



COMMENTARY

Special Edition Women's Cardiovascular Health

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About the Guest Editor

Dr. Gladys P. Velarde is Associate Professor of Medicine/Cardiology at The University of Florida, Jacksonville where she directs the Women's Cardiovascular Health Program and is Director of the Cardiovascular Disease Fellowship training program.

A Peruvian native, Dr. Velarde earned her medical degree from the New York University School of Medicine in New York and went on to complete her residency training in Internal Medicine at Columbia Presbyterian Medical Center and Cardiovascular Disease fellowship training at Mount Sinai Hospital in New York and Boston University. Dr. Velarde is a Fellow of the American College of Cardiology, an elected member of the American College of Cardiology Prevention Council and Women in Cardiology Leadership Council. She is immediate past - Chairperson of the American College of Cardiology Disparities Working Group and Steering Committee member of the National Forum for Heart Disease and Stroke Prevention and Co-Chair of the National Minority Cardiovascular Health Alliance. Her publications have appeared in local and national media and her most recent local honors are being named a 2014 Health Care Hero by the Jacksonville Business Journal and receiving the Gifted Teacher Award from the Florida Chapter of the American

College of Cardiology in 2017. She has published a comprehensive text book titled Management of Cardiovascular Disease in Women through collaboration between the Divisions of Cardiology at the University of Rochester and University of Florida in Jacksonville.

Cardiovascular Disease in Women: A Potpourri of Maladies

Recent decades have witnessed great progress in the treatment of cardiovascular disease (CVD). Due to improved therapies, preventive strategies and increased public awareness, CVD (stroke, heart failure, ischemic heart disease, peripheral arterial disease and congenital heart disease) mortality has been on the decline over this span of time for both genders. Unfortunately, the decline has been less prominent for women, especially women of color. Once viewed as a man's disease, CVD remains the leading cause of mortality for women in the United States and is responsible for a third of all deaths of women worldwide and half of all deaths of women over 50 years of age in developing countries. In the United States, CVD far outpaces all other causes of death, including all forms of cancer combined. The statistics are sobering with about one female death in the United States every 80 seconds from CVD. That represents close to 400,000 deaths per year according to the more recent statistics. Of these, more than one quarter of a million women will die this year from ischemic heart disease (IHD) which includes obstructive and non-obstructive coronary disease, and about 64% of women who die suddenly of IHD have no prior symptoms. Despite a

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significant number of females with known CVD and increased awareness among women of heart disease as their major health threat, a substantial proportion of women (46% as per the most recent American Heart Association survey) remain unaware of their cardiovascular risk and continue to fail to recognize its significance.

This lack of awareness is more profound (over 60% unaware) among women in higher-risk groups, racial and ethnic minorities, and has changed little in decades.

Poorly understood sex/gender differences in pathobiologic mechanisms, clinical presentation, management and application of diagnostic and therapeutic and preventive strategies have contributed to this gap. A critically important factor has been the underrepresentation of women in CVD research to date. In fact, only one-third of CVD clinical trials report sex-specific results despite The Food and Drug Administration regulations requiring sex stratification data, as well as the National Institute of Health recommendations of increased inclusion of women in clinical trials. This makes it difficult for researchers and clinicians to draw accurate conclusions about sex differences in mechanisms of disease, accuracy of specific diagnostic modalities and risks or benefits of a particular drug or device for the treatment of women with CVD. Furthermore, physicians and other healthcare providers continue to underestimate women's cardiovascular risk, in part because of utilization of traditional approaches which can lead to over-testing or inappropriate risk assessment without accurate differentiating who is truly at risk and inadequate use of preventive therapies for women.

The goal of this special edition of the journal is to shed some light on specific topics that dominate the spectrum of CVD in women. It does not pretend to be all-encompassing, but will cover a variety of important topics.

This issue opens with Dr. Sonia Henry and colleagues' review of the challenges of accurate CVD risk prediction and stratification in women. They review existing flaws and limitations in traditional risk models and scores. They examine the role of sex and the relative impact of specific coronary risk factors, traditional and nontraditional, and how these affect risk prediction and stratification.

Next, Drs. Rohan Sampson and Keith Ferdinand examine sex specific differences in the epidemiology and pathophysiology of IHD, with emphasis on non-obstructive coronary artery disease (NOCAD). Differences in coronary anatomy, microcirculation, vascular tone and differences in the atherosclerosis process are reviewed while stressing the importance of key risk factors in women such as hypertension, obesity and inflammation and its association not only with sex but ethnicity.

Drs. Khadeja Esmail and Dominick Angiolillo then bring us a detailed review of the available evidence on antiplatelet therapy for IHD, chronic-stable and unstable, and how female sex platelet biology has important implications on outcomes. Some important sex considerations in therapy emerge from this paper which emphasizes that despite biological differences and a high bleeding risk, women do receive benefit from current and novel antiplatelet agents and how these are still underutilized in women. The impact of gender on outcomes in pivotal recent trials is summarized in the form of a table that the reader will find very useful.

Dr. Viviany Taqueti follows with a valuable provocative insight into the importance of advanced noninvasive imaging tools like CCTA, PET, and CMR in enabling very sensitive assessments of anatomic atherosclerotic plaque burden, macro and micro-vessel related ischemia, and myocardial fibrosis respectively. She emphasizes the importance of low coronary flow reserve (CFR) as a potential link to understanding the hidden biological risk of stable IHD among women where abnormal coronary reactivity often co-exists with diffuse, nonobstructive CAD, a phenotype more prevalent in women and less amenable to focal revascularization. Dr. Taqueti explains how the pathophysiology of obstructive and nonobstructive coronary disease renders itself to a more accurate diagnosis with the appropriate utilization of these novel modalities.

A thorough review of the impact of psychosocial stressors, is tackled by Drs. Tomas Cabeza de Baca and Michelle Albert. They stress the importance of psychosocial factors, such as anxiety, depression, and inadequate social economic resources and their impact on adverse cardiovascular outcomes in women. This topic, often neglected, is an important

contributing risk factor, especially in ethnic minority women.

Next, this issue explores Peripartum cardiomyopathy. Drs. Dmitry Yaranov and Jeffrey Alexis provide an excellent update in this poorly understood condition that affects roughly 1/1000 women in the US in the peripartum period and disproportionately affects African American women and the Southern region of the US. This excellent review examines the epidemiology and etiologic factors such the role of angiogenic imbalance and pre-eclampsia as well as a treatment role of prolactin antagonists. The latest Investigations of Pregnancy Associated Cardiomyopathy study (IPAC) recommendations are also heavily referenced.

We move to the poorly understood and understudied topic of Heart Failure with Preserved Ejection Fraction (HFpEF) which especially affects women and the elderly. Drs. Juan Vilaro, Ahmed Mustafa and Juan Aranda review the importance of the heterogeneity of this condition and its implications on therapeutic approaches. Although there are no sex-specific recommendations regarding the evaluation and management of HFpEF in women compared

with men, women are more likely to have the HFpEF phenotype than HFrEF.

Finally, Drs. Nimeh Najjar, Peter Staiano and Mariam Louis review important sex differences in the association of Obstructive Sleep Apnea (OSA) and CVD with some data suggesting women may have different susceptibility to the effects of OSA. They stress that although OSA is a common condition, it remains grossly underdiagnosed in women. Drs. Tracy Ashby and Mariam Louis provide further important analysis regarding circadian misalignment and its association with CVD completing this excellent subsection.

In summary, our contributing authors tackle a potpourri of topics we feel will enhance the gender specific CVD knowledge of all health professionals but particularly that of cardiovascular specialists who care for the millions of women afflicted by CVD.

As our knowledge of the specific cardiovascular differences in women continues to evolve, we will be better poised to reduce sex/gender and ethnic CVD disparities that have been present for decades.