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Sex Differences in Outcomes Following Percutaneous Coronary Intervention According to Age

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Abstract

Background—Women <50 years of age with coronary artery disease (CAD) may represent a group at higher risk for recurrent ischemic events following percutaneous coronary intervention (PCI); however, no long-term, multi-center outcomes assessment exists in this population.

Methods and Results—Using the NHLBI Dynamic Registry we evaluated the association of sex and age on cardiovascular-related outcomes in 10,963 patients (3,797 women, 394 <50 years) undergoing PCI and followed for 5 years. Death, myocardial infarction (MI), coronary artery bypass graft surgery (CABG), and repeat PCI were primary outcomes comprising major adverse cardiovascular events (MACE). While procedural success rates were similar by sex, the cumulative rate of MACE at 1 year was higher in young women (27.8 vs. 19.9%, $p=0.003$) driven largely by higher rates of repeat revascularizations for target vessel or target lesion failure (CABG: 8.9% vs.

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3.9%, $p < 0.001$, adjusted hazard ratio [aHR] 2.4, 95% CI 1.5-4.0; PCI: 19.0% vs. 13.0%, $p = 0.005$, aHR 1.6, 95% CI 1.2-2.2). At 5 years, young women remained at higher risk for repeat procedures (CABG: 10.7% vs. 6.8%, $p = 0.04$, aHR 1.71, 95% CI 1.01-2.88; repeat PCI [target vessel]: 19.7% vs. 11.8%, $p = 0.002$, aHR 1.8, 95% CI 1.24-2.82). Compared to older women, younger women remained at increased risk of MACE, while all outcome rates were similar in older women and men.

Conclusions—Young women, despite having less severe angiographic CAD have an increased risk of target vessel and target lesion failure. The causes of this difference deserve further investigation.

Clinical Trial Registration—URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT00005677.

Keywords

acute coronary syndrome; restenosis; myocardial infarction; revascularization

Female sex has been linked to a poorer prognosis following coronary revascularization with the higher risk of death and myocardial infarction (MI) in women undergoing percutaneous coronary intervention (PCI) attributed to older age, a greater prevalence of co-morbid conditions, and a higher coronary artery disease (CAD) risk profile [1-4]. Although women less than 50 years of age are, at lower risk for developing CAD, they may be at higher risk for adverse events once diagnosed, thereby representing a subgroup of patients at increased risk for adverse cardiovascular events. To date, there are limited data on PCI long-term outcomes in young women. Prior studies suggest that in young adults, female sex is a predictor of adverse outcomes including in-hospital mortality, vascular complications, MI, and target vessel revascularization by coronary artery bypass graft surgery (CABG) [5-8]; however, these data have been limited to a single center's experience [7,8] or to multi-center registries that lack outcomes assessment beyond hospital discharge [5,6].

Over 200,000 PCIs are performed annually in women in the United States, and approximately 21% are in patients <55 years of age [9]. Therefore, understanding the sex-associated risk in younger women is critical given that these women have decades of future life expectancy and quality of life placed at risk by CAD. The aim of the current analysis is to evaluate the association between sex, age, and procedural, in-hospital, and long-term outcomes of PCI using the multi-center National Heart, Lung, and Blood Institute (NHLBI)-sponsored Dynamic Registry.

METHODS

The Dynamic Registry is a multi-center, prospective, observational study of consecutive patients undergoing PCI in 27 North American centers between June 1997 and May 2006 [10]. Five recruitment waves of approximately 2,000 patients each, with an emphasis on enrollment of women and minorities, were followed prospectively. All study subjects were contacted at 1 year, and participants enrolled in waves 2, 4, and 5 were contacted annually for up to 5 years. Institutional Review Boards of the Coordinating Center at the University of Pittsburgh and at all clinical sites approved the study protocol and all subjects gave written

informed consent. Trained research coordinators recorded baseline clinical, angiographic, and procedural data and contacted the study participants via telephone annually to ascertain information on follow-up events. Race was self-reported. In addition to directly contacting patients, study personnel contacted referring physicians and treating institutions to collect additional clinical follow-up data when necessary. Medical records were reviewed for hospitalizations occurring after the index PCI when available. With the use of the Social Security Administration's Death Master File (www.ntis.gov/products/ssa-dmf.asp), coordinators periodically evaluated the vital status of patients who were lost to follow-up. Follow-up rates were > 90% at 1 year and 80.0% at 5 years.

Statistical analysis

Primary outcomes included cumulative incidence of death, MI, or repeat revascularization (CABG or PCI). Death was defined as all-cause mortality. MI was defined by evidence of at least one of the two following criteria: (1) evolutionary ST-segment elevation, development of new Q-waves in 2 or more contiguous leads on an electrocardiogram (ECG), or new or presumably new left bundle branch block pattern on the ECG; (2) biochemical evidence of myocardial necrosis manifested as either total creatine kinase (CK) or CK-MB 3 times the upper limit of normal or troponin level above the upper limit of normal. Repeat PCI included any unplanned PCI during the follow-up period, including TVR and TLR but excluding staged PCI. TVR was defined as a subsequent PCI in the index vessel, including revascularization for restenosis or progressive CAD. TLR was defined as a subsequent PCI within 5 mm proximal or distal to the index lesion. Major adverse cardiovascular event (MACE) was defined as a composite of death, MI, CABG, or repeat PCI. Procedural success was defined as total or partial angiographic success without in-hospital death, Q wave MI, or emergent CABG.

Patients were stratified by sex and age, with age dichotomized at 50 years (an age shown to be an important cut-point in prior cardiovascular outcomes investigations [5,11]). Baseline clinical, angiographic, procedural, and in-hospital outcomes data were compared in women and men in age-stratified groups using the chi-square test or Fisher's exact test (categorical data) or the Wilcoxon rank-sum test or Student's t-test (continuous data). One-year and five-year cumulative event rates were calculated using the Kaplan-Meier method and compared by the log-rank statistic. Time was defined as the time from the procedure to the date of last contact or death. Patients lost to follow-up were censored at the date of last contact.

Multivariable Cox proportional hazards regression modeling was used to estimate the independent effect of sex. Sequential models were fit with the initial model including no covariates (unadjusted), and the final model including covariates selected based on clinical and biological relevance as well as observed imbalances by sex in the baseline data. All models included the following covariates: race, body mass index, current smoking, hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease, prior MI, prior CABG, multi-vessel disease, acute coronary syndrome, stent use, and stent type. All analyses were also adjusted for year of procedure and age was only included in the adjusted models for younger versus older women. Proportional hazards assumptions were evaluated

and satisfied for all outcomes. Statistical analyses were performed with SAS software (version 9.3), and a two-sided P value of 0.05 or less was considered statistically significant.

Results

In total, 10,963 patients were enrolled, including 394 women <50 years old (3.6%), 1,141 men <50 years old (10.4%), 3,403 women ≥50 years old (31%), and 6,025 men ≥50 years old (55%). Cardiovascular risk factors and comorbid conditions varied by age and sex, with women presenting with a higher prevalence of hypertension, diabetes, and cerebrovascular disease compared to men irrespective of age (Table 1). Smoking was more common in young women (52.6% prevalence). Despite a greater prevalence of risk factors, young women had less extensive angiographic CAD, while the prevalence of markers of CAD complexity, such as ACC/AHA class C lesions [12], calcified lesions, or bifurcation lesions, were comparable in younger women and men. While stents were used less frequently in young women compared to young men (79% vs. 84%, $p=0.02$), the frequency of drug eluting stent (DES) use was numerically higher in young women than men but statistical significance was not reached. Prescribing patterns of guideline-recommended secondary prevention pharmacotherapy and anti-anginal therapy at the time of discharge were comparable in young men vs. young women.

Compared to older women, younger women had a greater body mass index and a lower prevalence of hypertension, diabetes, and hypercholesterolemia, with a substantially higher prevalence of current smoking (52.6% vs 19.1%, $p<0.001$). Younger women had a lower prevalence of cerebrovascular and peripheral vascular disease. Acute MI as an indication for the PCI was significantly greater in younger women (34.6% vs 25.8%, $p<0.001$). Younger women were also more likely to be prescribed a statin and a beta blocker than older women (Table 1)

Unadjusted procedural success rates, in-hospital mortality rates, and in-hospital MI rates were comparable by sex in each age group (Table 2). While older women experienced higher rates of major access site complications (7.0% vs. 3.5%, $p < 0.001$), bleeding (3.0% vs. 0.9%, $p<0.001$), and stroke (0.6% vs. 0.2%, $p < 0.001$) compared to older men, these differences in in-hospital adverse events were not seen in younger PCI patients. Older women did experience higher rates of major access site complications, bleeding and stroke compared to younger women.

At 1 year, young women had a higher incidence of MACE compared to men of similar age (27.8% vs. 19.9%, $p=0.003$, Table 3). Cumulative rates of death and MI were comparable by sex; thus, the higher MACE rate was attributable to higher rates of CABG (8.9% vs. 3.9%, $p < 0.001$) and repeat PCI (19.0% vs. 13.0%, $p=0.005$) compared to young men within 1 year of the index PCI (Table 3). Analysis of lesion-specific data revealed higher rates of TVR (14.7% vs. 7.8%, $p<0.001$) and TLR (11.2% vs. 6.2%, $p=0.002$) in young women compared to young men at 1 year. After multivariable adjustment, young women remained at higher risk of repeat revascularizations compared to men of similar age, while the adjusted risks of death and MI were comparable by sex (Figure 1a). A sensitivity analysis that included all patients receiving at least 1 bare-metal stent and patients receiving at least 1 drug-eluting

stent demonstrated that the magnitude of the event rates were similar to the overall cohort (Supplemental Table 1).

These differences were not observed when comparing older women with older men (Figure 1b). At 1 year, compared to older women, younger women had an increased rate of MACE (27.8% vs 22.6%, $p=0.04$) while the risk of death was lower (2.2% vs 5.8%, $p=0.004$). The CABG, repeat PCI, CABG/PCI, TVR and TLR rates were significantly greater in younger compared to older women (all $p<0.001$); after multivariable adjustment younger women remained at a higher risk of repeat MACE ($p<0.001$) repeat PCI/CABG ($p=0.02$) and TVR ($p=0.02$, Figure 2).

Varying our definition of “young” from <50 years of age to <55 or <65 years yielded similar results, with women in the younger strata having consistently higher rates of repeat revascularizations compared to men of similar age (Supplement Table 2). Younger women at all age cut-points experienced higher MACE rates compared to older women at 1-year, with the differences in event rates shrinking with the increasing age cut-points. Younger men continue to experience lower MACE rates compared to older men regardless of age definition (Supplemental Figure).

These differences in repeat revascularization rates persisted at 5 years (Table 3) with young women experiencing higher cumulative rates of CABG (10.7 vs. 6.8%, $p=0.04$; adjusted HR [aHR] 1.71, 95% CI 1.01-2.88), need for any repeat revascularization (36.2 vs 31.3%, $p=0.06$, [aHR] 1.35, 95% CI 1.03-1.76), and TVR (19.7% vs. 11.8%, $p=0.002$; aHR 1.8, 95% CI 1.24-2.82) compared to men of similar age. Cumulative incidence rates of MACE, death, and MI were comparable in young women and young men at 5 years. In contrast to the findings in younger patients, there were no statistically significant differences in 1-year or 5-year cumulative rates of MACE, death, MI, CABG or repeat PCI in women and men 50 years following the index PCI (Table 3, Supplement Figure). However, at 5 years older women maintained an increased risk of CABG, repeat PCI, CABG/repeat PCI, TVR and TLR compared to younger women.

Discussion

This study found that women under the age of 50 years had a disproportionate risk for adverse clinical events following PCI of the index lesion, despite having less severe angiographic disease compared to men under 50. While there were no sex-associated differences in procedural success rates or in 1-year cumulative rates of death or MI, younger women experienced a higher unadjusted rate of MACE at 1 year follow-up and a higher adjusted risk of repeat coronary revascularizations, including CABG, repeat PCI, TVR, and TLR compared to men of similar age. The sex difference in rates of repeat revascularizations, reflecting restenosis and/or progression of CAD, persisted throughout the five-year follow-up period, as young women remained at higher risk of CABG and TVR at 5 years. In this detailed “real-world” registry, baseline clinical, angiographic, and procedural characteristics did not account for the observed differences in long-term outcomes. Furthermore, prescribing patterns of guideline-recommended secondary prevention pharmacotherapy at the time of discharge were comparable in young patients according to

sex and are thus unlikely to explain the elevated risk in young women. While female sex was associated with poorer outcomes among younger patients, female sex was not associated with the long-term risk of adverse events in older patients.

Percutaneous Coronary Intervention in Women

Using the NHLBI Coronary Angioplasty Registry (1985-1986), Kelsey et al (13) showed that women had a higher peri-procedural angioplasty mortality risk compared to men (2.6% vs 0.3%) and a higher death rate at 4 years (10.8% vs 6.6%) despite similar angiographic success rates. At 4 years, the risk of MI and revascularization either by CABG or PCI was slightly lower in women and there was a similar improvement in symptoms to men. Srinivas et al (6) showed that women less than 50 years of age had a significantly greater risk of in-hospital mortality (0.70% vs 0.22%) and serious vascular complications (0.82% vs 0.24%) after balloon angioplasty. Female sex remained a significant predictor of death, stroke or CABG in multivariable analysis.

Alfonso et al (14) assessed the initial results and long-term risk of bare metal stenting and showed that gender was an independent predictor of procedural failure with an increase in the risk of death in women compared to men (6% vs 2%) as well as an increased incidence of vascular complications (7% vs 2%). Anderson et al (15) assessed outcomes in patients >65 years of age who underwent PCI using a stent and showed that women had a slightly higher, but statistically significant, procedural risk than men (in-hospital death 2.2% vs 1.6%, peri-procedural MI 1.3% vs 1.2%, bleeding 4.4% vs 2.3%, vascular complications 1.3% vs 0.7%) but better long-term survival. The use of drug eluting stents was associated with a similar benefit for women and men. Stefanini et al (16) showed a reduction in the risk of death and MI at 3 years in women with 2nd generation drug-eluting stents (9.2% vs 10.9% in 1st generation drug-eluting stents and 12.8% in bare metal stents). The use of drug-eluting stents was associated with a significant decrease in the TLR rate compared to bare-metal stents only (2nd generation: 6.3%, 1st generation: 7.8%, bare-metal: 18.6%, $p < 0.0001$).

Potential Explanations for Sex Differences in PCI Outcomes among Younger Women

There are several plausible explanations for higher rates of repeat coronary revascularizations in young women. Repeat revascularizations may be related to younger women with premature atherosclerosis having an aggressive form of CAD. Consistent with prior data revealing a clustering of cardiovascular risk factors in women with premature CAD [17], young women in the Dynamic Registry had a higher prevalence of multiple cardiovascular comorbidities including hypertension, diabetes, cerebrovascular disease, obesity, and smoking. Previous data showed that young and middle aged women (<60 years) were less likely to develop coronary artery disease compared to men; however, the risk is equalized in the setting of diabetes mellitus [18]. Hence, the increased incidence, in combination with the more injurious effect of diabetes in young women may have increased the rate of repeat revascularization. As such, we postulated that our findings of higher rates of repeat revascularizations in young women were in part a reflection of an aggressive atherosclerotic phenotype in women with premature CAD despite angiographically less extensive CAD.

While biology is one plausible mechanism for higher rates of repeat revascularizations, the disproportionate risk in young women was notably not explained by traditional cardiovascular risk factors in our adjusted analyses, thus raising the question of whether mediators of CAD progression beyond conventional risk factors are needed to better characterize future cardiovascular risk in young women. Among the unmeasured potential mediators of CAD progression to consider in young women are depression, estrogen-state, inflammation, underlying hematologic and rheumatologic [19-24] disorders that may predispose to atherothrombosis.

Higher rates of TVR and TLR suggest that many repeat PCIs in young women were driven by subsequent revascularization for restenosis and progressive lesion development in the target vessel and it is plausible that younger women may be more prone to restenosis, as sex steroid hormones have numerous known and potentially unknown effects on vascular biology [25]. The effect of trajectory patterns of sex steroid hormones across the menopause transition has not been explored and previous studies assessing sex differences in angiographic and clinical restenosis have yielded inconsistent results [26-28]. While most post-hoc analyses from clinical trials have not demonstrated sex differences in in-stent restenosis at routine angiographic follow-up [27,28], clinically significant restenosis, including TVR and TLR, was higher in women compared to men receiving paclitaxel-eluting stents, although the higher risk in women was mitigated after adjustment [27]. Likewise, our results suggest that young women are more likely to undergo clinically-driven repeat revascularizations of the target vessel and target lesion compared to men of similar age.

An additional explanation for differential rates of repeat revascularizations may be that women are more likely to report post-PCI angina reflecting sex differences in the perception and communication of anginal symptoms. Although the mechanism is unclear, women are more likely to report chest pain during daily activity and mental stress but less likely during exercise, and they are more likely to report functional disability related to angina, despite less extensive anatomic disease [29,30]. During exercise stress testing with perfusion imaging, women with angina and ischemia grade their angina to be more intense than men with similar characteristics [31], and women are also more likely to experience angina during rest, sleep, and emotional stress [32]. In the current study 30% of the surviving young women reported recurrent angina in the previous 6 weeks at their 1-year contact, compared to 18% of young men and 21% of older women, indicating that both sex and age may be a factor influencing angina presentation. Since post-PCI angina prevalence and intensity likely correlate with repeat catheterization, differences in angina prevalence may have prompted increased surveillance for obstructive CAD in young women, in turn resulting in higher rates of repeat revascularizations.

Younger women are less likely to be educated on the risk of heart disease

There has been a steep decline in coronary heart disease mortality since 1979, however, the decline has largely been restricted to older patients. Women less than 55 years of age had the lowest decline in estimated annual percentage change in coronary heart disease with minimal to no reduction since 1990 [33] Given that poor control of cardiovascular risk

factors has been associated with MACE, repeat revascularizations may reflect failed secondary prevention efforts, including low adherence to a healthy lifestyle and pharmacotherapy, and/or poor knowledge and control of CAD risk factors. In a 2012 AHA national survey of American women, younger women were less aware that cardiovascular disease was the leading cause of death in women and were less likely to engage in activities that reduce cardiovascular risk [34]. Koopman et al, showed that women less than 55 years of age were less likely to be prescribed a lipid lowering agent for primary prevention [35]. Hawkins et al demonstrated that the rate of prescriptions for secondary prevention in stable angina was 10% lower in younger women than men [36]. In the Virgo study, at 1 year, women <55 years were less likely to be on optimal therapy following a myocardial infarction due to a disparity in treatment initiation rather than treatment adherence despite more likely to have had a previous PCI [37,38]. While virtually all women, in VIRGO had at least one potentially modifiable risk factor they were 11% less likely than men to have been informed that they were at risk for heart disease and 16% less likely to have been told methods to modify risk prior to the index MI [39]. In the current study, with the exception of aspirin, prescribing rates of statins, beta blockers, ACE inhibitors and thienopyridines were similar in younger patients (Table 1).

Strengths

The strengths of our study include a population-based, prospective design, a large sample-size, and long-term outcomes assessment. Women have historically been underrepresented in cardiovascular clinical trials [40] and prior multi-center studies investigating sex-based differences in PCI outcomes in the young were limited to inhospital outcomes assessment [5,6]; therefore the NHLBI Dynamic Registry is unique in that it enriched the sample size of women by design to increase the availability of sex-specific data on interventional approaches to CAD management. To our knowledge, our study is the first multi-center study to evaluate the long-term effects of premature CAD and PCI in women.

Limitations

This is a prospective observational study, and we cannot account for biases in patient selection for the index PCI and for subsequent repeat angiography and intervention; however, the Dynamic Registry enrolled a non-selected, non-clinical-trial-based population and is thus reflective of real-world cardiovascular care. Second, lack of information on medical therapy and compliance after hospital discharge could affect the results. Lastly, as our cohort comprised patients enrolled from 1997-2006, some patients did not receive treatments reflective of current practices, including a subset of patients treated with PCI before the advent of drug-eluting stents and/or the use of second generation drug eluting stents. However, by a sensitivity analysis the results were consistent between those receiving stents and the overall cohort (Supplemental Table1). Also 2nd generation drug-eluting stents have been shown to reduce the risk of death or MI and stent thrombosis but not TLR compared to early drug-eluting stents [16]. Among recipients of 2nd generation stents women as a group still have been shown to have had an increased risk of major adverse events and target vessel failure compared to men up to 3 years [41]. In the current study young women had consistently higher rates of repeat revascularizations throughout the 9 year enrollment period regardless of whether angioplasty or bare-metal or drug-eluting

stents were used or recruitment wave, suggesting that evolution in practice patterns and technology has not corrected the sex difference in post-PCI outcomes in the young.

Conclusion

Because of their many years of remaining life expectancy that are threatened by early-onset CAD, young women with CAD are a population that warrants special attention. Current trends reveal a incidence of adverse cardiovascular events in women with premature CAD, including both rising coronary death rates [42] and hospitalizations for MI [43]. Young women with CAD are at greater risk for adverse outcomes, including inhospital and 2-year mortality following MI [11,34,44,45] in part due to young women being less likely to receive reperfusion therapy [46]. In-hospital mortality following CABG [47] is also greater compared to men of similar age. Our finding of higher rates of repeat coronary revascularizations in young women represents another complication of CAD in this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is Known

- Women have higher risks of adverse outcomes following percutaneous coronary intervention.
- The steep decline in coronary heart disease since 1979 has been largely limited to older patients.
- There is little known on the outcomes of percutaneous coronary intervention in women younger than 50 years.

What the Study Adds

- Women less than 50 years had less severe coronary artery disease than men under 50. Despite this, young women undergoing percutaneous coronary intervention had greater risks of adverse clinical events.
- At 5 years follow-up young women had a higher adjusted risk of repeat revascularization.
- Major adverse clinical events were similar in older women and men.

Figure 1.

Adjusted Hazard Ratios and 95% confidence intervals for one-year adverse cardiovascular events after PCI. A) Women 50 vs men 50 years. B) Women 50 vs men 50 years. CABG=coronary artery bypass surgery, HR=Hazard ratio, MACE=major adverse cardiovascular events, MI=myocardial infarction, PCI=percutaneous coronary intervention, TLR=target lesion revascularization, TVR=target vessel revascularization

Figure 2.
Cumulative event rates by gender and age.

Table 1

Baseline, procedural, and angiographic characteristics, by age and sex

	Age < 50			Age 50			Women Age < 50 vs 50
	Women	Men	P- value	Women	Men	P- value	P-value
	(N = 394)	(N = 1141)		(N = 3403)	(N=6025)		
Patient Characteristics							
Age (median)	45	46	0.91	69	65	< 0.001	--
Race (%): White	66.8	71.1	<0.001	75.6	81.4	<0.001	<0.001
Black	25.6	15.7		15.8	9.3		
Hispanic	6.1	7.1		5.6	5.4		
Asian	1.5	5.4		2.8	3.8		
Other	0	0.7		0.2	0.2		
Body Mass Index (kg/m ² , mean)	30.9	29.8	0.10	29.3	28.5	<0.001	<0.001
Prior PCI (%)	29.7	29.4	0.92	28.7	33.8	<0.001	0.72
Prior CABG (%)	6.9	8.5	0.30	15.4	22.0	<0.001	<0.001
Prior Myocardial Infarction (%)	24.4	32.9	0.002	27.8	30.9	0.002	0.15
Congestive Heart Failure (%)	4.4	4.1	0.82	13.9	9.8	<0.001	<0.001
Cerebrovascular Disease (%)	5.4	1.6	<0.001	8.4	7.1	0.02	0.04
Renal disease (%)	4.6	4.9	0.80	7.1	6.8	0.67	0.07
Peripheral Vascular Disease (%)	4.3	2.6	0.09	9.1	8.6	0.40	0.002
Pulmonary Disease (%)	5.6	2.7	0.007	10.5	7.8	<0.001	0.002
Cancer (%)	1.8	1.2	0.41	7.7	8.1	0.44	<0.001
Diabetes (%)	31.9	22.0	<0.001	38.3	28.2	<0.001	0.01
Hypertension (%)	61.4	52.6	0.003	79.0	69.4	<0.001	<0.001
Hypercholesterolemia (%)	62.9	66.0	0.28	70.4	70.4	0.77	0.003
Smoking (%): Current	52.6	48.7	0.003	19.1	21.7	<0.001	<0.001
Former	17.8	26.3		31.8	49.2		
Never	29.6	25.0		49.1	29.1		
Angiographic Characteristics							
Number of Significant lesions, mean	2.2	2.5	0.003	2.9	3.2	<0.001	<0.001
Vessel Disease: 1	60.8	48.6	<0.001	41.5	33.7	<0.001	<0.001
2	23.4	32.8		31.3	33.6		
3	15.5	18.5		27.0	32.4		
Left main 50%	2.0	1.7	0.63	4.8	7.0	<0.001	0.01

	Age < 50			Age 50			Women Age < 50 vs 50
	Women	Men	P-value	Women	Men	P-value	P-value
	(N = 394)	(N = 1141)		(N = 3403)	(N=6025)		
stenosis							
Technically amenable to complete revascularization with PCI	91.6	88.5	0.10	85.3	82.4	<0.001	0.001
Number of lesions	(N = 517)	(N = 1571)		(N = 4670)	(N=8500)		
Reference vessel diameter (mm)	2.9	3.1	<0.001	2.9	3.1	<0.001	0.14
Evidence of thrombus	18.1	23.4	0.01	14.6	16.4	0.007	0.04
Calcified lesions	15.2	16.7	0.42	29.7	27.6	0.02	<0.001
Bifurcation lesions	12.8	13.0	0.89	11.2	11.4	0.74	0.29
ACC/AHA Class C lesions	20.3	20.8	0.05	21.3	21.9	0.01	0.60
Lesion treated successful, %	97.3	96.1	0.19	96.5	95.9	0.08	0.35
Procedural Characteristics							
Number of patients	(N = 394)	(N = 1141)		(N = 3403)	(N=6025)		
Indication for Revascularization							
Acute Myocardial Infarction	34.6	36.6	0.48	25.8	23.7	0.02	<0.001
Unstable Angina	38.2	35.5	0.34	44.0	39.5	<0.001	0.03
Stable Angina	20.4	18.6	0.44	19.5	23.0	<0.001	0.68
Stent use, %	78.7	84.2	0.01	83.0	84.3	0.11	0.03
Drug eluting stent use (%) *	78.5	75.2	0.40	77.2	78.2	0.54	0.77
Discharge Medications							
Number of patients alive at discharge	(N = 393)	(N = 1137)		(N = 3351)	(N=5950)		
Aspirin	94.4	96.6	0.05	94.3	95.3	0.03	0.93
Statin	68.7	69.7	0.71	63.1	67.2	<0.001	0.03
Beta blocker	78.4	79.3	0.75	72.8	74.6	0.06	0.01
ACE inhibitor	42.2	42.7	0.86	42.7	44.8	0.05	0.86
Thienopyridines	86.3	86.3	0.98	84.0	86.4	0.001	0.25
Warfarin	7.4	6.4	0.52	6.1	7.3	0.02	0.30

No formal comparison was made for age between the two groups of women given the stratification by age.

* Only includes patients from Waves 4 and 5 when drug eluting stents were available. Adjudication of angiographic variables was made by the performing interventionalists. Complete revascularization was defined as successful intervention of all hemodynamically significant lesions, including total occlusions. PCI-percutaneous coronary intervention, CABG-coronary artery bypass graft surgery.

Table 2

In-Hospital Adverse Events and Outcomes, by age and sex

	Age < 50			Age ≥ 50			Women Age < 50 vs ≥ 50
Adverse Event	Women (N = 394)	Men (N = 1141)	P- value	Women (N = 3403)	Men (N=6025)	P- value	P-value
Death (%)	0.3	0.4	0.61	1.5	1.3	0.28	0.04
Myocardial Infarction (%)	1.3	1.7	0.58	2.2	2.7	0.18	0.22
CABG (%)	0.8	0.9	0.83	1.0	0.9	0.56	0.65
Stroke (%)	0	0.2	0.40	0.6	0.2	<0.001	0.13
Major Entry Site Complication (%)	2.3	2.9	0.52	7.0	3.5	<0.001	<0.001
Bleeding requiring transfusion (%)	0.5	0.4	0.67	3.0	0.9	<0.001	0.004

Table 3

One-year and Five-Year Cumulative Event Rates.

	Age < 50			Age ≥ 50			Women Age < 50 vs ≥ 50
	Women (N=394)	Men (N=1142)	P-value	Women (N=3403)	Men (N=6025)	P-value	P-value
One-Year Events (%)							
MACE	27.8	19.9	0.003	22.6	21.2	0.15	0.04
Death	2.2	2.4	0.84	5.8	4.9	0.07	0.004
MI	6.3	4.6	0.25	5.4	5.1	0.67	0.57
CABG	8.9	3.9	<0.001	4.7	4.4	0.46	<0.001
Repeat PCI	19.0	13.0	0.005	12.1	11.1	0.16	<0.001
CABG/Repeat PCI	24.8	15.9	<0.001	15.7	14.6	0.19	<0.001
	N=389	N=1135		N=3385	N=5985		
TVR	14.7	7.8	<0.001	8.3	7.2	0.05	<0.001
TLR	11.2	6.2	0.002	6.5	5.9	0.31	<0.001
Five-Year Events (%)*							
	N=247	N=647		N=1918	N=3578		
MACE	42.7	37.8	0.10	42.6	42.5	0.77	0.61
Death	11.0	7.2	0.11	20.7	18.5	0.7	0.001
MI	12.1	11.7	0.81	12.1	10.2	0.8	0.99
CABG	10.7	6.8	0.04	5.9	7.2	0.19	0.005
Repeat PCI	30.3	27.4	0.24	21.6	21.5	0.75	<0.001
CABG/repeat PCI	36.2	31.3	0.06	25.4	26.6	0.63	<0.001
TVR	19.7	11.8	0.002	10.7	10.0	0.5	<0.001
TLR	10.5	7.3	0.08	6.6	6.3	0.88	0.02