Unstable angina in the Myocardial Infarction Triage and Intervention Registry (MITI): Short- and long-term outcomes in men and women

Catherine Kim, MD, MPH,a Carol H. Schaaf, MN,b Charles Maynard, PhD,c and Nathan R. Every, MD, MPHd
Seattle, Wash

Background Studies of unstable angina have focused on hospital mortality; long-term mortality studies have been limited by small numbers of patients or health care providers. The objectives of this study were to determine whether men and women with unstable angina had different presentations, mortality rates, and procedure utilization.

Methods We analyzed a prospective observational registry of 4305 men (60%) and 2847 women (40%) with unstable angina who were admitted to coronary care units in King County, Washington, between 1988 and 1994. We compared the rates of symptoms, survival, and procedure utilization between sexes after adjustment for age, race, insurance status, and medical history.

Results Women were older and had higher rates of hypertension and congestive heart failure than men but had lower rates of cigarette smoking, previous myocardial infarction, and previous procedure use (P < .0001). Women had significantly higher rates of dyspnea, nausea, and epigastric pain and less diaphoresis than men did (P < .0001). Women underwent fewer procedures, but after adjustment for age and medical history this difference was no longer significant except for coronary bypass grafting (odds ratio 0.50, 95% confidence interval [CI] 0.37-0.69); after index hospitalization, men and women underwent procedures at similar rates. Although women had higher rehospitalization rates than men, early mortality (odds ratio 0.89, 95% CI 0.55-1.4) and late mortality (hazard ratio 0.98, 95% CI 0.95-1.0) were similar between men and women after adjustment for age.

Conclusions Women and men with unstable angina have different risk factors and symptoms upon presentation but have similar procedure use and mortality rates. (Am Heart J 2001;141:73-7.)

Unstable angina accounts for 1 million hospital admissions annually1 and is one of several acute syndromes of coronary insufficiency.2 Few prospective studies have specifically compared long-term outcomes in men and women with unstable angina. Studies addressing sex differences have focused on myocardial infarction (MI). These studies found that women have less typical chest pain than men, women undergo fewer procedures than men, and women have greater early relative mortality than men, but that mortality is greater in men over longer follow-up.3,4 Studies of early mortality after unstable angina have found that women have similar outcomes to men5 or better outcomes than men.6 When patients were followed up for longer periods of time, men were actually at higher risk. One of these studies was limited by small numbers,8 whereas another was restricted to one group of health care providers.9 To determine whether there were sex differences in presentation, rehospitalization rates, procedure use, and early and late mortality for patients diagnosed with unstable angina, we analyzed patients diagnosed with unstable angina in the Myocardial Infarction Triage and Intervention Registry (MITI). The registry is a prospective observational registry with 45,260 patients designed to assess clinical outcomes of patients with cardiovascular ischemia, including unstable angina.

Methods Study setting and design From January 1988 through June 1994, 45,260 patients with chest pain were admitted to coronary care units in 19 hospitals in King County, Washington, which includes the city of Seattle and suburban areas. The diagnosis of unstable angina at discharge was established in review of coronary care unit logs and discharge diagnoses from medical records by extensively trained abstractors. Excluded from this analysis were patients...
with cardiac arrest on admission and those with an unknown or unrecorded admission diagnosis. The analysis included patients with the primary International Classification of Diseases, 9th Edition (ICD-9) code of 411 for unstable angina, and excluded patients with an ICD-9 code of 410 for acute MI except for initial diagnosis recorded in Table I. Medical histories, symptoms on admission, and treatments were entered in the MITI registry on unstable angina patients between January 1991 and February 1993; mortality information was entered between January 1989 and February 1993. A total of 4305 men and 2847 women with unstable angina were included in the analysis.

The registry was matched with subsequent hospitalization information from the State of Washington’s Death and Illness Database for 1988 through 1993, which is a combination of the death certificate files from the state’s Center for Health Statistics and the Comprehensive Hospital Abstract Reporting System. Coronary angiography, angioplasty, and bypass surgery utilization were identified with ICD-9 diagnosis and procedure codes. Events that took place in hospitals outside Washington State could not be determined for rehospitalization and procedure utilization.

### Analysis

Comparisons between categorical variables were evaluated with chi-square analysis and between continuous variables with t tests. We conducted multivariate logistic regression with hospital mortality as the outcome sex as the variable of interest, entered covariates of cardiac risk factors, prior procedure use, and race, and reported the main effects in odds ratios (ORs) and 95% confidence intervals (CIs). The interactions between sex and covariates were calculated, and if significant, were entered into the model. We conducted a similar analysis to ascertain whether sex was associated with cardiac procedure use during the course of hospitalization. Because the total number of cardiac events was relatively low, an alternate model using stepwise regression was also performed to avoid model overfitting; however, results from this model did not differ substantially.

Cox regression analysis was used to determine whether sex was an independent predictor of survival. Covariates of cardiac risk factors, prior procedure use, and race were entered into the model, and sex was forced into the model to determine its association with survival. When covariates did not fit the proportional hazards assumption, a stratified analysis was performed. All statistical calculations were conducted with Stata software.

### Results

#### Index hospitalization

Between 1988 and 1994, 4305 men (60%) and 2847 women (40%) with unstable angina were admitted to coronary care units in King County, Washington. Although the proportion of men and women with unstable angina was similar, significantly more women were discharged with noncardiac chest pain than with acute MI (Table I). Women were also primarily diagnosed with other cardiac diagnoses more frequently than men, including structural heart disease, congestive failure, and arrhythmias, as opposed to ischemia.

#### History and symptoms on presentation

Baseline characteristics of patients with unstable angina are shown in Table II. Women were significantly older and had a higher proportion of Medicare insurance as opposed to private insurance than men did (P < .0001). Although they had lower rates of current smoking and previous MI than men (P < .001), they had higher rates of hypertension and congestive heart failure than men (P < .0001). Women also had fewer procedures before hospitalization, particularly fewer coronary artery bypass grafts (CABG) (P < .0001).

On presentation, women had significantly less chest pain and diaphoresis than men and instead had higher rates of dyspnea, nausea, and epigastric pain (P < .0001) (Table II). Subanalysis by race did not reveal any difference in symptom reporting between African American women and white women or between African American men and white men.

#### Mortality during index hospitalization

When we examined unadjusted hospital mortality rates, we found that mortality was similar in men (1%)
and women (1%, \( P = .62 \)). This similarity persisted after adjustment for age, medical history, and procedure performance (Table III). The CIs are wide, reflecting the low hospital mortality in patients hospitalized for unstable angina. The only variable that was significantly correlated with survival to discharge was CABG (OR 17, 95% CI 3.3-85). No interaction was present between sex and other covariates. Mortality was less than 0.1% (95% CI 3.3-85). Procedures during index hospitalization

When we examined unadjusted procedure rates for the index hospitalization, women had lower rates of coronary catheterization than men (50% vs 59%, \( P < .0001 \)), lower rates of percutaneous transluminal coronary angioplasty (PTCA) (16% vs 20%, \( P < .0001 \)), and lower rates of CABG (11% vs 18%, \( P < .0001 \)). Before adjustment, women were about three fourths less likely to receive cardiac catheterization or PTCA than men and about half as likely to receive CABG than men (Table IV). They were discharged on \( \beta \)-blockers at the same rate as men (16% vs 17%, \( P = .53 \)) but discharged on aspirin less frequently (37% vs 46%, \( P < .0001 \)).

After adjustment for age, medical history, and prior procedures, this difference was no longer significant for coronary catheterization and PTCA, although women still underwent CABG less often than men (Table IV). This difference in the CABG rate persisted even in the subset of patients who underwent angiography.

Long-term mortality rates

The mean duration of follow-up was 3 years. In men with unstable angina, there were 636 deaths per 12,651 person-years of follow-up, and in women there were 488 deaths per 8328 person-years of follow-up. There was a trend toward worsening survival in women with longer follow-up. However, women and men had an overall similar risk of death (Cox hazard ratio 1.0, 95% CI 0.96-1.1). The unadjusted mortality rates at 1 year of follow-up (men 7.1% vs women 7.8%, \( P = .29 \)) and 2 years of follow-up (men 12% vs women 12%, \( P = .5 \)) were not significantly different between men and women. However, at 3 years (men 16% vs women 18%, \( P = .03 \)) and 4 years (men 19% vs women 23%, \( P = .01 \)), women had higher unadjusted mortality rates. When age was not included in the model, no factors predicted long-term mortality.

Adjustment for age, medical history, and cardiac procedure utilization did not significantly change the ratio. After age, history of MI, and angiography were stratified, the only factor that predicted long-term mortality was history of congestive heart failure (Cox hazard ratio 1.3, 95% CI 1.1-1.5).

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<tr>
<th>Table III. OR of female to male sex with hospital mortality as the outcome, adjusted for covariates</th>
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<td>Adjusted for age, race, insurance status, angioplasty, catheterization, and CABG</td>
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*Significant at \( P < .05 \).
†Medical history variables included a history of MI, angina pectoris, congestive heart failure, angioplasty, CABG, hypertension, diabetes, hypercholesterolemia, and current smoking.

Reshospitalization rates

Women had lower rates of rehospitalization 30 days after admission, but at longer follow-up women had significantly more hospitalizations (Table V). Factors that predicted rehospitalization included older age (OR 1.03, 95% CI 1.01-1.05), history of MI (OR 2.2, 95% CI 1.6-3), history of hypertension (OR 1.6, 95% CI 1.2-2.2), and catheterization (OR 0.91, 95% CI 0.85-1.3) or PTCA (OR 1.9, 95% CI 1.2-3.0) performed during the index hospitalization. The difference between men and women disappeared after adjustment for age, insurance status, and race.

Procedures during rehospitalization

Women did not necessarily have more procedures during rehospitalization because they continued to have lower unadjusted rates of PTCA and CABG than men (Table V). After adjustment for age, race, and insurance status, procedure rates at 1 year of follow-up did not vary between men and women for catheterization (OR 1.1, 95% CI 0.87-1.3), PTCA (OR 0.90, 95% CI 0.69-1.2), or CABG (OR 0.86, 95% CI 0.63-1.2). Similar results for procedure performance were found at 2 and 3 years of follow-up.

Discussion

In the MITI registry women and men with unstable angina have different distributions of risk factors and symptoms, but these differences do not predict hospital mortality. Although women underwent fewer procedures than men, women’s survival was similar to men’s survival after 4 years of follow-up.

Studies of cardiovascular risk factors have found that women have a different pattern of risk factor distribution than men. Women tend to be older and have lower rates of smoking, previous MI, and prior revascularization.3,13,14 We also found that similar risk factor differ-
ences existed for patients with unstable angina. Women were older than men and more often had a history of congestive heart failure and hypertension. However, they smoked less and had histories of MI and revascularization less often than men, as seen in prior studies.6,7

Women eventually diagnosed with MI by cardiac enzymes, electrocardiogram, or angiography have a different presentation than men, with less frequent Q-wave infarction and early ST elevation6,14 and a higher proportion of silent events.6,15 Previous examination of patients in the MITI registry with acute MI have found that women were as likely as men to have chest pain, dyspnea, diaphoresis, nausea, and epigastric pain.15 In patients with unstable angina, we found that women and men had different symptoms, with both groups presenting with high frequencies of chest pain but women having diaphoresis less often than men and other symptoms such as dyspnea, nausea, and epigastric pain more often.

Studies of patients with acute MI, including the MITI registry, have found that women have relatively higher early mortality after MI5,16-18 and others found that this effect was more evident in younger patients.4 This difference has been attributed to biologic reasons19,20 such as different plaque physiologic features in men and women or higher rates of vasospasm in young women. Women and men may have different pathophysiologic mechanisms of cardiovascular disease because of the multiple functions of estrogen.21 However, we did not find that women had higher hospital mortality rates than men in unstable angina. This is similar to other studies of early mortality rates in unstable angina and may be partially attributed to the fact that mortality was low during the index hospitalization and to the fact that women with unstable angina have less extensive coronary disease with better left ventricular function on catheterization than men do.6,14 In addition, women were not at a disadvantage with longer follow-up. We found that women and men had similar long-term mortality rates after adjustment for age.

The sex mortality difference has also been attributed to differences in management, particularly to the fact that women are referred less often than men for cardiovascular procedures.22-27 In the MITI registry, women with acute MI were underreferred for cardiac catheterization compared with men, even after adjustment. However, subsequent PTCA and CABG in hospital were similar between men and women after adjustment for this discrepancy in catheterization rates.15,16 In patients with unstable angina, we found that procedure use was similar in women after adjustment for medical history during the index hospitalization, except for CABG, which was lower in women. Often on initial presentation a distinction cannot be made between unstable angina and MI in the absence of ST-segment elevation.2 Patients with unstable angina may have received

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<th>Table IV. OR of female to male sex with procedure performance as the outcome, adjusted for covariates</th>
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<td><strong>Cardiac catheterization</strong></td>
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<td>Adjusted for age, race, insurance status, and medical history†</td>
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*Significant at P < .05.
†Medical history variables included a history of MI, angina pectoris, congestive heart failure, coronary angioplasty, CABG, hypertension, diabetes, hypercholesterolemia, and current smoking.
aggressive treatment which eliminated any sex differences for this group but that would be evident when analyzed together with other coronary syndromes.

Although women underwent fewer procedures than men and had similar mortality rates, they were rehospitalized more often than men. The fact that the differences disappeared after adjustment for age, race, and insurance status most likely reflects the fact that women were older and tended to have Medicare insurance and also had a higher rate of comorbidities and more ambiguous symptoms.

Limitations

Because mortality rates were low, this study may have been underpowered to find significant differences in long-term survival despite the large number of participants. In addition, most of the participants were white, and the findings might not extend to a more ethnically diverse group of patients. Because the registry only included patients admitted to the coronary care unit, the patients in the MITI registry may be sicker than patients on telemetry only with unstable angina; although the registry was community based. Finally, the registry contained limited clinical information on patients with unstable angina; information that would have helped to analyze process of care such as electrocardiographic changes, cardiac enzyme data, catheterization results, and medications during index admission was not available.

Conclusions

Although women may have a higher relative mortality rate than men after MI, this difference does not extend to women with unstable angina. This may be partially attributed to the fact that women with unstable angina have less extensive coronary disease with better left ventricular function on catheterization than men do. Further work needs to address the pathophysiologic factors that affect the transition from incomplete coronary occlusion to complete coronary occlusion and why this transition seems more common in men.

References