

SEX DIFFERENCES IN THE MANAGEMENT OF CORONARY ARTERY DISEASE

RICHARD M. STEINGART, M.D., MILTON PACKER, M.D., PEGGY HAMM, PH.D.,
 MARY ELLEN COGLIANESE, R.N., BERNARD GERSH, M.D., EDWARD M. GELTMAN, M.D.,
 JOSEPHINE SOLLANO, R.N., STANLEY KATZ, M.D., LEM MOYÉ, M.D., PH.D., LOFTY L. BASTA, M.D.,
 SANDRA J. LEWIS, M.D., STEPHEN S. GOTTLIEB, M.D., VICTORIA BERNSTEIN, M.D.,
 PATRICIA MCEWAN, M.D., KIRK JACOBSON, M.D., EDWARD J. BROWN, M.D., MARRICK L. KUKIN, M.D.,
 NIKI E. KANTROWITZ, M.D., AND MARC A. PFEFFER, M.D., PH.D., FOR THE SURVIVAL
 AND VENTRICULAR ENLARGEMENT INVESTIGATORS*

Abstract Background. Despite the fact that coronary artery disease is the leading cause of death among women, previous studies have suggested that physicians are less likely to pursue an aggressive approach to coronary artery disease in women than in men. To define this issue further, we compared the care previously received by men and women who were enrolled in a large postinfarction intervention trial.

Methods. We assessed the nature and severity of anginal symptoms and the use of antianginal and anti-ischemic interventions before enrollment in the 1842 men and 389 women with left ventricular ejection fractions ≤ 40 percent after an acute myocardial infarction who were randomized in the Survival and Ventricular Enlargement trial.

Results. Before their index infarction, women were as

likely as men to have had angina and to have been treated with antianginal drugs. However, despite reports by women of symptoms consistent with greater functional disability from angina, fewer women had undergone cardiac catheterization (15.4 percent of women vs. 27.3 percent of men, $P < 0.001$) or coronary bypass surgery (5.9 percent of women vs. 12.7 percent of men, $P < 0.001$). When these differences were adjusted for important covariates, men were still twice as likely to undergo an invasive cardiac procedure as women, but bypass surgery was performed with equal frequency among the men and women who did undergo cardiac catheterization.

Conclusions. Physicians pursue a less aggressive management approach to coronary disease in women than in men, despite greater cardiac disability in women. (N Engl J Med 1991; 325:226-30.)

CORONARY artery disease is the leading cause of death in women. It is estimated that 500,000 women die of the disorder each year, a mortality rate in this group that exceeds that for all neoplastic diseases combined.¹ However, several lines of evidence suggest that coronary artery disease is treated less aggressively in women than in men. Although women experience chest pain as their chief symptom more frequently than men,² fewer women are referred for noninvasive tests for coronary artery disease. Even when the noninvasive evaluation indicates a high likelihood of coronary artery disease, fewer women than men are referred for coronary arteriography and coronary bypass surgery — a difference that cannot be explained by sex-related differences in the prevalence of cardiovascular disease.^{3,4} Finally, even after a decision is made to refer a patient for cardiac catheterization and coronary bypass surgery, women are referred later in the course of their disease than men.

Several theories have been proposed to explain this sex-related difference in patient care. Since chest pain is more often associated with normal epicardial arteries in women than in men, many physicians believe that angina in women is less likely to be followed by

serious cardiovascular events.⁵ This may explain why physicians are more likely to attribute anginal symptoms in women to noncardiac causes.³ In addition, many noninvasive tests used for the evaluation of coronary artery disease are believed to be less accurate in women than in men.⁶ Hence, it is possible that the less aggressive diagnostic and therapeutic approach followed by physicians who care for women with angina is justified. Previous studies^{3,4} that have reported the existence of a sex-related bias have been unable to evaluate this possibility, since the patients in these studies were identified by a physician's decision to perform a diagnostic or therapeutic intervention rather than by the occurrence of a serious complication of coronary artery disease. If physicians possess the clinical judgment needed to identify high-risk patients correctly, then sex-related differences should not be apparent in the treatment of angina in patients who have had similar cardiovascular events. The present analysis was carried out to test this hypothesis.

METHODS

Study Patients

Patients were eligible for analysis in this study if they were enrolled in the Survival and Ventricular Enlargement Study (SAVE), a multicenter trial being carried out in the United States and Canada to evaluate the effect of an angiotensin-converting-enzyme inhibitor (captopril) on ventricular function and mortality in patients who have abnormal left ventricular function after an acute myocardial infarction. The SAVE trial is being conducted at 112 hospitals, which function as 45 clinical centers. Patients were enrolled in our study from January 1987 to January 1990.

All 2231 patients enrolled in the SAVE study were included in the present analysis. All patients had had an acute myocardial infarction within the previous 3 to 16 days; the presence of an infarction was confirmed by a combination of typical symptoms and characteristic changes in cardiac enzyme levels and the electrocar-

*The Survival and Ventricular Enlargement (SAVE) investigators are listed in the Appendix.

From Winthrop—University Hospital, Mineola, N.Y. (R.M.S., M.E.C., S.K., N.E.K.); University of Texas Health Science Center at Houston, Houston (P.H., L.M.); Mount Sinai School of Medicine, New York (M.P., J.S., M.L.K.); Mayo Clinic, Rochester, Minn. (B.G.); Washington University School of Medicine, St. Louis (E.M.G.); Tulsa Heart Center, Tulsa, Okla. (L.L.B.); University of Maryland at Baltimore, Baltimore (S.S.G.); University of British Columbia, Vancouver (V.B.); Wellesley Hospital, Toronto (P.M.); Oregon Heart Institute, Portland (S.J.L.); Sacred Heart Hospital, Eugene, Oreg. (K.J.); State University of New York at Stony Brook, Stony Brook (E.J.B.); and Brigham and Women's Hospital, Boston (M.A.P.). Address reprint requests to Dr. Steingart at Winthrop—University Hospital, 259 First St., Mineola, NY 11501.

diagram. All patients had left ventricular ejection fractions (as determined by radionuclide ventriculography) of 40 percent or less. Patients were excluded from participation if either their clinical course or an exercise-tolerance test after their index infarction indicated a high likelihood of myocardial ischemia but they did not have coronary arteriography. Patients were also excluded if coronary arteriography was performed and revascularization was recommended but not performed. The decision to recommend catheterization or revascularization was made by the patient's referring physician.

Data Collection

All data for the study were prospectively collected with use of uniform procedures for data collection and entry; the procedures were detailed in a manual of operations and reinforced at training sessions conducted before the start of patient enrollment. The following information was collected for each patient: the presence of coronary risk factors; number of previous hospitalizations (if any) for myocardial infarction, cardiac catheterization, coronary angioplasty, or coronary bypass surgery; presence and severity of anginal symptoms and functional status within three weeks before the index infarction; and medications received within 72 hours of the index infarction. The patients were asked whether they had ever been told by a physician that they were having angina; symptoms of angina three weeks before the index infarction were also assessed with the Rose questionnaire.⁷ Functional status was assessed with three scales: the New York Heart Association (NYHA) functional classification,⁸ the Karnofsky score,⁹ and the Goldman scale¹⁰; the first two scales assess the ability to perform general activities, whereas the third assesses the capacity to carry out specific activities. Both the Karnofsky score and the NYHA classification use the patient's own sense of usual activity as the reference by which current disability is measured, whereas the Goldman scale uses objective external standards. Higher scores indicate less functional impairment for the Karnofsky score (1 to 10) but greater impairment for the NYHA classification (I to IV) and the Goldman scale (1 to 4).

Statistical Analysis

Differences between groups were evaluated for statistical significance by the chi-square statistic for discrete variables and by the z score for the continuous variables. We used multiple logistic regression to determine the likelihood of a patient's undergoing cardiac catheterization or coronary-artery bypass surgery as a function of sex while controlling simultaneously for all other clinically cogent variables that might influence the diagnostic evaluation.¹¹ The 95 percent confidence limits for these odds ratios were computed. A two-tailed P value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Of the 2231 patients enrolled in the SAVE trial, 1842 were men and 389 were women. Before the qualifying myocardial infarction, coronary risk factors were more prevalent and more severe in the women than in the men. The women were older (61.7 ± 10.9 vs. 58.9 ± 10.5 years, $P < 0.001$) and more likely to have a family history of heart disease (53 vs. 44 percent, $P = 0.002$) and a history of diabetes (32 vs. 20 percent, $P < 0.001$) or hypertension (53 vs. 41 percent, $P < 0.001$) (Table 1). Accordingly, the use of insulin and oral hypoglycemic agents as well as diuretics and other antihypertensive agents within 72 hours of the infarction was more common in women than in men (all $P < 0.001$) (Table 2). Eighty-six percent of the women were postmenopausal. Women were more likely than men to be current smokers (63 vs. 51 percent, $P < 0.001$) (Table 1).

The men and women had similar histories of angina before their index infarction. Twenty-six percent of

Table 1. Clinical Characteristics before the Index Hospitalization.

CHARACTERISTIC	Men (N = 1842)	Women (N = 389)	P VALUE*
	percent (number)		
Clinical diagnosis of angina	25.8	24.4	NS
Suspected angina	5.2	6.9	NS
Angina on Rose questionnaire	18.6	18.0	NS
Angina	25.8 (476)†	24.4 (95)	
No. of angina episodes per wk			NS
0	24.8	26.3	
1-3	52.1	47.4	
>3	22.1	26.3	
Precipitants of angina			NS
Heavy activity	35.1	26.3	
Light activity	14.1	16.8	
Not related to activity	7.7	13.7	
Angina at rest	43.1	43.2	
Cardiac risk factors			
Current smoker	51.0	63.3	<0.001
History of diabetes	19.9	31.6	<0.001
History of hypertension	40.9	53.2	<0.001
Family history of heart disease	44.4	53.2	0.002

*NS denotes not significant.

†Data for five men were missing.

the men and 24 percent of the women had been told by a physician that they had angina. According to the responses to the Rose questionnaire, administered by study personnel, 19 percent of the men and 18 percent of the women had angina at least three weeks before their infarction. Among those with ischemic symptoms, the frequency of anginal attacks was similar for men and women: nearly 75 percent of both sexes had at least one episode per week. The duration of anginal symptoms varied widely in both men and women, with a few reporting symptoms for less than 1 month and some reporting symptoms for more than 10 years. Angina was precipitated by similar degrees of activity in both sexes; more than 40 percent of the men and women with angina had symptoms at rest within three weeks of their infarction (Table 1). The use of antianginal drugs (nitrates, beta-blockers, and calcium-channel blockers) during this time was also similar; however, more men received aspirin ($P = 0.008$) (Table 2).

Although the prevalence and frequency of angina were similar in the two sexes, women were more likely

Table 2. Drugs Taken within 72 Hours before the Index Hospitalization.*

TYPE OF DRUG	Men (N = 1842)	Women (N = 389)	P VALUE†
	percent		
Beta-blocker	20.7	20.8	NS
Calcium-channel blocker	23.0	21.9	NS
Nitrate	20.8	17.5	NS
Aspirin	22.3	16.2	0.008
Insulin	5.2	11.1	<0.001
Oral hypoglycemic agent	8.4	14.4	<0.001
Diuretic	21.4	30.3	<0.001
Other antihypertensive agent	4.5	11.1	<0.001
Tranquilizer	7.1	9.5	NS

*Drugs were taken as part of long-term therapy.

†NS denotes not significant.

than men to report disability from ischemic symptoms before their index infarction. This was true whether symptoms causing disability were assessed by the NYHA classification ($P < 0.001$), the Karnofsky score ($P = 0.009$), or the Goldman scale ($P < 0.001$) (Table 3). Only 35 to 50 percent of the women reported no functional limitation (according to the NYHA functional class or the Goldman scale), as compared with 60 to 70 percent of the men.

Despite reporting greater disability as a result of their anginal symptoms, the women were less likely to be referred for cardiac catheterization (15.4 vs. 27.3 percent) and coronary bypass surgery (5.9 vs. 12.7 percent) than men ($P < 0.001$ for both). This difference was not related to differences in the frequency of angina or infarction in the two groups. Although more men than women had a history of acute myocardial infarction (37 vs. 27 percent, $P < 0.001$), men underwent catheterization and bypass surgery more frequently than women whether or not they had a diagnosis of angina or an infarction before their index infarction. Specifically, cardiac catheterization was carried out in 58 percent of the men with a previous infarction but only 44 percent of the women ($P < 0.008$), and in 9 percent of the men without a previous infarction but only 5 percent of the women ($P = 0.032$). Similarly, cardiac catheterization was performed in 64 percent of the men who had a history of angina but only 44 percent of the women, and in 15 percent of the men without angina but only 6 percent of the women ($P < 0.001$ for both). Multiple logistic regression analysis showed that sex was associated

Table 4. Odds of Catheterization and Cardiac Surgery before the Index Infarction.*

VARIABLE	ODDS OF CATHETERIZATION		ODDS OF CARDIAC SURGERY	
	ODDS RATIO	95% CONFIDENCE LIMITS	ODDS RATIO	95% CONFIDENCE LIMITS
Male sex	1.87	1.27, 2.75	1.84	1.11, 3.05
Ejection fraction	1.00	0.98, 1.02	1.00	0.98, 1.02
Age ≤ 64 yr	2.12	1.61, 2.80	1.51	1.09, 2.08
Previous infarction	8.51	6.53, 11.11	4.56	3.20, 6.50
History of angina	4.63	3.44, 6.23	2.53	1.77, 3.63
Angina for > 5 yr	1.75	1.19, 2.56	2.09	1.44, 3.05
Ever smoked	1.15	0.84, 1.58	1.32	0.89, 1.96
Education $<$ high school	0.73	0.56, 0.95	0.85	0.62, 1.15
Married	1.05	0.78, 1.40	1.20	0.84, 1.71
History of diabetes	0.89	0.66, 1.21	0.81	0.56, 1.17
History of hypertension	1.18	0.92, 1.52	1.12	0.83, 1.50
Family history of heart disease	1.55	1.21, 1.99	1.50	1.12, 2.01
NYHA class I	1.19	0.82, 1.73	0.93	0.60, 1.44
Goldman scale, class I	0.71	0.51, 1.01	0.82	0.54, 1.23
Karnofsky scale, score of 10	0.95	0.70, 1.30	1.15	0.79, 1.68

*Odds ratios for each variable were calculated by including all the other variables listed in this table in the multivariate logistic regression model.

with the use of cardiac catheterization and bypass surgery independently of other clinical variables. After controlling for the other relevant variables listed in Table 4, we found that men were twice as likely as women to undergo cardiac catheterization and bypass surgery (Table 4). Once a woman underwent cardiac catheterization, however, sex-related differences in the use of surgery were less apparent: of the patients who had catheterization before their index infarction, 46 percent of the men and 38 percent of the women subsequently had bypass surgery (P not significant).

The presentation of the index infarction was similar for men and women, and both sexes had a similar hospital course and were equally likely to undergo cardiac catheterization and revascularization after their index infarction (Table 5). However, to be considered eligible for randomization in the SAVE study, patients were required to undergo cardiac catheterization and revascularization if they had symptoms or signs of myocardial ischemia after the index infarction. To determine whether these requirements may have biased the selection of patients for this analysis, we examined whether men and women who were otherwise eligible for the study were differentially excluded because of failure to undergo an indicated cardiac procedure in the presence of signs and symptoms of myocardial ischemia. There were 262 such patients; the sex of 241 was reported. Twenty percent of the excluded patients were women, a proportion similar to that of the randomized study population. Women were excluded for different reasons than men, however ($P < 0.05$); among patients who had clinical ischemia after their index infarction, women were twice as likely as men to be excluded because catheterization was not performed (42 vs. 21 percent). Yet once a woman underwent catheterization and revascularization was rec-

Table 3. Functional Rating and Employment before the Index Hospitalization.*

VARIABLE	MEN (N = 1842)	WOMEN (N = 389)	P VALUE
	<i>percent</i>		
Functional rating†			
Karnofsky score			0.009
8-10	89.9	85.3	
5-7	9.6	13.6	
1-4	0.4	0.5	
Goldman scale			< 0.001
1	62.4	35.0	
2	21.1	35.0	
3	14.9	28.5	
4	0.8	1.0	
NYHA clinical class			< 0.001
I	69.3	49.9	
II	25.1	39.6	
III	5.5	10.0	
IV	0.1	0.3	
Employment			< 0.001
Full time	45.2	18.0	
Part time	6.6	9.5	
Retired	36.8	40.4	
Unemployed	7.3	25.2	

*Values do not sum to 100 percent because of rounding.

†A Karnofsky score of 8 to 10 indicates normal activity; 5 to 7, less than normal activity, with the patient possibly requiring assistance; and 1 to 4, disability. The Goldman scale is based on the patient's ability to carry out specific activities requiring different levels of metabolic equivalents (METS): I ≥ 7 METS, II ≥ 5 METS, III ≥ 2 METS, and IV < 2 METS. The NYHA clinical class I indicates that the patient has no limitations, II slight limitations, and III marked limitations; class IV indicates that the patient cannot engage in any activity without discomfort.

Table 5. Course during Index Hospitalization before Randomization in the SAVE Study.*

VARIABLE	MEN (N = 1842)	WOMEN (N = 389)	P VALUE
Mean peak CK value (% of normal)	1327	1569	NS
Mean (\pm SD) ejection fraction (%)	30.8 \pm 6.9	31.8 \pm 6.0	0.012
Mean time from MI to randomization (days)	11	11	NS
Killip class within 72 hr of MI (% of patients)†			NS
I	60	54	
II	32	36	
III	5	7	
IV	2	2	
Procedures between MI and random- ization (% of patients)			
Cardiac catheterization	55	55	NS
Cardiac surgery	9	9	NS
PTCA	17	19	NS

*CK denotes creatine kinase, NS not significant, MI myocardial infarction, and PTCA percutaneous transluminal coronary angioplasty.

†Values do not sum to 100 percent because of rounding.

ommended, she was as likely as a man to undergo coronary bypass surgery (Table 6).

DISCUSSION

This study demonstrates that women with coronary heart disease undergo cardiac catheterization and coronary bypass surgery less often than men. The difference between the two groups was apparent even though women had symptoms of myocardial ischemia as frequently as men and reported significantly more disability as a result of their symptoms. This finding could not be explained by differences in coronary risk factors or cardiovascular medications, which might lead physicians to pursue a less aggressive approach. Even after controlling for all clinical variables, including the severity and duration of anginal symptoms, we found that men were twice as likely as women to undergo a cardiac procedure.

Two previous studies have suggested that physicians are less likely to recommend cardiac procedures in women than in men. Tobin and coworkers³ noted that men were 10 times more likely than women to undergo cardiac catheterization after an abnormal result on exercise testing. This difference seemed to be related to the finding that symptoms of chest pain in women, although more frequent, were more likely to be attributed to noncardiac causes. This finding raised the possibility that referring physicians overused radionuclide exercise testing in women. In a study of 2297 patients referred for coronary bypass surgery, Khan and associates⁴ noted that women had severe manifestations of coronary heart disease more often than men. This difference was related to the fact that men were referred more frequently for catheterization and surgery (with no or minimal symptoms) because they had a positive exercise test. These data are compatible with the hypothesis that coronary bypass surgery may have been overused in men who were at low risk of serious cardiovascular events.¹² Hence, although the studies of Tobin and coworkers³ and Khan

and coworkers⁴ identified sex-related differences in the use of health care resources, these reports could not rule out the possibility that such patterns of use merely represented inappropriate use of resources and were not associated with adverse clinical consequences. In addition, both studies were conducted at single hospitals with data bases that were collected in the early to mid-1980s and then analyzed retrospectively.

The present study addresses many of the limitations of these two earlier reports. Our study was carried out from 1987 to 1989 in 112 hospitals throughout the United States and Canada. The patients were asked about symptoms and cardiac procedures with the use of uniform methods and validated questionnaires. Most importantly, patients were selected for inclusion on the basis of the occurrence of a similar cardiovascular event, rather than on the basis of a physician's decision to recommend a cardiac procedure. Using the data on these high-risk patients, we were able to confirm previous findings that women undergo potentially useful cardiac procedures less often than men.

How can we explain the lower use of cardiac catheterization and coronary bypass surgery in high-risk women than in high-risk men? Many physicians believe that angina is a benign symptom in women, because many women with chest pain do not have coronary artery disease. This conclusion was based on experience in young women,¹³ however, and is not valid when the analysis includes older women. Many physicians also believe that stress testing is not accurate for the diagnosis of coronary disease in women. However, this conclusion is based on studies that failed to give adequate consideration to the lower prevalence of coronary disease in premenopausal women^{14,15} and failed to account for avoidable pitfalls in the interpretation of tests (e.g., breast artifact causing anterior-wall thallium defects).^{16,17} Finally, it is possible that fewer women are referred for cardiac procedures because of concern that women undergoing coronary bypass surgery have a higher operative mortality rate than men.¹⁸⁻²⁰ This higher mortality may be

Table 6. Reasons for Exclusion of Patients Otherwise Eligible for the SAVE Study, According to Sex.*

EXCLUSION CRITERION†	MEN (N = 191)	WOMEN (N = 50)
	percent	
Clinical ischemia, no catheterization	21.4	42.0
Markedly positive ETT, no catheterization	24.1	16.0
Thrombolytic therapy, no ETT or catheterization	4.2	2.0
Catheterization performed, revascularization recommended but not performed	50.3	40.0

*0.05 > P > 0.025 for the comparison of men with women.

†ETT denotes exercise-tolerance test.

the result, rather than the cause, of a referral bias, however, since women have more advanced disease at the time of referral.^{4,18-21}

On the basis of our findings, we cannot conclude whether cardiac catheterization and coronary bypass surgery were underused in women or overused in men. However, it is disturbing to note that by all measures employed, women reported more cardiac disability than men before their infarction but were less likely to undergo procedures that are known (at least in men) to lessen symptoms and improve functional capacity. Unfortunately, despite years of use, the ability of these procedures to reduce disability in women remains incompletely defined, because few women are enrolled in randomized trials of therapeutic interventions.²² In the present study, even among patients who had recurrent ischemia after their index infarction, women were twice as likely as men to be excluded from participation in the trial because they did not have an indicated cardiac catheterization that was required for enrollment.

APPENDIX

SAVE study centers: Albany Medical Center, Albany, N.Y. — T. Biddle, M.D.; Albert Einstein Medical Center, Philadelphia — J. Wertheimer, M.D.; Bowman Gray School of Medicine, Winston-Salem, N.C. — H. Miller, M.D.; Brigham and Women's Hospital, Boston — G. Lamas, M.D.; Iowa Heart Center, Des Moines — D. Gordon, M.D.; Geisinger Medical Center, Danville, Pa. — F. Menapace, M.D.; Hôpital du Sacré-Coeur, Montreal — J.L. Rouleau, M.D., and M. Klein, M.D.; Hôpital Notre-Dame, Montreal — F. Sestier, M.D., Ph.D.; Hospital of the Medical College of Pennsylvania, Philadelphia — P. Kowey, M.D.; Howard University Hospital, Washington, D.C. — O. Randall, M.D.; Jackson Clinical Foundation, Madison, Wis. — J. Farnham, M.D.; Jewish General Hospital, Montreal — J. McCans, M.D.; Kingston General Hospital, Kingston, Ontario — J. Parker, M.D.; Laval Hospital, Ste.-Foy, Quebec — G.R. Dagenais, M.D., and J. Rouleau, M.D.; Lutheran General Hospital, Park Ridge, Ill. — R. Sorkin, M.D.; Maine Medical Center, Portland — C. Lambrew, M.D.; Massachusetts General Hospital, Boston — R. Zusman, M.D.; Mayo Clinic, Rochester, Minn. — D. Hayes, M.D., and B. Gersh, M.D.; Memorial University of Newfoundland, St. John's — B. Sussex, M.D.; Mount Sinai Medical Center, Cleveland — D. Adler, M.D.; Mount Sinai Medical Center, New York, and Winthrop-University Hospital, Mineola, N.Y. — M. Packer, M.D., and R. Steingart, M.D.; Oregon Heart Institute, Portland — S. Lewis, M.D.; Sacred Heart Hospital, Eugene, Oreg. — K. Jacobson, M.D.; Sharp Hospital, San Diego, Calif. — S. Smith, Jr., M.D.; State University of New York, Stony Brook — E. Brown, Jr., M.D.; Tulsa Heart Center, Tulsa, Okla. — L. Basta, M.D.; University of Arizona, Tucson — S. Goldman, M.D.; University of Arkansas, Little Rock — H. Dinh, M.D.; University of British Columbia, Vancouver — V. Bernstein, M.D.; University of California-Davis, Sacramento — E. Amsterdam, M.D.; University of Connecticut, Farmington — D. Hager, M.D.; University of Louisville, Louisville, Ky. — J. Kupersmith, M.D.; University of Manitoba, Winnipeg — T. Cuddy, M.D.; University of Maryland, Baltimore — S. Gottlieb, M.D.; University of Massachusetts, Worcester — J. Alpert, M.D.; University of Missouri, Columbia — G. Flaker, M.D.; University of New Mexico, Albuquerque — J. Abrams, M.D.; University of South Florida, Tampa — S. Glasser, M.D.; University of Tennessee, Memphis — B. Hackman, M.D.; University of Texas at Galveston, Galveston — J. Wallace, M.D.; University of Toronto, Toronto — P. McEwan, M.D.; University of Wisconsin at Madison, Madison — N. Bittar, M.D.; Victoria Hospital, London, Ontario — M. Arnold, M.D.; Wadsworth Veterans Affairs Hospital, Los Angeles — B. Singh, M.D., Ph.D.; and Washington University, St. Louis — E. Gelman, M.D.; *Principal investigator:* Marc A. Pfeffer, M.D., Ph.D.; *Chairman, steering committee:* Eugene Braunwald, M.D.; *Policy board:* Richard

Gorlin, M.D., Mount Sinai Medical Center, New York; William W. Parmley, M.D., University of California San Francisco, San Francisco; James Ware, Ph.D., Harvard School of Public Health, Boston; and Karl T. Weber, M.D., University of Missouri, Columbia; *Data coordinating center:* University of Texas Health Science Center, Houston: C. Morton Hawkins, Sc.D., Barry Davis, M.D., Ph.D., Lemuel A. Moyé, M.D., Ph.D., and Peggy Hamm, Ph.D.; *Clinical coordinating center:* Brigham and Women's Hospital, Boston: Marc A. Pfeffer, M.D., Ph.D., Gervasio A. Lamas, M.D., John D. Rutherford, M.D., L. Howard Hartley, M.D., and Kathleen Connors, R.N.; *Mortality and end-points committee:* Milton Packer, M.D. (Chairman), Victoria Bernstein, M.D., Thomas E. Cuddy, M.D., Barry Davis, M.D., Ph.D. (University of Texas at Houston), Kirk Jacobson, M.D., Gervasio A. Lamas, M.D., Sandra Lewis, M.D., John McCans, M.D., Otelio Randall, M.D., Bruce Sussex, M.D., and John H. Wertheimer, M.D.; *Core directors:* Electrocardiography — John D. Rutherford, M.D.; radionuclide ventriculography — Frans J. Th. Wackers, M.D.; echocardiography — Martin St. John Sutton, M.D.; and cardiac catheterization — Gervasio A. Lamas, M.D.

REFERENCES

- Eaker ED, Packard B, Thom TJ. Epidemiology and risk factors for coronary heart disease in women. *Cardiovasc Clin* 1989; 19:129-45.
- Kannel WB, Abbott RD. Incidence and prognosis of myocardial infarction in women: The Framingham Study. In: Eaker ED, Packard B, Wenger NK, Clarkson T, Tyroler HA, eds. *Coronary artery disease in women*. New York: Haymarket-Doyma, 1987:208-14.
- Tobin JN, Wassertheil-Smoller S, Wexler JP, et al. Sex bias in considering coronary bypass surgery. *Ann Intern Med* 1987; 107:19-25.
- Khan SS, Nessim S, Gray R, Czer LS, Chau A, Matloff J. Increased mortality of women in coronary artery bypass surgery: evidence for referral bias. *Ann Intern Med* 1990; 112:561-7.
- Wenger NK. Gender, coronary artery disease, and coronary bypass surgery. *Ann Intern Med* 1990; 112:557-8.
- Sketch MN, Mohiuddin SM, Lynch JD, Zencka AE, Runco V. Significant sex differences in the correlation of electrocardiographic exercise testing and coronary arteriograms. *Am J Cardiol* 1975; 36:169-73.
- Rose GA. The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. *Bull World Health Organ* 1962; 27:645-58.
- The Criteria Committee of the New York Heart Association. *Nonmenclature and criteria for diagnosis of diseases of the heart and great vessels*. 6th ed. Boston: Little, Brown, 1964.
- Grieco A, Long CJ. Investigation of the Karnofsky Performance Status as a measure of quality of life. *Health Psychol* 1984; 3:129-42.
- Goldman L, Cook F, Mitchell N, Flatley M, Sherman H, Cohn PF. Pitfalls in the serial assessment of cardiac functional status. *J Chronic Dis* 1982; 35:763-71.
- Walker SH, Duncan DB. Estimation of the probability of an event as function of several independent variables. *Biometrika* 1967; 54:167-79.
- Weiner DA, Ryan TJ, McCabe CH, et al. The role of exercise testing in identifying patients with improved survival after coronary artery bypass surgery. *J Am Coll Cardiol* 1986; 8:741-8.
- Kannel WB, Feinleib M. Natural history of angina pectoris in the Framingham Study. *Am J Cardiol* 1972; 29:154-63.
- Weiner DA, Ryan TJ, McCabe CH, et al. Exercise stress testing: correlations among history of angina, ST-segment response and prevalence of coronary-artery disease in the Coronary Artery Surgery Study (CASS). *N Engl J Med* 1979; 301:230-5.
- Steingart RM, Scheuer J. Assessment of myocardial ischemia. In: Hurst J, ed. *The heart*. 7th ed. New York: McGraw-Hill, 1990:351-68.
- Meller J, Goldsmith SJ, Rudin A, et al. Spectrum of exercise thallium-201 myocardial perfusion imaging in patients with chest pain and normal coronary angiograms. *Am J Cardiol* 1979; 43:717-23.
- Hung J, Chaitman BR, Lam J, et al. Noninvasive diagnostic test choices for the evaluation of coronary artery disease in women: a multivariate comparison of cardiac fluoroscopy, exercise electrocardiography and exercise thallium myocardial perfusion scintigraphy. *J Am Coll Cardiol* 1984; 4:8-16.
- Kennedy JW, Kaiser GC, Fischer LD, et al. Clinical and angiographic predictors of operative mortality from the collaborative study in coronary artery surgery (CASS). *Circulation* 1981; 63:793-802.
- Loop FD, Golding LR, MacMillan JP, Cosgrove DM, Lytle BW, Sheldon WC. Coronary artery surgery in women compared with men: analyses of risks and long-term results. *J Am Coll Cardiol* 1983; 1:383-90.
- Fisher LD, Kennedy JW, Davis KB, et al. Association of sex, physical size, and operative mortality after coronary artery bypass in the Coronary Artery Surgery Study (CASS). *J Thorac Cardiovasc Surg* 1982; 84:334-41.
- Penckofer SM, Holm K. Women undergoing coronary artery bypass surgery: physiological and psychosocial perspectives. *Cardiovasc Nurs* 1990; 26:13-8.
- Hilts PJ. N.I.H. starts women's health office. *New York Times*. September 11, 1990:C-9.