Cardiovascular Disease in Women

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KEYWORDS

- Cardiovascular disease in women • Nonobstructive coronary artery disease
- Spontaneous coronary artery dissection • Takotsubo cardiomyopathy
- Pregnancy-related cardiac conditions • Preeclampsia and cardiovascular disease
- Cardiotoxicity of breast cancer therapy

KEY POINTS

- The clinical presentation of cardiovascular disease in women differs from that in men. These differences may be related specifically to genetic differences between men and women; anatomic and physiologic distinctions based on gender; and psychosocial, cultural, or economic differences.
- Traditional cardiovascular risk factors have a different impact in women than in men. Tobacco use, type 2 diabetes mellitus, obesity, depression, and psychosocial stress have a more potent effect on cardiovascular disease in women.
- Hormonal changes at different stages of a woman's life have an impact on the development of cardiovascular disease. These changes influence the cardiac conduction system, microvascular and endothelial function, and systemic inflammation.
- Pregnancy and breast cancer treatments have an impact on the development and presentation of cardiac disease. Other presentations predominantly affecting women include spontaneous coronary artery dissection and Takotsubo cardiomyopathy and likely reflect unique gender-based pathophysiology.
- Current cardiovascular prevention and treatment guidelines are developed from data obtained from mostly male subjects. These fail to account for sex-based differences that may alter risk, clinical presentation, evaluation, and therapy. The diagnosis, evaluation, and treatment of female patients should respect these guidelines, while considering distinct differences between the genders. New research specifically focusing on cardiovascular disease in women is imperative.

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EPIDEMIOLOGY OF CARDIOVASCULAR DISEASE IN WOMEN

Cardiovascular disease (CVD) affects 6.6 million women in the United States annually and is the leading source of morbidity and mortality among women.[1–3] Sadly, only 56% of women are aware of these statistics.[4,5] Among women diagnosed with cardiovascular disease, 2.7 million have a history of myocardial infarction. Each year more than 53,000 women die of a heart attack and 262,000 are hospitalized because of CVD.[4] One in 4 female patients presenting with a first myocardial infarction die within a year of diagnosis. Women under 45 have a higher mortality rate compared with men.[6] Although overall rates of CVD are declining, women continue to experience a disproportionately higher mortality rate.

It is projected that by 2030, $918 billion will be spent annually on CVD.[7] Although male and female patients often present differently, the long-term disease burden is similar. Female patients tend to present later in the disease process and with greater associated morbidity and mortality. Although women with CVD can present with some symptoms similar to those in men, there are clear distinctions. Women with CVD often present with broader range of symptoms than men. Obstructive coronary artery disease in women is identified less frequently than in men when relying exclusively on typical "anginal" symptoms. Often, these symptoms are commonly dismissed as noncardiac in female patients, inherently altering diagnosis and treatment patterns.

Because obstructive epicardial coronary artery atherosclerosis is less prominent as a disease in women, the term, *ischemic heart disease* (*IHD*), better approximates the nature of coronary pathophysiology seen in the female population. IHD in women includes classic coronary atherosclerosis and includes disorders, such as coronary microvascular dysfunction, endothelial dysfunction, vasomotor abnormalities, and spontaneous coronary artery dissection (SCAD).[8] Other conditions thought not primarily due to a coronary cause but which predominantly affect women include postpartum and stress-induced cardiomyopathy. The classification of CVD in women, therefore, encompasses many forms of coronary and noncoronary pathology.[9] A greater variation of the cause of IHD and the diminished sensitivity and specificity of current cardiovascular testing techniques have all led to misdiagnosis and underdiagnosis of cardiac-based chest pain syndromes in women, contributing to a disproportionately greater cardiovascular morbidity and mortality.

CORONARY MICROVASCULAR DYSFUNCTION

In women, underlying CVD must be considered prominently in the differential diagnosis of chest pain syndromes regardless of age. IHD may involve both limited coronary flow reserve and endothelial dysfunction with or without atherosclerotic epicardial coronary disease.[10] Endothelial dysfunction is a vascular pathophysiology[11] that may be more common in states with low levels of estrogen.[4,10] Endothelial dysfunction may be the primary mechanism by which conditions, such as menopause, premature ovarian failure, and functional hypothalamic amenorrhea, are associated with a higher risk of CVD.[12,13] Endothelial dysfunction is also associated with inflammatory conditions, including autoimmune disorders, such as lupus or rheumatoid arthritis, the prevalence of which is increased in female patients.[5] Endothelial dysfunction leads to poor vasodilatory responsiveness, vascular smooth muscle proliferation, and increased lipid deposition.

Endothelial dysfunction, however, does not fully explain cardiac chest pain in the presence of patent coronary arteries, especially in younger women. Women may present with classic anginal symptoms and show objective evidence of inducible ischemia on stress testing but still have normal angiographic findings with either