

Sauce for the Goose Versus Sauce for the Gander

Should Men and Women Play the Same Game But With Different Rules?

Articles, see p 771 and p 781

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Traditionally, coronary heart disease was considered a problem for men. As a consequence, women were understudied, underdiagnosed, and undertreated, with adverse outcomes. With the advent of representation of women in clinical research studies and the elucidation of gender-based differences in the recognition and management of a spectrum of aspects of coronary heart disease, the favorable outcomes have been stunning. Since 2000, cardiovascular mortality declined precipitously in women, more so than among their male peers. In 2014, for the first time since 1984, fewer US women than men died of cardiovascular disease.¹

Coronary heart disease in women is characteristically more complex than for men. In addition to the traditional atherosclerotic obstructive disease of the epicardial coronary arteries, women have nonobstructive coronary atherosclerosis, microvascular disease, or a combination of these attributes. The extent to which these features determine the clinical presentations and outcomes has not yet been ascertained, but ongoing studies are beginning to fill the knowledge gap and contribute to improved clinical decision making.

In this issue of *Circulation*, data from the VIRGO study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) highlight sex differences in the presentation and perception of symptoms among young patients with myocardial infarction² based on prospective patient interviews during the index myocardial infarction hospitalization. Although chest pain was the predominant symptom for both sexes, women presented with a greater array of nonchest pain symptoms, independent of the presence of chest pain, including epigastric symptoms, palpitations, and pain or discomfort in the jaw, neck, arms, or between the shoulder blades. Among the patients who sought care for their symptoms before hospitalization, both the women and their healthcare providers were less likely to attribute these prodromal symptoms to heart disease than were men. Because most of the young patients in VIRGO had ≥ 1 traditional cardiac risk factor, physicians should be attuned to consider the diagnosis of coronary heart disease in young patients who even mention chest pain, pressure, tightness, or discomfort in their presenting history but in particular those with multiple cardiac risk factors. The women were significantly more likely than the men to have perceived their symptoms as a result of stress or anxiety, and a greater proportion of the women sought medical care because of concern about another health problem such as diabetes mellitus rather than cardiac disease. Again, although the women sought care more frequently in the week before hospitalization than did the men, they were less likely to be told that their presenting symptoms related to cardiovascular disease. Perception of risk may be particularly important in this relatively young population, in that >40% of

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patients reported that they did not consider themselves at risk before their myocardial infarction despite a substantial burden of cardiac risk factors. Although >50% of women identified chest pain as associated with acute myocardial infarction, few considered less traditional symptoms such as fatigue, nausea, and shortness of breath as warning symptoms, with awareness lower for younger than for older women.

The public and professional educational gaps are substantial. Physicians must appreciate the importance of the mention of chest pain in the context of a greater number of nonchest pain symptoms among women. In this scenario of multiple symptoms, the prompt recognition of acute myocardial infarction may be delayed with adverse consequences. Again, the risk factor burden and often the family history of heart disease may be important variables, although apparently healthcare professionals traditionally consider young women to be at low risk.

Public education programs must be addressed specifically to young women and the importance of traditional and nontraditional risk factors explored.^{3,4} Not available in this study is the proportion of the young women who had nontraditional risk factors, including hypertensive complications of pregnancy, systemic autoimmune disease, and so on. The presence of multiple risk factors or a family history of cardiovascular disease, which place women at risk, should alert them to respond promptly to symptoms that may represent acute myocardial infarction.

As background, despite >15 years of public awareness campaigns addressing heart disease in women, including the National Heart, Lung, and Blood Institute's "Heart Truth" campaign⁵ and the American Heart Association's "Go Red for Women" initiatives,⁶ and although the awareness of heart disease as the major cause of morbidity and mortality for women has risen from ≈33% to slightly >50%, this awareness has plateaued in recent years, with the awareness being lowest in the most vulnerable women, those of racial and ethnic minorities.⁷ Selective and culturally appropriate education to this high-risk population is paramount.

A second article in this issue presents results from the STICH trial (Surgical Treatment for Ischemic Heart Failure), exploring sex differences in patients with ischemic heart failure undergoing surgical revascularization.⁸ Despite the underrepresentation of women (12%) in STICH, the data regarding long-term outcomes with medical therapy alone versus medical therapy plus coronary artery bypass graft surgery (CABG) provide valuable guidance for prospective clinical decision making. The small percentage of women in STICH had more coronary risk factors and lower rates of prior CABG surgery, but they had higher New York Heart Association class and lower 6-minute walk capacity and health-related quality of life Kansas City Cardiomyopathy Questionnaire summary scores. Thus, they appeared as a higher risk population for both

surgery and unfavorable long-term outcomes. Despite these variables, after 10 years of follow-up, all-cause and cardiovascular mortality were significantly lower in women. It is important to note that surgical deaths were not statistically different between the sexes among the patients randomized to CABG as the initial treatment per protocol. The authors' conclusion is that sex should not influence treatment decisions regarding CABG in these patients because sex was not associated with the effect of CABG on all-cause mortality, cardiovascular mortality, and the composite of death, cardiovascular hospitalization, or surgical deaths in these patients with ischemic left ventricular dysfunction. As the heart team assesses a revascularization strategy in patients with ischemic heart failure with left ventricular dysfunction, women appear by all scores to have high preoperative risk profiles, but in this study they did not have higher surgical risks. Given their improved long-term outcomes, sex should not influence initial treatment decisions regarding CABG recommendations for these women.

This point is highly relevant because physicians are less likely to pursue an aggressive approach to CABG in women than in men, with female sex conventionally considered a risk factor for open heart surgery and an inclusion characteristic as a prognostic factor in multiple cardiac operative risk evaluation scores such as Euro Score II, Society of Thoracic Surgeons score, modified Parsonnet's score, New York's Cardiac Surgery Reporting System score, and the Northern New England Cardiovascular Disease Study Group score. Many of these scores were based on earlier surgical data, at times on datasets with a higher percentage of women undergoing urgent CABG, and possibly before improved surgical techniques. Obviously, data from the STICH and other more recent trials must be included to revise the estimates in these scoring systems.

What are the next steps on the journey? The risk factor burden for women is a recurring theme. Women, including young women, must be educated that the female heart is vulnerable to coronary heart disease and that risk recognition and intervention when appropriate has the potential to delay or avert coronary events. Interventions include both lifestyle and pharmacotherapy. Both women and their healthcare providers should be aware of the nontraditional risk factors that increase the vulnerability of women to coronary events. Hypertensive complications of pregnancy, preeclampsia, small-for-gestational-age babies, and preterm birth identify a subset of women at increased coronary risk. Coronary risk factors are also prominent among women with systemic autoimmune disease and offer an opportunity for preventive interventions. A concomitant task relates to the accrual of an expanded evidence base. Increased participation of women in clinical trials will provide a more robust database for recommendations for coronary care. This requires the increased participation and retention of women and disaggregation of trial results

by sex as well as defined elements in the clinical protocol to capture the spectrum of symptoms of coronary disease prevalent among women. Emotion-precipitated symptoms, as well as, those consequent to physical activity should be examined, and measures of psychosocial variables, including depression and anxiety, should be included. Data items should address potentially relevant attributes for women, including hormonal status, oral contraceptive use, and use of menopausal hormone therapy, among others,⁹ that is, protocols designed to capture the unique features of the women participants in a cardiovascular clinical trial.

ARTICLE INFORMATION

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Disclosures

None.

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