Journal of the American College of Cardiology
© 2002 by the American College of Cardiology Foundation
Published by Elsevier Science Inc.
Vol. 40, No. 2, 2002
ISSN 0735-1097/02/$22.00
PII S0735-1097(02)01949-6

Women Do Have an Improved Long-Term Outcome After Non–ST-Elevation Acute Coronary Syndromes Treated Very Early and Predominantly With Percutaneous Coronary Intervention

A Prospective Study in 1,450 Consecutive Patients

Christian Mueller, MD,*† Franz-Josef Neumann, MD, FACC,* Helmut Roskamm, MD, FACC,* Peter Buser, MD, FACC,† John McB. Hodgson, MD, FACC,‡ Andrè P. Perruchoud, MD,† Heinz J. Buettner, MD*

Bad Krozingen, Germany; Basel, Switzerland; and Cleveland, Ohio

OBJECTIVES This study sought to assess gender-based differences in long-term outcome after very early aggressive revascularization for non–ST-elevation acute coronary syndromes (NSTACS).

BACKGROUND The Fragmin and fast Revascularization during InStability in Coronary artery disease (FRISC) II study suggested that women have less to gain from an early invasive strategy.

METHODS We conducted a prospective cohort study in 1,450 consecutive patients with NSTACS undergoing coronary angiography and subsequent coronary stenting of the culprit lesion as the primary revascularization strategy within 24 h of admission. The combined primary end point was defined as death or nonfatal myocardial infarction (MI) and recorded for a mean of 20 months.

RESULTS Percutaneous coronary intervention was performed in more than 50% of patients in women and men and accompanied with stenting in 80%. The percutaneous coronary intervention: coronary artery bypass grafting ratio was 4:1 in men and 5:1 in women. The primary end point occurred in 29 (7.0%) women as compared with 108 (10.5%) men (hazard ratio for women, 0.65; 95% confidence interval [CI] 0.42 to 0.99; p = 0.045). Backward-stepwise multivariate Cox regression analysis identified female gender as an independent predictor of death or MI (hazard ratio for female gender, 0.51; 95% CI, 0.28 to 0.92; p = 0.024). Kaplan-Meier analysis showed that women had consistently lower event rates during the entire follow-up period (p = 0.037 by log-rank for death or MI).

CONCLUSIONS Women treated with very early aggressive revascularization with coronary stenting of the culprit lesion as the primary revascularization strategy have a better long-term outcome as compared with men. (J Am Coll Cardiol 2002;40:245–50) © 2002 by the American College of Cardiology Foundation

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in both women and men. The percentage of female patients is rising and was 43% in 1995 (1). Observational studies (2–13) have shown a worse in-hospital and long-term outcome for acute myocardial infarction (MI) in women as compared with men. It is currently unknown whether these differences reflect differences in baseline characteristics (2–16), pathophysiologic distinctions (17–21) or gender differences in the diagnosis and treatment of CAD (2,3,6,22–27) to the detriment of women.

Each year, 1.5 million patients are hospitalized for acute coronary syndromes (ACS) in the U.S. An increased risk of death and recurrent MI has consistently been reported for women treated with fibrinolysis for ST-elevation ACS (2–13,15). For non–ST-elevation acute coronary syndromes (NSTACS), recent studies (14–16,28) have been controversial. In the Fragmin and fast Revascularization during InStability in Coronary Artery Disease (FRISC) II study (16), an invasive strategy with coronary angiography within the first seven days did not reduce the risk of future events among women, in contrast with its beneficial effect in men. In fact, multivariate analysis including the presence or absence of angiographically significant stenoses found female gender to be an independent risk factor for death or MI.

Very early (within 24 h) revascularization has been proposed as a novel potentially superior management strategy in patients with NSTACS (28,29). The long-term outcome of women as compared with men in NSTACS treated with a very early invasive strategy remains to be established.

We sought to determine if very early aggressive revascularization with coronary stenting of the culprit lesion as the primary revascularization strategy might result in identical outcome for both women and men.

METHODS

Patient population. From January 1996 to December 1999, consecutive patients admitted to our center with NSTACS were treated with a very early invasive strategy.

From the *Herz-Zentrum Bad Krozingen, Bad Krozingen, Germany; †University Hospital Basel, Basel, Switzerland; and ‡MetroHealth Medical Center, Cleveland, Ohio.

Manuscript received December 7, 2001; revised manuscript received March 19, 2002, accepted April 19, 2002.

Abbreviations and Acronyms

ACS	= acute coronary syndromes
CABG	= coronary artery bypass grafting
CAD	= coronary artery disease
CI	= confidence interval
CK	= creatine kinase
ECG	= electrocardiogram
FRISC	= Fragmin and fast Revascularization during InStability in Coronary artery disease study
MI	= myocardial infarction
NSTACS	= non–ST-elevation acute coronary syndrome
PCI	= percutaneous coronary intervention
TACTICS-TIMI 18	= Treat Angina with Aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis In Myocardial Infarction 18 trial

Patients were eligible for inclusion in this study if they had symptoms of myocardial ischemia occurring at rest (in general Braunwald class IIIB unstable angina [30]). Patients with de novo angina pectoris on exertion or worsening angina during exertion only (Braunwald class 1A to 1C), patients with persistent ST-elevation and patients with postinfarction angina (Braunwald class 1C, 2C, 3C) were excluded. Fifteen patients in whom angiography was not performed due to patient refusal (n = 6) or extremely severe concomitant disease (n = 9) had to be excluded from this analysis.

The study was carried out according to the principles of the Declaration of Helsinki. Informed consent was obtained from all participating patients.

Very early revascularization. Patients with persistent chest pain underwent immediate coronary angiography. In patients asymptomatic while on medical therapy, coronary angiography was performed within 24 h of admission. Whenever possible, coronary stenting of the culprit lesion was done directly after angiography. Stenting was not restricted to patients with one- and two-vessel disease, but also favored in patients with three-vessel disease, if the target lesion seemed accessible. If percutaneous coronary intervention (PCI) was not possible (unprotected left main disease, diffuse three-vessel disease) but revascularization seemed necessary, patients were scheduled for urgent coronary artery bypass grafting (CABG).

Follow-up. All patients were scheduled for out-patient visits at six months. In addition, patients were contacted by questionnaire in September 2000, nearly five years after enrollment of the first patient. For patients reporting cardiac symptoms, at least one clinical and electrocardiographic examination was performed in the outpatient clinic or by the referring physician. All information derived from contingent hospital readmission records or provided by the referring physician or by the outpatient clinic was reviewed and entered into the computer database.

End points and statistical analysis. The prespecified combined primary end point was defined as death from all causes or nonfatal MI. Myocardial infarction was defined as typical chest pain at rest followed by an increase in creatine phosphokinase (creatine kinase [CK] and CK-MB beyond two times the upper limit of normal and five times the upper limit of normal after CABG) or new Q waves in the electrocardiogram (ECG). All patients received ECG recordings directly after PCI or CABG and on the following morning. In addition, cardiac markers (CK and CK-MB) were determined at 8 to 24 h after the intervention and additionally whenever ischemic symptoms developed. The statistical analyses were performed using the SPSS/PC (version 11.0, SPSS Inc., Chicago, Illinois) software package. Discrete variables were expressed as percentage (95% confidence interval [CI]), continuous variables as means (95% CI), and a statistical significance level of 0.05 was used. Comparisons were made using analysis of variance for independent samples and chi-square tests as appropriate. All hypothesis testing was two-tailed. Cox proportional hazards regression analysis was used as the appropriate method throughout. Backward-stepwise multivariate Cox regression analysis was performed to identify independent predictors of death or MI. Gender, age, previous MI, previous CABG, previous PTCA, diabetes, mechanical resuscitation, defibrillation, cardiogenic shock, chest pain within the last 24 h, non–Q-wave MI, new ST-segment depression of at least 1 mm, new T-wave inversion, C-reactive protein >10 mg/l, troponin T ≥ 0.1 μg/l, baseline platelet count, baseline creatinine and the number

Table 1. Baseline Patient Characteristics

	Women (n = 417)	Men (n = 1,033)	p Value
Age (yrs)	68 (67–69)	64 (63–64)	0.01
Prior MI	24 (20–28)	37 (34–40)	0.01
Prior CABG	6 (4–9)	17 (14–19)	0.01
Prior coronary angioplasty	21 (17–25)	24 (21–26)	0.20
Diabetes	23 (18–28)	19 (16–22)	0.15
Hypercholesterolemia	70 (64–76)	68 (64–71)	0.55
Hypertension	72 (66–77)	60 (56–64)	0.01
Smoking	21 (15–26)	33 (30–37)	0.01
Angina pectoris at rest >48 h	20 (16–24)	16 (14–18)	0.07
Angina pectoris at rest <48 h	67 (63–72)	69 (66–72)	0.52
Non–Q-wave MI	13 (9–16)	15 (13–17)	0.28
Cardiogenic shock	1 (0–2)	1 (0–2)	0.54
New ST depression at entry	12 (9–15)	10 (8–12)	0.28
New T-wave inversion	34 (29–38)	27 (24–30)	0.01
Troponin T ≥ 0.1 μg/l	52 (46–58)	58 (54–61)	0.11
CRP > 10 mg/l	24 (19–29)	26 (23–30)	0.47
Creatinine (mg/dl)	0.78 (0.73–0.83)	1.00 (0.95–1.05)	0.01
Platelet count ($\times 10^3/\mu l$)	248 (241–255)	229 (225–234)	0.01

Data are expressed as mean or percentage (95% confidence interval).
CABG = coronary artery bypass grafting; CRP = C-reactive protein; MI = myocardial infarction.

Table 2. Baseline Angiographic and Procedural Characteristics

	Women (n = 417)	Men (n = 1,033)	p Value
Coronary vessels with ≥50% stenosis			0.01
0	21 (17–25)	11 (9–13)	0.01
1	26 (22–31)	24 (22–27)	0.45
2	24 (20–29)	23 (20–25)	0.44
3	29 (24–33)	42 (39–46)	0.01
Percutaneous coronary intervention	53 (48–58)	56 (53–59)	0.27
Proportion with stent	80 (74–85)	80 (76–83)	0.97
Proportion with glycoprotein IIb/IIIA inhibition	14 (9–19)	11 (7–15)	0.55
Coronary artery bypass grafting	11 (8–14)	15 (13–17)	0.02
Medical therapy	36 (32–41)	28 (26–31)	0.01

Data are expressed as mean or percentage (95% confidence interval).

of coronary vessels with ≥50% stenosis at angiography were entered into the model. The cumulative survival curves were constructed with the use of the Kaplan-Meier method.

RESULTS

There were 417 women and 1,033 men in this study (Tables 1 and 2). Baseline characteristics were considerably different between women and men. The women were significantly older and less often had prior MI or prior CABG. More women had arterial hypertension and more men were smokers. At admission, there was no difference in the rate of ST-segment depression. However, T-wave inversion was seen more often in women. Troponin T was elevated in more than 50% of patients in both groups. Serum creatinine was lower and platelet count higher in women. There were more patients without a high-grade coronary lesion among the women, and less patients with three-vessel disease. Accordingly, CABG was chosen more often in men (15% vs. 11%, p = 0.02) and medical therapy more often in women (36% vs. 28%, p = 0.01). Percutaneous coronary intervention was performed in more than 50% of patients of both genders, and accompanied with stenting in 80%. All together, two-thirds of patients underwent revascularization. The PCI:CABG ratio was 4:1 in men and 5:1 in women.

Eighty-three deaths and 59 MIs occurred during a mean follow-up of 20 months (range, 1 to 60). The combined primary end point of death or MI was recorded in 29 (7.0%) women as compared with 108 (10.5%) men (Table 3). Therefore, the risk of death or MI was significantly lower for women (hazard ratio, 0.65; 95% CI, 0.42 to 0.99; p = 0.045). Total mortality was 4.1% in women as compared with 6.4% in men (hazard ratio, 0.62; 95% CI, 0.23 to 1.66; p = NS). The incidence of nonfatal MI was 3.1% in women versus 4.5% in men (hazard ratio, 0.66; 95% CI, 0.34 to 1.28; p = NS). During the in-hospital phase, there was a trend in favor of women; however, none of the outcome differences reached statistical significance.

Backward-stepwise multivariate Cox regression analysis including baseline characteristics, ECG findings, markers of inflammation and myocardial necrosis, as well as the angiographic extent of CAD identified female gender as an independent predictor of death or MI (Table 4). In this model, female gender had a major impact with an hazard ratio of 0.51 (95% CI, 0.28 to 0.92; p = 0.02).

Kaplan-Meier curves for the cumulative probability of death (Fig. 1) and the cumulative probability of death or MI (Fig. 2) were considerably different for women and men. Women had consistently lower event rates during the whole follow-up period (p = 0.0899 by log-rank test for death and p = 0.0366 by log-rank test for death or MI).

DISCUSSION

This study of 1,450 consecutive patients with NSTACS treated with an aggressive revascularization strategy showed important differences in baseline clinical characteristics be-

Table 3. Association Between Female Gender and Outcome

	Women (n = 417)	Men (n = 1,033)	Hazard Ratio (95% CI)	p Value
In-hospital				
Death or MI	3.8 (2.0–5.7)	4.7 (3.4–5.9)	0.81 (0.44–1.48)	0.496
Death	1.2 (0.2–2.3)	2.0 (1.2–2.9)	0.64 (0.38–1.10)	0.105
Q-wave MI	0.7 (0.0–1.5)	0.3 (0.0–0.6)	2.49 (0.50–12.36)	0.263
Non–Q-wave MI	1.9 (0.6–3.2)	2.3 (1.4–3.2)	0.75 (0.30–1.86)	0.530
During follow-up				
Death or MI	7.0 (4.5–9.4)	10.5 (8.6–12.3)	0.65 (0.42–0.99)	0.045
Death	4.1 (2.2–6.0)	6.4 (4.9–7.9)	0.62 (0.23–1.66)	0.346
MI	3.1 (1.5–4.8)	4.5 (3.2–5.7)	0.66 (0.34–1.28)	0.219

Data are expressed as percentage (95% confidence interval [CI]).
MI = myocardial infarction.

Table 4. Independent Predictors of Death or Myocardial Infarction During Follow-Up in Multivariate Analysis

	Hazard Ratio (95% CI)	p Value
Female gender	0.51 (0.28–0.92)	0.024
CRP > 10 mg/l	2.43 (1.55–3.81)	0.001
Coronaries with ≥50% stenosis	1.52 (1.11–4.29)*	0.001
Serum creatinine	1.21 (1.04–1.41)	0.016
Age	1.05 (1.03–1.08)*	0.001
Platelet count	1.004 (1.001–1.006)*	0.002
T-wave inversion	0.51 (0.28–0.91)	0.024

*For an increase in age of 1 year, serum creatinine of 1 mg/dl, platelet count of $10^3/\mu l$ and one coronary with ≥50% stenosis.
CI = confidence interval; CRP = C-reactive protein.

tween women and men. Most importantly, women were older but less often had prior MI or prior CABG. In addition, the angiographic extent of CAD was less severe in women. These findings are consistent with various previous studies (2–16). The treatment strategy applied in our patient is novel in two aspects: 1) timing and 2) preferred method of revascularization. Coronary angiography and subsequent coronary stenting of the culprit lesion as the primary revascularization method were performed within 24 h of admission in all patients. The PCI:CABG ratio was 4:1 in men and 5:1 in women. This treatment was associated with a significantly better long-term outcome in women as compared with men.

Our analysis has four particular strengths. First, it is derived from a prospective study of consecutive unselected patients rather than a randomized trial. This eliminates selection bias and eases the extrapolation of findings into clinical practice. Women are notoriously underrepresented in randomized controlled trials (31) of NSTACS. Therefore, this prospective study in consecutive patients may be particular valuable for the investigation of gender-based differences. Second, it includes long-term follow-up. Third, a uniform revascularization strategy was applied in all patients. Fourth, the extent of CAD was quantified in all patients and included in the multivariate analysis as a potential cofounder. This enables us to investigate the impact of female gender independent of the extent of CAD.

Our patient cohort with NSTACS seems similar to the patients included in the FRISC II (16) and Treat angina with Aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy (TACTICS) (28) studies. The FRISC II study excluded patients with previous CABG and patients with advanced age. However, most baseline patient characteristics were comparable. Three-vessel disease was present in 38% of patients in this study, as compared with 23% in FRISC II and 34% in TACTICS, prior MI in 33% of patients in this study, as compared with 23% in FRISC II and 39% in TACTICS, and a troponin T ≥0.1 μg/l in 56% of patients in this study, as compared with 58% in FRISC II and 54% in TACTICS.

Comparison with FRISC II. The outcome of women in our study is in marked contrast with the results of the revascularization strategy used in FRISC II (16). With coronary angiography performed within the first seven days and a PCI:CABG ratio of 1:1, women randomized to the invasive strategy had a worse outcome as compared with men. In fact, in multivariate analysis, female gender in-

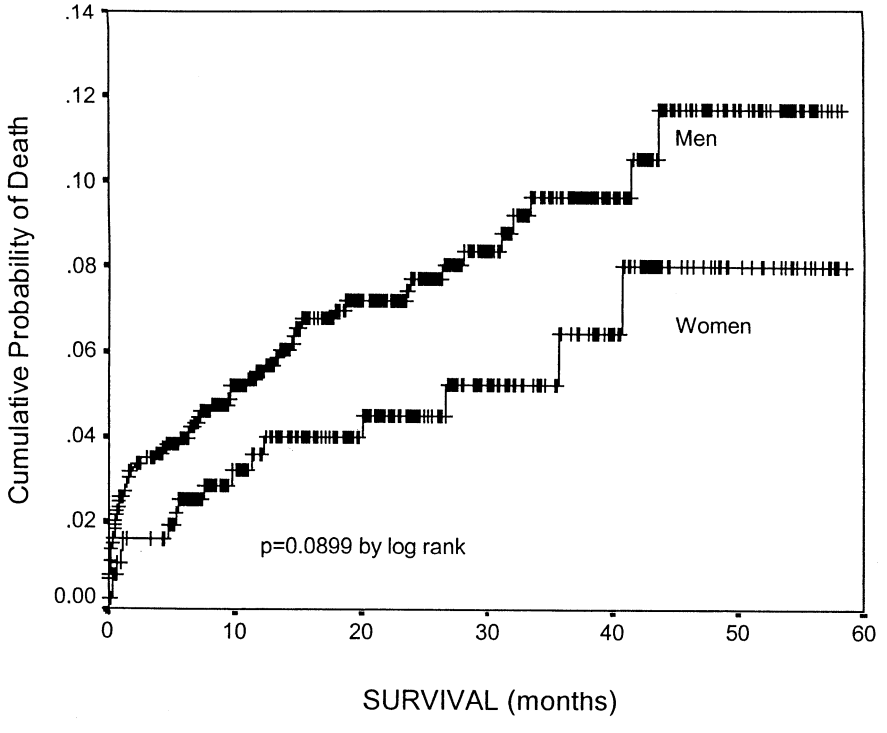

Figure 1. Cumulative probability of death for women and men during long-term follow-up.

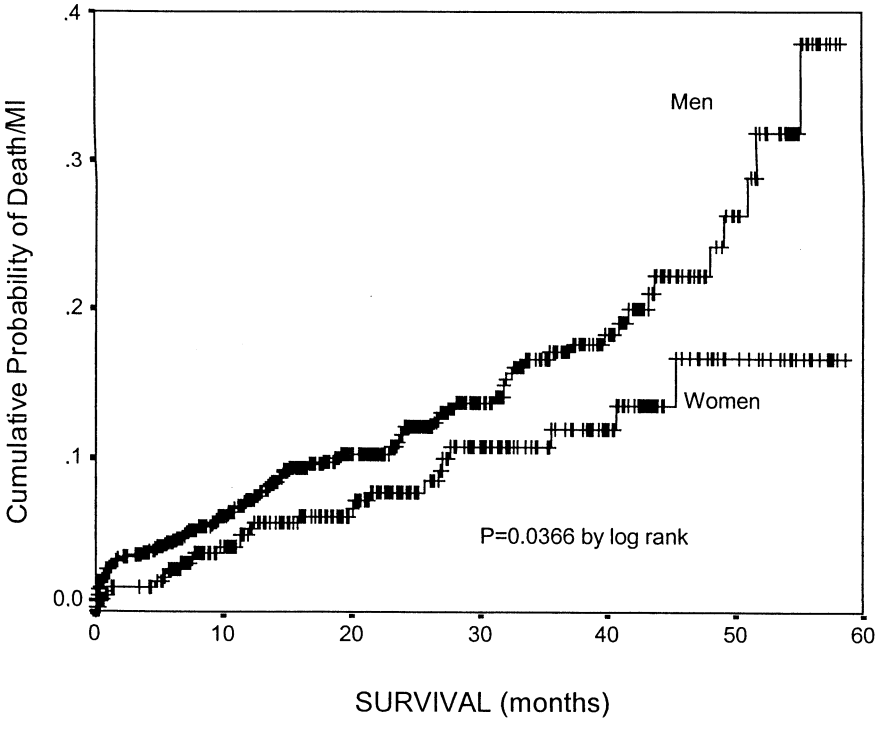

Figure 2. Cumulative probability of death or myocardial infarction for women and men during long-term follow-up.

creased the risk for death or MI (hazard ratio, 1.7; p = 0.014) in the invasive group in FRISC II. This difference seemed solely due to an excess hazard in women undergoing CABG. Therefore, the PCI:CABG ratio of the revascularization strategy seems to be an important contributor to gender differences in the outcome of patients with NSTACS. In fact, with PCI-based very early revascularization, female gender was found to be a significant independent predictor of event-free survival. In multivariate analysis, female gender reduced the risk of death or MI by 49%.

Comparison with TACTICS-Thrombolysis In Myocardial Infarction (TIMI) 18. In addition to our findings, there are other contemporary data (28) that do not support the conclusion of the FRISC II study, that "women have less to gain from an early invasive strategy." The TACTICS-TIMI 18 trial (28) compared an early invasive strategy, which included routine catheterization within 4 h and 48 h and revascularization as appropriate with a selectively invasive strategy, in which catheterization was performed if the patient had objective evidence of recurrent ischemia or an abnormal stress test. The primary end point, a composite of death, nonfatal MI and rehospitalization for an acute coronary syndrome at six months, was reduced with the use of the early invasive strategy in both men and women. However, the event rate was slightly higher in women as compared with men (17.0% vs. 15.3%, p = NS). Of note, the PCI:CABG ratio was 2:1 in the TACTICS-TIMI 18 trial. This supports our hypothesis of a direct relation between the PCI:CABG ratio and the relative outcome of women as compared with men.

The timing of the revascularization procedure may be another important contributor to gender differences in the outcome of patients with NSTACS. Several pathophysiologic distinctions (17–21) have been reported between women and men. Women seem to form less coronary collaterals as compared with men (20). Therefore, they may benefit particularly from a rapid correction of the epicardial obstruction during NSTACS. In addition, the benefit of extended antithrombotic treatment before revascularization may well be different for women and men (17–19).

Conclusions. Women treated with very early aggressive revascularization with coronary stenting of the culprit lesion as the primary revascularization strategy have a better long-term outcome as compared with men. In multivariate analysis, female gender independently reduced the risk of death or MI by 49%.

Acknowledgments

The authors thank Kika Peitz and her wonderful team for assistance in the catheter laboratory, Anita Abels for her help in data acquisition, as well as Martin Brutsche, MD, PhD, for his expert advice.

Reprint requests and correspondence: Dr. Christian Mueller, Medizinische Intensivstation, Medizinische Universitätsklinik, Petersgraben 4, CH-4031, Basel, Switzerland. E-mail: chmueller@uhbs.ch.

REFERENCES

1. Goldberg RJ, Yarzebski J, Lessard D, Gore JM. A two-decades (1975 to 1995) long experience in the incidence, in-hospital and long-term

case fatality rates of acute myocardial infarction: a community-wide perspective. J Am Coll Cardiol 1999;33:1533–9.
2. Maynard C, Litwin PE, Martin JS, Weaver WD. Gender differences in the treatment and outcome of acute myocardial infarction: results from the Myocardial Infarction Triage and Intervention Registry. Arch Intern Med 1992;152:972–6.
3. Chiriboga DE, Yarzebski J, Goldberg RJ, et al. A community-wide perspective of gender differences and temporal trends in the use of diagnostic and revascularization procedures for acute myocardial infarction. Am J Cardiol 1993;71:268–73.
4. Fiebach NH, Viscoli CM, Horwitz RI. Differences between women and men in survival after myocardial infarction: biology or methodology? JAMA 1990;263:1092–6.
5. Robinson K, Conroy RM, Mulcahy R, Hickey N. Risk factors and in-hospital course of first episode of myocardial infarction or acute coronary insufficiency in women. J Am Coll Cardiol 1988;11:932–6.
6. Kostis JB, Wilson AC, O'Dowd K, et al. Sex differences in the management and long-term outcome of acute myocardial infarction: a statewide study. Circulation 1994;90:1715–30.
7. Stone GW, Grines CL, Browne KF, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75:987–92.
8. Weaver WD, White HD, Wilcox RG, et al. Comparisons of characteristics and outcomes among women and men with acute myocardial infarction treated with thrombolytic therapy. JAMA 1996;275:777–82.
9. Lincoff AM, Califf RM, Ellis SG, et al. Thrombolytic therapy for women with myocardial infarction: is there a gender gap? J Am Coll Cardiol 1993;22:1780–7.
10. White HD, Barbash GI, Modan M, et al. After correcting for worse baseline characteristics, women treated with thrombolytic therapy for acute myocardial infarction have the same mortality and morbidity as men except for a higher incidence of hemorrhagic stroke. Circulation 1993;88:2097–103.
11. Becker RC, Terrin M, Ross R, et al. Comparison of clinical outcomes for women and men after acute myocardial infarction. Ann Intern Med 1994;120:638–45.
12. Kober L, Torp-Pedersen C, Ottesen M, Rasmussen S, Lessing M, Skagen K. Influence of gender on short- and long-term mortality after acute myocardial infarction. Am J Cardiol 1996;77:1052–6.
13. Tofler GH, Stone PH, Muller JE, et al. Effects of gender and race on prognosis after myocardial infarction: adverse prognosis for women, particularly black women. J Am Coll Cardiol 1987;9:473–82.
14. Hochman JS, McCabe CH, Stone PH, et al. Outcome and profile of women and men presenting with acute coronary syndromes: a report from TIMI IIIB. J Am Coll Cardiol 1997;30:141–8.
15. Hochman JS, Tamis JE, Thompson TD, et al. Sex, clinical presentation, and outcome in patients with acute coronary syndromes. N Engl J Med 1999;341:226–32.
16. Lagerqvist B, Säfström K, Stähle E, et al. Is early invasive treatment of unstable coronary artery disease equally effective for both women and men? J Am Coll Cardiol 2001;38:41–8.
17. Conlan MG, Folsom AR, Finch A, et al. Associations of factor VIII and von Willebrand factor with age, race, sex, and risk factors for atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) study. Thromb Haemost 1993;70:380–5.
18. Tracy RP, Bovill EG, Fried LP, et al. The distribution of coagulation factors VII and VIII and fibrinogen in adults over 65 years: results from the Cardiovascular Health Study. Ann Epidemiol 1992;2:509–19.
19. Stegnar M, Pentek M. Fibrinolytic response to venous occlusion in healthy subjects: relationship to age, gender, body weight, blood lipids and insulin (Erratum, Thromb Res 1993;72:173). Thromb Res 1993; 69:81–92.
20. Johansson S, Bergstrand R, Schlossman D, Selin K, Vedin A, Wilhelmsson C. Sex differences in cardioangiographic findings after myocardial infarction. Eur Heart J 1984;5:374–81.
21. Levenson J, Pessana F, Gariepy J, Armentano R, Simon A. Gender differences in wall shear-mediated brachial artery vasoconstriction and vasodilation. J Am Coll Cardiol 2001;38:1668–74.
22. Ayanian J, Epstein A. Differences in the use of procedures between women and men hospitalized for coronary heart disease. N Engl J Med 1991;325:221–5.
23. Bergelson BA, Tommaso CL. Gender differences in clinical evaluation and triage in coronary artery disease. Chest 1994;108:1510–3.
24. Clarke KW, Gray D, Keating NA, et al. Do women with acute myocardial infarction receive the same treatment as men? BMJ 1994;309:563–6.
25. Dellborg M, Swedberg K. Acute myocardial infarction: difference in the treatment between men and women. Qual Assur Health Care 1993;5:261–5.
26. Kudenchuk PJ, Maynard C, Martin JS, Wirkus M, Weaver WD. Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women. Am J Cardiol 1996;78:9–14.
27. Tunstall-Pedoe H, Morrison C, Woodward M, Fitzpatrick B, Watt G. Sex differences in myocardial infarction and coronary deaths in the Scottish MONICA population of Glasgow 1985–1991: presentation, diagnosis, treatment, and 28-day case fatality of 3,991 events in men and 1,551 events in women. Circulation 1996;93:1981–92.
28. Cannon CP, Weintraub WS, Demopoulos LA, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med 2001;344:1879–87.
29. Scull GS, Martin JS, Weaver D, et al. Early angiography versus conservative treatment in patients with non-ST-elevation acute myocardial infarction. J Am Coll Cardiol 2000;35:895–902.
30. Braunwald E. Unstable angina: a classification. Circulation 1989;80: 410–4.
31. Lee PY, Alexander KP, Hammill BG, Pasquali SK, Peterson ED. Representation of elderly persons and women in published randomized trials of acute coronary syndromes. JAMA 2001;286:708–13.

APPENDIX

The following interventional cardiologists were involved in the present study: Jens Petersen, MD; Klaus Werner, MD; Heinz J. Buettner, MD; Hans-Peter Bestehorn, MD; Thomas Comberg, MD; Axel W. Frey, MD, PhD; Valerio Basignana, MD; and Michael Gick, MD.