

EDITORIAL

Pearls and Purple: The Dawn of a Modern Age

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We as a society made history with our election of the first woman Vice President and with her inauguration on January 20, 2021. For the first time, a woman holds the second-highest office in the country. Why does this shock us? For centuries, our society has downplayed the huge role of women and has underestimated the abundance of stressors women have endured. In this issue of the *Journal of the American Heart Association (JAHA)*, “Associations of Job Strain, Stressful Life Events, and Social Strain With Coronary Heart Disease in the Women’s Health Initiative Observational Study,” Wang et al assessed the impact of psychosocial stressors on the incidence of coronary heart disease (CHD) in women.¹

See Article by Wang et al.

The longitudinal data were obtained retrospectively from 80 825 participants from the WHI (Women’s Health Initiative) Observational Study. Under the leadership of its first female director, Dr Bernadine Healy, the National Institutes of Health founded the WHI Observational Study and dedicated >\$500 million to find strategies for preventing heart disease, breast/colorectal cancer, and osteoporosis in women. Data collection began in 1991 and ended in 2005. These chronic diseases are major causes of death, disability, and frailty in older women of all races and socioeconomic backgrounds. Data from the WHI Observational Study continue to shed light on women’s health issues, including the study by Wang et al.

The elegant and detailed study by Wang et al used 3 previously validated stress measures, allowing examination of the unique impacts of different stress domains and their potential interaction with

the development of CHD in women. It was found that stressful life events and social strain were both associated with increased risk of CHD among women. For job strain, the increased CHD risk was confounded by socioeconomic factors. Exposure to job strain and social strain interacted synergistically and produced a higher risk of CHD than would be expected from exposure to either stressor alone. These findings support the public health concern about the harmful impact of stress on well-being and, in particular, on cardiovascular risk.

Addressing stress may have an important role in the prevention of CHD in women, especially for women who experience stress both at work and at home. The findings from this study are robust. However, equally important is the mechanism through which stress impacts the development of CHD. How can we expound on these data and potentially broaden the arc to other disease manifestations related to women, stress, and life? In addition, what are the modulators for this connection? Is the mechanism genetic predisposition, inflammation, or mediation by chemical transmissions in the body? The focus of the study by Wang et al was specific to the development of CHD, and most of the participants were retired White women. Over the time period during which these data were collected and followed (2005–2015), there was no open dialogue about burnout, the understanding of stress on other cardiac disease manifestations was not thoroughly explored, and there was no global pandemic that would change our lives forever.

Burnout is a negative affective state characterized by emotional exhaustion, physical fatigue, and cognitive weariness symptoms. Burnout was found to be an independent risk factor for future incidence of CHD in a study of >8800 employed Israeli men and women.

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Individuals with high levels of burnout (upper quintile) had a significantly higher risk of developing CHD, compared with those with low levels of burnout.² Mehta et al surveyed 10 798 members of the American College of Cardiology to assess burnout. Of the 2274 cardiologists who responded to the survey (58% men [n=1321] and 42% women [n=953]), the results showed that 26.8% reported burnout and nearly half reported being stressed, a precursor to burnout. Burnout was significantly more common in women than in men (31% versus 24%, respectively; $P < 0.001$).³

Women often hold work positions with less professional autonomy; and in their private lives, most women have the primary responsibility for children and the household, and they are seldom given time or space for themselves.^{4,5} Women are often responsible for taking care of others and sacrifice their own needs.^{6,7}

A dramatic manifestation of stress-induced cardiovascular disease is stress cardiomyopathy, which occurs more frequently ($\geq 90\%$) in postmenopausal women (mean age, ≥ 66 years).⁸ Postmenopausal women also report more anxiety, depression, and sleep disturbances.⁹ Women have more cardiovascular events after menopause, which may be caused by many different reasons, including increased sympathetic drive and endothelial dysfunction. In addition, psychological and/or physical stresses may lead to myocardial dysfunction in some people but not in everyone. Stress can cause a complex neocortical and limbic response through an activation of brainstem noradrenergic neurons and stress-related neuropeptides (ie, neuropeptide Y). The increased levels of norepinephrine and neuropeptide Y in response to intense stress are transmitted to the myocardial level and may induce a direct toxic effect and/or cause epicardial and microvascular dysfunction. The increased sympathetic drive and high levels of neuropeptide Y have been associated with impaired coronary reserve, which can lead to stress cardiomyopathy⁸ and CHD.

Partly attributable to visceral adiposity, women have higher levels of inflammatory markers, including high-sensitivity CRP (C-reactive protein), interleukin-6, serum amyloid A, D-dimer, and lipoprotein phospholipase A2. In addition, levels of other novel biomarkers, such as circulating soluble urokinase-type plasminogen activator receptors, which are associated with CHD, were found to be significantly higher in women relative to men. Levels of the nonsoluble and soluble urokinase-type plasminogen activator receptors have been found to be higher in women, even after adjusting for demographics, risk factors, medication use, and systemic inflammation, measured as circulating high-sensitivity CRP levels. High levels of soluble urokinase-type plasminogen activator receptors were associated with higher mortality in both women and men.¹⁰ Population-based studies

have shown that there is an association between psychological stress and inflammation, and both contribute to CHD risk.¹¹

Future studies are necessary to find the missing link(s) between stress and the development of CHD. The finding by Wang et al in the WHI Observational Study that postmenopausal women with both high social strain and high job strain experience a 21% increase in risk of developing CHD is not insignificant. Studies are needed among higher-risk patient populations, Black women,¹² and certain ethnic groups, such as South Asian women,¹³ to study the association of stress with CHD. To reduce this risk, the complex and intertwining confounders must be addressed. This will require input from diverse sources, including women, healthcare agencies, and our executive administration. We are optimistic that a woman Vice President of Black and South Asian descent can make a significant impact in helping high-risk groups decrease their cardiovascular risk by prioritizing prevention of chronic disease on the presidential agenda. As the twin pressures of the pandemic and US politics steadily increase CHD risk, our wish to the executive office is this: may pearls and purple reign to protect vulnerable populations from the cardiovascular impacts of stress!

ARTICLE INFORMATION

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