Corporation, College Station, Tex.) and SAS (SAS Institute, Cary, N.C.) statistical software. We estimated that a sample of 1600 patients was needed to detect an absolute difference of 6% in the presence or absence of an intervention between men and women (two-tailed $\alpha = .05$, $\beta = 0.20$).

RESULTS

A total of 1669 patients (631 women, 1038 men) were available for our analysis. Baseline characteristics by sex are displayed in Table 1. Men were significantly younger, less likely to be African American, less likely to be Medicaid insured, more likely to smoke, and less likely to have diabetes mellitus ($P < .05$) than women. In the univariate analysis (Table 2), women had significantly higher rates of hospital mortality ($P < .01$) and diabetes ($P < .01$) and a longer mean length of stay in the hospital ($P = .01$). Men had significantly higher rates of stent placement ($P < .01$) and CABG ($P < .01$).

We found no significant difference between men and women for hospital mortality, time in the ICU, total time in the hospital, stent placement, angiogram, angioplasty, or the 3 catheterization procedures combined in the multivariate analysis (Table 3). Men had significantly more CABG (relative risk [RR] 1.96, 95% confidence interval [CI] 1.41-2.76) than women.

In a separate analysis of patients who underwent CABG ($n = 211$), men had significantly more 3-vessel coronary disease and advanced left anterior descending artery disease (LAD >50%) than women (Table 4). There was no difference between men and women undergoing CABG for either single-vessel or double-vessel coronary artery disease. The extent of coronary artery disease was only known for patients who were catheterized ($N = 1204$). Again comparing sex regarding the risk of CABG, but additionally controlling for the extent of coronary artery disease (LAD >50% and 3-vessel CAD), now reveals no significant increase associated with male sex (RR 1.30, 95% CI 0.82-2.08).

TABLE 4
**EXTENT OF CORONARY ARTERY DISEASE IN PATIENTS
 UNDERGOING CABG, BY PATIENT'S SEX (N = 211)**

Extent of Disease	Relative Risk (95% CI)*
Single vessel	0.79 (0.29-1.19)
Two vessel	0.86 (0.45-1.21)
More than 2 vessels	1.44 (1.10-1.88) †
Left anterior descending artery > 50%	1.58 (1.14-2.04) †

* Men compared with women (ie, men who underwent CABG were more likely to have extensive disease than were women who underwent CABG).
 † $P < .05$.
 CABG denotes coronary artery bypass grafting.

DISCUSSION

In our study, men had significantly higher rates of bypass surgery and all procedures combined, as has been found in previous studies.¹⁰⁻¹² Age was the greatest confounder for the mortality outcome. Mortality rates were significantly higher in women with all confounding variables in the logistic model except age. The close similarity between the mortality outcome in this study and the findings of Vaccarino et al¹ may be explained by the considerably smaller sample size of the current investigation. Alternatively, this similarity may reflect greater recognition of sex disparities and changing practice patterns since those studies were published.

The increased adjusted risk of bypass surgery and of all procedures is explained in part by the anatomic differences in coronary artery disease as found in our study and in others.^{3,14} Men undergoing CABG had significantly more 3-vessel and advanced left main disease than women. In our data, controlling for the extent of coronary artery disease eliminated any sex bias. We are limited, however, by not having data on all men and women who had an acute MI and by knowing only the coronary anatomy of those undergoing coronary catheterization. Future research should address this question. Because the prevalence of diabetes is higher in women, they may have more generalized coronary artery disease that is less amenable to bypass surgery and angioplasty, as was the case in the GUSTO IIb trial.³

Other factors may still play a role in the observed differences between the sexes. Women may be more likely to have surgery on an outpatient basis after discharge from the hospital. Our study did not investigate this possibility. Women may need more time to decide whether they want to undergo surgery, thereby delaying a procedure. Another possibility is that the age of women who are having an MI is greater than that of men having an MI; women may therefore refuse surgery more often than men

because of their age. The research has not examined whether women tend to refuse or delay these procedures more often than men. Further research should be done in this area, including outpatient procedures, women's views on surgery, and other potential barriers to surgery.

The current study has several limitations. For example, data regarding congestive heart failure (CHF) was not available for inclusion in the analysis. Previous studies found that CHF was more common in women than in men. In addition, comorbidities were analyzed as dichotomous variables. Data on the severity of preexisting conditions could not be assessed. The study lacks any data on the severity of illness during hospitalization. The sample size was smaller than that of some previous work in this area. Finally, we lacked data on the number of vessels involved for all patients in the study. Therefore, it is possible that women had an equal risk of 3-vessel and left main coronary disease, but were not referred for CABG.

CONCLUSIONS

After being admitted for an acute MI, men and women had no significant difference in mortality, time spent in the ICU, total time in the hospital, frequency of stent placement, angiograms, or angioplasty. Men, however, had a significantly higher rate of CABG. Among those undergoing bypass surgery, men had significantly more advanced left-main coronary disease and 3-vessel disease than women. Controlling for the extent of coronary artery disease eliminated any bias for sex in the number of CABGs performed.

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