

RESEARCH LETTER

# Long-Term Outcomes are Similar Despite Sex Disparities in High-Intensity Statin Use in Patients With Nonobstructive Coronary Artery Disease Diagnosed Via Invasive Coronary Angiography

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In current practice, high intensity statins are prescribed for patients diagnosed with obstructive or nonobstructive coronary artery disease (CAD). Studies have shown that women are commonly undertreated with statins.<sup>1,2</sup> We sought to determine medication usage patterns and outcomes by sex at long-term follow-up.

The data that support the findings of this study are available from the corresponding author upon reasonable request. All patients who underwent index invasive coronary angiography (ICA) at the University of Virginia for high pretest probability of CAD between January 1, 2012 and December 31, 2013 were included (n=1579). Patients with known CAD, history of myocardial infarction, or emergent indications for invasive coronary angiography (ST-elevation myocardial infarction, cardiogenic shock, postcardiac arrest) were excluded. Invasive coronary angiographies performed for preoperative evaluation for transplant or cardiothoracic surgery were also excluded. This study cohort included 925 patients. The University of Virginia institutional review board gave approval for the study protocol and rendered waiver of informed consent. At a median time of follow-up at 6.0 years, complete long-term follow-up data were available for 850 patients (91.9%). There were no statistically significant differences between the

initial 925 patients and the 850 patients comprising this follow-up cohort ( $P>0.05$  for all clinical characteristics across all stenosis groups). Patients were classified as having normal/near-normal coronary arteries ( $\leq 20\%$  stenosis, n=264), nonobstructive CAD (21%–49% stenosis, n=114), or obstructive CAD ( $\geq 50\%$  stenosis, n=472). Outcomes (cardiac death, nonfatal myocardial infarction, and late revascularization) were gathered prospectively and compared between groups by Kaplan-Meier survival analysis. We gathered baseline and follow-up data on statin usage on the 850 patients with follow-up data available and compared usage in the 3 groups by sex via chi-square analysis and Fisher's exact test where appropriate. The alpha level of significance was set at  $<0.05$ . All statistical analyses were performed using SAS (version 9.3; SAS Institute Inc, Cary, NC).

Baseline mean low-density lipoprotein cholesterol values were 103 in men and 113 in women ( $P<0.001$ ). At a median follow-up of 6.0 years, there was an increase in overall statin use regardless of sex (Table). No differences in aspirin, beta blocker, or overall statin usage by sex were seen across all stenosis groups ( $P>0.05$  for all medications). No differences in high-intensity statin use (atorvastatin 40/80 mg or rosuvastatin 20/40 mg) were seen between the sexes in

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**Table. Study Cohort Statin Usage Subdivided by Severity of Angiographic Coronary Stenosis**

Sex	Total cohort, n (%)		Severity of coronary stenosis					
			≤20%, n (%)		21%–49%, n (%)		≥50%, n (%)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Male	222 (46.9)	350 (74.6)	42 (34.7)	64 (52.9)	24 (45.3)	37 (69.8)	156 (52.2)	249 (84.4)
High intensity			*	*	*	23 (43.4)	*	153 (51.9)
Female	187 (49.5)	253 (67.6)	63 (44.1)	73 (51.4)	37 (60.7)	40 (66.7)	87 (50.0)	140 (81.9)
High intensity			*	*	*	12 (20.0)	*	88 (51.5)

\*High-intensity statin usage data were not gathered in these groups.

patients with obstructive CAD (51.9% of men versus 51.5% of women,  $P=0.78$ ). Interestingly, there was a significant difference in usage of high-intensity statins by sex in patients with nonobstructive CAD (43.4% of men versus 20.0% of women,  $P=0.001$ ). Yet, outcomes were similar between the sexes across all stenosis groups ( $P>0.05$  for all groups).

Fewer women with CAD are treated with statins compared with their male cohorts despite evidence showing similarly improved cardiovascular outcomes with statin therapy for primary or secondary prevention.<sup>3,4</sup> Commonly cited causes of this treatment disparity include a lower rate of statin prescribing by physicians, higher rates of declined statin therapy when offered, and higher rates of statin therapy discontinuation after starting.<sup>2</sup> Our study demonstrated overall similar usage of statins across all stenosis groups and similar high-intensity statin usage by sex in patients with obstructive CAD. This similarity in usage by sex in obstructive CAD could be explained by the patient population's relatively high cardiovascular risk, leading to high rates of high-intensity statin usage regardless of sex.<sup>5</sup> However, there was a significant difference in statin usage between sexes in patients with nonobstructive CAD. Despite this disparity in treatment, we found that outcomes remained similar between sexes across all stenosis groups. One possible explanation for this could be differences in coronary anatomic features, where higher risk lesions were more aggressively treated with medical therapy. Unfortunately, this possibility was not assessed during our angiographic review. These similar outcomes could also be a result of a relatively low sample size, highlighting the need for further study, but could represent an area for optimization of medical therapy in female patients with nonobstructive CAD.

## ARTICLE INFORMATION

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### Disclosures

Dr Bourque is a consultant for Pfizer and GE Healthcare. The other authors have nothing to disclose.

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