Comparison of Outcomes of Coronary Revascularization for Acute Myocardial Infarction in Men Versus Women

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This study sought to examine the differences in the characteristics and outcomes between men and women who underwent percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) for acute myocardial infarction (AMI) in contemporary US practice. The Nationwide Inpatient Sample was used to identify patients who underwent revascularization for AMI between January 1, 2003 and December 31, 2016. The primary outcome was in-hospital mortality. Propensity score matching was utilized to account for differences in baseline characteristics. In total, 3,603,142 patients were included, of whom only 1,180,436 (33%) were women. Compared with men, women were older and had higher prevalence of key co-morbidities including diabetes, hypertension, congestive heart failure, and chronic kidney and lung disease (p <0.001). In the PCI cohort, women were significantly less likely to undergo multivessel PCI, to receive mechanical circulatory support, or to undergo atherectomy. In the CABG group, women were more likely to have concomitant valve surgery. In the propensity-matched cohorts, in-hospital mortality was higher for women than men regardless of revascularization strategy: 7.6% versus 6.6% for PCI in ST-elevation myocardial infarction, 2.0% versus 1.9% for PCI in non-ST-elevation myocardial infarction, and 5.7% versus 4.3% for CABG in any AMI (p <0.001). Women also had higher rates of major complications, longer hospitalizations, higher costs, and were less likely to be discharged home (vs nursing facility). These sex-based differences persisted over the study 14-year period. In conclusion, in a contemporary nationwide analysis of propensity score-matched patients, women who undergo revascularization for AMI have worse in-hospital outcomes than men regardless of revascularization mode. **(Am J Cardiol 2020;132:1−7)**

Differences in the presentation, management, and outcomes of acute myocardial infarction (AMI) between men and women have been well documented. There is a large body of literature demonstrating worse outcomes of AMI in women, who were also less likely to be referred for invasive angiography and to undergo revascularization.[1−3] However, the impact of sex on the outcomes of patients who undergo coronary revascularization specifically in the setting of AMI is less studied. Several studies have shown worse outcomes of percutaneous coronary intervention (PCI) in women compared with men overall, but without stratification of outcomes according to PCI indication.[4−8] Similarly, a few studies have shown worse outcomes of coronary artery bypass grafting (CABG) in women, but those studies did not distinguish between CABG performed for stable indications and those performed in the setting of an AMI.[9−12] In addition, considerable changes have been reported in the trends in PCI and CABG in recent years including a substantial reduction in procedural rates, and an increasing proportion of patients with AMI in all patients who underwent revascularization.[13] Hence, we sought to examine the differences in outcomes between men and women who underwent PCI or CABG for AMI in contemporary US practice.

Methods

The Nationwide Inpatient Sample (NIS) was used to derive patient-relevant information between January 2003 and December 2016. The NIS is the largest publicly available all-payer administrative claims-based database and contains information about patient discharges from ≈1,000 nonfederal hospitals in 47 states. It contains clinical and resource utilization information on 5 million to 8 million discharges annually, with safeguards to protect the privacy of individual patients, physicians, and hospitals. These data are stratified to represent ≈20% of US inpatient hospitalizations across different hospital and geographic regions and act as a random sample. National estimates of the entire US hospitalized population were calculated using the Agency for Healthcare Research and Quality sampling and weighting method. The institutional review board exempted the study because it utilizes public, deidentified data.

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Funding: No funding was used to support this study.

See page 6 for disclosure information.

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https://doi.org/10.1016/j.amjcard.2020.07.014

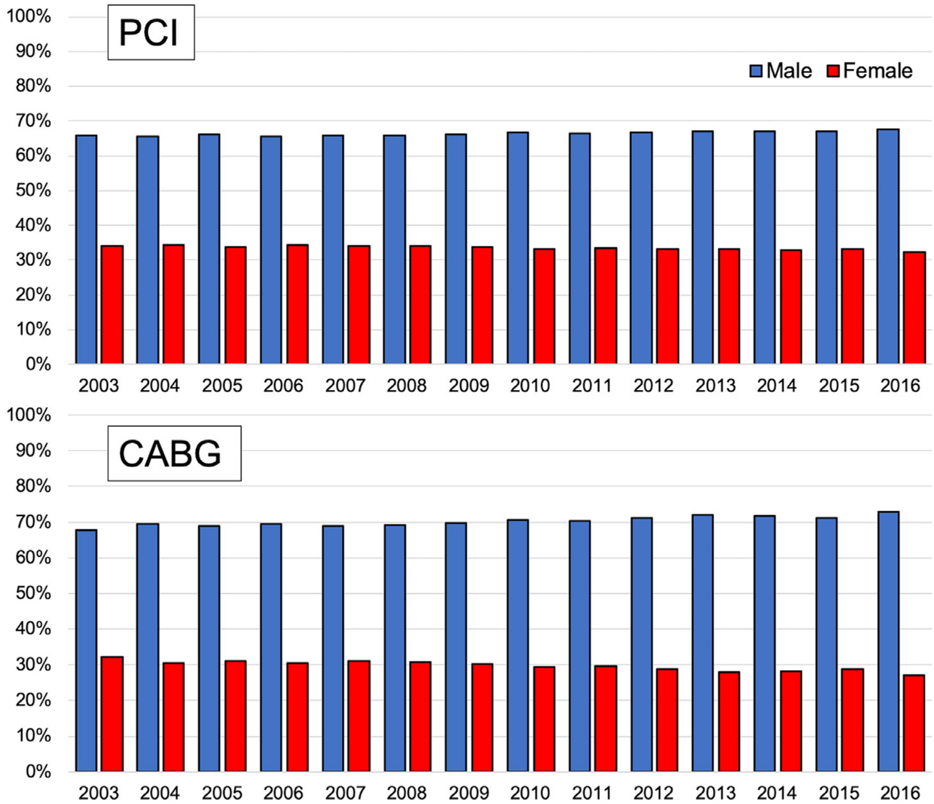

Figure 1. Distribution of revascularization after acute myocardial infarction by sex over time as a percentage of annual cases. CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

Adult patients with a primary discharge diagnosis of AMI who underwent revascularization through PCI or CABG were identified in the NIS database using International Classification of Diseases-9th, 10th Clinical Modification (eTable 1). The PCI cohort was further subdivided according to presentation as ST-elevation myocardial infarction (STEMI) or non-ST-elevation myocardial infarction (NSTEMI). Baseline co-morbidities were described, and in-hospital morbidity and mortality were assessed and compared between sexes. We excluded patients in whom information about gender (male vs female) was missing (n = 1,301).

The primary end point for all patients was in-hospital death. Secondary outcomes for patients who underwent surgical revascularization included clinical stroke, acute kidney injury, need for hemodialysis, pneumonia, cardiac tamponade, gastrostomy tube placement, tracheostomy, prolonged mechanical ventilation >72 hours, urinary tract infection, discharge disposition, length of stay, and cost. For patients who underwent PCI, secondary outcomes included clinical stroke, acute kidney injury, need for hemodialysis, vascular complication, blood transfusion, discharge disposition, length of stay, and cost.

Descriptive statistics are presented as frequencies with percentages for categorical variables. Continuous variables are reported as mean ± standard deviation. Baseline characteristics were compared using a Pearson chi-square test for categorical variables and an independent-samples *t* test for continuous variables. Trend weights accounting for changes in the NIS sampling design are available only for data between 1998 and 2011. For 2012 and 2013, trend weights were not available, and the standard survey weights were used. Matched categorical variables were presented as frequencies with percentages and compared using the McNemar test. Matched continuous variables are reported mean ± standard deviation and compared using a paired-samples *t* test.

To account for potential confounding factors and to reduce the effect of selection bias, propensity score-matching models were developed using logistic regressions to derive matched groups for comparative outcomes analysis. Patients who underwent revascularization (PCI or CABG) were entered into a nearest neighbor 1:1 variable ratio, parallel, balanced propensity score-matching model using a caliper of 0.01 to ensure perfect matching; variables included age, year of presentation, and baseline characteristics (complete variables provided in eTable 2). We performed multiple imputations to impute missing values for race (missing in 14% of observations) using the fully conditional specification method (an iterative Markov chain Monte Carlo algorithm) using age, sex, insurance status, co-morbid conditions, hospital region, and clinical characteristics. This method adheres to the recommendations provided by the Healthcare Cost and Utilization Project for handling missing racial data. To estimate the cost of hospitalization, the NIS data were merged with cost-to-charge ratios available from the Healthcare Cost and Utilization Project. We estimated the cost of each inpatient stay by

Table 1
Baseline characteristics of men and women who underwent percutaneous coronary intervention for myocardial infarction

Baseline characteristic	PCI for STEMI			PCI for NSTEMI		
	Men (n = 603,198)	Women (n = 252,385)	p value	Men (n = 1,315,027)	Women (n = 714,126)	p value
Age (mean ± SD)	60 ± 12	66 ± 14	<0.001	63 ± 13	68 ± 13	<0.001
Race/ethnicity						
White	77.2%	77.4%	<0.001	78.3%	74.9%	<0.001
Black	7.2%	10.0%	<0.001	8.0%	12.2%	<0.001
Hispanic	8.1%	6.9%	<0.001	7.4%	7.2%	<0.001
Medical co-morbidities						
Diabetes mellitus	26.1%	32.6%	<0.001	34.2%	41.4%	<0.001
Hypertension	58.7%	65.7%	<0.001	70.4%	75.2%	<0.001
Prior sternotomy	2.9%	2.5%	<0.001	8.5%	6.1%	<0.001
Chronic renal disease	7.3%	9.4%	<0.001	14.3%	16.3%	<0.001
Chronic lung disease	11.3%	16.2%	<0.001	16.3%	21.9%	<0.001
Vascular disease	5.5%	7.7%	<0.001	10.4%	12.4%	<0.001
Atrial fibrillation	9.6%	12.7%	<0.001	12.1%	13.4%	<0.001
Conduction disorders	4.0%	4.2%	<0.001	4.8%	4.7%	0.002
Carotid artery disease	0.6%	1.0%	<0.001	1.5%	2.2%	<0.001
Prior stroke/TIA	2.3%	3.6%	<0.001	3.9%	5.1%	<0.001
Dialysis	0.1%	0.2%	<0.001	0.3%	0.5%	<0.001
Anemia	8.3%	16.6%	<0.001	11.9%	19.7%	<0.001
Congestive heart failure	3.2%	4.6%	<0.001	3.8%	5.2%	<0.001
Cardiogenic shock	9.9%	12.0%	<0.001	2.4%	2.7%	<0.001
Use of MCS device	10.7%	10.8%	0.24	2.8%	2.7%	<0.001
Atherectomy	4.0%	3.3%	<0.001	1.5%	1.4%	<0.001
Multivessel PCI	14.8%	13.9%	<0.001	19.1%	17.9%	<0.001
Elixhauser co-morbidities		<0.001		<0.001		
0	11.2%	9.7%		9.9%	8.7%	
1 or 2	49.4%	49.7%		49.7%	49.1%	
≥3	39.4%	40.6%		40.4%	42.1%	
Medicare insurance	42.2%	64.0%	<0.001	52.7%	70.3%	<0.001
Lowest income tertile	26.0%	29.0%	<0.001	27.1%	30.7%	<0.001

MCS = mechanical circulatory support; n = number; NSTEMI = non-ST-elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction; SD = standard deviation; TIA = transient ischemic attack.

multiplying the total hospital charge with cost-to-charge ratios. A type I error rate of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 24 (IBM Corp) and R, version 3.3.1 (R Foundation for Statistical Computing).

Results

In total, 3,603,142 patients underwent revascularization for AMI from 2003 to 2016 in the NIS, of whom 1,180,436 (32.8%) were women. Of the total sample, 2,884,736 patients (80.1%) underwent PCI and 718,406 (19.9%) underwent CABG. Figure 1 illustrates the percentages of women and men who underwent revascularization by PCI or CABG for AMI annually from 2003 to 2016.

In the PCI cohorts, baseline characteristics differed between women and men; as illustrated in Table 1. Men were younger than women overall and when separated by indication (STEMI: men, 60 ± 12; women, 66 ± 14 years; NSTEMI: men, 63 ± 13; women, 68 ± 13 years, p <0.001 for both); they were also more likely to be white (p <0.001). Compared with men, women were more likely to have significant co-morbidities by Elixhauser co-morbidity score, including higher prevalence of diabetes mellitus, hypertension, carotid and peripheral vascular disease, renal insufficiency, chronic lung disease, and congestive heart failure (p <0.001 for all). Women were more likely to be in cardiogenic shock, but less likely to receive mechanical circulatory support, to be treated with atherectomy, or to undergo multivessel PCI, and this was consistent for both STEMI and NSTEMI.

In the CABG cohort, differences in baseline characteristics between women and men were comparable to those observed in the PCI cohort (Table 2). Men were younger than women (65 ± 12 vs 68 ± 11 years, p <0.001), more likely to be white, and had higher rates of smoking, atrial fibrillation, and conduction disease (all p <0.001). Women, however, had higher mean Elixhauser co-morbidity scores, and higher prevalence of diabetes mellitus, hypertension, carotid stenosis, vascular disease, chronic renal insufficiency, chronic lung disease, liver disease, congestive heart failure, and cardiogenic shock (all p <0.001). Women were more likely to undergo concomitant valve surgery (aortic: 4.9% vs 4.7%, p = 0.004; mitral: 4.6% vs 2.5%, p <0.001) and less likely to receive mechanical circulatory support (p <0.001).

With PSM, baseline characteristics of the PCI group became well matched between the women and men as shown in eTable 3. In the unmatched cohorts, women had worse morbidity, mortality, length of stay, and cost compared with men as shown in eTable 4. The mortality difference between men and women persisted over the study 14-

Table 2
Baseline characteristic of men and women who underwent coronary artery bypass grafting

Baseline characteristics	Men (n = 504,481)	Women (n = 213,925)	p value
Age, mean ± SD	65 ± 11	68 ± 11	<0.001
Race/ethnicity		<0.001	
White	77.7%	73.7%	
Black	6.6%	11.0%	
Hispanic	8.3%	8.5%	
Medical co-morbidities			
Diabetes mellitus	39.9%	46.9%	<0.001
Hypertension	70.0%	72.2%	<0.001
Carotid artery disease	4.7%	5.9%	<0.001
Smoking	24.0%	18.4%	<0.001
Anemia	27.6%	33.0%	<0.001
Atrial fibrillation	30.4%	29.0%	<0.001
Conduction disorders	4.4%	3.8%	<0.001
Chronic renal insufficiency	16.0%	16.7%	<0.001
Dialysis	0.3%	0.3%	0.80
Chronic lung disease	23.2%	25.5%	<0.001
Congestive heart failure	4.7%	6.2%	<0.001
Liver disease	0.5%	0.4%	<0.001
Vascular disease	13.2%	15.1%	<0.001
Cardiogenic shock	8.1%	9.0%	<0.001
Mechanical circulatory support use	17.9%	17.3%	<0.001
Concomitant surgery			
Aortic valve surgery	4.7%	4.9%	0.004
Mitral valve surgery	2.5%	4.6%	<0.001
Elixhauser co-morbidities		<0.001	
0	9.4%	8.7%	
1 or 2	50.3%	49.4%	
≥3	40.4%	41.9%	
Nonteaching hospital	40.2%	38.8%	<0.001
Medicare\medicaid insurance	56.2%	70.6%	<0.001
Lowest income	27.9%	31.2%	<0.001

n = number; SD = standard deviation.

year period after PCI for STEMI or NSTEMI (Figure 2). After rigorous PSM, in-hospital mortality remained higher in women than in men. The magnitude of difference was higher in the STEMI subgroup (7.6% vs 6.6%, p <0.001) compared with NSTEMI (2.0% vs 1.9%, p = 0.003; Table 3). Women also had higher rates of stroke, acute kidney injury, vascular complications, and were more likely to require blood transfusions in both the STEMI and NSTEMI

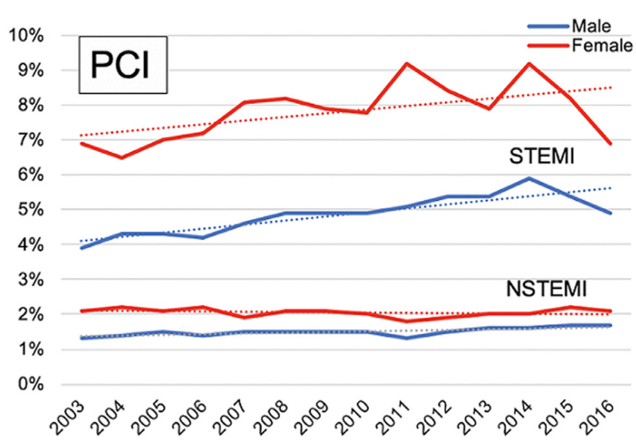

Figure 2. Rate of annual in-hospital mortality by sex for patients who underwent percutaneous coronary intervention according to clinical indication. PCI = percutaneous coronary intervention.

subgroups (all p <0.001). Nonhome discharges were more common in women. However, cost became nonstatistically different.

With PSM-matching, baseline characteristics of the CABG group became well matched between the women and men as shown in eTable 5. In the unmatched cohorts, women had worse morbidity, mortality, length of stay, and cost compared with men (eTable 6). The mortality difference between men and women persisted over the 14-year study period (Figure 3). After PSM, in-hospital mortality remained higher in women than in men (5.7% vs 4.3%, p <0.001) as were key complications, such as acute kidney injury, prolonged ventilation, tracheostomy, and urinary tract infections (p <0.001; Table 4). Nonhome discharge, length of stay, and cost remained significantly higher in women than in men.

Discussion

The major findings of this study are as follows: first, over twice as many men as women underwent revascularization in the setting of AMI over a 14-year period in the United States. Second, there were sex-specific differences in risk profiles and procedural techniques; older age and relevant co-morbidities were more common in women. Third, in a propensity score-matched group, women had higher rates of in-hospital mortality for both PCI and CABG, more

Table 3
Outcomes of percutaneous coronary interventions in propensity matched cohorts of men and women presenting with acute myocardial infarction

Clinical outcomes post-PCI	PCI for STEMI			PCI for NSTEMI		
	Men (n = 245,456)	Women (n = 244,983)	p value	Men (n = 694,002)	Women (n = 693,972)	p value
In-hospital mortality	6.6%	7.6%	<0.001	1.9%	2.0%	0.003
Clinical stroke	1.0%	1.3%	<0.001	0.8%	1.1%	<0.001
Acute kidney injury	11.9%	10.1%	<0.001	11.3%	10.9%	<0.001
Need for hemodialysis	0.6%	0.6%	0.97	0.8%	0.7%	<0.001
Vascular complication	3.6%	6.0%	<0.001	3.2%	5.4%	<0.001
Blood transfusion	3.7%	6.0%	<0.001	4.0%	6.0%	<0.001
Disposition		<0.001		<0.001		
Home discharge	89.5%	87.1%		91.5%	89.1%	
Nonhome discharge	9.6%	12.5%		8.1%	10.7%	
Length of stay − median (IQR)	3 (2-5)	3 (2-6)	<0.001	3 (2-5)	3 (2-6)	<0.001
Cost − median (IQR)	$20,626 (15,467-29,247)	$20,642 (15,513-29,045)	<0.001	$19,516 (14,703-27, 330)	$19,625 (14,750-27,553)	0.97

$ = dollar; IQR = interquartile range; PCI = percutaneous coronary intervention.

complications, longer hospital stays, and were less likely to be discharged home.

The preponderance of men included in this study is consistent with some prior studies[5,11,12] and may be partially explained by the higher incidence of myocardial infarction (MI) in men, which according to updated national heart disease and stroke statistics released earlier this year by the American Heart Association, occurs 1.4 times more often in men.[14] Other factors that may contribute to the disparity include the increased likelihood of women presenting with so-called "atypical" symptoms and/or silent MIs leading to delayed diagnoses and missed opportunities for revascularization.[15] Additionally, it is conceivable that physicians aware of the disparity in outcomes are less likely to offer revascularization to women.

The differences in baseline characteristics seen here are in line with meta-analyses on the topic, which show distinctive risk profiles between sexes.[3,6,16] The older age of women likely reflects their longer life expectancy and tendency to develop disease later in life.[14] Differences in procedural techniques, including the lower rates of mechanical circulatory support utilization in all women as well as decreased performance of atherectomy and multivessel PCI may reflect differences in disease extent or severity, which have been observed elsewhere.[16] Other studies have also

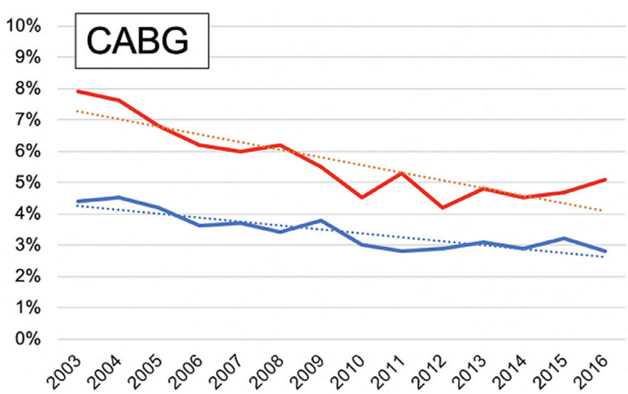

Figure 3. Rate of annual in hospital mortality by sex for patients who underwent coronary artery bypass grafting during the study period. CABG = coronary artery bypass grafting.

noted difference in technique; IVUS was less frequently used in women than men in 1 meta-analysis.[8] However, the decreased implementation of these techniques may reveal less complete revascularization in women, which could contribute to their increased mortality.

Sex-related differences in mortality after AMI have been inconsistent over time and sometimes are eliminated when adjusting for other clinical factors or treatment strategies.[1−3,17] In the present study, sex remained a significant and independent predictor of in-hospital mortality when taking into account revascularization strategies and patient characteristics. As noted above, AMI in women, diabetics and the elderly are less likely to present with chest pain, which can lead to greater delay in care and worse mortality.[6,18−20] Periprocedural MI has been cited as accounting for differences in outcome both in PCI and CABG[8,9,21]; our data are insufficient to confirm or dispute this hypothesis. The reasons behind a decrease in mortality after CABG over time but not after PCI are likely multifactorial and include changes in patient demographics, procedural techniques, and operator experience.[13]

Our findings of worse in-hospital mortality in women after revascularization for AMI despite rigorous propensity score matching are in keeping with other studies that demonstrate worse outcomes after revascularization for other indications.[4−7,10−12,22] Possible drivers of this disparity include later time to presentation for and decreased recognition of ACS in women; anatomic differences dictating smaller stent diameters[6,8] or less suitable LIMAs; differences in procedural techniques such as those reported here as well as the important disparity in rate of LIMA utilization published elsewhere,[9,11,23] and rates of serious complications including bleeding and vascular or access-related complications.[4,5,7,24] Finally, there may be additional variables whose impact is unrecognized or that are simply not easy to measure.

Although the differences presented here may not be completely unforeseen, they are incompletely understood. Such sex disparities in cardiovascular care have prompted a scientific statement from the American Heart Association specific to women[25] as well as period public calls for more balanced inclusion in cardiovascular trials.[26,27] Finally, as suggested by a recent editorial, the higher prevalence of

Table 4
Outcomes of coronary artery bypass grafting in propensity matched cohorts of men and women presenting with acute myocardial infarction

Clinical outcomes post-CABG	Men (n = 212,111)	Women (n = 212,228)	p value
In-hospital mortality	4.3%	5.7%	<0.001
Clinical stroke	2.1%	2.9%	<0.001
Acute kidney injury	21.4%	20.1%	<0.001
Need for hemodialysis	1.9%	2.0%	0.29
Pneumonia	7.3%	7.3%	0.77
Cardiac tamponade	0.4%	0.4%	0.37
Gastrostomy	1.5%	1.5%	0.70
Tracheostomy	2.5%	2.9%	<0.001
Prolonged mechanical ventilation	5.8%	6.7%	<0.001
Urinary tract infection	5.7%	15.3%	<0.001
Disposition			
Home discharge	73.2%	63.3%	<0.001
Nonhome discharge	26.70%	36.6%	
Length of stay, median (IQR)	10 (7-14)	11 (8-15)	<0.001
Cost, median (IQR)	$42,326 (31,526-60,480)	$43,929 (32,617-62,833)	<0.001

CABG = coronary artery bypass grafting; $ = dollar; IQR = interquartile range.

cardiovascular disease unrelated to obstructive epicardial atherosclerosis in women likely signifies a different pathobiology that should mandate different treatment strategies.[28] First, patients admitted for AMI who were medically managed were not included in this sample, nor were ACS patients who presented with unstable angina. This may include patients with AMI due to causes other than plaque rupture, for example, spontaneous coronary artery dissection (more common in women and unlikely to be intervened upon[29]) or patients with type 2 MIs, whose pathophysiology and clinical courses would be expected to differ; however, it is unclear whether 1 gender would be more likely to suffer type 2 MI.[30] Second, NIS is an administrative database that gathers data for billing purposes and, as such, can be impacted by coding errors; however, the Healthcare Cost and Utilization Project quality control measures minimize this risk, and errors for hard outcomes such as in-hospital mortality are likely rare. Although the NIS allows assessment of in-hospital outcomes, it lacks some data of clinical interest including procedural details (such as stent size or success of intervention), echocardiographic data (such as ejection fraction), and laboratory results. In addition, long-term mortality data are unavailable. Finally, the potential for unmeasured confounders may bias the outcome results in the propensity score-matched cohorts; however, we believe that our rigorous propensity matching is likely to minimize the impact of this selection bias.

In conclusion, in a contemporary nationwide analysis of propensity score-matched patients, women who undergo revascularization for AMI have worse in-hospital outcomes than men, including rates of death and complications.

Authors' Contributions

Madeline Mahowald: Drafting of the manuscript, data presentation.

Fahad Alqhatani: Conceptualization, statistical analysis, critical revision to the manuscript.

Mohamad Alkhouli: Conceptualization, critical revision to the manuscript, data presentation, supervision.

Disclosures

The authors declare that they have no known competing financial interests or personal relations that could have appeared to influence the work reported in this study.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.07.014.

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