Characteristics and Outcomes of Women Veterans Undergoing Cardiac Catheterization in the Veterans Affairs Healthcare System

Insights from the VA CART Program

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Background—The number of women veterans is increasing, yet little is known about their cardiovascular risk factors, coronary anatomy, cardiac treatments, and outcomes after cardiac catheterization. Prior studies have shown that nonveteran women have more risk factors, receive less aggressive treatment, and have worse outcomes, despite having less obstructive coronary artery disease than men. Whether these differences exist among women veterans in the veterans affairs healthcare system is unknown.

Methods and Results—Data on 85 936 veterans (3181 women) undergoing initial cardiac catheterization between October 1, 2007, and September 30, 2012, were examined using the national veterans affairs Clinical Assessment Reporting and Tracking (CART) Program. Sex differences in demographics, indications, coronary anatomy, cardiac treatments, and outcomes were analyzed. Women veterans were younger (56.9 versus 63.0 years, $P<0.0001$) with fewer traditional cardiovascular risk factors, but with more obesity, depression, and posttraumatic stress disorder than men. Women had lower rates of obstructive coronary artery disease than men (22.6% versus 53.3%). Rates of procedural complications were similar in both genders. Adjusted outcomes at 1 year showed women had lower mortality (hazard ratio, 0.74; confidence interval, 0.60–0.92) and less all-cause rehospitalization (hazard ratio, 0.87; confidence interval, 0.82–0.93), but no difference in rates of unplanned percutaneous coronary intervention.

Conclusions—Women veterans undergoing catheterization are younger, have more obesity, depression, and posttraumatic stress disorder, less obstructive coronary artery disease, and similar long-term outcomes, compared with men. These findings suggest a significant portion of women veterans may have chest pain not attributable to obstructive coronary artery disease. Further research into possible causes, such as endothelial dysfunction or concurrent psychological comorbidities, is needed. (***Circ Cardiovasc Qual Outcomes*. 2015;8:S39-S47. DOI: 10.1161/CIRCOUTCOMES.114.001613.**)

Key Words: cardiac catheterization ■ coronary artery disease ■ outcomes research ■ sex ■ women

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Coronary artery disease (CAD) remains the leading cause of death among women in the United States.[1] Prior research has demonstrated that women with CAD are typically older than men and have more risk factors, such as diabetes mellitus,[2] hypertension,[3,4] hyperlipidemia,[5] obesity,[6] and congestive heart failure.[4,7] Despite these higher rates of CAD risk factors, women have less obstructive CAD.[4,8] Studies are conflicting regarding whether women are treated less aggressively than their male counterparts.[9–15] Women tend to have more complications and worse outcomes after cardiac catheterization[16] and are less likely to receive evidence-based medical therapy after discharge.[17]

Women who have served in the military may have an even higher risk of CAD than nonveteran women, given the overall worse health status and higher number of CAD risk factors in the veteran population,[18–20] but little is known about the characteristics and treatment of women veterans suspected of having clinically significant CAD. The number of women seeking care at veterans affairs (VA) facilities has doubled over the past decade,[21] providing a unique opportunity to understand cardiac care and outcomes among women veterans. By extension, these lessons could improve our understanding of the sex differences noted in nonveteran cardiac populations.

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WHAT IS KNOWN

- Despite having less obstructive coronary artery disease than men, women have higher rates of cardiovascular risk factors and worse cardiovascular outcomes.
- It is not known whether these characteristics apply to women veterans undergoing cardiac catheterization in the VA healthcare system.

WHAT THE STUDY ADDS

- This national study demonstrates that women veterans undergoing cardiac catheterization in the VA system have higher rates of nonobstructive coronary artery disease or normal coronary arteries than men, even when presenting with acute coronary syndromes.
- Women veterans have a higher burden of obesity, depression, and posttraumatic stress disorder, fewer traditional cardiovascular risk factors, and similar 1-year outcomes compared with men.
- Chest pain in the absence of obstructive coronary disease is common in women veterans and may represent a complex interplay of psychological stressors and somatic disease, but further research is needed.

Using data from the national VA Clinical Assessment, Reporting, and Tracking (CART) Program, we sought to evaluate sex differences among veterans undergoing initial diagnostic catheterization in the VA. The specific aims of this study were to determine whether there were sex differences in (1) clinical characteristics and comorbidities, (2) coronary anatomy and treatment, and (3) procedural complications and long-term outcomes after diagnostic catheterization.

Methods

Launched in 2005, the VA CART Program is a national VA clinical quality program for coronary procedures conducted in all VA cardiac catheterization laboratories nationwide.[22] A key feature of the CART Program is a clinical software application designed to collect data on catheterization laboratory procedures in a standardized fashion. The software is embedded in the VA electronic health record and allows providers to enter patient and procedural information for all cardiac catheterizations and percutaneous coronary interventions (PCI) as part of routine clinical workflow. Once data entry is complete, the data elements automatically populate a clinical note for the patient electronic health record. These data also populate a clinical data repository that supports the quality assessment, quality improvement, and clinical research missions of the CART Program.

The CART software uses standardized definitions and features, such as pull-down menus, to ensure uniformity of data entry by different providers and in different catheterization laboratories. Core data elements conform to the definitions and standards of the American College of Cardiology's National Cardiovascular Data Registry.[23] Quality checks of the data are periodically conducted, and it has been shown to be complete, timely, and accurate.[24] CART data are combined with longitudinal data in the VA patient electronic health record, including vital status, inpatient hospitalizations, clinic visits, pharmacy prescriptions and refills, and laboratory results. The data are also merged with VA claims data for veterans' care for hospitalizations that occur outside the VA system. The Colorado Multiple Institutional Review Board approved this study.

Study Cohort

This study included data from all men and women veterans undergoing initial diagnostic catheterization between October 1, 2007, and September 30, 2012, at any of the 77 VA catheterization laboratories. Patients <18 years of age were excluded. All patients with a prior catheterization, PCI, or coronary artery bypass grafting (CABG) were excluded to evaluate the risk factor profile and subsequent care after the initial catheterization.

Exposure

Patient sex was determined from the CART database and VA patient treatment files.

Outcomes

Both peri-procedural and 1-year outcomes were assessed. Peri-procedural outcomes included in-laboratory complications and bleeding complications requiring transfusion. One-year outcomes included all-cause death, all-cause rehospitalization, rehospitalization for myocardial infarction (MI), unplanned catheterization, unplanned PCI, and unplanned CABG. In-laboratory complications were defined as access-site hematoma, dysrhythmia, hives, stroke, emergent PCI, acute respiratory distress, acute pulmonary edema, death, peri-procedural MI, acute cardiogenic shock, limb ischemia, anaphylactic shock, retroperitoneal hematoma, emergent CABG, or new cardiac tamponade.

Covariates

Patient demographic, clinical comorbidity, catheterization indication, coronary anatomy, and postprocedural treatment information were collected from the CART and VA patient data files. Demographic information included age, race, and Hispanic ethnicity. Race was defined as white, black or African American, or other, which included American Indian or Alaska Native, Asian, Native Hawaiian, or other Pacific Islander. Racial and ethnic classifications were based on patient self-report, and the methodology for racial classification has been described elsewhere.[25] Clinical comorbidity information included diabetes mellitus, hyperlipidemia, hypertension, chronic kidney disease, tobacco use, congestive heart failure, cerebrovascular disease, peripheral arterial disease, obesity, chronic obstructive pulmonary disease, posttraumatic stress disorder (PTSD), depression, sleep apnea, procedural indication, and Framingham risk. Obesity was defined as a body mass index ≥30. Framingham risk was calculated using methods previously described[26] and was categorized by the 10-year predicted coronary heart disease risk as low (<10%), intermediate (10% to 20%), or high (>20%). Indications for cardiac catheterization were collected from CART data and categorized into acute coronary syndrome (ACS), elective, or other. Elective indications included chest pain, stable angina, and positive functional study. Positive functional study was defined as any cardiac stress test that was suggestive of ischemia. Other indications for cardiac catheterization included valvular heart disease, cardiomyopathy, ischemic heart disease, cardiac transplant, cardiac tamponade, cardiogenic shock, coronary heart disease, heart failure, dysrhythmia, research study, and unknown.

Coronary anatomy was classified into obstructive CAD, nonobstructive CAD, or normal coronary arteries. In addition, the extent of CAD was classified into 1, 2, or 3-vessel distribution. In line with prior studies,[25] obstructive CAD was defined as any coronary stenosis >70% in any epicardial artery or 50% in the left main coronary artery. Nonobstructive CAD refers to coronary stenosis that is ≥20%, but <70%, in any epicardial artery or ≥20%, but <50%, in the left main coronary artery. Normal coronary anatomy was defined as <20% stenosis in all coronary arteries. We then categorized patients as having single, double, or triple-vessel or left main obstructive disease. Vessel

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Table 1. Demographics and Clinical Characteristics

	Women (N=3181)	Men (N=82 755)	*P* Value
Demographics			
Age, median (IQR)	56.9 (51.1–62.5)	63 (58.3–69)	<0.0001
Hispanic, % (n)	6.8 (216)	7.9 (6508)	0.0269
Race: White, % (n)	63.9 (2033)	73.4 (60 756)	<0.0001
Race: Black, % (n)	25.9 (824)	17.4 (14 394)	<0.0001
Race: Other, % (n)	10.2 (324)	9.2 (7605)	0.0569
Clinical Comorbidities			
Obese, % (n)	57.2 (1794)	46.6 (38 149)	<0.0001
BMI, median (IQR)	31.2 (26.7–36.6)	29.5 (26–33.8)	<0.0001
Hypertension, % (n)	75.7 (2409)	82.7 (68 469)	<0.0001
Hyperlipidemia, % (n)	71.2 (2265)	77.5 (64 117)	<0.0001
Diabetes mellitus, % (n)	32.7 (1041)	39.4 (32 644)	<0.0001
Depression, % (n)	55.3 (1758)	31.4 (26 002)	<0.0001
Congestive heart failure, % (n)	13.4 (426)	20 (16 551)	<0.0001
Cerebrovascular disease, % (n)	10.2 (323)	12.6 (10 394)	<0.0001
Framingham risk: high, % (n)	2.9 (92)	24.6 (20 337)	<0.0001
Framingham risk: medium, % (n)	38.6 (1229)	54.6 (45 173)	<0.0001
Framingham risk: low, % (n)	58.5 (1860)	20.8 (17 245)	<0.0001
Tobacco use, % (n)	48.9 (1556)	57.7 (47 760)	<0.0001
Prior myocardial infarction (MI), % (n)	4.8 (152)	7.8 (6438)	<0.0001
COPD, % (n)	17.5 (557)	20 (16 545)	0.0006
Chronic kidney disease, % (n)	6.6 (210)	14.2 (11 714)	<0.0001
Family history of CAD, % (n)	1.3 (40)	0.5 (431)	<0.0001
Peripheral vascular disease, % (n)	6.9 (220)	14.9 (12 309)	<0.0001
PTSD, % (n)	20.1 (638)	16.3 (13 481)	<0.0001
Sleep apnea, % (n)	15.3 (488)	16.8 (13 870)	0.0352
Pre-catheterization stress test			
Stress test ≤30 days prior, % (n)	30.4 (966)	28.1 (23 233)	0.0048

BMI indicates body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; and PTSD, posttraumatic stress disorder.

distribution was classified into the left anterior descending and its branches, the left circumflex artery and its branches, and the right coronary artery and its branches. Postprocedural treatments included PCI, CABG, or medical therapy. PCI that occurred on the same day as the initial catheterization or as part of a staged PCI were considered part of the treatment episode and not counted as an outcome. CABG that occurred within 30 days of the index catheterization, without an intervening unplanned catheterization or PCI, was considered a planned procedure. All other CABG procedures were considered unplanned. Medications at the time of discharge after cardiac catheterization were analyzed, including β-blockers, statin therapy, antiplatelet agents (clopidogrel or prasugrel), long-acting nitrates, and calcium-channel blockers.

Statistical Analyses

Patient demographics and clinical characteristics, procedural indications, presence of coronary stenoses, pharmacological treatment, and revascularization procedures were collected and compared by sex. The cohort was further stratified and analyzed by indication (ACS, elective, or other). Continuous data were compared using Wilcoxon nonparametric tests and categorical data using Chi-square or Fisher's exact tests, as appropriate.

Unadjusted rates of peri-procedural and 1-year outcomes were calculated and compared using Kaplan–Meier curves. To evaluate adjusted differences in 1-year outcomes for men and women after initial cardiac catheterization, a Cox proportional hazards model was fitted for each of 6 outcomes, adjusted using the covariates listed earlier and including an interaction between sex and indication for catheterization to assess sex differences by indication category. Spline terms were included in the models to account for the nonlinearity of age. For all outcomes, patients were censored on death or at 1 year if they did not experience an event. Crude and adjusted estimates of the hazard ratios for women compared with men were calculated. Data were complete for all covariates with the exception of obesity, which resulted in exclusion of 920 (1.1%) patients. These patients were excluded from both adjusted and unadjusted models. Adjustment for the peri-procedural outcomes was not performed because of low numbers of events. Sex differences in clinical characteristics were also assessed by stratifying the cohort by race (white, black, and other).

Statistical analyses were performed using SAS software (version 9.4, SAS Institute, Cary, NC) and R 3.1.1 (R Core Team (2014)). All analyses were performed at the CART Coordinating Center, housed at the VA Eastern Colorado Healthcare System.

Results

Clinical Characteristics

A total of 82 755 males (96%) and 3181 (4%) women met criteria for inclusion in this analysis. The median age for women was 56.9 years and for men was 63.0 years (P<0.0001). Baseline demographics for the entire population revealed that women had fewer traditional cardiovascular risk factors than men, including hypertension, hyperlipidemia, diabetes mellitus, and tobacco use (Table 1). Notably, women veterans had higher rates of obesity, depression, and PTSD than men veterans (Table 1). The same findings were apparent when analyzed by race. Women in each racial group (white, black, and other) were younger, had lower rates of traditional cardiovascular risk factors (hypertension, hyperlipidemia, diabetes mellitus, and tobacco use), and higher rates of obesity, depression, and PTSD than their male counterparts.

Table 2 shows the demographics and clinical characteristics of veterans by indication for catheterization (ACS, elective, and other). Regardless of catheterization indication, women had lower rates of hypertension, hyperlipidemia, diabetes mellitus, and tobacco use than men. In each category, women had more obesity, depression, and PTSD than men. Among the entire cohort, women more commonly presented with chest pain as an indication for cardiac catheterization than men (52.1%, n=1656 versus 39.3%, n=32 549, P<0.0001). Although stress testing was performed equally often in men and women, irrespective of indication for catheterization (Table 2), a relatively low percentage of patients presented for catheterization with the indication of positive functional study, and women were somewhat less likely to present with this indication than men (13.3%, n=423 versus 14.8%, n=12 212, P=0.023).

Coronary Anatomy and Treatment

Women were found to have normal coronary arteries at the time of catheterization significantly more often than men (45.9% versus 17%, P<0.0001; Table 3). Rates of nonobstructive CAD were similar but women had less single and multivessel obstructive disease. Rates of treatment with PCI and medical therapy were lower in women (Table 3). Analysis

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Table 2. Demographics and Clinical Characteristics by Indication

	ACS			Elective			Other		
	Women (N=401)	Men (N=14 052)	*P* Value	Women (N=2132)	Men (N=46 309)	*P* Value	Women(N=648)	Men (N=22 394)	*P* Value
Demographics									
Age, median (IQR)	58.7 (52.4–65.4)	63.5 (58.6–71.6)	<0.0001	56.2 (50.6–61.6)	62.6 (57.8–67.5)	<0.0001	58 (51.6–65)	63.8 (59.2–71.5)	<0.0001
Hispanic, % (n)	10.7 (43)	11.2 (1572)	0.7713	6.4 (136)	7.3 (3374)	0.1143	5.7 (37)	7 (1562)	0.2115
Race: White, % (n)	60.1 (241)	72.6 (10 199)	<0.0001	64.4 (1374)	73.7 (34 121)	<0.0001	64.5 (418)	73.4 (16 436)	<0.0001
Race: Black, % (n)	27.9 (112)	17.5 (2455)	<0.0001	25.9 (552)	17.1 (7896)	<0.0001	24.7 (160)	18.1 (4043)	<0.0001
Race: Other, % (n)	12 (48)	9.9 (1398)	0.1835	9.7 (206)	9.3 (4292)	0.5398	10.8 (70)	8.6 (1915)	0.0441
Clinical comorbidities									
Obese, % (n)	50 (188)	40.5 (5566)	0.0002	61.2 (1296)	50.1 (23 036)	<0.0001	48.1 (310)	43.1 (9547)	0.0116
BMI, median (IQR)	30 (25.3–34.8)	28.7 (25.2–32.7)	0.001	31.9 (27.6–37.2)	30 (26.6–34.3)	<0.0001	29.6 (25.2–35.5)	29 (25.3–33.4)	0.0065
Hypertension, % (n)	75.6 (303)	81.1 (11 391)	0.0057	75.8 (1617)	83.7 (38 750)	<0.0001	75.5 (489)	81.8 (18 328)	<0.0001
Hyperlipidemia, % (n)	66.1 (265)	74.2 (10 424)	0.0003	74 (1578)	81.1 (37 552)	<0.0001	65.1 (422)	72.1 (16 141)	0.0001
Diabetes mellitus, % (n)	31.7 (127)	38.9 (5473)	0.0032	33.6 (716)	40.3 (18 666)	<0.0001	30.6 (198)	38 (8505)	0.0001
Depression, % (n)	45.4 (182)	28.9 (4068)	<0.0001	58.7 (1251)	34.2 (15 844)	<0.0001	50.2 (325)	27.2 (6090)	<0.0001
Congestive heart failure, % (n)	12 (48)	15 (2106)	0.0944	6.5 (138)	11.9 (5522)	<0.0001	37 (240)	39.8 (8923)	0.1498
Cerebrovascular disease, % (n)	15 (60)	14.3 (2005)	0.6953	9.2 (197)	11.7 (5435)	0.0004	10.2 (66)	13.2 (2954)	0.0254
Framingham risk: high, % (n)	4.7 (19)	31 (4352)	<0.0001	2.5 (54)	23.8 (11 024)	<0.0001	2.9 (19)	22.2 (4961)	<0.0001
Framingham risk: medium, % (n)	47.9 (192)	53.4 (7497)	0.0304	37.9 (808)	54.7 (25 347)	<0.0001	35.3 (229)	55.1 (12 329)	<0.0001
Framingham risk: low, % (n)	47.4 (190)	15.7 (2203)	<0.0001	59.6 (1270)	21.5 (9938)	<0.0001	61.7 (400)	22.8 (5104)	<0.0001
Tobacco use, % (n)	54.1 (217)	58.5 (8226)	0.0763	49.5 (1055)	59.2 (27 398)	<0.0001	43.8 (284)	54.2 (12 136)	<0.0001
Prior myocardial infarction, % (n)	12.5 (50)	16 (2246)	0.0576	3.8 (81)	5.8 (2672)	0.0001	3.2 (21)	6.8 (1520)	0.0004
COPD, % (n)	18.5 (74)	19.3 (2715)	0.6643	15.9 (338)	18.8 (8699)	0.0007	22.4 (145)	22.9 (5131)	0.7489
Chronic kidney disease, % (n)	10 (40)	16.2 (2280)	0.0008	4.8 (103)	12 (5545)	<0.0001	10.3 (67)	17.4 (3889)	<0.0001
Family history of CAD, % (n)	1.7 (7)	0.4 (58)	0.0021	1.4 (29)	0.6 (298)	<0.0001	0.6 (4)	0.3 (75)	0.287
Peripheral vascular disease, % (n)	9.2 (37)	16.2 (2277)	0.0002	6 (128)	13.9 (6434)	<0.0001	8.5 (55)	16.1 (3598)	<0.0001
PTSD, % (n)	18 (72)	13.8 (1939)	0.0177	22.4 (477)	18.7 (8651)	<0.0001	13.7 (89)	12.9 (2891)	0.5373
Sleep apnea, % (n)	10 (40)	12.8 (1795)	0.0969	16.7 (356)	18.7 (8655)	0.0208	14.2 (92)	15.3 (3420)	0.4532
Pre-Catheterization stress test									
Stress test ≤30 days prior, % (n)	11.2 (45)	12.4 (1744)	0.4759	37.9 (809)	37.6 (17 435)	0.7825	17.3 (112)	18.1 (4054)	0.5933

BMI indicates body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; and PTSD, posttraumatic stress disorder.

by race (white, black, and other) showed that women in all groups had less obstructive CAD and were less likely to be treated with PCI or medications (β-blockers, statins, clopidogrel or prasugrel, and long-acting nitrates).

When differentiated by indication for catheterization (Table 4), women continued to have higher rates of normal coronaries than men (19.2% versus 5.0%, *P*<0.0001, in the ACS group). Among patients with ACS, women had similar rates of single-vessel coronary disease, and higher rates of nonobstructive and normal coronaries, compared with men. Women had less 2-vessel and 3-vessel or left main CAD than men, regardless of the indication for catheterization, and had less treatment with PCI. At discharge, women were less likely to receive treatment with β-blockers, statins, and antiplatelet agents (clopidogrel or prasugrel), even among patients presenting with ACS (Table 4).

Outcomes

In-laboratory complications were similar among all women and men veterans (1.5% versus 1.6%, p=NS). Women were

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Table 3. Coronary Anatomy, Postprocedural Medications, and Unadjusted Outcomes

	Women (N=3181)	Men (N=82 755)	*P* Value
Coronary anatomy and treatment			
3-Vessel/left main obstructive, % (n)	4.5 (142)	17.1 (14 132)	<0.0001
2-Vessel Obstructive, % (n)	5.3 (170)	14.3 (11 842)	<0.0001
1-Vessel Obstructive, % (n)	12.8 (407)	21.9 (18 103)	<0.0001
Non-Obstructive, % (n)	28.7 (913)	27.2 (22 482)	0.0563
Normal, % (n)	45.9 (1461)	17 (14 108)	<0.0001
PCI-Treatment, % (n)	11.7 (372)	21.8 (18 070)	<0.0001
Postprocedural Medications			
Beta-blocker, % (n)	55.5 (1764)	70.5 (58 337)	<0.0001
Statin, % (n)	57.3 (1823)	71.2 (58 907)	<0.0001
Clopidogrel, prasugrel, % (n)	16.8 (533)	32.1 (26 540)	<0.0001
Long-acting Nitrate, % (n)	24.1 (768)	31.3 (25 902)	<0.0001
Calcium channel blocker, % (n)	23 (733)	22.9 (18 974)	0.8795
Procedural complications			
In-laboratory complications, % (n)	1.5 (49)	1.6 (1318)	0.8172
Transfusion within 30 days, % (n)	3.4 (109)	5.8 (4839)	<0.0001
Unadjusted 1-year outcomes			
Death, % (n)	2.7 (86)	5.6 (4668)	<0.0001
Rehospitalization All-Cause, % (n)	30.6 (973)	41.5 (34 383)	<0.0001
Rehospitalization for MI (day 15-1yr), % (n)	0.8 (24)	1.2 (952)	0.0387
Repeat Catheterization, % (n)	7.5 (239)	11.8 (9776)	<0.0001
Unplanned PCI, % (n)	3 (95)	5.7 (4698)	<0.0001
Unplanned CABG, % (n)	1.3 (40)	5.1 (4227)	<0.0001

CABG indicates coronary artery bypass grafting; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

less likely to have bleeding complications requiring transfusion. At 1 year, women had lower rates of death (2.7% versus 5.6%), unplanned PCI (3.0% versus 5.7%), and unplanned CABG (1.3% versus 5.1%; all $P<0.0001$) than men (Table 3). Women were less likely to be rehospitalized for all causes. Similar sex differences in long-term outcomes were demonstrated in proportional hazards models adjusted for the presence of obstructive disease as well as multiple factors. Women veterans had similar rates of unplanned PCI (hazard ratio [HR], 1.03; confidence interval [CI], 0.84–1.27; $P=0.78$) and rehospitalization for MI (HR, 1.19; CI, 0.79–1.80; $P=0.41$). Women were less likely than men to die (HR, 0.74; CI, 0.60–0.92; $P=0.007$), undergo unplanned CABG (HR, 0.58; CI, 0.42–0.79; $P<0.001$), or be rehospitalized for any cause (HR, 0.87; CI, 0.82–0.93; $P<0.001$).

Analysis by indication for catheterization revealed no sex differences in in-laboratory complications and similar or lower rates of bleeding complications among women (Table 4). Unadjusted outcomes for patients with ACS showed that women had lower mortality, all-cause rehospitalization, unplanned PCI, and unplanned CABG. Women and men with ACS had similar rates of rehospitalization for MI and unplanned catheterizations (Table 4). Adjusted models, including the interaction between sex and indication, showed women with ACS were less likely to die (HR, 0.45; CI, 0.23–0.88; $P=0.014$), but equally likely to be rehospitalized, require an unplanned catheterization, PCI, or CABG (Figure 1). Women with elective catheterizations had lower rates of death, rehospitalization for all causes, and unplanned catheterizations by 1 year (Figure 2). Women and men undergoing catheterization for other indications had no significant differences in outcomes (Figure 3).

Discussion

This is the first study of national VA data to investigate sex differences in the clinical characteristics, treatment, and outcomes of veterans undergoing cardiac catheterization. Our results show that women veterans had fewer classic CAD risk factors than men but higher rates of obesity, depression, and PTSD. Women more often presented with chest pain as an indication for catheterization than men. Furthermore, women veterans had lower rates of obstructive CAD, similar or lower rates of procedural complications, and lower 1-year death and all-cause rehospitalization rates, regardless of catheterization indication. These findings suggest that the clinical presentation that prompts referral of women veterans to VA catheterization laboratories is not as attributable to obstructive CAD as men. Accordingly, exploration of other causes for women's clinical presentation, such as endothelial dysfunction or concurrent psychological comorbidities, should occur.

Our findings both contradict and confirm prior studies of women and cardiovascular disease in several important ways. In contrast to the general population, in which women are typically older and have more cardiovascular risk factors than men,[7] women veterans were younger and had fewer conventional risk factors. In addition, women veterans had higher rates of depression and PTSD than men veterans, highlighting mental health as a potential risk factor for CAD and adverse outcomes.[27,28] Depression, anxiety, and other psychological disorders can also manifest physical symptoms, such as chest pain, even in the absence of CAD.[29–31] Because depression and PTSD are associated with decreased quality of life, persistent chest pain, increased cardiovascular risk, and worse cardiovascular outcomes,[32–35] the high rates observed in the veteran population clearly warrant attention.

Similar to studies in civilian populations, women veterans have less obstructive CAD than men.[8,15,36] Women had normal coronary arteries more often than men, regardless of catheterization indication. In the ACS population, women were also more likely to have nonobstructive CAD and less multivessel disease. Possible reasons for less obstructive disease in women with cardiac symptoms have been explored, including disorders of the coronary microvasculature and endothelial dysfunction.[37–39] Studies have shown that PTSD is associated with chest pain and that there is an association between PTSD and subsequent development of CAD, although this association has not been studied in women veterans specifically. Postulated mechanisms include sympathetic activation, which may over time result in cardiac autonomic dysfunction.[32,33] However, the low diagnostic yield of cardiac catheterization among women veterans might also indicate that screening and referral for catheterization needs improvement. Additional research is needed to better understand the referral

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Table 4. Coronary Anatomy, Postprocedural Medications, and Unadjusted Outcomes by Indication

	ACS			Elective			Other		
	Women (N=401)	Men (N=14 052)	*P* Value	Women (N=2132)	Men (N=46 309)	*P* Value	Women (N=648)	Men (N=22 394)	*P* Value
Coronary anatomy and treatment									
3-Vessel/left main obstructive, % (n)	11.2 (45)	26.8 (3772)	<0.0001	3.7 (78)	15.9 (7357)	<0.0001	2.9 (19)	13.4 (3003)	<0.0001
2-Vessel obstructive, % (n)	13.5 (54)	22.8 (3202)	<0.0001	4.3 (91)	13.4 (6222)	<0.0001	3.9 (25)	10.8 (2418)	<0.0001
1-Vessel obstructive, % (n)	31.2 (125)	32.2 (4527)	0.6591	10.3 (219)	20.8 (9633)	<0.0001	9.7 (63)	17.6 (3943)	<0.0001
Nonobstructive, % (n)	22.7 (91)	11.7 (1645)	<0.0001	29.3 (624)	29.1 (13 473)	0.8622	30.6 (198)	32.9 (7364)	0.2134
Normal, % (n)	19.2 (77)	5 (699)	<0.0001	50 (1065)	18.4 (8534)	<0.0001	49.2 (319)	21.8 (4875)	<0.0001
PCI treatment, % (n)	38.2 (153)	48.1 (6764)	<0.0001	8.9 (190)	20 (9252)	<0.0001	4.5 (29)	9.2 (2054)	<0.0001
Postprocedural medications									
Beta-blocker, % (n)	74.3 (298)	83.3 (11 708)	<0.0001	51.1 (1089)	66.1 (30 612)	<0.0001	58.2 (377)	71.5 (16 017)	<0.0001
Statin, % (n)	74.6 (299)	84.2 (11 838)	<0.0001	56.5 (1204)	70.8 (32 775)	<0.0001	49.4 (320)	63.8 (14 294)	<0.0001
Clopidogrel, prasugrel, % (n)	50.4 (202)	63.6 (8933)	<0.0001	12.6 (269)	29.9 (13 867)	<0.0001	9.6 (62)	16.7 (3740)	<0.0001
Long-acting Nitrate, % (n)	44.9 (180)	49.4 (6940)	0.0755	23.3 (497)	31 (14 358)	<0.0001	14 (91)	20.6 (4604)	<0.0001
Calcium channel blocker, % (n)	21.9 (88)	21.1 (2963)	0.6776	23.3 (496)	24.5 (11 329)	0.2075	23 (149)	20.9 (4682)	0.1983
Procedural complications									
In-laboratory complications, % (n)	2.5 (10)	1.9 (261)	0.3543	1.2 (26)	1.4 (653)	0.4642	2 (13)	1.8 (404)	0.7036
Transfusion within 30 days, % (n)	8 (32)	10.1 (1418)	0.1653	1.7 (37)	4.1 (1914)	<0.0001	6.2 (40)	6.7 (1507)	0.5767
Unadjusted 1-year outcomes									
Death, % (n)	3.2 (13)	9.4 (1320)	<0.0001	1.3 (28)	3.1 (1443)	<0.0001	6.9 (45)	8.5 (1905)	0.1589
Rehospitalization all-cause, % (n)	37.7 (151)	42.5 (5968)	0.0543	24.7 (526)	36.5 (16 883)	<0.0001	45.7 (296)	51.5 (11 532)	0.0035
Rehospitalization for MI (day 15-1 year), % (n)	2.7 (11)	2.6 (359)	0.8138	0.5 (10)	0.9 (397)	0.0548	0.5 (3)	0.9 (196)	0.2635
Repeat catheterization, % (n)	17.2 (69)	18.6 (2615)	0.4764	5.6 (120)	10.8 (5010)	<0.0001	7.7 (50)	9.6 (2151)	0.1068
Unplanned PCI, % (n)	8.5 (34)	11.2 (1580)	0.083	2.1 (45)	4.9 (2257)	<0.0001	2.5 (16)	3.8 (861)	0.0712
Unplanned CABG, % (n)	1.2 (5)	3.8 (527)	0.0087	1.1 (23)	5.1 (2365)	<0.0001	1.9 (12)	6 (1335)	<0.0001

ACS indicates acute coronary syndrome; CABG, coronary artery bypass grafting; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

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patterns at the VA; unfortunately, details about the description and nature of chest pain were not available in the current study. In addition, information about stress test results was not available. Efforts are ongoing to capture this important information in VA patients, and future studies will be able to provide insight into catheterization referral patterns. Additional research is also needed to determine why women veterans with cardiac signs or symptoms have less obstructive disease, and what potential treatments can effectively address their symptoms because it is known that women without obstructive CAD frequently have persistent chest pain[40] associated with increased healthcare costs,[41] rehospitalization,[38] and adverse cardiovascular outcomes, including higher rates of MI and mortality.[42]

Outcomes for women veterans after diagnostic catheterization were similar or better compared with men veterans. Women had lower mortality at 1 year, even when adjusted for age, presence of obstructive disease, and multiple comorbidities. This is in contrast to some prior research that has indicated that women have worse outcomes than men,[17] but studies are conflicting.[43] Although our findings seem reassuring, caution is needed when interpreting these results. Because women have significantly less obstructive CAD than men, but similar rates of rehospitalization for MI and unplanned PCI at 1-year, this may indicate that the presence of nonobstructive disease carries a significant healthcare burden.

This study has important clinical implications, not only for practitioners who will care for increasing numbers of women

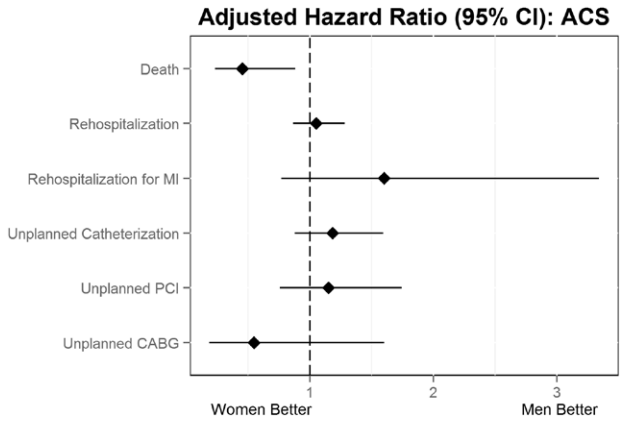

Figure 1. Adjusted Cox model results for 1-year adverse outcomes for women veterans, relative to men veterans, undergoing catheterization for acute coronary syndrome (ACS). CABG indicates coronary artery bypass grafting; CI, confidence interval; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

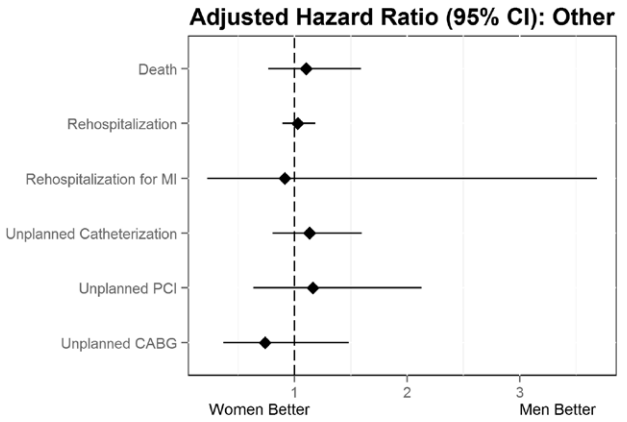

Figure 3. Adjusted Cox model results for 1-year adverse outcomes for women veterans, relative to men veterans, undergoing catheterization for other indications. CABG indicates coronary artery bypass grafting; CI, confidence interval; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

veterans at both VA and non-VA facilities, but also for providing insight into the pathophysiology of CAD in women. Efforts are needed to better understand why women experience chest pain in the absence of obstructive CAD.[40] The optimal method of diagnosis and therapy for patients with chest pain in the absence of obstructive CAD warrants increased attention; greater emphasis on noninvasive testing methods, such as CT coronary angiography, may be indicated. Finally, the interplay between psychological factors and the presence of chest pain merits further research. As the population of women veterans continues to age and develop additional cardiac risk factors, rates of obstructive CAD and associated complications may rise.

This is the first nationwide study of women veterans undergoing cardiac catheterization. VA CART data are an optimal means of capturing this data; however, several limitations deserve consideration. First, although CART data have been shown to be highly accurate,[24] misclassification may still occur, and more detailed information regarding stress testing types and results was not available. In addition, detailed symptom description, biomarker, and EKG data were not available. In the absence of this granular data, we were unable to explore possible predictors of obstructive or nonobstructive CAD. Second, there is potential for overfitting of the Cox models of long-term outcomes, particularly for rehospitalization caused by MI because of lower event rates in this group. Third, the cause of death could not be separated into cardiac-specific mortality because this is not collected in VA data sets. Additional variables, such as aspirin use and left ventricular ejection fraction, were also not available. Finally, the groups of men and women were significantly different in terms of age and clinical demographics. As a result of these large differences, the use of regression adjustment may not have been sufficient to account for the residual confounding effect of age and other clinical differences. Therefore, these findings should be interpreted accordingly.

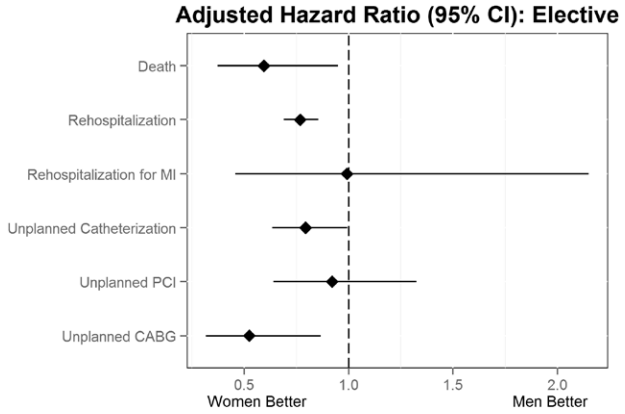

Figure 2. Adjusted Cox model results for 1-year adverse outcomes for women veterans, relative to men veterans, undergoing catheterization for elective indications. CABG indicates coronary artery bypass grafting; CI, confidence interval; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

Conclusions

This is the first study of national VA data to investigate sex differences in the clinical characteristics, treatment, and outcomes of veterans undergoing cardiac catheterization. Our results show that women veterans had fewer classic CAD risk factors than men but higher rates of obesity, depression, and PTSD. Furthermore, women veterans had lower rates of obstructive CAD, similar or lower rates of procedural complications and subsequent rehospitalization, and lower 1-year death rates, regardless of catheterization indication. These findings suggest that the clinical presentation that prompts referral of women veterans to VA catheterization laboratories is not as attributable to obstructive CAD as it is in men. Accordingly, exploration of other causes for women's clinical presentation, such as endothelial dysfunction or concurrent psychological comorbidities, should occur. Further investigation into the reasons behind these findings and application of those insights into effective treatments could potentially address some of the sex differences noted in nonveteran cardiac populations.

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Disclosures

None.

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Characteristics and Outcomes of Women Veterans Undergoing Cardiac Catheterization in the Veterans Affairs Healthcare System: Insights from the VA CART Program

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