ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 11, Issue 01, Jan-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

CARDIOVASCULAR IMAGING IN CORONARY HEART DISEASE IN WOMEN ORGANIZM

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Abstract: Heart disease is the leading cause of death among men and women. Women have a unique coronary heart disease phenotype with fewer calcified lesions, more non-obstructive plaque, and a higher prevalence of microvascular disease compared with men, which may partly explain why current risk models for identifying obstructive coronary artery disease (CAD) may fail. so do women. This article summarizes sex differences in the functional and anatomical assessment of CAD in women with stable chest pain and proposes an approach to using multimodality imaging to evaluate suspected CAD in women according to recently published American Heart Association/American Heart Association data. College of Cardiology guidelines for the assessment and diagnosis of chest pain. A paradigm shift in the approach to imaging women with coronary artery disease is needed, including updated risk models, a better understanding of CAD in women in whom nonobstructive disease is more common, and algorithms focused on the assessment of ischemia in nonobstructive CAD and myocardial infarction in nonobstructive CAD.

Key words: Cardiovascular diseases; heart disease in women; visualization; ischemia.

Heart disease is the leading cause of death among men and women. Recent reports have documented a reduction in cardiovascular disease (CVD) mortality in women, but the reduction is lower compared to men.[1] Women have a unique phenotype of coronary artery disease with fewer calcified lesions, more non-obstructive plaque, and a higher prevalence of microvascular disease compared with others. with men, which may partly explain why current models for detecting obstructive coronary heart disease (CHD) may not perform as well in women.[2] This article summarizes sex differences in the functional and anatomical assessment of CAD in women with stable chest pain. and provides an approach to the use of multimodal imaging to evaluate suspected coronary artery disease (CAD) in women, consistent with recently published American Heart Association (AHA)/American College of Cardiology (ACC) guidelines for the assessment and diagnosis of chest pain. [3] A paradigm shift in the approach to imaging women with coronary artery disease is needed, including updated risk models, a better understanding of CAD in women in whom nonobstructive disease is more common, and algorithms focused on assessing ischemia in nonobstructive coronary artery disease. disease (INOCA) and myocardial infarction with non-obstructive coronary artery disease (MINOCA).[4] Another important disease is MINOCA, in which patients present with symptoms of ACS but without coronary obstruction. Women with ACS are less likely to develop obstructive CAD than men, but are more likely to have blood clots and plaque erosion. dysfunction, stress-induced Takotsubo cardiomyopathy, and myocarditis should be considered. As mentioned in the previous text, recent evidence confirms that CMR plays a critical role in identifying the cause, which may alter therapeutic strategies. The recently published ACC/AHA Guidelines for the Evaluation and Diagnosis of Chest Pain gave CMR a Class 1 recommendation in patients with MINOCA, recognizing its value as an effective tool for differentiating myopericarditis from other causes, including myocardial infarction. [3]. The most obvious pathophysiological differences between women and men in relation to CVD are linked to sex hormones. Relatively protected against CVD before menopause, women's risk exceeds men's risk

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after menopause, highlighting the cardioprotective influence of sex hormones, particularly estrogens [2]. Conversely, female-specific diseases associated with dysregulation of sex hormones, such as polycystic ovary syndrome and premature menopause, increase cardiovascular risk [3]. 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 [8]. 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 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

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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. To provide optimal care for women with angina, a paradigm shift is required that takes into account sex differences in risk factors, coronary physiology and pathophysiology, and clinical symptoms. More emphasis needs to be placed on primary prevention in women with non-obstructive CAD and assessment of INOCA and MINOCA, as supported by recent chest pain guidelines. With our current arsenal of noninvasive cardiovascular imaging tools, we are well positioned to meet the challenges of this paradigm shift.

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