Editorial

Angina and Cardiac Care
Are There Gender Differences, and If So, Why?

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The report by Daly et al\textsuperscript{14} in this issue of \textit{Circulation} represents a useful step toward filling this gap. This multinational investigation is the largest evaluation of management and outcome of chronic stable angina according to gender in recent years. It reports on 2197 male and 1582 female patients who received a new diagnosis of stable angina by a cardiologist in 197 participating cardiology services in Europe. Clinical information on the patients and management strategies performed or planned were recorded, and patient follow-up was obtained at 1 year. The results of this study indicate a systematically lower utilization of treatments and diagnostic procedures in women than in men, even though both groups had received a diagnosis of angina pectoris from a cardiologist, and women had a higher angina class. At the initial assessment, women were less likely to be prescribed antiplatelet and statin therapy (despite similar rates of hyperlipidemia) and to be referred for further evaluation with exercise ECG (73% of women and 78% of men) and coronary angiography (31% of women and 49% of men). Adjustment for comorbidity, symptom characteristics, and other factors did not account for the gender differences in procedures, and observed management differences persisted almost unaltered at 1 year.

One obvious explanation for the lower referral of women for coronary angiography is the lower rate of positive stress tests in this group; however, among patients with a positive ECG stress test, a significantly lower proportion of women (56%) than men (65%) received coronary angiography at 1 year. Additionally, among patients with demonstrated CAD by angiography, women had 30% lower adjusted odds of receiving revascularization than men. Even differences in severity of CAD at angiography did not explain gender-based variations in revascularization when added to the model. The latter results are in contrast to other investigations showing that once coronary anatomy is defined by coronary angiography, gender is not an independent predictor of revascularization procedures.\textsuperscript{3,15,16}

A strength of the present study was the examination of patients’ outcomes, because this may shed some light on the clinical implications of withholding appropriate patient care. In the entire population, there were no differences in angina symptoms and major cardiovascular events (death or MI) between men and women; however, among patients with confirmed CAD at angiography, women experienced worse outcomes. They continued to experience more angina and had approximately twice the rates of death or MI at 1 year as compared with men. There are 2 possible explanations of these results. First, differential referral by gender was appropriately due to the lower risk of women,\textsuperscript{17} but because women with confirmed CAD received fewer secondary prevention...
treatments than men, worse outcomes in this group were due to undertreatment of women. Surprisingly, however, adjustment for use of statin and antiplatelet medications at the initial assessment did not change the gender-related hazards ratio of death or MI, and adjustment for revascularization tended to widen rather than narrow the gender difference in outcome. A second and more likely explanation for the findings is that differential referral by gender was not appropriate and led to selection bias. Patients needed to undergo coronary angiography, with or without prior noninvasive testing, to confirm the diagnosis of CAD; the women selected for these tests were probably at higher risk than their male counterparts. Their higher-risk status may not have been accounted for completely in the statistical analysis and may have superseded any other factors that potentially contributed to the gender differences, such as treatment.

What accounts for gender differences in the management of chronic angina? One factor likely to play a role is uncertainty about the diagnostic value of exercise stress testing in women, a problem that has been known for quite some time. The lower prevalence of obstructive CAD in women results in lower diagnostic accuracy with a higher rate of false-positive results; in addition, women’s poorer physical performance as compared with men’s at the time of testing further limits the value of the test in many cases. In contrast to exercise stress testing, stress imaging studies are highly accurate for the detection of CAD in women, and pharmacological stress can be used in patients who cannot exercise. Thus, if a perception of lower accuracy of treadmill testing was a factor in the study by Daly et al, one would have expected a preferential use of stress cardiac imaging in women. This, surprisingly, was not the case; cardiac imaging studies were used infrequently in both men and women. Despite the limitations of exercise treadmill testing, a recent American Heart Association consensus statement has concluded that evidence is insufficient to remove this test as a first-line evaluation for symptomatic women at intermediate or high pretest likelihood of CAD; the women referred for coronary angiography for chest pain did not have an abnormal rest ECG, stress cardiac imaging is more appropriate.

Another possible explanation for gender differences in the management of angina is the perception that women are at lower risk than their male counterparts, which may translate into a lack of attention to early symptoms and signs of CAD in women. Indeed, a current study shows that physicians are more likely to classify women at a lower-risk category for CAD in women and the adverse consequences of this disease, at least the same attention should be paid to appropriately investigate chest pain in women as in men. The results of this study indicate that we need to continue striving toward the improvement of the cardiac care of women. Two key areas include the use of appropriate noninvasive diagnostic techniques in women with chest pain and a better education of clinicians toward risk assessment and management of women with suspected or confirmed CAD. It is crucial that an effective diagnostic strategy for women with chest pain be disseminated, leading to interventions aimed at preventing MI in women.

Disclosure
Dr Vaccarino has served as an advisory board member for CV Therapeutics.

References


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