

Improving the Cardiovascular Health of Women in the Nation

Moving Beyond the Bikini Boundaries

Despite recent declines in cardiovascular mortality in women over the past decade, cardiovascular disease (CVD) remains the number 1 killer of women.¹ Deaths attributable to CVD outnumber the deaths attributable to breast, ovarian, uterine, cervical, or vaginal cancers, or childbirth combined, and yet, when the medical community refers to women's health, they continue to focus on the bikini boundaries.

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SEX DIFFERENCES IN TREATMENT FOR CVD

Women continue to be labeled as a special population in many guidelines relating to CVD, despite being the majority of the population. Nonetheless, when presenting with an acute coronary syndrome, it is women, in particular, younger women, who are less likely to receive guideline-recommended therapies, timeliness of care, or diagnostic and invasive therapies resulting in worse outcomes in comparison with men.² Women who experience cardiac arrest are less likely to receive bystander CPR than men, and less likely to receive guideline-recommended therapies. The prevalence of heart failure is greater in women than in men, and, despite the sex differences in the causes and types of heart failure, women with heart failure with reduced ejection fraction are less likely to receive evidence-based therapies, including medications, implantable cardioverter defibrillators, ventricular assist devices, and heart transplant, despite improved survival and quality of life when receiving these therapies. Asymptomatic peripheral artery disease is twice as common in women as in men, and once a diagnosis of peripheral artery disease is made, women have greater functional impairment, lower rates of revascularization, and an increased likelihood of emergent procedures. This persistent pattern of poorer cardiovascular outcomes appears predominantly attributable to suboptimal use of guideline-recommended therapy in women, despite the strong evidence that management of CVD with evidence-based therapies benefits both sexes equally.

SEX-SPECIFIC CVD RISK FACTORS

There are unique CVD risk factors for women related to pregnancy or hormonal influences. The effect of adverse pregnancy outcomes is emerging as an important predictor of future CVD risk. Pregnancies associated with preterm delivery, gestational diabetes, gestational hypertension, preeclampsia, and eclampsia increase the risk of future CVD. Pregnancy appears to be a natural stress test identifying at-risk women, but because these conditions disappear postpartum, the increased CVD risk is often not translated to women. These adverse pregnancy outcomes are also not assessed when using current CVD risk assessment tools. Other unique risk factors for women include polycystic ovarian syndrome, functional hypothalamic amenorrhea, menopausal status and hormone use, also not assessed in con-

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porary risk assessment tools (Table). These risk factors should be assessed in women, and increase the need to ensure that traditional CVD risk factors are controlled and periodically reassessed.

SEX DIFFERENCES IN CVD RISK FACTORS

Traditional risk factors affect both sexes but can affect them differently. The presence of type 1 or 2 diabetes mellitus increases the risk for CVD in women to a greater degree than it does in men. Smoking is one of the strongest risk factors for CVD in both sexes, but, for women, smoking combined with oral contraceptives increases the risk of stroke. There are also certain CVD risk factors that are not sex specific but female predominant, particularly autoimmune disorders, including rheumatoid arthritis, systemic lupus erythematosus, and scleroderma. Breast cancer and its treatment increase the risk of CVD, manifest just 7 years after the breast cancer diagnosis³ (Table).

SEX DIFFERENCES IN CVD

Certain cardiac conditions occur exclusively in women (female-specific), whereas other conditions are seen more frequently in women (female-predominant). Peripartum cardiomyopathy occurs only in women and requires focused CVD management, given its effect during gestation, lactation, and future pregnancies. Cardiac conditions seen more frequently in women include nonobstructive ischemic heart disease, myocar-

dial infarction with nonobstructive coronary arteries, Takotsubo cardiomyopathy, spontaneous coronary artery dissection, postural orthostatic tachycardia syndrome, coronary vasospasm, and pulmonary hypertension (Table), many of which have no proven diagnostic or therapeutic approaches, because of limited research and clinical trials.

THE EFFECT OF SEX ON MEDICATIONS

Women have been understudied in most trials of cardiac medications. The underrepresentation of women in the majority of CVD drug trials limits the ability to draw sex-specific conclusions. Nonetheless, there is a significant increase in bleeding in women with many anticoagulants, complicating CVD outcomes when these are needed. If one needs further evidence that women are physiologically different than men, randomized controlled trials have demonstrated a differential effect of aspirin in women in comparison with men, with a reduction of stroke versus myocardial infarctions, respectively.⁴

THE NEED FOR WOMEN'S CARDIOVASCULAR HEALTH PROGRAMS

Because of the sex differences in CVD and CVD outcomes outlined above, there is an overwhelming need for women's cardiovascular health programs. There remains a lack of physician awareness of CVD in women, ultimately affecting the morbidity and mortality of women.² In ad-

Table. Female Sex and Cardiovascular Disease Risk Factors and Conditions

Female-Specific Cardiovascular Disease Risk Factor	Female-Predominant Cardiovascular Disease Risk Factors	Female-Specific Cardiovascular Disease Conditions	Female-Predominant Cardiovascular Disease Conditions
Adverse pregnancy outcomes Pregnancy-related hypertension: Gestational hypertension Preeclampsia Eclampsia Gestational diabetes mellitus Preterm delivery	Autoimmune inflammatory diseases: Rheumatoid arthritis Systemic lupus erythematosus Scleroderma	Peripartum cardiomyopathy	Myocardial infarction with nonobstructive coronary arteries
Polycystic ovarian syndrome	Breast cancer		Takotsubo cardiomyopathy/apical ballooning syndrome/stress-induced cardiomyopathy Nonobstructive ischemic heart disease Coronary microvascular dysfunction Endothelial dysfunction
Functional hypothalamic amenorrhea			Heart failure with preserved ejection fraction
Reproductive hormones			Spontaneous coronary artery dissection
			Postural orthostatic tachycardia syndrome
			Coronary vasospasm
			Pulmonary hypertension

dition, there remains a significant knowledge gap within the medical community in understanding the pathophysiological differences in CVD in women because of many factors, including limited formal curriculum in medical schools related to CVD in women, lack of required rotations in women's CVD programs for residents and fellows, and self-selected continued medical education for practicing physicians. This has resulted in persistent sex-specific gaps in the application of our guideline-recommended prevention strategies, in addition to diagnostic and therapeutic adherence in CVD management in women. The fact that guidelines are endorsed by major professional associations, but their application is not routinely translated into practice in women (whether sex specific or not), leaves significant room for improvement beyond what is currently being achieved.

Women's cardiovascular health programs have been developed across the country to focus on the unique and complicated CVD issues in women. Historically, women have been underrepresented in clinical trials until the past 2 decades, limiting our understanding of CVD in over half of our population. Women's cardiovascular programs are positioned to identify at-risk women and prevent CVD, ensuring adherence to primary and secondary prevention guidelines. In addition, their role reaches beyond prevention by identifying and phenotyping women with specific forms CVD.⁵

Specifically, the roles of women's heart centers in our academic settings and communities have the potential to improve the health of women in the following ways:

1. Improve CVD prevention and reduce disparities in care for women: Increase the awareness of the medical community of issues related to women with CVD, with an expected improvement in primary and secondary CVD prevention and outcomes.
2. Improve CVD diagnosis and treatment for female-specific/female-predominant conditions: Serve as a referral center, providing expertise and specialization of women's CVD diagnosis and treatment.
3. Advance research in women's cardiovascular health: Uniquely positioned to participate in research, by participating in registries of sex-specific CVD conditions. In addition, given that women remain underrepresented in clinical trials, investigators are often seeking sites with women's cardiovascular programs to increase women recruitment.
4. Improve education on women's CVD in the community: Those situated within academic settings have the ability to influence medical school curriculum to include sex-specific aspects of CVD. Clinical rotations in women's CVD should be mandatory for internal medicine and cardiology training. Currently, most trainees receive limited training in sex differences in CVD, yet awareness and incorporation of sex-specific information into practice

will improve CVD outcomes. There is also a need to extend our educational focus to provide interprofessional education to primary care, including obstetricians and gynecologists, who are often the first to identify risk factors in women.⁵ Education of women directly to understand their CVD risk, treatment options, and advocacy have been an invaluable part of most women's cardiovascular programs. These programs also often establish support groups for women living with CVD.

Despite the wealth of evidence that sex is one of the strongest modulators of CVD risk, CVD pathophysiology, and impacts diagnostic testing and response to treatment, the consideration of sex in clinical decision making is rarely considered.⁴ Given the evidence showing poorer management and outcomes for women with CVD, women's cardiovascular programs are essential to correct the persistent inequities of CVD care and prevention in women. The potential of these programs is also their ability to impact existing research gaps. Last, improving the education of future and practicing physicians on sex differences in CVD is the first step to providing precision medicine for the care of women. When consideration of sex becomes incorporated in all CVD risk assessment and management, perhaps the need for women's cardiovascular health programs will disappear. For now, this special population needs far more than bikini medicine.

DISCLOSURES

None.

AFFILIATION

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FOOTNOTES

Circulation is available at <http://circ.ahajournals.org>.

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