



THE ROLE OF THE IMMUNE SYSTEM IN THE PROGRESSION OF CORONARY HEART DISEASE IN MENOPAUSAL WOMEN

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<https://doi.org/10.5281/zenodo.7491083>

ARTICLE INFO

Received: 19th December 2022

Accepted: 28th December 2022

Online: 29th December 2022

KEY WORDS

Coronary heart disease, estrogens, cardioprotection, postmenopausal period, risk factors, immune system.

ABSTRACT

The main cause of morbidity and mortality in the population worldwide is cardiovascular disease (CVD). Coronary heart disease is the most important cause of cardiovascular mortality in women worldwide. Because most data on CHD are still largely from men, the true incidence of CHD in women may be underestimated. Risk calculations are primarily based on mortality rates rather than overall CHD rates, for which women tend to have higher rates of nonfatal events. In addition, women have lower income and lower socioeconomic status than men, which generally contribute to poorer health outcomes. Also, the adaptive immune response has recently emerged as an important factor in a wide range of cardiovascular diseases, including atherosclerosis, hypertension, cardiac remodeling, and heart failure; however, its role is not fully understood. Although the risk of cardiovascular disease increases with the onset of menopause, it cannot be distinguished from aging. The Women's Ischemia Syndrome Evaluation Study showed that the presence of cardiovascular risk factors was responsible for comparable CHD lesions in premenopausal and postmenopausal women.

Cardiovascular disease is reported to be the leading cause of death worldwide. In 2019, 12.4 million people died of heart attack and stroke. Of these, 78% came from low- and middle-income countries. High-income countries had lower mortality rates because of more effective prevention and treatment programs [1, 17, 123]. Although several clinical and biochemical risk factors

have been identified, the role of psychological factors has also become increasingly important over the past few decades. Several risk factors associated with coronary heart disease (CHD) have been identified, which include causal risk factors (hypertension, hyperlipidemia, and diabetes), conditional risk factors (triglycerides and lipoproteins), and



predisposing risk factors (obesity, physical activity, gender, family history, socioeconomic factors, insulin resistance, and psychological factors) [2, 3, 20]. Data from various studies have shown a strong association between psychological stress and CHD. Cardiovascular diseases represent a serious health problem in industrialized countries in terms of excessive morbidity and mortality. It is clear from the literature review that there is a strong association between coronary heart disease and certain psychological factors. Psychological variables such as stress, personality, anxiety, and lifestyle contribute along with high blood pressure and obesity; sedentary lifestyle, cigarette smoking, and high blood cholesterol to the development of CHD [3, 21, 28, 29]. The present study is a comparative study between patients with coronary heart disease and those without coronary heart disease regarding lifestyle.

A large number of clinical and biochemical factors have been identified in the development of CHD; the role of psychosocial factors has also become increasingly important over the past few decades. The World Health Organization has stated that since 1990, 80-90% of people dying from CHD had one or more lifestyle-related risk factors [4, 38, 47]. Lifestyle is a person's way of life. It includes a person's health behaviors, social interactions, attitudes, values, beliefs, and, essentially, how a person perceives himself or herself and sometimes how he or she is perceived by others. Lifestyle is one of the main factors that have shown a close relationship with CHD [38, 48, 64, 65]. Lifestyle is based on subjective perception, purposeful and goal-oriented. It is motivated by the desire to overcome

feelings of inferiority combined with the desire to succeed. The overall goals of lifestyle are to understand, predict and control life and the self. Lifestyle, as indicated earlier, has been found to affect a person's health, environmental adaptation, psychosomatic and mental illness [21, 28]. Health psychologists have found that a healthy lifestyle and dietary habits are associated with positive effects on blood cholesterol levels [21, 26]. Diet, sleep patterns, smoking, and alcohol use have negative effects on health [26, 33, 36].

Many scientists [123, 138] have observed in young patients with coronary disease that prolonged emotional strain has been associated with work-related responsibilities. The Framingham study demonstrated the importance of lifestyle, employment, and interpersonal stress. Showing that in men younger than 65 years of age, anxiety about aging, daily stress and tension were associated with an increased risk of developing CHD, and in men and women older than 65 years; family dissatisfaction or disagreement were risk factors for CHD [9, 15, 16]. A high-fat diet, obesity, and lack of exercise increase the risk of heart disease. Tobacco use, whether smoking or chewing tobacco, increases the risk of cardiovascular disease [26, 33].

There is a positive relationship between heart disease and fat consumption, obesity, smoking, and lack of exercise. The association between smoking and risk of CHD is simple and direct. Smoking has several negative effects on the cardiovascular system [26, 33, 100]. Job dissatisfaction and workload in men have become a predictive factor for CHD [17,115,116,118].

Cardiovascular disease in women: clinical perspectives



Cardiovascular disease (CVD) remains the leading cause of death in women. Over the past three decades there has been a sharp decline in mortality from heart disease among both men and women. observed, especially in the age group > 65 years. However, recent data suggest that rates of morbidity and mortality from coronary heart disease are not observed, especially among younger women (<55 years) [23, 35, 39]. It is imperative that we understand the mechanisms that contribute to a worsening risk factor profile in young women in order to reduce future atherosclerotic cardiovascular disease (CVD) morbidity and mortality. Greater recognition of the prevalence of traditional CVD risk factors and their differential impact on women, as well as new nontraditional risk factors unique to women or more common in women, contributes to a new understanding of the mechanisms that lead to worse outcomes for women. Finally, diagnosis of acute coronary syndromes (ACS) in women, especially young women, is often challenging, and it is important to recognize differences in signs and symptoms at presentation to improve patient management and outcomes [39, 42].

Coronary heart disease (CHD) can be defined as a vascular disease limited to the epicardial coronary arteries and should not be confused with coronary heart disease (CHD), which includes coronary artery disease, microcirculation or myocardial imbalance. In women in particular, the use of the terminology "CHD" has advantages over "CHD" because of the lower prevalence of anatomically obstructive coronary artery disease, even higher rates of myocardial ischemia and associated

mortality in women compared with men of the same age. Women with CHD have persistent suboptimal treatment patterns, higher mortality, and poorer CVD outcomes compared with men [52, 56, 58]. In an environment where cardiologists have traditionally been trained to equate CHD with angiographically defined obstructive CHD, the failure to recognize these unique aspects of CHD in women has contributed to less aggressive lifestyle and medical preventive interventions in women compared with men and may contribute to a sex-specific mortality gap. Thus, a paradigm shift beyond a purely anatomic description of obstructive CHD is needed to turn it into early detection of CHD risk and treatment in women [60, 61, 63].

Biological differences between men and women are called sex differences and are often reproduced in animal models. Sex differences in the cardiovascular disease system are due to differences in gene expression from sex chromosomes, which can be further altered by sex differences in hormones, resulting in gene expression and function unique to sex. These differences lead to variations in the prevalence and manifestations of cardiovascular conditions, including those related to autonomic regulation, hypertension, diabetes, and vascular and cardiac remodeling. In contrast, gender differences are unique to humans and arise from sociocultural practices (behavior, environment, lifestyle, and diet). To promote gender- and sex-specific care, this review will review recent clinical perspectives on cardiovascular disease in women. focusing on new and unique aspects of cardiovascular health in women and on the sex and gender differences associated with clinical practice in the



prevention, diagnosis, and treatment of cardiovascular disease. This review will also present current approaches to the evaluation and treatment of ACS and other cardiovascular diseases that have a higher prevalence or unique features in women [67, 77, 78].

Endogenous estrogens support vasodilation and promote blood pressure control in premenopausal women. Women develop hypertension about ten years after men, and it is more common in older women than in older men. No sex differences in the clinical manifestations of hypertension other than pregnancy-related hypertension have been described. Hypertension is often poorly controlled in older women; only 23% of women compared with 38% of men over age 80 have blood pressure (BP) <140/90 mm Hg. There is currently no evidence that antihypertensive medications differentially affect BP response, but many studies of antihypertensives have not reported sex-specific efficacy profiles or side effects analyses [78, 80, 85].

Dyslipidemia has the highest population risk in women, 47.1%, compared with all other known risk factors for CHD. However, this higher risk of CVDs is usually not seen before menopause, even if cholesterol levels are significantly elevated. Lifestyle modifications, including diet and exercise, are critical for primary and secondary prevention of CVD. Pharmacological therapy for hyperlipidemia for secondary prevention has been clearly shown to be equally effective in women and men in reducing recurrent cardiac events and CVD mortality [87, 91]. For primary prevention, data on women are more limited. Primary prevention guidelines for statin prescribing

have recently been adapted to include sex in the American Heart Association (AHA)/American College of Cardiology (ACC) pooled cohort formula for determining risk of CVDs. Statins should be administered to patients at moderate or high risk of CVD according to the new ACA/ACC recommendations [91,96,100].

Pre-menopausal women are relatively protected against CVDs compared with men of the same age. However, after the onset of menopause, this sex gap shrinks. This long-standing observation led to the assumption that ovarian steroid hormones, and estrogens in particular, were cardioprotective, initially supported by retrospective observational studies [78, 85, 101]. However, such conclusions have been refuted by randomized clinical trials (RCTs) of both primary and secondary prevention of ASCVD. The inconsistency was unexpected in light of the beneficial physiological effects of estrogen on vascular endothelium at the cellular and molecular levels, on blood vessels in animal models of CVD, and on lipids and biomarkers of insulin resistance; Thus, menopausal hormone therapy (MHT) has become one of the most controversial areas of female health. The results of major RCTs, the Women's Health Initiative and the Heart Estrogen/Progestin Replacement Study (HERS), led to a dramatic change in clinical practice in the mid-2000s with a marked decline in MHT use worldwide. Since then, clinicians and scientists have critically analyzed randomized controlled trials in an attempt to explain discrepancies with observational data. The median age of inclusion in the WHI study was 63 years, more than 12 years older than the age at which MHT typically begins in clinical practice, for an indication for



treatment of vasomotor symptoms in postmenopause. When the WHI researchers analyzed the results by age group (50-59, 60-69, 70-79 years), the results of CHD with MHT were more favorable in younger women than in older women, especially in the E-alone study [103, 104]. Consistent with these trends, a meta-analysis of more than 39,000 women participating in 23 clinical trials showed that MHT reduced the risk of CHD in women younger than 60 years of age, but not in older women. The "time hypothesis" debate continues, and recent randomized controlled trials have focused on surrogate endpoints such as mean carotid intima-media thickness and CA. These trials have also produced conflicting results, including null results for carotid intima and CA in the Kronos Early Estrogen Prevention Study (KEEPS) and evidence supporting the time hypothesis in the Early and Late Estradiol Intervention Study (ELITE). Overall, a consensus has been

reached that MHT at the lowest effective dose remains an appropriate treatment for early (i.e., within 5 years) menopausal symptoms in the absence of contraindications, but should never be prescribed for the explicit purpose of preventing CVD [108, 111].

In medicine, a proper distinction between sex and gender effects is usually unattainable, so they are often collected for clinical purposes. Gender- and sex-specific studies of CHD have led to a new understanding of the pathophysiology of coronary heart disease in women, which includes, but is not limited to our common understanding of atherosclerosis. CHD in women includes not only atherosclerotic obstructive CHD, but also an expanded spectrum of coronary diseases, including coronary microvascular dysfunction (CMD), endothelial dysfunction, vasomotor abnormalities, spontaneous coronary artery dissection (SCAD) and stress-induced cardiomyopathy [21, 111].

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