

# Women & Heart Disease: Non-Invasive Testing in the Diagnosis of CAD

Coronary artery disease (CAD) continues to be underdiagnosed in women which contributes to a higher mortality rate. Dr. Shanks and Dr. Cujec explore the important role played by non-invasive testing in the diagnosis of CAD in women.

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Coronary artery disease (CAD) is the leading cause of mortality for women in Canada. CAD is more difficult to diagnose in women than in men and the continued underdiagnosis of CAD contributes to the high mortality rates in women.

Although coronary angiography is the gold standard for the diagnosis of CAD, it is an expensive, invasive test that is only appropriate in a minority of women who present with chest pain.

Non-invasive testing plays an important role in identifying women with CAD, so that preventive and therapeutic interventions can be appropriately used to decrease the risk of MI and improve survival.

## *How do women with coronary disease differ from men?*

The average age at presentation of CAD (either angina or MI) for women is about 10 years older than men. Women are often > 60-years-old when they initially present with symptomatic CAD. Angina typically presents as retrosternal squeezing discomfort occurring with exertion or emotional stress and relieved within a few minutes by rest or by sublingual nitroglycerin. The usual duration is < 15 minutes. Women are more likely to complain of dyspnea and often have a mixed picture, with both typical and atypical features. It is useful to ask the patient what she does in terms of physical activity and to determine whether there is any limitation in these activities because of either chest discomfort or dyspnea, which may be secondary to myocardial ischemia.

It is more common for women with exertional angina to also have rest angina, nocturnal angina and angina with mental stress, than it is for men. Women also tend to be less concerned with the fact that they might have CAD and are less likely to attribute exertional symptoms to a cardiac problem. This may influence the way they interpret and report their exertional symptoms. Because of their more advanced age at presentation, women also have more co-morbidities,

- such as:
- arthritis,
  - renal insufficiency,
  - hypertension and
  - diabetes.

## *When to suspect CAD in a woman with chest pain*

Age, sex and type of chest pain are predictive of the presence of CAD (Table 1). In addition to a careful history of the chest discomfort in terms of quality, provoking factors and duration, it is important to assess the patient's baseline risk for CAD. Major risk factors for CAD in women are:

- age > 65 years,
- diabetes and
- peripheral vascular disease.

Intermediate risk factors are:

- hypertension,
- smoking and
- hypercholesterolemia.

**Table 1**  
**ACC/AHA practice guidelines on exercise testing: Pretest probability of CAD in women by age and symptoms<sup>1</sup>**

Age	Typical/definite angina*	Atypical/probable angina**	Non-anginal chest pain***
30-39	Intermediate	Very low	Very low
40-49	Intermediate	Low	Very low
50-59	Intermediate	Intermediate	Low
60-69	High	Intermediate	Intermediate
≥70	High	Intermediate	Intermediate

\* Typical angina: all three criteria fulfilled  
 \*\* Atypical angina: two out of three criteria fulfilled  
 \*\*\* Non-anginal chest pain: None to one criteria fulfilled

ACC: American College of Cardiology  
 AHA: American Heart Association

Criteria for chest pain:  
 1. Location: retrosternal +/- radiating to the left/both arms, or the neck  
 2. Provoking factors: exercise, cold or emotional stress  
 3. Relieving factors: rest and/or nitroglycerin. Duration < 15 minutes

A woman has a high probability (> 80%) of CAD if she has typical angina and has either one major or two intermediate risk factors for CAD. A woman with atypical chest discomfort who is > 65 years of age and has hypertension or dyslipidemia has an intermediate probability of CAD (between 20% and 80%).

Age is a very important predictor of CAD and a premenopausal woman with no risk factors is very unlikely to have CAD (< 20% probability).

*Tests to order when you suspect a woman may have CAD*

*Electrocardiogram*

An electrocardiogram is an essential test and is usually normal. Some women (more frequently than men) will have non-specific ST and T wave changes.

*Exercise Stress Testing*

If a woman has low probability of CAD, no further testing is indicated (Figure 1). If a woman has intermediate or high probability of CAD, based on history of typical angina and the presence of at least some risk factors, the best test to start off with is an exercise electrocardiogram (stress test), as long as the patient is able to walk on a treadmill and has a relatively normal electrocardiogram (Figure 2).

The stress test has a sensitivity of 60% to 65% and specificity of about 70% for the diagnosis of CAD in women. This lower sensitivity is related to a number of factors, including lower prevalence of multivessel CAD in women and inadequate exercise duration because of physical deconditioning in older women.

**About the authors...**

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A woman must be able to achieve 85% of her age-predicted maximal heart rate in order to have a diagnostic stress electrocardiogram. (Formula = 220 - age in years).

Specificity is also decreased so that a positive stress test with ST segment depression does not necessarily mean that the woman has CAD. ST segment criteria for diagnosis of myocardial ischemia (*i.e.*, 1 mm of horizontal or downsloping ST segment depression) were established in men. Women without CAD are more likely to have ST segment depression on the electrocardiogram, both at rest and during exercise, than compared to men. The reason for this is not known, but is probably—in part—related to estrogens. Estrogen has a chemical structure similar to digitalis and may affect myocardial repolarization currents.

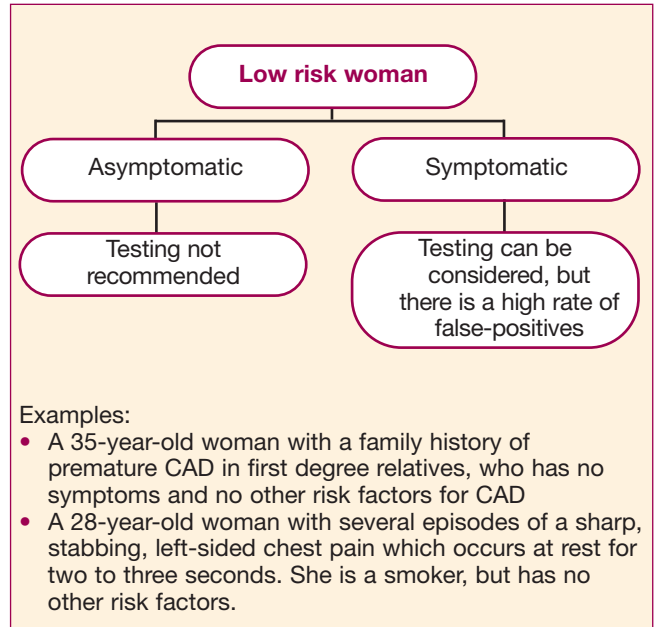


Figure 1. Diagnostic strategy for women who are at low risk of CAD (age < 65 years and no atherosclerotic risk factors present)

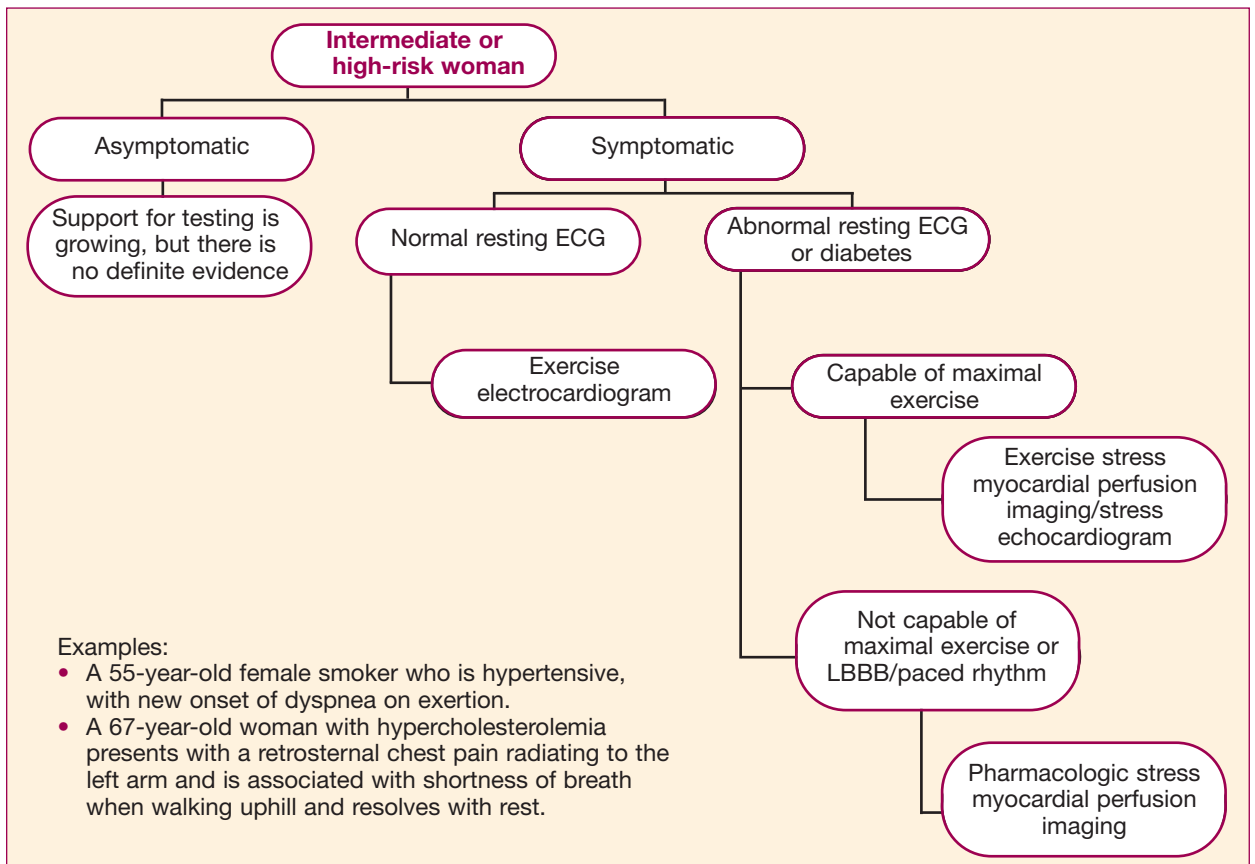


Figure 2. Diagnostic strategy for women at intermediate or high risk of CAD (age > 65 years or atherosclerotic risk factors present).

**Table 2**  
**Comparison of different stress tests in women**

	Description	Test characteristics	Advantages	Disadvantages
<b>Stress electrocardiogram</b>	ECG and BP monitoring during graded treadmill exercise	Sensitivity = 60% Specificity = 70%	<ul style="list-style-type: none"> <li>• Widely available</li> <li>• Inexpensive</li> <li>• Brief test (&lt; 1 hour)</li> <li>• Predicts outcome</li> </ul>	<ul style="list-style-type: none"> <li>• Must be able to exercise on treadmill to achieve 85% of maximal heart rate</li> <li>• Must not have LBBB, LVH or significant ST depression</li> <li>• Lower test accuracy for diagnosis of CAD</li> </ul>
<b>Nuclear myocardial perfusion imaging (sestamibi scan)</b>	Technetium or thallium-based radioisotope used for myocardial perfusion imaging during exercise or with pharmacologic stress (dipyridamole or dobutamine)	Sensitivity = 80% to 90% Specificity = 80%	<ul style="list-style-type: none"> <li>• Defines territory/ extent of myocardial ischemia</li> <li>• Accurate test in women with suspected heart disease</li> <li>• Can often provide assessment of LVEF</li> <li>• Predicts outcome</li> </ul>	<ul style="list-style-type: none"> <li>• Expensive</li> <li>• Often 2-day protocol used with imaging after radioisotope injection at rest and during stress</li> <li>• Breast/diaphragm attenuation artifacts may lead to fixed defects</li> </ul>
<b>Stress echocardiography</b>	Wall motion abnormalities are detected	Sensitivity = 80% to 85% Specificity = 85% immediately after treadmill exercise or with dobutamine infusion if patient is unable to exercise	<ul style="list-style-type: none"> <li>• Can assess LVEF and any valvular disease</li> <li>• Predicts outcomes</li> </ul>	<ul style="list-style-type: none"> <li>• Need good acoustic windows (difficult in women with large breasts)</li> </ul>

CAD: Coronary artery disease  
LVEF: Left ventricular ejection fraction

LVH: Left ventricular hypertrophy

Because of frequent false positive stress test results in women, a stress test is not indicated in a woman with a low probability of CAD.

ST segment depression on the stress electrocardiogram is not the only important predictor of CAD. Duration of exercise is an important prognostic indicator. The Duke score improves the predictive value of the stress test in women. (Formula for The Duke treadmill score = Exercise time [minutes on Bruce protocol] – [5 x maximum ST segment deviation] –

[4 x angina index, where 0 = no angina, 1 = non-limiting angina and 2 = exercise limiting]). A score of > +5 indicates a low risk patient with an annual mortality of < 0.25%. The moderate risk group has a score of -10 to +4, with an average annual mortality of 1.25%. The high risk group has a Duke score < -10, with an annual mortality of 5%.

For example, a 25-year-old woman who is able to complete 15 minutes on a Bruce protocol may have ST segment depression of 2 mm, but no chest discomfort.

Her calculated Duke score is +5, which puts her in a low-risk category with an annual mortality of 0.25%.

*Pharmacologic imaging test*

A pharmacologic imaging test needs to be performed if a woman is unable to exercise because of:

- chronic obstructive lung disease,
- peripheral vascular disease,
- arthritis, or
- stroke.

This can either be a dipyridamole (persantine) sestamibi scan or a dobutamine echocardiogram (Table 2). A dipyridamole sestamibi scan is also preferred in patients with a left bundle branch block, as the conduction abnormality in and of itself can result in decreased septal uptake during stress.

A stress imaging study should be ordered, such as a stress sestamibi scan or a stress echocardiogram, as these are more accurate than the stress electrocardiogram, if the woman is able to exercise, but has:

- an abnormal electrocardiogram with left ventricular hypertrophy or ST depression of > 1 mm,
- a history of prior coronary angioplasty,
- coronary artery bypass surgery or
- diabetes.

Because stress imaging tests have a higher sensitivity (about 80%) for detection of CAD, these tests are preferred over the stress electrocardiogram in women with diabetes who are more likely to have CAD.

*The average age at presentation of CAD (either angina or MI) for women is about 10 years older than men.*

*Results of non-invasive testing*

A woman likely has multivessel CAD and should be referred to a cardiologist for assessment regarding coronary angiography and revascularization if she has an intermediate-to-high probability of CAD (e.g., > age of 65 years or has diabetes with typical angina) and:

- her stress test shows ST segment depression of 2 mm or more within the first six minutes of exercise,
- if the BP drops during exercise, or
- she develops ST segment elevation during exercise.

High-risk indicators on perfusion imaging include:

- a large territory of myocardial ischemia,
  - multiple territories of myocardial ischemia,
  - increased lung uptake and transient ischemic dilatation indicating increased left ventricular diastolic pressure and decreased systolic function.
- These patients should also be referred to a cardiologist.

If the stress test shows significant ST segment depression, but the patient is at low-risk for CAD, a sestamibi scan or stress echocardiogram should be done as these tests are more specific for myocardial ischemia.

*Treating CAD*

All patients who have CAD should be on acetylsalicylic acid and a statin. They should be advised with regards to smoking cessation and maintaining an optimal weight. It is important that patients are aware of the symptoms of unstable angina and MI, so that they can present promptly to the ER. Hormonal replacement therapy is not indicated for either the primary or the secondary prevention of cardiovascular events. A  $\beta$ -blocker or calcium channel blocker is used, as necessary, for the control of angina. An angiotensin-converting enzyme inhibitor should be added if the patient has:

- diabetes,
- left ventricular dysfunction or
- hypertension.

### Take-home message

- Women with suspected CAD should have initial risk stratification based on their clinical presentations and risk factors
- A stress electrocardiogram should be the initial test in women with intermediate-to-high pretest likelihood of CAD and who have normal resting electrocardiogram as well as good exercise tolerance
- Women with a low likelihood of CAD do not generally require any non-invasive testing. A positive stress electrocardiogram in this setting is likely falsely positive and needs confirmation with a more specific imaging test (either sestamibi myocardial perfusion imaging or stress echocardiography)
- Cardiac imaging (nuclear or stress echocardiography) is recommended for symptomatic women with:
  - established CAD (*i.e.*, prior percutaneous coronary intervention or coronary artery bypass surgery),
  - suspected CAD and an abnormal resting 12 lead electrocardiogram or diabetes and for women who are unable to adequately exercise on a treadmill

### New coronary artery imaging modalities

#### Coronary artery calcium score

Coronary artery calcium score has been used in asymptomatic patients to screen for CAD. This score does not assess the degree of luminal obstruction or the functional significance of atherosclerotic lesions and needs to be supplemented with a stress test. This test may have a role in women with intermediate probability of CAD.

#### Cardiac magnetic resonance imaging


Cardiac magnetic resonance imaging at rest and with dobutamine stress can assess myocardial perfusion

and coronary anatomy, but the limited availability and the claustrophobia some patients experience inside the magnet remain a problem.

#### Coronary CT angiograph

Using a 64 or 128 slice CT scanner, high quality images of the coronary arteries can be obtained and the degree of coronary stenosis qualified. This technique provides anatomic information about the coronary arteries but no functional information about perfusion. For example, a coronary artery may be occluded yet there might not be any ischemia because of adequate collaterals which are not seen on CT angiography. Coronary CT angiography also has decreased specificity if there is significant coronary calcification or the presence of a coronary stent. Coronary CT angiography is a promising technique for assessing coronary disease in women with intermediate probability of CAD but outcome studies are lacking.

### Conclusion

The good news is that evidence-based therapy for CAD is as effective in women as it is in men. It is important to accurately diagnose women with CAD so that the institution of appropriate therapies may improve the quality of life and survival. 

#### Reference

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#### Resources

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