Gender differences in diagnostic testing for suspected coronary artery disease?

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Over the years, many clinical trials have provided evidence that there are substantial gender differences in the pathophysiology, clinical presentation, diagnosis, and treatment of coronary artery disease (CAD). Although women have a higher atherosclerotic burden, are more symptomatic, and have a worse clinical outcome, they have a lower prevalence of obstructive coronary disease than men [1, 2]. The pathophysiology of heart disease in women is a spectrum and, therefore, one must consider a unique evaluation approach, which in some cases will spread beyond the detection of epicardial stenosis to include evaluation of the atherosclerotic burden as well as an evaluation of coronary reactivity of the microvasculature and endothelium [3].

An interesting question is whether diagnostic tests for the detection of CAD have similar diagnostic accuracies in men as in women. This holds both for the (exercise) ECG and diagnostic imaging procedures [4–6]. As a first step one should evaluate the baseline ECG in women suspected for CAD, together with risk factors and symptoms, to establish the pre-test likelihood of disease. Assessment of the patient's functional capacity is important to assess prognosis, but also to appropriately choose the best noninvasive stress testing modality [7–11]. Current evidence supports the use of the exercise ECG as the *test of choice* for symptomatic women with a normal resting ECG, an adequate exercise tolerance, and an intermediate pre-test likelihood of disease [12]. The calculation of functional capacity and

clinical scores further improves the ability to diagnose and assess prognosis in women.

Cardiac imaging with stress echocardiography or stress perfusion imaging (SPECT) provides incremental information over clinical variables and the exercise ECG in symptomatic women with suspected CAD. Local expertise should guide selection of the appropriate test. According to the American Heart Association (AHA) consensus statement, symptomatic women with questionable exercise capacity, abnormal baseline ECG, and those with diabetes mellitus, should undergo cardiac imaging with exercise or pharmacological stress as the *initial* test in the evaluation of symptoms [13]. Cumulative data analysis of over 1000 women has shown the mean sensitivity of stress echocardiography to detect physiologically significant coronary disease to be 81 %, with a specificity of 86 %. For the diagnosis of physiologically significant CAD in symptomatic women, the sensitivity of exercise myocardial perfusion imaging ranges from 78 % to 88 %, with a specificity of 64 % to 91 %. Pharmacological vasodilator perfusion imaging has been shown to be accurate in detecting physiologically significant CAD in women with a sensitivity and specificity for coronary artery stenosis >50 % of 91 % and 86 %, respectively. Positron emission tomography (PET) and cardiovascular magnetic resonance (CMR) are newer methods that can be very useful in symptomatic women with no evidence of obstructive CAD to evaluate the coronary microvasculature for evidence of subendocardial ischaemia or abnormal coronary reserve. For instance, dobutamine CMR has shown to be a valuable noninvasive stress imaging modality for identifying disease in women at risk, with a sensitivity and specificity for detecting obstructive CAD in women of 85 % and 86 %, respectively [14]. Evolving evidence supports the use of advanced imaging techniques such as coronary CT angiography (CCTA) in the setting of an abnormal or equivocal stress cardiac imaging

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study [15]. In a series of 51 women and 52 men, the diagnostic sensitivity and specificity was *similar by sex* at 85 % and 99 %, respectively [16].

To summarise, exercise ECG testing and the use of imaging modalities provide very useful information for both women and men suspected for CAD. Diagnostic accuracies and predictive values do not show important gender-specific differences, implying similar clinical significance. This holds in particular for the current myocardial imaging modalities such as stress echocardiography and myocardial SPECT imaging. Emerging novel imaging technologies and protocols using PET, CMR and CCTA, assessment of carotid intima-media thickness, and brachial artery flow-mediated dilatation will be useful to further identify the atherosclerotic burden and define the unique pathophysiology of ischaemic heart disease in symptomatic women without evidence of obstructive CAD [17]. Future imaging protocols that focus on analysing endothelial function, platelet function and detection of subclinical atherosclerosis will likely be integrated into diagnostic and prognostic algorithms for women at risk for ischemic heart disease [18, 19].

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