

Cardiovascular risk in women

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Cardiovascular disease (CVD) is the leading cause of death in women worldwide. In Europe, more women (51%) died from CVD compared with men (42%). However, the misconception of CVD as a man's disease and breast cancer as the greatest threat to women is still prevalent. In fact, CVD causes over 50% of death compared to 3% of death caused by breast cancer in women [1]. Women have higher prevalence of persistent chest pain, rehospitalisation and mortality from ischemia heart disease (IHD) than men, along with higher financial costs [2]. Women also have greater patient-related delays that have remained unchanged for more than a decade [3]. Despite substantial risk in heart disease, women are less likely to receive guideline-directed care and counselling on their risk reduction from their clinicians than men. Importantly, once diagnosis is correctly made, women with heart disease responded well to symptoms after prescription of cardiac medication [2]. This evidence highlights the important gap in risk assessment, diagnosis, management and prevention of heart disease in women.

Women have different clinical presentations of heart disease compared with men. It is frequently stated that 'typical' symptoms during a heart attack include chest pain radiating to the left arm, crushing substernal chest pain and diaphoresis. However, women with acute coronary syndromes tend to experience non-specific symptoms, such as pain located in the neck and shoulder regions, shortness of breath, nausea, generally unwell or unexplained fatigue [4, 5]. These symptoms are often called 'atypical', but in fact, are typical for women. These different set of symptoms are more noticeable in younger women compared to their male counterparts. Young women often present with no chest pain or other non-specific symptoms leading to delayed presentation to the health facility for a timely diagnosis, which were linked to increased risk of mortality after an acute myocardial infarction (AMI) [6].

Even after seeking help, women are less likely to receive the guideline-recommended treatment. A recent study using data from US Atherosclerosis Risk in Communities surveillance showed women aged 35-54 years with AMI were substantially less likely than men to receive coronary revascularization and lipid-lowering therapies [7]. This study also reported the worrying upward trend in AMI hospitalisations for young women between 1995 to 2014[7].

Gender differences in the presentation of heart disease suggest that a higher proportion of women develop microvascular angina (MVA) rather than obstructive coronary artery disease (CAD) which is more common in men [5]. MVA plays an important role in the IHD pathophysiology of women. MVA is a condition that affects the smallest coronary artery blood vessels, characterised by having chest pain with evidence of myocardial ischemia in the absence of obstructive CAD (<50% stenosis) [8] [9]. Vascular plaque erosion remains the most common cause of acute coronary thrombosis leading to sudden cardiac death in women younger than 50 years old [10]. However, the sex-differences in coronary structure make it difficult to visualise the abnormalities of the micro-coronary vessels using traditional diagnostic devices [8]. Therefore, the traditional diagnostic strategies such as coronary angiography that are used to detect severe coronary stenosis may not be adequate to screen the risk of heart disease in women [4, 6].

Traditional risk factors such as diabetes, hypertension drawn from research emphasizing men may underestimate the risk of IHD in women. Women have different risk factor profiles compared with men. Women are more likely to have systemic autoimmune diseases which are associated with accelerated atherosclerosis and increased cardiac risk [10]. Several female

related-factors have been shown to increase cardiac risk in women, such as oestrogen deficiency, polycystic ovary syndrome, premature menopause [4-6, 11]. Furthermore, women have greater risk of heart disease during pregnancy, which is accompanied by increased overall demand on maternal cardiovascular system [10, 12]. During the pregnancy, women are more likely to have cardiac arrhythmias and risk for AMI and certain pregnancy-related complications such as gestational diabetes, hypertension, and pre-eclampsia that increase women's risk of heart disease later in life [10].

Despite the significant risk in women, lack of awareness of CVD as a women's leading health threat is common among women and their health care providers. An international survey showed only 45% of women known CVD is the top killer of women [13]. The lack of awareness and identification of symptoms in women often lead to a delayed response in seeking care for a timely treatment, which contributes to poor outcomes. This is evident in a retrospective analysis of 4,360 patients with AMI during a 16-year time span that found women had greater delay to hospital arrival from symptom than men, which was associated with significantly higher in-hospital mortality [3]. Moreover, women are less likely to receive routine cardiovascular risk assessment as the part of routine screenings. Research reveals only 16% of primary care physicians and 22% of cardiologist performed guideline-recommended risk assessment in women [13].

The lack of awareness in combination with non-specific symptoms, difference in coronary anatomy and unique risk factors present a challenge for the prevention, assessment, and management in heart disease in women. However, management and research of CVD in women have received less attention and are, therefore, under-investigated [4]. For example,

the above-mentioned female-specific risk factors are not included in current risk prediction models. Existing guidelines for managing heart disease is directed by the presence of obstructive CAD without accounting for different risk factors profiles and higher prevalence of symptoms considered 'atypical' in women with MVA [14]. Subsequently, women with MVA are often under-diagnosed and received less guideline recommended counselling and care [5].

Failure to recognise the CVD risks and lack of sex-specific guidelines in women are likely multifactorial. Evidence suggests gender concordance improves the cardiac outcomes in women. An analysis of 571,797 MI patients over nearly two decades demonstrated female patients were more likely to survive and experienced better outcomes if they were treated by female doctors in the hospitals [15]. However, in UK, women remain underrepresented in many specialities, particularly in cardiology, with only 13% of cardiologists being women [16]. Furthermore, women have been underrepresented in cardiovascular research from which the guidelines were developed. Moreover, women tend to develop obstructive CAD about 10 years later than men. In a clinical trial, use of arbitrary upper age limits for inclusion criteria could potentially exclude older women participating in studies. Subsequently, the eligible women enrolled in research may not represent women with the heart disease in the general population [12].

Given the greater risk and substantial disparity in the knowledge, awareness and management of CVD in women, it is time to act and enhance sex-specific approach to clinical care and research. Raising awareness is the first step to improve better outcomes. Women health clinicians and researchers are needed to improve health in clinical settings, and to conduct

research to improve cardiovascular health in women. Future clinical trials and research must take account for the women-specific factors to achieve balanced number of women and men and report sex-specific analysis and results [12].

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