ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 11, Issue 02, Fev-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

MODELS FOR IDENTIFYING OBSTRUCTIVE CORONARY ARTERY DISEASE

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Abstract: Heart disease is the leading cause of death for both men and women. However, women have a unique coronary heart disease (CHD) phenotype, with fewer calcified lesions and more non-obstructive plaque. This may partly explain why risk models for obstructive CHD in men may not accurately predict the risk of CHD for women. This article summarizes the differences in functional and anatomical assessments of CHD between men and women with stable chest pain. It also proposes an approach for using multimodal imaging to evaluate women with suspected CHD, based on recent American Heart Association (AHA) guidelines.A paradigm shift is needed in the approach to imaging women with coronary artery disease (CAD), including updated risk models, a better understanding of CAD in women, in whom non-obstructive disease is more common. Algorithms focused on the assessment of ischemia in non-obstructive CAD and myocardial infarction in women with non-obstructive CAD are also needed.

Key words:Coronary artery; heart disease in women; myocardial infarction; pathophysiological differences .

Heart disease is the leading cause of death for both men and women. However, recent reports have shown a reduction in the mortality rate from cardiovascular disease (CVD) in women compared to men. This reduction is lower for women than for men. Women have a unique type of coronary artery disease, with fewer calcified lesions and more non-obstructive plaques, as well as a higher prevalence of microvascular diseases compared to men. These differences may explain why current methods for detecting obstructive coronary heart disease (CHD) do not work as well for women. This article summarizes the sex differences in functional and anatomical assessments of CAD in women with stable chest pain and provides an approach for using multimodal imaging to diagnose suspected CAD in women, in line with recently published guidelines from the American Heart Association (AHA) and the American College of Cardiology (ACC).[3] There is a need for a paradigm shift in the way we approach imaging women with coronary artery disease, including updating risk models, gaining a better understanding of CAD in women who have non-obstructing disease more commonly, and developing algorithms that focus on assessing ischemia in non-obstructive CAD (INOCA) as well as myocardial infarction with nonobstructing coronary artery disease (MINOCA). Another important condition is MINOCA, where patients present with the symptoms of ACS (Acute Coronary Syndrome) but without coronary obstructions. Women with ACS are less likely to develop obstructing CAD than men, but they are more likely to experience blood clots and plaque erosion due to dysfunction, stress-induced Takotsubo cardiomyopathy (TCM), and myocarditis. As mentioned in the previous paragraph, recent evidence suggests that CMR (Cardiac Magnetic Resonance) plays a crucial role in identifying the underlying cause, which could alter therapeutic approaches.The recently published American College of Cardiology (ACC) and American Heart Association (AHA) guidelines for the evaluation and diagnosis of chest pain have given cardiac magnetic resonance (CMR) a Class 1 recommendation for patients with myocarditis, recognizing its value as an effective tool for differentiating this condition from other causes, such as myocardial infarction. These guidelines also

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emphasize the importance of CMR in differentiating between these conditions. One of the most obvious differences in pathophysiology between women and men with regard to cardiovascular disease (CVD) is linked to sex hormones. Before menopause, women are relatively protected from CVD, but their risk exceeds that of men after menopause. This highlights the cardioprotective effect of sex hormones, especially estrogens. Conversely, specific female-related diseases associated with dysregulated sex hormones, such as polycystic ovarian syndrome and premature menopause, can increase cardiovascular risk. Mutiple pathophysiological mechanisms are shared between both sexes but display a sexual dimorphism resulting in different phenotypes of CVD. Coronary microvascular dysfunction (CMVD) [4] is a condition of microvessel impairment leading to myocardial ischemia even in the absence of epicardial coronary artery stenosis [5]. Several sex-specific biological, hormonal, and neurological pathways promote CMVD, acting in isolation or synergistically [6]. Indeed, CMVD is favored by low-grade systemic inflammation and increased sympathetic activity, which are more pronounced in women compared to men, as well as by the decrease of estrogens in postmenopausal women [7]. Importantly, CMVD is thought to be the common soil of various CVDs affecting most frequently postmenopausal women, such as ischemia with no obstructive coronary artery disease (INOCA), heart failure (HF) with preserved ejection fraction (HFpEF), Takotsubo cardiomyopathy (TTC, also termed stress-induced cardiomyopathy, apical ballooning syndrome or broken-heart-syndrome), peripartum cardiomyopathy (PPCM), and cardiomyopathy related to antineoplastic treatments [7], all of which will be discussed in this review. Negative emotions can also trigger CVD via the so-called brain–heart axis .An elevated amygdalar metabolic activity, a brain region involved in the processing of emotions, is associated with an increased risk of future major adverse cardiovascular events (MACE) [5]. In women, but not in men, an association between the presence of myocardial ischemia and an increased amygdalar metabolic activity has recently been shown and is consistent with a high prevalence of mental stress in women with CVD . Similarly, women are at a higher risk of mental stress-induced myocardial ischemia than men, which might be associated with the increased baseline sympathetic activity in older women. Sympathetic hypertonia also plays a detrimental role in HF and TTC and may account, at least in part, for the gender bias and sex-specific phenotypes seen in these conditions. Coronary artery disease (CAD) differs between women and men in terms of risk factors—with a higher impact of traditional cardiovascular risk factors (CVRFs) in women, despite a lower overall risk burden , clinical presentation—more often atypical in women [3], mechanisms—with lower atherosclerotic plaque burden in women [3], and outcomes—worse prognosis in women, despite lower CAD burden [5]. In addition, women more frequently report non-traditional CVRFs, such as mental stress and depression . Mechanistically, plaque composition differs between sexes with women presenting more often with plaque erosion during an acute coronary syndrome (ACS) (as compared to plaque rupture in men), less necrotic core, and less plaque calcification . These sex differences in plaque composition could account for the higher prevalence of ischemia with non-obstructive CAD in women , a central feature in the female population of both acute and chronic coronary syndromes (CCS). Consequently, the ongoing paradigm that CAD imaging consists of detecting epicardial coronary stenosis must be reconsidered in women . In ACS, the majority of cases occur due to a plaque rupture which leads to a coronary occlusion, and is more frequent in men [7]. However, a subgroup of individuals displays myocardial infarction (MI) with no obstructive coronary arteries (MINOCA), of which the majority are women [5]. MINOCA is defined as (i) an acute MI (as per the 4th universal definition) [4], (ii) with no obstructive coronary arteries on invasive coronary angiography (ICA), (iii) and no specific differential diagnosis, which requires excluding myocarditis and TTC [5]. While MINOCA remains of unknown origin in 8–25% of cases [3], it can also be induced by specific conditions with high

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female prevalence, including coronary spasm and spontaneous coronary artery dissection [1]. Spontaneously resolving coronary plaque erosion can also cause MINOCA [3]. Given the specific etiologies of ACS in women, a new classification has been proposed in this population. Indeed, using the universal definition of MI, 1 out of 8 young women (< 55 years) with ACS remains unclassified [3]. The VIRGO : Role of Gender on Outcomes of Young AMI Patients) classification, which groups patients according to their clinical features, reduces the rate of unclassified cases thereby helping to tailor management strate. This review highlights sex-specific considerations that are critical for selecting the most appropriate cardiac imaging modality—with particular focus on challenges and opportunities of contemporary CVD management in women. Indeed, awareness about female attributes in cardiac imaging, considering technical implications and female-specific conditions, might help alleviate the burden of CVD in this subpopulation. Consequently, there is an urgent need for imaging guidelines that are tailored to women and men. While efforts have been made in this direction, substantial knowledge gaps still exist. Future imaging studies and recommendations require the integration of sex as an algorithm-modifying variable. In the era of precision medicine, accounting for sex disparities seems crucial to provide the best possible cardiovascular care to women and men.

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