

## Ischemic Heart Disease in Women. Contemporary Diagnostic Assessment

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### Abstract

Coronary artery disease (CAD) is the leading cause of death and disability worldwide, both for women and men, partially due to increased life expectancy and the coronary risk factors epidemics. But women have been very frequently understudied, underdiagnosed, and undertreated, and this fact has influenced clinical outcomes. The term ischemic heart disease (IHD) considers a higher risk status associated with symptomatic patients with obstructive and nonobstructive CAD, including coronary microvascular disease. In addition to the atherosclerotic obstructive disease of the epicardial coronary arteries, women frequently have nonobstructive CAD and microvascular disease as well as inequity in medical and interventional treatments compared to men. Coronary atherosclerosis in women has a complex pathophysiology and the clinical picture is also complex because women have frequently atypical symptoms. Thus, the IHD diagnosis and risk stratification in women poses a challenge to the clinician, who should apply a cost-effective approach for choosing the best diagnostic test in each case. The focus of contemporary evaluation is to document myocardial ischemia and the burden of nonobstructive and obstructive CAD, with the aim of determining IHD risk and guiding therapeutic decisions. Strengthening clinical research encouraging women-specific trials in prevention, risk stratification and image-guided therapy is necessary; in addition, a coordinated approach which involves medical professionals, governments, scientific societies, international organizations, and female patients may help to reduce morbidity and mortality due to IHD in women. In conclusion, more emphasis needs to be placed on cardiovascular care in women. Doing the right test for the right patient in the right way with a cost-effective approach is the key to optimal care. Clinical management combining prevention, guidelines and clinical judgment is required.

**Keywords:** *Ischemic Heart Disease; Women; Diagnosis; Risk Stratification*

### Abbreviations

CAD: Coronary Artery Disease; CFR: Coronary Flow Reserve; CMR: Cardiac Magnetic Resonance; ECG: Electrocardiogram; IHD: Ischemic Heart Disease; MACE: Major Adverse Cardiac Events; MPI: Myocardial Perfusion Imaging; NSTEMI: Non ST-Elevation Myocardial Infarction; PET: Positron Emission Tomography; STEMI: ST-Elevation Myocardial Infarction

### Introduction

Coronary artery disease (CAD) is the leading cause of death and disability worldwide, both for women and men, partially due to increased life expectancy and the coronary risk factors epidemics. In the United States almost 200 000 women die due to CAD every year [1].

Nevertheless, during many years CAD has been considered a “men’s problem”. As a consequence, women have been very frequently understudied, underdiagnosed, and undertreated, and this fact has influenced clinical outcomes. Hopefully, during the last decade new approaches to the management of ischemic heart disease (IHD) in women were introduced, and more women were represented in clinical research studies.

The term ischemic heart disease considers a higher risk status associated with symptomatic patients with obstructive and nonobstructive CAD, including coronary microvascular disease [2]. However, the presentation of a silent ischemia should also be considered.

It is important to point out that there is generally a misconception at public level about the importance of CAD in females, e.g. CAD do not get as much coverage as breast cancer campaigns, which leads to an underestimate of the magnitude of the problem.

### Diagnosis and management

In addition to the atherosclerotic obstructive disease of the epicardial coronary arteries, women frequently have nonobstructive CAD and microvascular disease as well as inequity in medical and interventional treatments compared to men.

Coronary atherosclerosis in women has a complex pathophysiology, including abnormal coronary reactivity, microvascular dysfunction, plaque erosion and distal microembolization [3-5].

The clinical picture is also complex, because women have frequently atypical symptoms. In addition to the traditional coronary risk factors, unique risk factors for women such as polycystic ovarian syndrome, functional hypothalamic amenorrhea, premature delivery, preeclampsia and pregnancy-associated hypertension, gestational diabetes, and cardiac complications observed during breast cancer treatment should also be considered [6].

Thus, the IHD diagnosis and risk stratification in women poses a challenge to the clinician, who should apply a cost-effective approach for choosing the best diagnostic test in each case.

In the past, the evaluation of women with suspected IHD focused on the detection of obstructive coronary stenosis and the subsequent revascularization, either surgical or by coronary percutaneous interventions. By the contrary, the focus of contemporary evaluation is to document myocardial ischemia and the burden of nonobstructive and obstructive CAD, with the aim of determining IHD risk and guiding therapeutic decisions.

The determination of a woman's risk status for IHD (low, intermediate, or high) should guide the clinical management. The recommended initial diagnostic test for an intermediate-risk woman is an exercise electrocardiogram (ECG) if functionally capable of exercising and with an interpretable resting ECG.

Women at intermediate to high risk who have an abnormal resting ECG or who are unable to exercise should be referred to a stress imaging: myocardial perfusion imaging (MPI), echocardiography or cardiac magnetic resonance (CMR) [7,8]. Test selection may consider team experience and resources availability in a specific setting. Focus should not be placed only on the diagnostic accuracy, but also on the effectiveness in improving outcomes. Post-stress test risk stratification should be based on the extent, localization and severity of ischemia induced by stress.

Approximately 60% to 70% of women and 30% of men undergoing coronary angiography to further evaluate suspected clinically stable IHD have nonobstructive CAD [9]. In the presence of nonobstructive CAD, microvascular and/or endothelial dysfunction, epicardial and microvascular spasm, myocardial bridging, and conduit vessel stiffening may contribute to myocardial ischemia [10,11]. The use of coronary flow reserve (CFR) measurement with positron emission tomography (PET) improves risk detection in women with obstructive CAD as well as in those with nonobstructive CAD and coronary microvascular dysfunction [8].

Regarding management of IHD in women, it is important to take into account that optimal medical therapy recommended for stable chronic angina, ST-elevation myocardial infarction (STEMI) or non ST-elevation myocardial infarction (NSTEMI) is the same for women and men, but women frequently receive less optimal therapy (both medical and interventional), and this fact influences prognosis. Thus, an ischemia-guided invasive strategy contributes to major adverse cardiac events (MACE) reduction in both sexes.

### Future Actions

Strengthening clinical research encouraging women-specific trials in prevention, risk stratification and image-guided therapy is necessary, both for obstructive and nonobstructive CAD.

In addition to this, a coordinated approach which involves medical professionals, governments, scientific societies and international organizations, as well as the female patients may help to reduce morbidity and mortality due to IHD in women.

### Conclusions

More emphasis needs to be placed on cardiovascular care in women. Doing the right test for the right patient in the right way with a cost effective approach is the key to optimal care. Finally, clinical management combining prevention, guidelines and clinical judgment is required.

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