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The Use of Multimodality Imaging in the Diagnosis of Ischemic Heart Disease in Women

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Abstract

Women with coronary artery disease have a worse short and long-term prognosis than men and the prevalence of atherosclerotic cardiovascular disease is rising. Women are less likely than men to present with classic anginal symptoms and are more likely to be misdiagnosed. There are several non-invasive imaging modalities available for diagnosing ischemic heart disease in women and many of these modalities can also help with prognosis and management. Choosing the best imaging modality to evaluate women with possible ischemic heart disease is a scenario that clinicians frequently face.

Earlier modalities, such as exercise treadmill testing, show significant gender differences in performance, whereas newer modalities, such as coronary CT angiography, myocardial perfusion imaging and cardiac magnetic resonance imaging, are highly specific and sensitive for detecting ischemia and coronary artery disease with greater gender parity. Individual factors such as availability, diagnostic performance and female-specific considerations such as pregnancy status may all have an impact on the decision to use one modality over another. Emerging techniques for diagnosing ischemia and coronary microvascular dysfunction include strain rate imaging, CT-myocardial perfusion imaging and cardiac magnetic resonance imaging.

Keywords: Coronary CT angiography • Myocardial perfusion imaging • Cardiac magnetic resonance imaging

Introduction

Women with coronary artery disease have a worse short and long-term prognosis than men and the prevalence of atherosclerotic cardiovascular disease is rising. Women are less likely than men to present with classic anginal symptoms and are more likely to be misdiagnosed. There are several non-invasive imaging modalities available for diagnosing ischemic heart disease in women and many of these modalities can also help with prognosis and management. Choosing the best imaging modality to evaluate women with possible ischemic heart disease is a scenario that clinicians frequently face.

Earlier modalities, such as exercise treadmill testing, show significant gender differences in performance, whereas newer modalities, such as coronary CT angiography, myocardial perfusion imaging and cardiac magnetic resonance imaging, are highly specific and sensitive for detecting ischemia and coronary artery disease with greater gender parity. Individual factors such as availability, diagnostic performance and female-specific considerations such as pregnancy status may all have an impact on the decision to use one modality over another. Emerging techniques for diagnosing ischemia and coronary microvascular dysfunction include strain rate imaging, CT-myocardial perfusion imaging and cardiac magnetic resonance imaging [1-3].

Cardiovascular disease is the leading cause of death and disability worldwide, accounting for roughly one-third of all deaths. It is the leading cause of death in the United States; coronary artery disease (CAD) and ischemic heart disease (IHD) continue to be the leading causes of death in men and women due to cardiovascular disease. Because of an increase in cardiac risk factors such as obesity, diabetes and hypercholesterolemia, as well as an ageing population, the incidence of atherosclerotic cardiovascular disease is increasing. However, age-adjusted mortality rates are decreasing, owing to improved medical therapies that allow patients with IHD to live longer lives. Although men are more likely to develop cardiovascular disease, women with CAD have a worse short and long-term prognosis. Furthermore, women who have angina symptoms or an abnormal cardiac stress test are less likely to be referred for additional diagnostic testing and started on guideline-directed medical therapies [4,5].

Literature Review

The pathogenesis of atherosclerosis begins in adolescence and early adulthood as fatty streaks, long before the disease manifests clinically. Atherosclerotic plaque containing lipids may ulcerate or rupture, resulting in thrombosis and ischemia. The most common cause of myocardial infarction (MI) in men and women is atherosclerosis, which results in plaque rupture or erosion. MI caused by nonobstructive coronary arteries (MINOCA) accounts for 5-10% of all MI. Similarly, in the absence of significant CAD, myocardial ischemia may occur with signs and symptoms of ischemia, which is classified as ischemia with no obstructive coronary artery disease (INOCA).

There is probably some overlap between MINOCA and INOCA. MINOCA is defined by the universal definition of MI criteria, which include a rise and/or fall in cardiac troponin (cTn) levels above the 99th percentile, as well as signs and symptoms of myocardial ischemia [6-8]. This can be manifested as new ischemic ECG changes, new ischemic wall motion abnormalities, loss of viable myocardium on noninvasive imaging, or identification of coronary thrombus by angiography or autopsy in the absence of obstructive coronary artery stenosis (50% stenosis) on angiography and myocarditis or Takotsubo cardiomyopathy. MINOCA, as opposed to acute MI caused by CAD, commonly affects younger patients, particularly women with fewer traditional cardiac risk factors. The cause of this condition is unknown, but it could be caused by plaque rupture or erosion, coronary vasospasm, spontaneous coronary artery dissection (SCAD), coronary artery embolization, or coronary microvascular disease. However, in the vast majority of cases, no aetiology is found. MINOCA can also cause cardiac arrest and heart failure and while the mortality rate is

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lower than in MI caused by CAD overall, outcomes are significantly worse than in MI caused by CAD.

INOCA is defined by the presence of angina with non-obstructive CAD on angiography (obstructive CAD is defined as >50-70% stenosis or fractional flow reserve (FFR) 0.8). Women account for roughly 60% of INOCA patients. INOCA can happen on its own or in conjunction with hypertension, severe aortic stenosis, severe anaemia, coronary vasospasm and myocardial bridging. Women with INOCA had an increased risk of all-cause mortality (13 vs. 2.8%) in the WISE study, which studied clinically stable women with signs and symptoms of myocardial ischemia, compared to a representative cohort of women who were matched for age, gender and observed over a similar time period.

Discussion

Non-obstructive plaque with high-risk histological features such as a large necrotic core, thin fibrous cap (65 mm), active inflammation, angiogenesis, plaque hemorrhage, positive remodeling and microcalcification confer an increased risk of erosion or rupture. Non-invasive imaging techniques such as CCTA, nuclear molecular imaging and CMR can detect some of these characteristics. High-risk plaque detected by CCTA is associated with an increased risk of future MACE (major adverse cardiovascular outcomes) and may be useful as an additional risk stratification tool, particularly in patients with nonobstructive coronary artery disease, women and younger patients.

Another cause of IHD in women is coronary microvascular dysfunction (CMD), which is characterised by epicardial, microvascular endothelial, or non-endothelial dysfunction. This results in decreased coronary perfusion, which is visible as decreased coronary flow reserve (CFR). CFR is defined as the maximum increase in flow through the coronary arteries above normal resting volume, which reflects the coronary circulation's ability to respond to increased oxygen demand. Although single-photon emission computed tomography (SPECT), magnetic resonance imaging (MRI), intravascular Doppler ultrasound and echocardiography have been used, positron emission tomography (PET) imaging remains the standard method for estimating CFR. A maximal hyperemia to baseline capacity ratio of 2.0 is considered abnormal. It is important to note that even if they have non-obstructive CAD, patients with CMD have an increased risk of major adverse cardiovascular events.

Spontaneous coronary artery dissection (SCAD) occurs when the intima and media separate due to hematoma formation within the medial layer, resulting in external compression of the true coronary arterial lumen and myocardial ischemia and/or infarction. SCAD is most likely the result of a combination of genetic, hormonal, arteriopathy and environmental factors. It is frequently associated with fibromuscular dysplasia, which is more common in female patients. A small percentage of cases are caused by inherited connective tissue disorders such as Marfan, Loeys-Dietz and Ehlers-Danlos syndrome. SCAD has a female predominance, affecting 87-95% of women.

Women with IHD may manifest differently than men. Women are less likely than men to present with classic chest pain (31% vs. 42%) and they are more likely to report dyspnea, weakness, back pain, palpitations, or loss of appetite. Importantly, patients with ACS who do not present with chest pain are more likely to be misdiagnosed and have a higher risk of death than those who do. Furthermore, the absence of chest pain has not been consistently linked to the severity of ACS. When compared to baseline, stress echocardiography reveals abnormal myocardial contractility during exercise, indicating inducible myocardial ischemia. Although exercise is preferred, a pharmacological stress agent such as dobutamine can be used to detect new or worsening LV regional wall motion abnormalities (RWMA). In addition to qualitative assessments of myocardial response to stress, quantitative measurements such as strain rate imaging (SRI) derived from tissue Doppler imaging (TDI) can be used to determine myocardial viability.

Strain describes the shortening, thickening and lengthening of the myocardium and can be used as a measure of regional left ventricular function on echocardiography, as well as detect characteristic findings suggestive of ischemic myocardium, such as decreased peak systolic strain, systolic lengthening and post-systolic shortening. This produces a contraction variable that is independent of the passive tethering effects from other regions that can influence the interpretation of TDI single point velocities and has been successfully used to differentiate between different myocardial viability states. Stress echocardiography is widely available and does not expose the patient to ionising radiation.

Conclusion

Uncontrolled hypertension, severe arrhythmias, significant left ventricular outflow tract obstruction, ACS and symptomatic severe aortic stenosis are all contraindications. Overall, stress echocardiography has a higher sensitivity and specificity in women than ETT, with sensitivity ranging from 70 to 96% and specificity ranging from 79 to 92%. The performance of stress echocardiography to detect inducible ischemia in men and women has been variable, with some studies demonstrating statistical differences while others did not. A recent trial with approximately 45% women found a sensitivity of 95.4% and a specificity of 96% for detecting obstructive CAD.

For the evaluation of patients with known or suspected CAD, SPECT-myocardial perfusion imaging (MPI) provides information about global and regional LV systolic contractility, LV volume and myocardial perfusion defects during exercise or pharmacological stress. At peak exercise or following vasodilator administration (agents such as adenosine, dipyridamole, or regadenoson) or dobutamine administration, radionucleotide tracers, most commonly 99m-technetium (Tc99m)-labeled perfusion agents, are injected intravenously. Typically, both rest and stress images are obtained; however, in certain patients, a stress-only protocol may be used, with rest images obtained only if the stress images are abnormal. Radiation exposure, estimated at 11 mSV in this modality, should also be considered, especially in younger patients. However, current radiation risk estimates do not show a difference in risk from SPECT-MPI in women versus men.

Acknowledgement

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Conflict of Interest

Authors declare no conflict of interest.

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