JACC: CARDIOVASCULAR IMAGING
© 2016 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER
VOL. 9, NO. 4, 2016
ISSN 1936-878X/$36.00
http://dx.doi.org/10.1016/j.jcmg.2016.02.012

iVIEW

EDITOR'S PAGE

Cardiovascular Imaging of Women

We Have Come a Long Way But Still Have a Ways to Go

Leslee J. Shaw, PhD,[a] Payal Kohli, MD,[b] Y. Chandrashekhar, MD,[c] Jagat Narula, MD, PhD[d]

In decades past, published reports and funded research rarely focused on sex-specific differences in cardiovascular disease, nor did we understand the importance of pathophysiologic differences that uniquely affect women. The public health message at the time was a focus on the burden of cardiovascular disease among men that resulted in a common (mis)perception that women were not at risk for major coronary and vascular diseases. Since that time, we have witnessed an unfolding of critical pieces of the puzzle, more clearly defining the magnitude of the disease burden among women. Our failure to consider the importance of sex across basic, translational, and clinical research has become an important limitation to our body of evidence in cardiovascular medicine. The statistics are clear that cardiovascular disease is the leading cause of morbidity and mortality for women. In fact, the case fatality rates are higher for women compared with men (1). Without a doubt, we have learned that cardiovascular disease is a potent killer of women and men alike, it was so in the past century and would remain so, and it afflicts women in developed and developing countries alike.

In this issue of *iJACC*, we highlight important research topics that have important health influences on the lives of our female patients. We present several systematic reviews on imaging for ischemic heart disease, valvular interventions, and screening, as well as original research on radiation exposure, observational comparisons on atherosclerotic plaque, and also secondary analyses from major studies including the PROMISE (Prospective Multicenter Imaging Study for Chest Pain Evaluation) trial and CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) registry. The diversity of these reports highlights the magnitude of the issues in the field of cardiovascular medicine that are relevant to women. We generally refer to sex-related research on cardiovascular imaging as that noting clear phenotypic and outcome differences or that related to varying quality-of-care patterns. Both are highly relevant but have different implications for the disparities, which are observed in women with worsening outcomes compared with men. Phenotypic nuances elucidate and inform working models and hypotheses to identify high-risk women compared with men. For example, a preponderance of evidence supports a higher rate of nonobstructive coronary artery disease in symptomatic women compared with men. Beyond this, evidence is far from definitive that we can identify a distinct atherosclerotic plaque signature in women that would support pathological studies of frequent occurrence of plaque erosion as the basis of acute coronary events (2,3). Some observational series note a varied prevalence of high-risk atherosclerotic plaque features unique to women, while others do not; at least in the stable state, it is difficult to find any different morphological attribute, as shown in several reports in this issue of *iJACC* (4,5). These examples illustrate the maturity of sex-specific research evidence and the extent to which clear differences between women and men with regard to cardiovascular pathophysiology can be documented.

There are important considerations when reviewing the reports in this issue. First, our knowledge base and enrollment of sufficiently powered samples of women remains a challenge. In many original research studies, as few as 100 women are compared with larger samples of men. Definitive statements regarding sex differences are challenging when such

From the [a]Emory Clinical Cardiovascular Research Institute, Atlanta, Georgia; [b]Kaiser Permanente, Denver, Colorado; [c]University of Minnesota & VA Medical Center, Minneapolis, Minnesota; and the [d]Icahn School of Medicine at Mount Sinai, New York, New York. Dr. Narula has received research support from Philips and GE Healthcare in the form of equipment grant to the institution. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

small and selected series of women are enrolled and compared with men. The extent to which our referral patterns or differential clinical presentations disadvantage women is unknown. Yet issues of selection or referral bias have tremendous implications for the use of and outcomes after cardiovascular imaging in women. Women consistently receive less intensive medical care and are underreferred to cardiovascular imaging procedures (6,7). In a recent randomized trial, fewer than 1 in 10 women with abnormal stress test results had any change in anti-ischemic therapies or referral to diagnostic angiography (8). On the other hand, the risk-benefit ratio for imaging in women is complicated by the fact that women bear an excess risk burden with imaging involving radiation. We need to know where we stand and only then will we know where to go.

Another issue plaguing the field of women's health research is the lack of funded clinical research aimed at identifying sex-specific differences and the development of targeted treatment trials aimed at improving clinical outcomes for women and men evaluated with cardiovascular imaging each year. Despite federal mandates, underrepresentation of women in clinical research is common, which further hinders our capacity to build a solid evidence base of female-centric research findings. When only small or selected samples of women are reported, the challenge remains to identify thematic patterns by sex from peer-reviewed research. Larger, more representative and unbiased samples of women are required to provide definitive answers with regard to whether we can identify clinical and imaging characteristics that would lead to defined diagnostic and therapeutic strategies of care for women. Moreover, we have yet to set consistent standards for sex comparisons, which further complicates our ability to examine thresholds of abnormality in women compared with men.

As the expression says, we have come a long way, but we have a ways to go before we meet our goals of health equity on sex-specific research. The "long way" that we have come is the enormous amount of data presented in this issue of *iJACC*, and for that we should all rejoice in this progress on women's health issues. The "ways to go" is whether we can commit to a strategic plan encompassing women's health as a primary goal for cardiovascular imaging research. Both praise and criticism lead to pathways of change, the next level of novelty in research, and ultimately altering the morbid and fatal consequences of cardiovascular disease affecting millions of women. Our focus on cardiovascular imaging in this issue of *iJACC* highlight a thoughtful approach to our current status and prompts contemplation on future research opportunities unique to women's health.

Research, in general, is becoming by necessity more transdisciplinary, and it is never more so than for women's health. Issues related to pregnancy, menopause, pathology, and endocrinology highlight other important contributions to unlocking critical female-specific differences in cardiovascular disease. Our approaches require a more thoughtful approach to women's health than a secondary analysis from a registry or trial. This vision requires that we embrace the "stepping stones and obstructing boulders" that describe present-day women's cardiovascular health research and use our current "milestones" to strategically guide our path toward success in improving the lives of female patients (9). Should we not owe our best when it comes to taking care of one-half of the population of the planet.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Jagat Narula, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, New York, New York 10029. E-mail: narula@mountsinai.org.

REFERENCES

1. Centers for Disease Control and Prevention. Women and heart disease fact sheet. Available at: http://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_women_heart.htm. Accessed February 26, 2016.

2. Arbustini E, Dal Bello B, Morbini P, et al. Plaque erosion is a major substrate for coronary thrombosis in acute myocardial infarction. Heart 1999;82:269–72.

3. Farb A, Burke AP, Tang AL, et al. Coronary plaque erosion without rupture into a lipid core. A frequent cause of coronary thrombosis in sudden coronary death. Circulation 1996;93:1354–63.

4. Schulman-Marcus J, ó Hartaigh B, Gransar H, et al. Sex-specific associations between coronary artery plaque extent and risk of major adverse cardiovascular events: the CONFIRM long-term registry. J Am Coll Cardiol Img 2016;9:364–72.

5. Bharadwaj AS, Vengrenyuk Y, Yoshimura T, et al. Multimodality intravascular imaging to evaluate sex differences in plaque morphology in stable CAD. J Am Coll Cardiol Img 2016;9:400–7.

6. Shaw LJ, Miller DD, Romeis JC, Kargl D, Younis LT, Chaitman BR. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120:559–66.

7. Mieres JH, Gulati M, Bairey Merz N, et al. Role of noninvasive testing in the clinical evaluation of women with suspected ischemic heart disease: a consensus statement from the American Heart Association. Circulation 2014;130:350–79.

8. Shaw LJ, Mieres JH, Hendel RH, et al. Comparative effectiveness of exercise electrocardiography with or without myocardial perfusion single photon emission computed tomography in women with suspected coronary artery disease: results from the What Is the Optimal Method for Ischemia Evaluation in Women (WOMEN) trial. Circulation 2011;124:1239–49.

9. Wenger NK. Coronary heart disease in women: highlights of the past 2 years—stepping stones, milestones and obstructing boulders. Nat Clin Pract Cardiovasc Med 2006;3:194–202.