Gender differences among patients with acute coronary syndromes undergoing percutaneous coronary intervention in the American College of Cardiology-National Cardiovascular Data Registry (ACC-NCDR)

Nausheen Akhter, MD,[a] Sarah Milford-Beland, MS,[b] Matthew T. Roe, MD, MHS,[b] Robert N. Piana, MD,[c] John Kao, MD,[a] and Adhir Shroff, MD, MPH[a] on behalf of the American College of Cardiology-National Cardiovascular Data Registry Investigators ***Chicago, IL; Durham, NC; and Nashville, TN***

Background Although prior studies have demonstrated disparities in the management and outcomes of women with acute coronary syndrome (ACS), there are limited large-scale contemporary data on gender differences in post-intervention outcomes in this population.

Methods We analyzed patients according to 2 ACS categories, unstable angina/non–ST-elevation myocardial infarction (UA/NSTEMI) and ST-elevation myocardial infarction (STEMI) who had a percutaneous coronary intervention in the ACC-NCDR from January 1, 2004, to March 30, 2006. Of 199,690 patients, 55,691 women presented with UA/NSTEMI, and 12,335 women presented with STEMI. Clinical and angiographic characteristics, procedural and treatment patterns, and in-hospital outcomes were examined.

Results Women presented more often with UA/NSTEMI than men (82% of women vs 77% of men, $P < .0001$). Despite having greater comorbidities, women in both ACS categories had fewer high risk angiographic features than men. Women were less likely to receive aspirin or glycoprotein IIb/IIIa inhibitors, and were less often discharged on aspirin or statin. For in-hospital mortality, the adjusted odds ratio for men compared to women was similar (odds ratio 0.97, $P = .5$). Women had higher rates of cardiogenic shock, congestive heart failure, any bleeding, and any vascular complications. Importantly, rates of subacute stent thrombosis were less in women compared to men (0.43% vs 0.57%, $P = .0003$).

Conclusions Although women had fewer high-risk angiographic features than men, they continue to have higher rates of in-hospital complications. This suggests the need for gender-tailored techniques to minimize post-intervention complications and maximize application of evidence-based antiplatelet therapies. (Am Heart J 2009;157:141-8.)

Cardiovascular disease is well recognized as the leading cause of death in women. It is estimated that the lifetime risk for developing coronary artery disease (CAD) in women after 40 years of age is 32%.[1] Acute coronary syndromes (ACS), including unstable angina (UA), non–ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI), represent a large portion of the clinical presentation of CAD. In 2003, a conservative estimate of hospital discharges for UA and myocardial infarction (MI) in women was 382,000.[1]

Previous studies have shown gender differences at each step along the treatment path for ACS patients. In a study of New York City hospitals, women who had an acute myocardial infarction were less likely than men to be admitted to hospitals with revascularization capability.[2] Several studies have demonstrated that in this high-risk population, women are offered cardiac catheterization and percutaneous coronary intervention (PCI) less frequently than men.[3-6] Even among women who undergo PCI, they experience a higher rate of complications and mortality than men.[2,4,7] On the other hand, a recent analysis from the Mayo Clinic showed that there was no difference in post-PCI complications at 30 days between women and men once baseline risk factors were taken into account.[8] Many of these older analyses were

From the [a]Division of Cardiology, University of Illinois at Chicago Medical Center, Chicago, IL, [b]Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, and [c]Vanderbilt University Medical Center, Nashville, TN.
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Reprint requests: Adhir Shroff, MD, MPH, Division of Cardiology, University of Illinois at Chicago Medical Center, 840 S. Wood Street Suite 926, M/C 715, Chicago, IL 60612.
E-mail: arshroff@uic.edu
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conducted in the bare metal stent era. Drug-eluting stents (DES) have been well documented to decrease target vessel and lesion revascularization[9,10] which is often the most common adverse event in contemporary stenting trials. In a study of DES, clinical need for revascularization was decreased similarly in men and women.[11] Women with ACS receive less optimal medical therapy compared to their male counterparts.[12-14]

We used a large, contemporary PCI registry to examine whether gender-based differences in clinical and angiographic characteristics, procedural and treatment patterns, and procedural outcomes persist within a select ACS patient population uniformly undergoing coronary intervention.

Methods

Data collection

The American College of Cardiolology-National Cardiovascular Data Registry (ACC-NCDR) is a national cardiac catheterization laboratory registry. Hospitals performing cardiac catheterization and PCI procedures voluntarily participate in data collection. Data are collected retrospectively or concurrently and represent consecutive patients treated at each institution. A standardized set of data elements and definitions, systematic data entry, and transmission procedures are used to ensure rigorous data quality standards. Patient demographics, clinical history, procedural information, and adverse events that occurred up to the hospital discharge are collected and sent to the ACC-NCDR on a quarterly basis.[15] Definitions for risk factors and other data elements within the ACC-NCDR are available online.[16] Details of the registry and copies of the case report form may be found on the ACC-NCDR's website.[16]

Patient population

We analyzed the index PCI procedure for each patient admission from January 1, 2004, to March 30, 2006. Four hundred seventy sites contributed data to the ACC-NCDR during this period. The contributing sites include both academic and non-academic institutions, free-standing laboratories, and adult cardiology practices that perform cardiac catheterizations. Of 309,351 patients with a PCI procedure, 199,690 of them had ACS. Acute coronary syndrome was defined as a clinical presentation consistent with UA/NSTEMI or STEMI within 8 days of admission.

Non–ST-segment elevation MI was defined as at least one of several biochemical indicators: (1) For troponin T or I: maximal concentration of troponin T or I more than the MI decision limit on at least one occasion during the first 24 hours after the index clinical event. (2) For creatine kinase–MB (CK-MB): (*a*) maximal value of CK-MB higher than 2× the upper limit of normal on one occasion during the first hours after the index clinical event, or (*b*) maximal value of CK-MB, preferable CK-MB mass, higher than the upper limit of normal on 2 successive samples. (3) For total CK: in the absence of availability of a troponin or CK-MB assay, total CK higher than 2× the upper limit of normal, or the MB fraction of CK may be used, but these last 2 biomarkers are considerably less satisfactory than CK-MB. NSTEMI definition also includes one of the following ECG changes: (1) either ST segment depression or T wave abnormalities; or (2) ischemic symptoms in the presence or absence of chest discomfort. Ischemic symptoms may include (*a*) unexplained nausea and vomiting; or (*b*) persistent shortness of breath secondary to left ventricular failure; or (*c*) unexplained weakness, dizziness, lightheadedness, or syncope.

ST-segment elevation MI was defined by the same biochemical parameters as NSTEMI and one of the following ECG changes: (1) ST-segment elevation—new or presumed new ST-segment elevation at the J point in ≥2 contiguous leads with the cutoff points ≥0.2 mV in leads V_1, V_2, or V_3, or ≥0.1 mV in other leads; or (2) development of any Q wave in leads V_1 through V_3, or the development of a Q wave ≥30 ms (0.03 seconds) in leads I, II, aVL, aVF, V_4, V_5, or V_6. (Q-wave changes must be present in any 2 contiguous leads and be ≥1 mm in depth.)[16]

The decision for PCI was made by individual operators at each contributing site.

Statistical methods

Demographic and baseline characteristics, treatment patterns, angiographic status, and in-hospital outcomes were compared between men and women overall and according to ACS status: UA/NSTEMI and STEMI. Because patients often had multiple lesions intervened upon during a single PCI laboratory visit, lesion characteristics were assigned as follows: for each characteristic, the highest risk value of any lesion intervened upon during the index PCI was recorded.

Continuous variables are described as medians (with interquartile ranges) and categorical variables are described as frequencies. Continuous and ordinal categorical variables were compared using stratum adjusted Wilcoxon rank sum tests, whereas nominal categorical variables were compared using stratum adjusted χ^2 tests where stratification is by hospital. User-defined missing values are treated as missing.

In examining the relationship between gender and outcomes, as well as gender and medical treatments, we initially performed comparisons adjusting for ACS status alone. Then, a multivariable logistic regression model was constructed to adjust for a broad range of potentially confounding patient preoperative and hospital characteristics.[16]

Of the procedural outcomes, any bleeding event was defined as percutaneous entry site, retroperitoneal, gastrointestinal, genital/urinary, or other/unknown cause. Any vascular event was defined as access site occlusion, peripheral embolization, dissection, or arteriovenous fistula, and psuedoaneurysm.[16]

Because patients within a hospital were more likely to be similar, all multivariable adjusted analyses were performed using generalized estimating equation models to account for correlations among clustered responses (ie within-hospital correlations). A P value of <.05 was established as the level of statistical significance for all tests. All analyses were performed using SAS software (versions 8.2, SAS Institute, Cary, NC).

Results

Clinical characteristics

A total of 199,690 patients, 131,664 men and 68,026 women, met the inclusion criteria for this study. Of these,

Table I. Baseline clinical characteristics in post-PCI population

	UA/NSTEMI (n = 157 652)			STEMI (n = 42 038)		
	Men (n = 101 961)	**Women (n = 55 691)**	***P***	**Men (n = 29 703)**	**Women (n = 12 335)**	***P***
Age (y)	62.0 (54.0, 72.0)	68.0 (58.0, 77.0)	<.01	57.0 (50.0, 67.0)	66.0 (55.0, 77.0)	<.01
BMI	28.7 (25.8, 32.6)	29.0 (24.9, 33.9)	<.01	28.1 (25.2, 31.6)	27.5 (23.9, 32.3)	<.01
White race	88.3	85.6	<.01	86.6	86.7	.97
Insurance payor			<.01			<.01
• Government	48.6	64.3		35.5	55.6	
• Commercial	32.9	21.8		37.5	24.0	
• HMO	13.4	10.0		14.3	11.8	
• None	5.1	4.0		12.5	8.4	
Previous MI (>7 d)	33.0	28.0	<.01	18.6	15.9	<.01
Previous CHF	9.8	14.0	<.01	3.6	6.9	<.01
Current CHF	8.1	11.4	<.01	8.2	12.5	<.01
• NYHA class IV	20.4	21.1	<.01	51.8	52.5	.13
DM			<.01			<.01
• Insulin-dependent DM	8.8	14.7		4.4	8.4	
• Nondependent DM	21.4	23.1		14.5	17.6	
HTN	74.2	82.4	<.01	55.2	66.8	<.01
Smoker			<.01			<.01
• Current	28.9	23.7		46.9	39.5	
• Former	40.3	28.0		24.9	18.2	
Dyslipidemia	75.3	74.6	.06	56.7	56.2	.27
PVD	11.8	13.4	<.01	5.8	8.1	<.01
CVA	10.7	14.8	<.01	5.5	9.5	<.01
Renal failure			.14			.003
• Nondialysis	4.0	3.8		2.3	2.8	
• Dialysis	1.4	2.1		0.7	1.1	
Family history of CAD (< 55 y)	29.3	29.8	.14	26.3	24.6	.001
Prior PCI	38.2	34.2	<.01	17.3	13.6	<.01
Prior CABG	24.1	17.0	<.01	6.2	4.8	<.01
Cardiogenic shock	1.1	1.2	.12	8.3	11.6	<.01

Data are presented as observed frequencies (percentage) except for BMI and age, which are presented as median (25th, 75th percentile). *BMI*, Body mass index; *HMO*, health care maintenance organization; *NYHA*, New York Heart Association; *DM*, diabetes mellitus; *PVD*, peripheral vascular disease; *CVA*, cerebral vascular accident.

157,652 patients presented with UA/NSTEMI and 42,038 patients presented with STEMI. A significant difference in presenting diagnosis based on gender was observed where a higher proportion of women presented with UA/NSTEMI than men (82% of women vs 77% of men, $P <$ .01). Women were older than men whether presenting with UA/NSTEMI or STEMI (Table I). Most patients were white (87%).

In both UA/NSTEMI and STEMI, women had a significantly ($P < .01$) higher prevalence of both insulin and non–insulin-dependent diabetes mellitus, hypertension (HTN), peripheral vascular disease, and cerebrovascular accident when compared to men. Women were significantly ($P < .01$) less likely to have a history of smoking, MI, or prior revascularization, either with PCI or coronary artery bypass graft (CABG). Women also had significantly ($P < .01$) higher rates of previous congestive heart failure (CHF) and current heart failure symptoms.

For patients presenting with STEMI, women had a higher incidence than men of cardiogenic shock (11.6% vs 8.3%, $P < .01$) and non–dialysis-dependent renal failure (2.8% vs 2.3%, $P = .003$).

Angiographic and procedural characteristics

Pertinent angiographic and procedural findings in this study are summarized on Table II. The ejection fraction (EF) was calculated by a left ventricular angiogram, a radionucleotide study, or an echocardiogram. The EF was known before catheterization or performed at the time of catheterization. Median EF in women was greater than that of men for UA/NSTEMI patients (58% vs 55%, $P < .01$) and comparable to that of men among STEMI population. In both UA/NSTEMI and STEMI groups, women had fewer high-risk angiographic features. Specifically, the highest risk lesion among women was more commonly classified as American College of Cardiology and American Heart Association lesion grade A or B, shorter in length, and less likely to be a bifurcation lesion.

There were no clinically significant differences in DES use by gender. In fact, DESs were used slightly more often in women in both UA/NSTEMI and STEMI presentations (85.4% vs 84.6%, $P < .01$ and 77.7% vs 77.4%, $P < .01$).

Medical therapy utilization

Although there was high compliance with evidence-based medical therapies in this registry, clinically

Table II. Angiographic and procedural characteristics in post-PCI population

Variable	UA/NSTEMI (n = 157 652)			STEMI (n = 42 038)		
	Men (n = 101 961)	Women (n = 55 691)	P	Men (n = 29 703)	Women (n = 12 335)	P
EF percentage	55.0 (45.0, 60.0)	58.0 (50.0, 61.0)	<.01	45.0 (40.0, 55.0)	45.0 (37.0, 55.0)	.96
Left main stenosis ≥50%	6.7	4.6	<.01	4.0	4.0	.70
1-Vessel CAD	40.8	48.2	<.01	45.8	47.3	<.01
2-Vessel CAD	30.2	28.9		32.0	32.4	
3-Vessel CAD	23.7	17.6		20.6	18.8	
Lesion risk			<.01			.007
• Non-high/non-ACC/AHA Class C	58.4	61.6		41.1	42.0	
Lesion length (mm)	16.0 (12.0, 23.0)	16.0 (12.0, 22.0)	<.01	20.0 (15.0, 24.0)	18.0 (13.0, 24.0)	<.01
Lesion bifurcation	12.9	12.1	.0003	11.5	11.0	.11
IABP	1.5	1.4	.68	9.6	10.5	.002
Stent use			<.01			<.01
• Some DESs used	84.6	85.4		77.4	77.7	
• No DES used but some stent used	8.4	7.5		14.7	13.0	
Total no. of lesions treated			<.01			.82
• 1	65.3	67.7		72.3	72.0	
• 2	25.9	24.8		21.8	21.7	

Data are presented as observed frequencies (percentage) except for EF percentage and lesion length, which are presented as median (25th, 75th percentile). *IABP*, Intra-aortic balloon pump.

significant differences in medical therapies were apparent. In the acute or admission setting, women were less likely to receive antiplatelet therapies, aspirin (odds ratio [OR] 1.16, 95% CI 1.13-1.20, $P < .01$) and glycoprotein IIb/IIIa (GpIIb/IIIa) inhibitor (OR 1.10, 95% CI 1.08-1.13, $P < .01$) (Table III). Conversely, women were more likely to receive β-blockers, direct thrombin inhibitors, and low-molecular-weight heparin (LMWH). At discharge, women received aspirin (OR 1.17, 95% CI 1.12-1.21, $P < .01$) and statin therapy (OR 1.10, 95% CI 1.07-1.13, $P < .01$) at lower rates than men.

Procedural outcomes

After risk adjustment using the entire ACS population, there was no difference in mortality rates between men and women (OR 0.97, 95% CI 0.88-1.07, $P = .52$). However, even after adjusting for confounding, women continued to be associated with significantly higher rates of several adverse outcomes, including the presence of CHF (OR 0.80, 95% CI 0.69-0.92, $P = .002$), cardiogenic shock (OR 0.82, 95% CI 0.75-0.89, $P < .01$), any bleeding (OR 0.55, 95% CI 0.52-0.58, $P < .01$), and any vascular events (OR 0.69, 95% CI 0.51-0.93, $P = .02$) (Table IV). The increased bleeding and vascular complications among women were derived primarily from access site complications (bleeding at the entry site, retroperitoneal bleed, pseudoaneurysm). Importantly, rates of subacute stent thrombosis were significantly less in women (0.43% vs 0.57%, $P = .0003$) (Table V).

Discussion

The ACC-NCDR reflects treatment patterns across the United States and affords an analysis of contemporary management of ACS patients undergoing PCI in the DES era. Our results demonstrate gender differences in clinical presentation, angiographic features, administration of antiplatelet therapies, and higher procedural complications in women with ACS who had a PCI during admission. Many of these differences persisted despite adjustment for baseline risk factors.

Women present significantly more often than men with UA/NSTEMI and often with atypical features. This difference in ACS presentation was also demonstrated by the Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO) IIb study. These differences may be accounted for by differences in anatomy, pathophysiology of CAD, and clinical characteristics in women vs men.[17] We demonstrate a higher prevalence of single-vessel disease in women, as well as several differences in clinical risk factors, including a lower prevalence of smoking in women. The reason for gender differences in ACS presentation is likely multifactorial. These differences in presentation may also account for the underutilization of acute antiplatelet therapy on hospital admission. As prior studies have shown, women with ACS are older and present with more comorbidities.[12-14,18] Our study indicates that this remains true in the DES era. The later development of CAD in women is attributed to differences in endogenous sex hormones, particularly estrogen.[19]

Other investigators have also shown that women with ACS present more often with both prior and current signs of CHF than men.[13] Interestingly, our analysis of left ventricular function demonstrated similar, if not better, EF percentage in women than in men. Women with UA/NSTEMI had HTN (>80%), normal median EF percentage, and significantly higher rates of current

Table III. Compliance to medical therapy by gender with ORs for use of men vs women

	Men (n = 131 664)	Women (n = 68 026)	Unadjusted OR	*Adjusted OR (95% CI)	Adjusted *P*
Acute Therapy					
Aspirin	91.7	90.2	1.26	1.16 (1.13-1.20)	<.01
Antithrombins					
Heparin	63.7	60.8	1.10	1.05 (1.03-1.07)	<.01
Any LMWH	21.5	22.7	0.94	0.95 (0.93-0.97)	<.01
Direct thrombin inhibitors	26.7	29.8	0.88	0.95 (0.93-0.97)	<.01
Any GpIIb/IIIa	57.3	51.3	1.25	1.10 (1.08-1.13)	<.01
β-Blocker	71.0	71.6	0.96	0.94 (0.92-0.96)	<.01
Clopidogrel	72.6	72.2	1.02	0.99 (0.97-1.01)	.39
Statin	55.3	54.6	1.03	1.06 (1.04-1.09)	<.01
Discharge therapy†					
Aspirin	95.6	94.7	1.30	1.17 (1.12-1.21)	<.01
β-Blocker	83.3	81.7	1.10	0.99 (0.97-1.02)	.65
Clopidogrel	95.0	94.9	1.02	0.99 (0.95-1.03)	.50
Statin	84.5	81.0	1.26	1.10 (1.07-1.13)	<.01

All data are presented as observed frequencies (percentage).
*Variables in the acute therapy models are as follows: age—linear spline with knots, at 50, 60, 70, 76, and 84; white; smoker; insurance—commercial, HMO, non-US/none, and government (reference); diabetes—insulin treated, non–insulin treated, and none (reference); hypercholesterolemia; hypertension; BMI—linear spline with knots at 18.5 and 35; glomerular filtration rate (GFR)/dialysis—linear spline with dialysis or GFR ≤30 patients (pts) set to GFR = 30 and knots at 60 and 90; CVD; chronic lung disease (CLD); PVD; family history of CAD; CHF; NYHA class IV; prior CABG; prior PCI; prior MI; prior CHF; prior valve surgery; cardiogenic shock; admission symptoms—non-STEMI, STEMI, and UA (reference); status—salvage, emergent, urgent, and elective (reference); and hospital characteristic—percentage of females per site.
†Variables in the discharge therapy models are the same as those in the acute therapy model with additional variables: preoperative IABP; subacute thrombosis in a major artery; acute PCI—yes-primary for STEMI, yes-rescue, yes-facilitated, yes-NSTEMI/UA, and no (reference); highest risk lesion characteristics; segment—left main, proximal left anterior descending (pLAD), proximal right coronary artery (pRCA)/mid left anterior descending (mLAD)/proximal circumflex (pCIRC), and other (reference); preprocedure stenosis 100%; preprocedure TIMI flow none; high/C risk; lesion bifurcation; lesion length—missing, 30+, and <30 (reference); and total number of lesions treated.

Table IV. Procedural outcomes in overall post-PCI population with OR for men vs women

	Men (n = 131 664)	Women (n = 68 026)	Unadjusted OR	Adjusted OR (95% CI)	Adjusted *P* value
Mortality	1.4	2.2	0.65	0.97 (0.88-1.07)*	.52
Cardiogenic shock	1.2	1.6	0.73	0.82 (0.75-0.89)†	<.01
CVA	0.6	0.7	0.74	0.83 (0.65-1.06)‡	.13
CHF	1.3	1.8	0.71	0.80 (0.69-0.92)§	.002
Renal failure	0.6	1.1	0.57	1.13 (0.99-1.29)*	.07
Any bleeding event	2.1	4.4	0.46	0.55 (0.52-0.58)*	<.01
Any vascular event	0.7	0.9	0.70	0.69 (0.51-0.93)‡	.02

All data are presented as observed frequencies (percentage).
*Variables in the mortality, renal failure, and bleeding models: age—linear spline with knots at 50, 60, 70, 76 and 84; white; smoker; insurance—commercial, HMO, non-US/none, and government (reference); diabetes—insulin treated, non–insulin treated, and none (reference); hypercholesterolemia; hypertension; BMI—linear spline with knots at 18.5 and 35; GFR/dialysis—linear spline with dialysis or GFR ≤30 pts set to GFR = 30 and knots at 60 and 90; CVD; CLD; PVD; family history of CAD; CHF; NYHA class IV; prior CABG; prior PCI; prior MI; prior CHF; prior valve surgery; cardiogenic shock; admission symptoms—NSTEMI, STEMI, and UA (reference); status—salvage, emergent, urgent, and elective (reference); preoperative IABP; subacute thrombosis in a major artery; acute PCI—yes-primary for STEMI, yes-rescue, yes-facilitated, yes-NSTEMI/UA, and no (reference), highest risk lesion characteristics, segment—left main, pLAD, pRCA/mLAD/pCIRC, and other (reference); preprocedure stenosis 100%; preprocedure TIMI flow none; high/C risk; lesion bifurcation; lesion length—missing, 30+, and <30 (reference); total number of lesions treated; and hospital characteristic—percentage of females per site.
†Variables in the cardiogenic shock model are the same as those in the mortality model except prior valve surgery is removed and acute PCI is categorized as follows: yes-primary for STEMI, yes-rescue, yes-facilitated or NSTEMI/UA, and no (reference).
‡Variables in the stroke and any vascular event models: age (linear), NYHA class IV, and hospital characteristic (percentage of females per site).
§Variables in the CHF model: age—linear; white; prior CABG; hypercholesterolemia; CVD; family history of CAD; CHF; NYHA class IV; status—salvage/emergent; urgent, and elective (reference); acute PCI—yes-primary for STEMI, yes-rescue, yes-facilitated or NSTEMI/UA, and no (reference); highest risk lesion characteristics—high/C risk; total number of lesions treated; and hospital characteristic—percentage of females per site.

heart failure symptoms than men (11.4% vs 8.1%, $P < .01$). This is highly suggestive that diastolic dysfunction was a large component of the presentation of heart failure in women with ACS. Others have also reported that women with CHF are older, have HTN, and more often have higher EFs.[20,21] It has also been well validated that diastolic dysfunction and elevated left ventricular filling pressures in the setting of an acute MI has prognostic implications.[22]

The use of multiple evidence-based classes of cardiovascular medications has been associated with an improved outcome free of death and MI.[23] Prior studies have demonstrated that American College of Cardiology and American Heart Association class I medical therapies

Table V. Bleeding and vascular complications—overall population

	Men (n = 131 664)	Women (n = 68 026)	P
Bleeding			
Blood products transfused after laboratory visit	3.55	7.62	<.01
Percutaneous entry site	0.80	1.85	<.01
Retroperitoneal bleed	0.23	0.84	<.01
GI	0.52	0.85	<.01
GU	0.21	0.13	.0002
Other/unknown	0.45	1.01	<.01
Vascular			
Access site occlusion	0.03	0.11	<.01
Peripheral embolization	0.05	0.12	<.01
Dissection	0.54	0.64	<.01
Pseudoaneurysm	0.29	0.73	<.01
AV fistula	0.06	0.09	<.01
Subacute stent thrombosis	0.57	0.43	.0003

All data are presented as observed frequencies (percentage). *GI*, Gastrointestinal; *GU*, genitourinary; *AV*, arterial-venous.

are given less frequently to women on admission and discharge.[6,12,13] In our study, multiple medical therapies were used at statistically lower rates for women compared to men, although these differences were generally small in absolute terms. The largest clinically significant differences were in the acute or admission administration of antiplatelet therapies such as aspirin, GpIIb/IIIa inhibitor, and aspirin at the time of discharge. These differences on discharge therapy may be due to the increased rates of adverse bleeding events and vascular complications among women. Interestingly, medical practitioners preferred acute administration of direct thrombin inhibitors, perhaps in hopes of curbing adverse bleeding outcomes; however, this did not appear to affect the increased rates of bleeding complications in women compared to men. There was also a greater use of LMWH in women, which may account for some of the increased bleeding complications that were observed. We did not have data on the activated clotting time with heparin administration to determine if this was contributing to the increased bleeding rate in women. It is particularly important to dose anticoagulants correctly to decrease bleeding rates in women. Further study of the pharmacokinetics of antiplatelet and anticoagulation therapies in women with ACS may aid in finding the optimal therapy to maintain efficacy and minimize complications.

In the past, women had higher mortality rates after PCI.[2,4,7] Fortunately, there has been a general trend toward improved in-hospital mortality outcomes in women after PCI.[18] When comparing National, Heart, Lung and Blood Institute registries from 1985 to 1994, in-hospital mortality rates post-PCI in women trended lower (2.6% vs 1.5%, P = nonsignificant).[24,25] There has been conflicting information about short-term mortality after an acute myocardial infarction. Younger women have been shown to have higher rates of death during hospitalization when compared to men of the same age.[26] However, others have reported no gender differences in 10-day mortality, even when women received less aggressive treatment during early management of an acute MI.[27] At 1 year, women had higher mortality (6.5% vs 4.3%, P = .02) and a higher combined end point of death, MI, and CABG (18.3% vs 14.4%, P = .03).[17,28] Consistent with a trend toward improvement in post-PCI mortality outcomes, our study did not find a significant gender difference in adjusted in-hospital mortality rates.

Higher rates of procedural complications have been reported in women. In particular, women are prone to more vascular and bleeding complications than men. From 1994 to 1998, a national database reported twice as many complications in women for stroke (0.4% vs 0.2%, $P < .001$) and vascular complications (5.4% vs 2.7%, $P < .001$).[29] Others have reported rates of major bleeding in women with STEMI at 2.9%[26] and rates of blood transfusions in women with NSTEMI at 17.2%.[13] Our findings suggest that bleeding and vascular complications in women appear to be driven by access site complications (bleeding at entry site, retroperitoneal bleed, pseudoaneurysm). Proactive measures to decrease access site complications, such as fluoroscopy of the groin before catheterization, smaller sheath size, increased attention to access management, should be considered routinely in women. Tavris et al[30] studied the association of gender, sheath size, and closure techniques and found that large sheath size and both manual compression and collagen plug devices to control femoral artery bleeding increased the relative risk of vascular complications for women. Therefore, these increased complications persist even in the era of closure devices. Gastrointestinal bleeding also occurred more frequently in women in the current study, which may have contributed to the decreased use of aspirin on discharge.

One might also expect higher rates of SAT among women due to smaller coronary luminal diameters, increased prevalence of diabetes, and less antiplatelet medication use. However, conversely, we found that women had significantly lower rates of SAT than men. This difference may be accounted for by the lower-risk angiographic lesions that were seen in women. Revascularization of more complex lesions, particularly bifurcation or in-stent restenosis lesions, increases the risk of stent thrombosis.[31]

We have demonstrated several important gender differences from clinical presentation to angiographic characteristics to administration of medical therapy that could account for the differences in procedural outcomes. However, there may still be inherent biological differences between genders that have yet to be defined that may also explain these outcomes.[20]

Given the large numbers of patients in the ACC-NCDR, many of the differences in this study are small but statistically significant. As in any large registry analysis, the clinical significance of this data should be considered when interpreting these results. The patients in this study were predominantly white. The data were self-reported, which may lead to under-reporting of complications or overreporting of success rates. We also only have a comparison of crude therapy rates and no information on contraindications to treatment. We did not have access to drug doses, which might be particularly relevant for anticoagulation therapy and bleeding complications. We only evaluated patients undergoing PCI, so this analysis cannot comment on different treatment patterns among patients who did not undergo PCI. We also could not evaluate relative timing of PCI among patients with STEMI, especially those who underwent primary PCI as the initial mode of reperfusion therapy. Unfortunately, we also did not have access to posthospitalization CABG procedures and long-term outcomes.

In this contemporary analysis of patients with ACS undergoing PCI in the US, we have reported high overall compliance to evidence-based medical therapies in women. Drug-eluting stents were also used equally between genders. However, morbidity post-intervention in women with ACS continues to be a major problem, particularly bleeding complications. Concerns about these potential complications may in fact deter application of beneficial invasive procedures and antiplatelet/antithrombotic therapies in some cases. Although these acute complications do not appear to translate into increased in-hospital mortality for women, long-term differences in survival cannot be excluded. Future research should investigate gender-tailored ways to minimize the early complications of PCI in women and maximize application of evidence-based antiplatelet therapies in this population.

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