Sex Differences in Outcomes Following Percutaneous Coronary Intervention According to Age

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

**Methods and Results**—Using the National Heart, Lung, and Blood Institute Dynamic Registry, we evaluated the association of sex and age on cardiovascular-related outcomes in 10,963 patients (3797 women, 394 <50 years) undergoing PCI and followed for 5 years. Death, myocardial infarction, coronary artery bypass graft surgery, and repeat PCI were primary outcomes comprising major adverse cardiovascular events. Although procedural success rates were similar by sex, the cumulative rate of major adverse cardiovascular events at 1 year was higher in young women (27.8 versus 19.9%; \(P=0.003\)), driven largely by higher rates of repeat revascularizations for target vessel or target lesion failure (coronary artery bypass graft surgery: 8.9% versus 3.9%, adjusted hazard ratio 2.4, 95% confidence interval 1.5–4.0; PCI: 19.0% versus 13.0%, \(P=0.005\), adjusted hazard ratio 1.6, 95% confidence interval 1.2–2.2). At 5 years, young women remained at higher risk for repeat procedures (coronary artery bypass graft surgery: 10.7% versus 6.8%, \(P=0.04\), adjusted hazard ratio 1.71, 95% confidence interval 1.01–2.88; repeat PCI [target vessel]: 19.7% versus 11.8%, \(P=0.002\), adjusted hazard ratio 1.8, 95% confidence interval 1.24–2.82). Compared with older women, younger women remained at increased risk of major adverse cardiovascular events, whereas all outcome rates were similar in older women and men.

**Conclusions**—Young women, despite having less severe angiographic coronary artery disease, 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.

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**Key Words:** acute coronary syndrome ▪ myocardial infarction ▪ restenosis ▪ revascularization

F**emale sex has been linked to a poorer prognosis after 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 comorbid conditions, and a higher coronary artery disease (CAD) risk profile.**1–4 Although women <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 (TVR) by coronary artery bypass graft surgery (CABG)5–8; however, these data have been limited to a single center’s experience7,8 or to multicenter registries that lack outcomes assessment beyond hospital discharge.5,6

Over 200,000 PCIs are performed annually in women in the United States, and ≈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

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S16
WHAT IS KNOWN

- Women have higher risks of adverse outcomes after 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 <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.

Methods

The Dynamic Registry is a multicenter, prospective, observational study of consecutive patients undergoing PCI in 27 North American centers between June 1997 and May 2006. Five recruitment waves of ≥2000 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 ≤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 (http://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 2 following criteria: (1) evolution of ST-segment elevation, development of new Q-waves in ≥2 contiguous leads on an 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 or creatine kinase-MB ≥3× 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 target lesion revascularization (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 investigations11). Baseline clinical, angiographic, procedural, and in-hospital outcome data were compared in women and men in age-stratified groups using the χ² test or Fisher exact test (categorical data) or the Wilcoxon rank-sum test or Student’s t test (continuous data). One-year and 5-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, multivessel 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 2-sided P value of ≤0.05 was considered statistically significant.

Results

In total, 10,963 patients were enrolled, including 394 women <50 years old (3.6%), 1141 men <50 years old (10.4%), 3403 women ≥50 years old (31%), and 6025 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 mellitus, and cerebrovascular disease compared with 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, whereas the prevalence of markers of CAD complexity, such as American College of Cardiology/American Heart Association class C lesions,12 calcified lesions, or bifurcation lesions, were comparable in younger women and men. Although stents were used less frequently in young women compared with young men (79% versus 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 was comparable in young men versus young women.

Compared with older women, younger women had a greater body mass index and a lower prevalence of hypertension, diabetes mellitus, and hypercholesterolemia, with a substantially higher prevalence of current smoking (52.6% versus 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% versus 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).
Table 1. Baseline, Procedural, and Angiographic Characteristics, by Age and Sex

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Age &lt;50</th>
<th>Age ≥50</th>
<th>Women Age &lt;50 vs ≥50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women (N=394)</td>
<td>Men (N=1141)</td>
<td>P Value</td>
</tr>
<tr>
<td>Age (median)</td>
<td>45</td>
<td>46</td>
<td>0.91</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>66.8</td>
<td>71.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black</td>
<td>25.6</td>
<td>15.7</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>6.1</td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>1.5</td>
<td>5.4</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m², mean</td>
<td>30.9</td>
<td>29.8</td>
<td>0.10</td>
</tr>
<tr>
<td>Prior PCI, %</td>
<td>29.7</td>
<td>29.4</td>
<td>0.92</td>
</tr>
<tr>
<td>Prior CABG, %</td>
<td>6.9</td>
<td>8.5</td>
<td>0.30</td>
</tr>
<tr>
<td>Prior myocardial infarction, %</td>
<td>24.4</td>
<td>32.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Congestive heart failure, %</td>
<td>4.4</td>
<td>4.1</td>
<td>0.82</td>
</tr>
<tr>
<td>Cerebrovascular disease, %</td>
<td>5.4</td>
<td>1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal disease, %</td>
<td>4.6</td>
<td>4.9</td>
<td>0.80</td>
</tr>
<tr>
<td>Peripheral vascular disease, %</td>
<td>4.3</td>
<td>2.6</td>
<td>0.09</td>
</tr>
<tr>
<td>Pulmonary disease, %</td>
<td>5.6</td>
<td>2.7</td>
<td>0.007</td>
</tr>
<tr>
<td>Cancer, %</td>
<td>1.8</td>
<td>1.2</td>
<td>0.41</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>31.9</td>
<td>22.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>61.4</td>
<td>52.6</td>
<td>0.003</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>62.9</td>
<td>66.0</td>
<td>0.28</td>
</tr>
<tr>
<td>Smoking, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>52.6</td>
<td>48.7</td>
<td>0.003</td>
</tr>
<tr>
<td>Former</td>
<td>17.8</td>
<td>26.3</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>29.6</td>
<td>25.0</td>
<td></td>
</tr>
</tbody>
</table>

Angiographic characteristics

<table>
<thead>
<tr>
<th>Vessel disease</th>
<th>Age &lt;50</th>
<th>Age ≥50</th>
<th>Women Age &lt;50 vs ≥50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of significant lesions, mean</td>
<td>2.2</td>
<td>2.5</td>
<td>0.003</td>
</tr>
<tr>
<td>Left main ≥50% stenosis</td>
<td>2.0</td>
<td>1.7</td>
<td>0.63</td>
</tr>
<tr>
<td>Technically amenable to complete revascularization with PCI</td>
<td>91.6</td>
<td>88.5</td>
<td>0.10</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Indication for revascularization</th>
<th>Age &lt;50</th>
<th>Age ≥50</th>
<th>Women Age &lt;50 vs ≥50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myocardial infarction</td>
<td>34.6</td>
<td>36.6</td>
<td>0.48</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>38.2</td>
<td>35.5</td>
<td>0.34</td>
</tr>
</tbody>
</table>

(Continued)
Unadjusted procedural success rates, in-hospital mortality rates, and in-hospital MI rates were comparable by sex in each age group (Table 2). Although older women experienced higher rates of major access site complications (7.0% versus 3.5%; \(P<0.001\)), bleeding (3.0% versus 0.9%; \(P<0.001\)), and stroke (0.6% versus 0.2%; \(P<0.001\)) compared with 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 with younger women.

At 1 year, young women had a higher incidence of MACE compared with men of similar age (27.8% versus 19.9%; \(P=0.04\); 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% versus 3.9%; \(P<0.001\)) and repeat PCI (19.0% versus 13.0%; \(P=0.005\)) compared with young men within 1 year of the index PCI (Table 3). Analysis of lesion-specific data revealed higher rates of TVR (14.7% versus 7.8%; \(P<0.001\)) and TLR (11.2% versus 6.2%; \(P=0.02\)) in young women compared with young men at 1 year. After multivariable adjustment, young women remained at higher risk of repeat revascularizations compared with men of similar age, although 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 DES demonstrated that the magnitude of the event rates were similar to the overall cohort (Table I in the Data Supplement).

These differences were not observed when comparing older women with older men (Figure 1B). At 1 year, compared with older women, younger women had an increased rate of MACE (27.8% versus 22.6%; \(P=0.04\)), whereas the risk of death was lower (2.2% versus 5.8%; \(P=0.004\)). The CABG, repeat PCI, CABG/PCI, TVR, and TLR rates were significantly greater in younger compared with 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 with men of similar age (Table II in the Data Supplement). Younger women at all age cut points experienced higher MACE rates compared with 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 with older men, regardless of age definition (Figure in the Data Supplement).

These differences in repeat revascularization rates persisted at 5 years (Table 3), with young women experiencing higher cumulative rates of CABG (10.7 versus 6.8%; \(P=0.04\); adjusted hazard ratio 1.71, 95% confidence interval 1.01–2.88), need for any repeat revascularization (36.2 versus 31.3%; \(P=0.06\); adjusted hazard ratio 1.35, 95% confidence interval 1.03–1.76), and TVR (19.7% versus 11.8%; \(P=0.002\); adjusted hazard ratio 1.8, 95% confidence interval 1.24–2.82) compared with 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 after the index PCI (Table 3; Figure in the Data Supplement). However, at 5 years, older women maintained an increased risk of CABG, repeat PCI, CABG/repeat PCI, TVR, and TLR compared with younger women.

### Discussion

This study found that women under the age of 50 years had a disproportionate risk for adverse clinical events after PCI of the index lesion, despite having less severe angiographic disease compared with men under 50. Although 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 with men of similar age. The sex difference in rates of repeat revascularizations, reflecting restenosis and progression of CAD, persisted throughout the 5-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. Although 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.
Youth Women Post PCI

Using the NHLBI Coronary Angioplasty Registry (1985–1986), Kelsey et al. showed that women had a higher peri-procedural angioplasty mortality risk compared with men (2.6% versus 0.3%) and a higher death rate at 4 years (10.8% versus 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. showed that women <50 years of age had a significantly greater risk of in-hospital mortality (0.70% versus 0.22%) and serious vascular complications (0.82% versus 0.24%) after balloon angioplasty. Female sex remained a significant predictor of death, stroke, or CABG in multivariable analysis.

Alfonso et al. assessed the initial results and long-term risk of bare metal stenting and showed that sex was an independent predictor of procedural failure with an increase in the risk of death in women compared with men (6% versus 2%), as well as an increased incidence of vascular complications (7% versus 2%). Anderson et al. 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% versus 1.6%, peri-procedural MI 1.3% versus 1.2%, bleeding 4.4% versus 2.3%, vascular complications 1.3 versus 0.7%) but better long-term survival. The use of DESs was associated with a similar benefit for women and men. Stefanini et al. showed a reduction in the risk of death and MI at 3 years in women with second-generation DESs (9.2% versus 10.9% in...
first generation DESs and 12.8% in bare metal stents). The use of DESs was associated with a significant decrease in the TLR rate compared with bare-metal stents only (second generation: 6.3%, first 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, young women in the Dynamic Registry had a higher prevalence of multiple cardiovascular comorbidities, including hypertension, diabetes mellitus, cerebrovascular disease, obesity, and smoking. Previous data showed that young and middle-aged women (<60 years) were less likely to develop CAD compared with men; however, the risk is equalized in the setting of diabetes mellitus. Hence, the increased incidence, in combination with the more injurious effect of diabetes mellitus 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.

Although biology is one plausible mechanism for higher rates of repeat revascularizations, the disproportionate risk in young women was 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, and underlying hematologic and rheumatologic 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 because sex steroid hormones have numerous known and potentially unknown effects on vascular biology. 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. Although most post hoc analyses from clinical trials have not demonstrated sex differences in in-stent restenosis at routine angiographic follow-up, clinically significant restenosis, including TVR and TLR, was higher in women compared with men receiving paclitaxel-eluting stents, although the higher risk in women was mitigated after adjustment. Likewise, our results suggest that young women are more likely to undergo clinically driven repeat revascularizations of the target vessel and target lesion compared with 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. During exercise stress testing with perfusion imaging, women with angina and ischemia grade their angina to be more intense than men with similar characteristics, and women are also more likely to experience angina during rest, sleep, and emotional stress. In the current study, 30% of the surviving young women reported recurrent angina in the previous 6 weeks at their 1-year contact, compared with 18% of young men and 21% of older women, indicating that both sex and age may be a factor influencing angina presentation. Because 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 <55 years of age had the lowest decline in estimated annual percentage change in coronary heart disease with minimal to no reduction since 1990. 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 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. Koopman et al showed that women <55 years of age were less likely to be prescribed a lipid-lowering agent for primary prevention. Hawkins et al. demonstrated that the rate of prescriptions for secondary prevention in stable angina was 10% lower in younger women than men. In the Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) study, at 1 year, women <55 years were less likely to be on optimal therapy after an MI because of a disparity in treatment initiation rather than treatment adherence, despite more likely to have had a previous PCI. Although 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 before the index MI. In the current study, with the exception of aspirin, prescribing rates of statins, beta blockers, angiotensin-converting enzyme 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, and prior multicenter studies investigating sex-based differences in PCI outcomes in the young were limited to in-hospital outcomes assessment. Therefore, the NHLBI Dynamic Registry is unique in that it enrolled a nonselected, nonclinical 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. Finally, because our cohort comprised patients enrolled from 1997 to 2006, some patients did not receive treatments reflective of current practices, including a subset of patients treated with PCI before the advent of DESs or the use of second-generation DESs. However, by a sensitivity analysis, the results were consistent between those receiving stents and the overall cohort (Table I in the Data Supplement). Also second-generation DESs have been shown to reduce the risk of death or MI and stent thrombosis but not TLR compared with early DESs. Among recipients of second-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 with men ≤3 years. 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 DESs 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.

Conclusions

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 an incidence of adverse cardiovascular events in women with premature CAD, including both rising coronary death rates and hospitalizations for MI. Young women with CAD are at greater risk for adverse outcomes, including in-hospital and 2-year mortality after MI in part because of young women being less likely to receive reperfusion therapy. In-hospital mortality after CABG is also greater compared with men of similar age. Our finding of higher rates of repeat coronary revascularizations in young women represents another complication of CAD in this population.

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