

Sex Differences in Evaluation and Outcome of Unstable Angina

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SEX DIFFERENCES IN THE DELIVERY of cardiac care have been clearly documented.¹⁻¹¹ Although considerable controversy remains concerning the appropriateness of such differences, there is evidence to suggest that once the diagnosis of coronary disease is established, such as after myocardial infarction (MI) or after coronary angiography, the delivery of cardiac care is similar for men and women.¹² Thus, it is of interest to examine sex differences at an earlier point in the diagnostic sequence, when the presence of coronary disease is not established. A recently published computerized survey of 720 primary care physicians indicated that sex independently influenced the management of chest pain,¹³ a frequent symptom in women and a frequent cause of emergency department (ED) visits. It is unknown whether a similar difference exists for patients receiving a diagnosis of unstable angina, and whether it affects outcomes.

This study tested the hypothesis that female sex was negatively associated with the care delivered to and the outcome of persons diagnosed in the ED with unstable angina.

For editorial comment see p 659.

Context The existence of sex bias in the delivery of cardiac care is controversial, and little is known about the association between sex and delivery of care and outcomes at an early point in the diagnostic sequence, such as when patients present for the evaluation of chest pain.

Objective To test the hypothesis that female sex is negatively associated with care delivered to and outcomes of persons diagnosed as having unstable angina.

Design Inception population-based cohort study with an average of 6 years of follow-up.

Setting Emergency departments (EDs) in Olmsted County, Minnesota.

Patients A total of 2271 Olmsted County residents (1306 men and 965 women) who presented to the ED for the first time with symptoms meeting criteria for unstable angina between 1985 and 1992.

Main Outcome Measures Use of cardiac procedures within 90 days of ED visit, overall mortality, and cardiac events (cardiac death, nonfatal myocardial infarction, nonfatal cardiac arrest, and congestive heart failure), compared by sex and Agency for Health Care Policy and Research cardiovascular risk category (low, intermediate, or high).

Results Women were older ($P < .001$), more likely to have a history of hypertension ($P = .001$), and less likely to present with typical angina ($P = .004$) than men. Men were more likely than women to undergo noninvasive cardiac tests (relative risk [RR], 1.27; 95% confidence interval [CI], 1.14-1.40) as well as invasive cardiac procedures (RR, 1.72; 95% CI, 1.51-1.97). After adjustment, male sex was associated with a 24% increase in the use of cardiac procedures. Survival of both men and women in the high and intermediate risk categories was significantly lower than expected per the general population ($P < .001$). Women had a worse outcome than men, but after multivariate adjustment, male sex was associated with a trend toward an increase in the risk of death (RR, 1.23; 95% CI, 0.99-1.54) and significantly associated with increased risk of cardiac events (RR, 1.21; 95% CI, 1.03-1.42).

Conclusions Our population-based data indicate that after an ED visit for symptoms of unstable angina, the use of cardiac procedures was lower in women, but after taking into account baseline characteristics, men experienced worse outcomes.

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METHODS

Study Setting

Epidemiologic research in Olmsted County, Minnesota, is possible because the county is relatively isolated from other urban centers and nearly all medical care is delivered to local residents by a handful of providers. Other than that a higher proportion of the working population is employed in the health care industry, the characteristics of the population of Olmsted

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County are similar to those of US whites in general.

Potential epidemiologic studies in the community are enhanced by the fact that each provider uses a medical record system, whereby all data collected on an individual are assembled in 1 place. Thus, the details of every encounter, including visits to the ED, and all laboratory results, pathology reports, and correspondence concerning each patient, can be accessed. The result is the linkage of medical records from all sources of medical care used by the Olmsted County population; these are easily retrievable because the Mayo Clinic has maintained extensive indices based on clinical and histologic diagnoses and surgical procedures since the early 1900s.^{14,15} Since 1966, similar indices have been developed for non-Mayo providers under the aegis of the Rochester Epidemiology Project.

Cohort Design

The Rochester Epidemiology Project indices, augmented by the log books of the EDs (St Mary's, Rochester Methodist, and Olmsted Community hospitals), were used to identify a population-based cohort of Olmsted County residents who had an initial ED visit for symptoms consistent with unstable angina between January 1, 1985, and December 31, 1992. The study was approved by the Mayo Clinic Institutional Review Board. Minnesota State law requires that patients seen after January 1997 must authorize use of their medical records for research studies, and patients who refused research authorization were excluded.

Residency in Olmsted County was verified with information from birth certificates and city and county directories.

Eligible patients included all residents presenting for the first time to the ED with chest pain meeting criteria for unstable angina during the study period. Eligibility was determined based on evidence available in the ED. Unstable angina was defined as 1 of the following: symptoms of angina at rest lasting longer than 20 minutes, new onset exer-

tional angina that met the Canadian Cardiovascular Society criteria for class 3 or higher, variant angina, or post-myocardial infarction (MI) angina.¹⁶ Patients were excluded if they presented to the ED with criteria for ongoing acute MI (ST-segment elevation ≥ 1 mm in 2 or more leads) or with definite other cause of chest pain, including pleuritic chest pain, pulmonary embolism, musculoskeletal cause, trauma, pneumonia, pericarditis, and dissecting aortic aneurysm.

The medical records were reviewed by a team of physicians and nurse abstractors to collect data with which to characterize patient demographics, clinical signs and symptoms, and cardiovascular disease risk factors (history of familial coronary disease, smoking, diabetes mellitus, hypertension, and hyperlipidemia defined by a total serum cholesterol level ≥ 5.7 mmol/L [220 mg/dL]). Elevated creatine phosphokinase (CPK) was defined as peak CPK greater than 1.5 times the upper limit of normal. The evaluation of symptoms was made from ED assessment or the physician's initial admission note and the information used to make this assessment always preceded test results. Patients were classified in 3 risk categories according to the guidelines for initial disposition of patients with unstable angina published by the Agency for Health Care Policy and Research (AHCPR, now the Agency for Healthcare Research and Quality).¹⁶ All electrocardiograms were read by cardiologists or ED physicians blinded to the hypothesis of the study and sex of the patient.

All end points were ascertained through record review. Disposition from the ED was categorized as intensive care unit admission, admission to telemetry or to general ward bed, or home dismissal. The use of cardiac and gastrointestinal procedures during the 90 days following the ED visit was examined. Cardiac procedures were categorized as noninvasive, including procedures performed at rest (echocardiography, resting radionuclide angiography, resting sestamibi study, and ultrafast com-

puted tomography) and stress tests (exercise and pharmacologic stress testing with or without nuclear or ultrasound imaging), or invasive, consisting of diagnostic coronary angiography. Gastrointestinal procedures included upper gastrointestinal radiography and upper gastrointestinal endoscopy, esophageal manometry, and reflux studies.

The Rochester Epidemiology Project obtains copies of death certificates for all Olmsted County residents known to have died. These are linked to the medical record of all Olmsted County residents. This ensures virtually 100% complete follow-up for the mortality end point.

Cardiac events included cardiac deaths, nonfatal MI, nonfatal cardiac arrest, and congestive heart failure. The definition of MI was based on the documentation in the medical record of the occurrence of chest pain typical for an ischemic origin, or characteristic changes in the electrocardiogram and/or cardiac enzymes. Congestive heart failure was defined as the occurrence of exertional or paroxysmal nocturnal dyspnea responding symptomatically to digitalis, diuretics, or afterload-reducing agents. The definition of cardiac arrest was based on documentation of this diagnosis by the clinician in the hospital records.

Statistical Analysis

Associations between sex and baseline characteristics with sex were tested by means of proportional hazards. The outcome measures examined were disposition from the ED, use of cardiac procedures within 90 days after ED visit, overall survival, and survival free of cardiac events (defined as cardiac death or nonfatal cardiac event, including nonfatal MI, nonfatal cardiac arrest, and congestive heart failure).

Among hospitalized patients, disposition from the ED (intensive care unit, telemetry, or nonmonitored hospital ward vs intensive care) was analyzed using logistic regression analysis adjusting for sex and AHCPR risk category.

Use of cardiac procedures within 90 days after the ED visit was analyzed by

means of proportional hazards modeling. Association between sex and use of any cardiac procedure was examined and proportional hazards modeling within the group undergoing cardiac procedures was used to examine the association between sex and use of invasive procedure. Survival was analyzed by means of the Kaplan-Meier method. Survival observed in each sex and AHCPR risk category was compared with the age- and sex-specific expected survival of the 1990 Minnesota population using the log-rank statistic. Proportional hazards modeling was used to examine the association between sex and time to all-cause death and between sex and time to first cardiac event.

Variables in the models included age; type of chest pain (typical or atypical for angina pectoris); AHCPR risk category; number of coronary disease risk factors; history of MI; ST-segment depression on an electrocardiogram; elevated CPK; and the exposure variable of interest, sex. Tests for first-order interactions between sex and other variables were examined.

RESULTS

Between 1985 and 1992, 6812 Olmsted County residents were evaluated in 1 of the Olmsted County EDs for chest pain. Screening of the records of these visits by a nurse abstractor under supervision of 1 of the authors (M.E.F.) resulted in the identification of individuals eligible for study entry. The reasons for exclusion from the study were residency outside Olmsted County (799), electrocardiogram criteria for acute MI with ST elevation ≥ 1 mm in 2 or more leads (247), nonincident nature of the episode of unstable angina during the study period (1082), noncardiac or noncoronary cause of chest pain (1647), angina pectoris but with no AHCPR criteria for unstable angina (47), refusal to be included in studies (82), and not meeting physician criteria (637).

Thus, during the study period, 2271 residents of Olmsted County (1306 men and 965 women) were seen in the ED for chest pain meeting criteria for unstable angina and constitute the study cohort.

Baseline Characteristics

At index ED visit, women were approximately 7 years older and less likely to be

smokers than men and were more likely to have a history of hypertension and hypercholesterolemia (TABLE 1). Prevalence of history of familial coronary artery disease or MI was the same in both sexes. In terms of symptom status at the time of the ED visit, the type of chest pain was more frequently described as atypical for angina pectoris in women, although similar percentages of men and women had prolonged pain. Women were more likely to have electrocardiogram abnormalities than men.

According to the AHCPR guidelines, the majority of patients (69%) were classified as intermediate risk, qualifying for admission to the intensive care unit or for telemetry; 19% as high risk, justifying admission to the intensive care unit; and 12% as low risk, potential candidates for outpatient observation. There was no association between risk category and sex, and the association of sex with baseline characteristics described above remained unchanged after adjustment for AHCPR risk category. The frequency of patients with elevated CPK was 18% for both men and women.

Table 1. Baseline Clinical Characteristics of Patients at the Time of Emergency Department Visit*

	Men (n = 1306)	Women (n = 965)	P Value
Age, mean (SD), y	60 (14)	67 (16)	<.001
Current smoker	26	16	.001
Diabetes mellitus	14	16	.06
History of hypertension	39	55	.001
History of hypercholesterolemia†	40	51	.001
History of familial CAD	27	25	.37
History of MI	39	40	.64
Typical angina	75	81	.004
Prolonged pain	82	85	.12
Electrocardiographic findings			
Normal	47	41	.01
Abnormal	53	59	
Pathological Q waves	11	10	.16
ST-segment depression ≥ 1 mm	6	8	.20
Other ST-T changes	26	33	.001
AHCPR risk category			
High	19	20	.55
Intermediate	69	67	
Low	12	13	

*Data are presented as percentages unless otherwise indicated. CAD indicates coronary artery disease; MI, myocardial infarction; and AHCPR, Agency for Health Care Policy and Research. Other ST-T changes denotes ST depression less than 1 mm in magnitude and dynamic T-wave changes. All P values are adjusted for AHCPR risk category.

†Serum cholesterol value was not recorded for 21% of subjects.

Management

ED Disposition. Few patients were dismissed to home (men, 4%; women, 6%) or admitted to a nonmonitored hospital ward (men, 1%; women, 2%). The majority of the patients were admitted to a monitored or intensive care unit. After adjustment for age and AHCPR risk category, there was no association between sex and the type of hospital unit to which patients were admitted, telemetry vs intensive care (odds ratio [OR], 1.13; 95% confidence interval [CI], 0.93-1.36).

Procedures Used Within 90 Days After ED Visit. A total of 1408 procedures were used in the 965 women and 2576 procedures in the 1306 men. The majority of procedures were cardiac, mainly stress tests and coronary angiography. The overall use of procedures was high (men, 87%; women, 76%) and men were 30% more likely to undergo any procedure than women (relative risk [RR] for men vs women,

Table 2. Use of Cardiac Procedures Within 90 Days After Emergency Department Visit for Unstable Angina

Procedure	Men, %* (n = 1306)	Women, %* (n = 965)	Crude Relative Risk (95% CI)†	P Value	Adjusted Relative Risk (95% CI)†	P Value
Noninvasive Diagnostic Tests						
Any noninvasive test	74	62	1.27 (1.14-1.40)	<.001	1.21 (1.09-1.35)	<.001
Echocardiography and other resting tests‡	35	36	0.96 (0.84-1.10)	.57	1.06 (0.91-1.22)	.45
Stress test	58	38	1.68 (1.48-1.90)	<.001	1.43 (1.26-1.63)	<.001
Noninvasive diagnostic tests only	34	39	0.84 (0.73-0.96)	.01	0.85 (0.74-0.98)	.03
Stress test only	21	18	1.17 (0.96-1.42)	.11	1.01 (0.83-1.24)	.89
Invasive Diagnostic Procedures						
Coronary angiography	50	33	1.72 (1.51-1.97)	<.001	1.59 (1.38-1.82)	<.001
Coronary angiography only	11	11	1.02 (0.79-1.31)	.88	0.93 (0.72-1.21)	.60
Noninvasive Test and Angiography						
	39	22	1.92 (1.64-2.26)	<.001	1.80 (1.53-2.12)	<.001

*Data presented as percentage of men and women who undergo the corresponding procedure.

†Relative risk is for men vs women; the adjusted relative risks are adjusted for age and Agency for Health Care Policy and Research risk category. CI indicates confidence interval.

‡Other resting tests include resting radionuclide angiography, sestamibi study, and ultrafast computed tomography.

1.31 [95% CI, 1.19-1.43]). Eighty-five percent of men and 72% of women underwent a cardiac procedure (RR, 1.34; 95% CI, 1.22-1.47). Women were more likely to undergo gastrointestinal procedures than men (RR, 0.74; 95% CI, 0.60-0.93). The percentage of men and women undergoing various types of cardiac procedures is shown in TABLE 2 along with the RRs for men vs women. Both the crude RRs and the RRs adjusted for age and AHCPR risk category are presented. Men were more likely to undergo noninvasive cardiac procedures, which reflects a greater use of stress testing in men. There was no sex difference in the use of echocardiography and other resting procedures. The use of coronary angiography was higher in men. These crude associations were minimally attenuated by adjustment for age and AHCPR risk category.

The intensity of procedure use was greater in men than in women. Twenty-four percent of women and 13% of men underwent no procedure, whereas 18% of women and 29% of men underwent more than 2 procedures (*P* for trend, .001).

TABLE 3 shows the model used to examine the association between sex and cardiac procedure use. After adjustment for other predictor variables including age, typical nature of the chest pain, presence of ST-segment depression, elevated CPK, and AHCPR risk

Table 3. Predictors of the Use of Any Cardiac Procedure Within 90 Days After Emergency Department Visit*

Variable	Crude Relative Risk (95% CI)†	P Value	Adjusted Relative Risk (95% CI)†	P Value
Male sex	1.34 (1.22-1.47)	<.001	1.24 (1.11-1.37)	<.001
Age	0.99 (0.989-0.994)	<.001	0.99 (0.986-0.992)	<.001
Typical chest pain	1.21 (1.08-1.36)	.001	1.23 (1.09-1.38)	<.001
ST-segment depression	1.29 (1.08-1.55)	.005	1.25 (1.03-1.52)	.02
Elevated CPK	1.44 (1.28-1.61)	<.001	1.49 (1.32-1.69)	<.001
AHCPR intermediate risk	1.08 (0.93-1.25)	.31	1.18 (1.00-1.38)	.049
AHCPR high risk	1.13 (0.95-1.34)	.16	1.22 (1.01-1.48)	.045

*CI indicates confidence interval; CPK, creatine phosphokinase; and AHCPR, Agency for Health Care Policy and Research (the low-risk category is the reference level).

†Relative risk is for men vs women; the adjusted relative risks are adjusted for all variables listed in the first column.

category, men were 24% more likely to undergo cardiac procedures (RR, 1.24; 95% CI, 1.11-1.37). This association remained similar when the analysis was restricted to the use of procedures performed within 30 days of the index event (RR, 1.22; 95% CI, 1.01-1.36).

Further analysis examined the association between sex and type of cardiac procedures used among the 1803 persons undergoing any cardiac procedure. After adjustment for other covariates (including age, AHCPR risk category, type of chest pain, elevated CPK, and cardiac risk factors), men were more likely to undergo coronary angiography than women were (RR for male sex, 1.40; 95% CI, 1.21-1.61; *P* < .001).

The mean (SD) length of stay in the hospital was 3.02 (2.80) days for the 198 patients (118 men and 80 women) who did not undergo any testing and 5.86

(8.81) days for the 1974 patients (1130 men and 844 women) who underwent at least 1 test.

Outcome

The mean (SD) duration of follow-up was 6.0 (3.1) years. In men, 358 deaths and 1050 cardiac events (179 cardiac deaths, 50 nonfatal ventricular arrhythmias, 240 nonfatal MIs, and 581 cases of congestive heart failure) occurred during 8054 person-years of follow-up. In women, 351 deaths and 881 cardiac events (171 cardiac deaths, 26 nonfatal ventricular arrhythmias, 187 nonfatal MIs, and 497 cases of congestive heart failure) occurred during 5502 person-years of follow-up.

All-Cause Mortality. The 6-year overall survival rate was 78% for men and 71% for women (*P* < .001). Observed survival was not different from

expected survival for men and women in the low-risk category. In the intermediate- and high-risk categories, an excess mortality was observed with significant differences between observed and expected survival for both men and women ($P < .001$). For women in the AHCPR high-risk category, the 3-year survival was 68% (95% CI, 61%-74%) vs an expected 3-year survival of 86%. Likewise for men in the high-risk category, the 3-year survival was 75% (95% CI, 69%-80%) vs an expected 3-year survival of 88%.

Associations between clinical variables and time to death are shown in

TABLE 4. Women fared worse than men in that male sex was univariately associated with a 31% decrease in the risk of death.

In addition to sex, age, AHCPR risk category, and cardiac risk factors, history of MI and elevated CPK and ST-segment depression were univariate predictors of time to death. After adding these variables to the model, there was a trend toward an excess risk of death in men. The analyses were repeated while examining the outcome during the first 30 days of follow-up and consistently indicated, by the direction of the association, an excess risk

of death in men (adjusted RR for male sex, 2.10; 95% CI, 0.81-5.44; $P = .14$).

Cardiac Events. The univariate 6-year survival free of cardiac events was 70% for men and 63% for women ($P = .001$). Associations between baseline characteristics and time to cardiac events are shown in TABLE 5.

Women fared worse than men, but, in addition to sex, age, AHCPR risk category, and cardiac risk factors, history of prior MI, ST-segment depression and elevated CPK were univariate predictors of time to cardiac event. After adding these variables in the model, there was a 21% excess risk of cardiac events in men.

There was no interaction between sex and the dependent variables included. The analyses were repeated while examining the outcome during the first 30 days of follow-up and indicated a 44% increase in the risk of cardiac events in men at 30 days (adjusted RR for male sex, 1.44; 95% CI, 1.02-2.05; $P = .04$).

COMMENT

This study tested the hypothesis that, among adults receiving an ED diagnosis of unstable angina, female sex is negatively associated with the delivery of cardiac care and subsequent outcome. We found an association between female sex and lesser use of cardiac procedures that could not be explained by measured sex differences in baseline characteristics. The majority (88%) of men and women receiving an ED diagnosis of unstable angina were classified as intermediate or high risk according to the AHCPR guidelines, and their survival was significantly worse than the expected survival. This indicates that unstable angina portends a poor prognosis irrespective of sex. In survival analyses and after adjustment for age and other baseline characteristics, men were at increased risk for cardiac events and death.

Unstable Angina as a Public Health Problem

Each year in the United States, approximately 5 million persons are evaluated in EDs for chest pain,¹⁷ underscoring the

Table 4. Predictors of Time to Death After Emergency Department Visit*

Variable	Unadjusted Relative Risk (95% CI)	P Value	Adjusted Relative Risk (95% CI)†	P Value
Male sex	0.69 (0.59-0.80)	<.001	1.23 (0.99-1.54)	.07
Age	1.08 (1.07-1.09)	<.001	1.07 (1.06-1.09)	<.001
AHCPR intermediate risk‡	5.18 (3.15-8.53)	<.001	0.93 (0.49-1.76)	.82
AHCPR high risk‡	9.70 (5.84-16.12)	<.001	1.34 (0.69-2.60)	.39
Smoking	0.52 (0.42-0.64)	<.001	1.20 (0.89-1.62)	.23
Diabetes mellitus	2.21 (1.87-2.62)	<.001	1.94 (1.56-2.41)	<.001
Hypertension	1.97 (1.69-2.28)	<.001	1.34 (1.09-1.65)	.006
Total serum cholesterol ≥ 5.7 mmol/L	0.81 (0.68-0.97)	.03	0.72 (0.58-0.88)	.002
History of MI	2.76 (2.37-3.21)	<.001	1.58 (1.28-1.95)	<.001
ST-segment depression	2.93 (2.46-3.49)	<.001	1.30 (0.95-1.76)	.10
Peak CPK $> 1.5 \times$ upper limit of normal	1.27 (1.07-1.52)	.008	1.15 (0.90-1.47)	.25

*CI indicates confidence interval; AHCPR, Agency for Health Care Policy and Research; MI, myocardial infarction; and CPK, creatine phosphokinase.

†Relative risks were adjusted for all variables listed in first column.

‡AHCPR low-risk category is the reference level.

Table 5. Predictors of Time to Cardiac Event After Emergency Department Visit*

Variable	Unadjusted Relative Risk (95% CI)	P Value	Adjusted Relative Risk (95% CI)†	P Value
Male sex	0.79 (0.69-0.91)	.001	1.21 (1.03-1.42)	.02
Age	1.06 (1.05-1.07)	<.001	1.06 (1.05-1.06)	<.001
AHCPR intermediate risk‡	11.26 (6.02-21.03)	<.001	2.73 (1.43-5.19)	.002
AHCPR high risk‡	20.44 (10.85-38.49)	<.001	3.42 (1.77-6.63)	<.001
Smoking	0.70 (0.58-0.84)	<.001	1.49 (1.20-1.85)	<.001
Diabetes mellitus	2.56 (2.18-3.00)	<.001	1.97 (1.65-2.35)	<.001
Hypertension§	2.20 (1.91-2.54)	<.001	1.40 (1.19-1.65)	<.001
Familial CAD	0.92 (0.78-1.07)	.28	1.15 (0.96-1.39)	.13
History of MI	2.80 (2.43-3.23)	<.001	1.47 (1.25-1.73)	<.001
ST-segment depression	2.60 (2.09-3.25)	<.001	1.15 (0.91-1.46)	.25
Peak CPK $> 1.5 \times$ upper limit of normal	1.99 (1.70-2.32)	<.001	1.85 (1.55-2.22)	<.001

*CI indicates confidence interval; AHCPR, Agency for Health Care Policy and Research; CAD, coronary artery disease; MI, myocardial infarction; and CPK, creatine phosphokinase.

†Relative risks were adjusted for all variables listed in first column.

‡AHCPR low-risk category is the reference level.

§Hypertension was defined as a diagnosis of hypertension recorded in the patient's chart or the use of antihypertensive medication.

importance of chest pain as a public health problem. Of these patients, those with unstable angina represent the greatest challenge to clinicians because of the risk, albeit small, of adverse cardiac outcomes.¹⁶ Extensive efforts have been made to define better triage mechanisms that would allow reliable identification of high-risk patients while minimizing the number of hospital admissions for chest pain syndromes in low-risk patients,¹⁸⁻²⁵ and practice guidelines have been published for the disposition of patients presenting to the ED with unstable angina.¹⁶ In the current series, a small percentage of the whole population of both sexes was classified as low risk, consistent with previously reported aggregate data.²⁶ The lack of sex difference in risk category and the small percentage of women in the low-risk group underscore the continuing challenge that the evaluation and management of chest pain syndromes continues to represent in both sexes.

Sex and Care Delivered for Unstable Angina

Little information is available on the association between sex and the delivery of care for unstable angina. A secondary analysis from the Acute Cardiac Ischemia Time-Insensitive Predictive Instrument (ACI-TIPI) clinical trial indicates that women with angina pectoris seen in the ED were less likely to undergo cardiac catheterization or revascularization.²⁷ This sex difference in the delivery of cardiac care was not observed with MIs.²⁷ Even though these data, which support the "Yentl syndrome," whereby to be treated as men, women would have to present like men, described by Healy,¹² are provocative, several points must be kept in mind. First, our study was not designed to investigate sex differences in the delivery of cardiac care as a primary hypothesis, and the observed differences may have been related to unmeasured confounding variables. Second, the delivery of care could conceivably have been influenced by the trial setting, thus compromising external validity.

Recently, Schulman et al¹³ reported the results of a survey of primary care phy-

sicians that examined referral to cardiac catheterization according to race and sex among case vignettes of patients presenting with chest pain. The authors reported that race and sex influenced physicians' recommendations for the management of chest pain, with women being less likely to be referred to cardiac catheterization. While the study design was free of some of the biases related to retrospective analyses, it addressed the management of chest pain but not unstable angina, a syndrome associated with the perception of a greater likelihood of adverse events. In addition, because hypothetical examples were used, the study could not examine the impact of the documented sex differences in care on outcome.

The current study extends the findings of previous studies by indicating a strong positive association between male sex and use of cardiac procedures in a geographically defined population diagnosed in the ED with unstable angina. One could hypothesize that reported sex differences in the sensitivity and specificity of noninvasive procedures, in particular, stress testing, could play a role in the sex differences in utilization that were noted in our study.²⁸⁻³²

Sex and Outcome of Unstable Angina

The data presented herein indicate that the majority of women and men receiving an ED diagnosis of unstable angina are classified in the high and intermediate AHCPR risk categories and experience excess mortality compared with the general population. The public health implications of these findings are that women with unstable angina constitute a relatively high-risk population. After accounting for age and other baseline characteristics, men experience worse outcomes than women do both at 30 days and throughout the entire follow-up, with an excess risk of cardiac events and a trend toward excess risk of death. The clinical implications of these data in terms of health care delivery are challenging. In particular, while women in this cohort were subjected to fewer cardiac procedures than

men, one cannot infer from these data that more aggressive management of women with unstable angina is warranted. Indeed, opposite inferences can be drawn from these analyses: that procedures are overutilized in men or underutilized in women. It is uncertain that performing more invasive cardiac procedures in women, who present with unstable angina at an older age than men, would result in better outcomes. This hypothesis would be best tested in a randomized trial, the relevance of which is underscored by the large proportion of persons who receive an ED diagnosis of unstable angina and belong to AHCPR risk categories associated with excess mortality.

Limitations

Underascertainment of persons presenting to the ED for the evaluation of unstable angina is unlikely because the resources of the Rochester Epidemiology Project provide access to all medical records for the care provided to Olmsted County residents. However, ascertainment of all patients seeking medical care for chest pain may have not been complete. Other settings in which such evaluations may occur theoretically could include office visits to primary care physicians or cardiologists. However, the intent of our study was to capture the cohort of patients with chest pain who meet criteria for unstable angina, and the likelihood that such symptoms would not result in a referral to the ED is small. Reliance on the medical records for measurement of potential confounding variables should be considered. The care delivered to the present cohort reflects practices in 1985-1992, which raises the issue of generalizability to more contemporary practices. While no data suggest that patterns of care have changed, this should be the subject of future studies.

As in any observational study, residual confounding should be considered as an alternate explanation of the findings reported herein; in particular, patient preference could not be captured.

Because this study was population-based, the potential effects of referral

bias are greatly diminished; however, the underrepresentation of minorities in this cohort, which was cared for essentially by 1 group of providers, compromises the generalizability to different racial and ethnic groups or to different health care environments. However, no single population or health care system can be expected to be completely representative of the general

population; thus, our findings should be further examined in different populations and care settings.

CONCLUSION

These population-based data indicate that after an ED visit for unstable angina, the utilization of cardiac procedures is lower in women. Men experience worse outcomes than women, with

an increased risk of death and cardiac events. Further studies are needed to examine whether such adverse outcomes can be altered by interventions.

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