



# Clinical Evaluation of Women with Ischemic Heart Disease

Gender differences and biases have the potential to influence investigation and management of coronary artery disease in women. Physicians must recognize these differences when faced with a woman with possible cardiovascular disease.

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**A**lthough coronary artery disease (CAD) has traditionally been considered a men's disease, cardiovascular disease is also the leading cause of death in North American women. Over

the last decade, there has been increasing awareness of both the importance of CAD in women and of the significant differences between men and women who have the disease. Potential gender biases, both within the medical community and within the general population of women themselves, also have been identified. These gender differences and biases have the potential to influence investigation and management of suspected or confirmed CAD in women, and should be taken into consideration when faced with a woman with potential cardiovascular disease. This article will focus specifically on the presentation of CAD and its appropriate clinical evaluation in women.



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## Heart Disease in Women

### CAD in Women

Chest pain in women is common and is often non-ischemic. Conversely, the presentation of atypical and non-chest pain CAD, including acute myocardial infarction (MI), is more common in women than men. Chest pain is the most common presentation of CAD in both genders. The initial presentation of chest pain occurs in the setting of acute MI twice as often in men as compared with women. Women presenting with acute MI tend to be older and have more co-morbidities. The presence of hypertension or diabetes increases the likelihood of acute MI, as does the presence of clinical congestive heart failure or significant electrocardiogram (ECG) changes.

Even in the setting of acute MI, women's presenting symptoms differ from those of men. Women are more likely to experience back, jaw, abdominal and neck pain, nausea, shortness of breath and congestive symptoms, while they are less likely to complain of diaphoresis. While some studies have suggested that women with acute MI present later after symptom onset than do men, other series have found no difference in the time to presentation. Women

have an increased incidence of silent or unrecognized MI, as compared with men.

Outside of suspected cases of acute coronary syndromes, chest pain in women accounts for a significant number of visits to primary-care physicians and subsequent referral to cardiovascular specialists. In fact, women are much more likely to present with angina than MI as their initial symptom of CAD. Chest pain has many potential etiologies, and women have a greater prevalence of non-coronary causes of chest pain than do men. Chest pain, whether "typical" or "atypical" is associated with less angiographically significant CAD in premenopausal women. The presence of "atypical" features in women, however, does not decrease the likelihood of CAD in women to the same degree as it does in men. Women may present with a mixed picture of both typical and atypical features, such as pain in locations other than the anterior chest, or chest pain equivalents, such as dyspnea, palpitations, fatigue, nausea or presyncope. Features, such as rest angina, nocturnal angina and angina with mental stress, are more commonly seen in women than in men with chronic stable angina.

#### Summary

### Clinical Evaluation of Women with Ischemic Heart Disease

- The workup of women presenting with chest pain should be guided by clinical stratification into low, intermediate or high-risk categories.
- Women with a low-probability profile should not undergo stress testing.
- Women with an intermediate-probability profile, who are able to exercise and who have a normal resting ECG, should undergo ECG stress testing with Duke Treadmill Score (DTS).
- Stress imaging studies should be performed in the case of non-diagnostic ECG stress testing or in the presence of baseline ECG abnormalities.
- Pharmacologic stress using nuclear or echocardiographic techniques can be performed where the patient cannot exercise adequately.
- Women with a high probability of CAD should undergo stress testing with DTS or coronary angiography, depending on the severity and stability of symptoms.

## Heart Disease in Women

There are also differences in the ways that men and women interpret cardiac symptoms and the ways that these are conveyed to health-care workers. Women are more likely to attribute their symptoms to non-cardiac etiologies, even in the setting of acute MI, and may bias their care by suggesting that their pain is due to a hiatus hernia or ulcer, *etc.*, rather than being of a cardiac nature. Women are also less likely than men to recognize their risk for the development of CAD, and are even less likely to recognize their risk of dying from CAD. The presence of atypical features on presentation, along with possible attribution of symptoms to non-cardiac causes by the patient herself, may deter health-care workers from probing into the symptoms and risk factors. There is some evidence, as well, that both race and gender affect the way physicians manage patients presenting with chest pain. For example, women, and in particular black women, are less likely to be referred for cardiac catheterization, even when presenting with clinical characteristics that are identical to that of men.

### Approach To Diagnosis Of Women With Suspected CAD

Since chest pain and other symptoms that may be associated with CAD occur commonly in women, and since these symptoms may have atypical features, the challenge is to establish whether or not there is evidence of significant CAD. While it is true that a patient's clinical characteristics and coronary risk factors can provide the information to estimate the likelihood of CAD, there is evidence to suggest that this prediction is more easily and accurately accomplished in men than in women. The prevalence of CAD, par-

#### Quick Facts

#### Practice Points

- Women are more likely to have angina than MI as their initial presentation of CAD. Typical features of coronary artery disease, both in the acute and chronic situation, do occur in women, however women have a higher likelihood of presenting with atypical symptoms than do men.
- Women are less likely than men to attribute their symptoms to cardiac disease, even in the setting of acute MI.

Shouldn't the first depression  
be the last depression?



## Heart Disease in Women

Table 1

### Classification of Chest Pain

#### Typical Features

- Substernal.
- Squeezing, burning, heavy.
- Exertional or precipitated by emotion.
- Promptly relieved by rest or nitroglycerin.

#### Atypical Features

- Left chest, abdomen, back, arm, without mid-chest pain.
- Sharp or fleeting.
- Repeated or very prolonged. Unrelated to exercise.
- Not relieved by rest or exercise.
- Relieved by antacids.
- Characterized by palpitations without chest pain.

Table 2

### Determinants of the Likelihood of CAD in Women

#### Major

- Post-menopausal status. (without HRT)/age > 65 years
- Diabetes.
- Peripheral Vascular Disease.

#### Intermediate

- Hypertension.
- Smoking.
- Lipid abnormalities.

#### Minor

- Obesity.
- Sedentary lifestyle.
- Family history of CAD.
- Other risks factors for CAD.

ticularly multivessel disease, in women, except in the older age group, is lower than in men, therefore, the predictive value of any symptom or non-invasive test is lower in women than in men. Since the utility of diagnostic testing is related to the pretest probability of disease, it is necessary to make a careful assessment of risk, including symptom characterization and risk factors, in order to guide the choice of diagnostic modalities or determine if any testing is required.

Despite the fact that women tend to have more atypical features when presenting with CAD than do men, the presence of typical chest pain is associated with a higher prevalence (60% to 75%) of angiographically significant CAD. Patients with some atypical features (“probable angina”) had less than 50% (30% to 40%) preva-

lence, and women with non-specific chest pain syndromes (only atypical features) had a very low (2% to 7%) prevalence of significant occlusive CAD on angiography. Pain characteristics, therefore, should be assessed, and pain classified as typical, atypical, or nonanginal, as one aspect of risk stratification. Typical chest pain is associated with three or more typical features (Table 1), atypical chest pain is associated with two of the typical features and nonischemic pain has one or none of the typical features.

While classic risk factors play a role in the risk of CAD in women, some are of greater significance and others are less important (Table 2). The presence of any type of chest pain, whether atypical or typical, is associated with a lower

Table 3

### Classification of Patients According To Their Probability of CAD

#### High Probability of CAD (>80%)

- *Typical angina* and any of:
  - Post-menopausal status / age > 65
  - Diabetes
  - Peripheral vascular disease
  - Two intermediate determinants
- *Atypical angina* and any of:
  - Post-menopausal status / age > 65 and > 1 intermediate determinant
  - Diabetes plus > 1 intermediate or minor determinants
  - Three intermediate or 2 intermediate plus minor determinants

#### Intermediate Probability of CAD (20-80%)

- *Typical angina* and:- 1 intermediate or > 2 minor determinants
- *Atypical angina* and:
  - Post-menopausal status / age > 65
- *Nonischemic pain* and:
  - Post-menopausal status / age > 65 or diabetes and > 2 intermediate and/or minor determinants

#### Low Probability of CAD (<20%)

- *Typical angina* and:
  - Premenopausal with no determinants
- *Atypical angina* and:
  - No major determinants
- *Nonischemic pain* and:
  - No major determinants

risk of CAD in premenopausal women than in men of the same age, however, the CAD likelihood increases after menopause. A woman's age and menopausal status, therefore, should be considered when assessing the risk of CAD. Besides age, diabetes is one of the most important risk factors for CAD, as it eliminates the age advantage in women over men and confers a substantially greater CAD mortality rate than in nondiabetic females. Diabetes is, therefore, an impor-

tant predictor of the presence and prognosis of CAD in women.

The Canadian Cardiovascular Society Consensus document on Women and Ischemic Heart Disease proposes the algorithm in Table 3 to classify patients as having a high, intermediate, or low probability of CAD, taking into consideration chest pain characteristics, age/menopausal status, diabetes and the presence of other risk factors.

## Heart Disease in Women

### Quick Facts

#### Practice Points:

- Patients should be classified as having a high, intermediate, or low probability of CAD, and appropriate investigations initiated accordingly by taking into consideration:
  - Chest pain characteristics
  - Age/menopausal status
  - Diabetes
  - Presence of other risk factors
- The presence of post-menopausal status or diabetes increases the likelihood of CAD, independent of chest pain characteristics.

### Diagnostic Evaluation of Women with Chest Pain

The diagnostic workup of women with suspected CAD can be problematic and is certainly challenging. The purpose of performing a clinical evaluation of these women is to identify those at very high risk, who would benefit from immediate coronary angiography, and, in lower-risk patients, to accurately identify those with significant CAD prior to the development of an acute coronary event. This must be accomplished in the setting of limited health-care resources and with the recognition that testing sensitivity and specificity may be less than optimal in some groups of patients. The overall goal is to improve the quality and efficiency of evaluating women with chest pain.

ECG stress testing is the most readily available and least expensive tool for risk stratification of women with chest pain, however, it may be less predictive of significant CAD in women than in men. Women are less likely to exercise to

target heart rate and have a generally reduced functional capacity than men. Women are also more likely to have resting ECG repolarization abnormalities, which reduce the diagnostic specificity of ECG stress testing. The fact that women tend to be older and have more comorbidities, such as hypertension and left ventricular hypertrophy, may be responsible for both the inability to exercise to target and the ECG abnormalities. Exercise-induced repolarization abnormalities, even in the absence of resting ECG abnormalities, may be related to the digitalis-like effect of estrogen on the ST segment, rather than to true ischemic changes. The sensitivity of ECG stress testing varies during the menstrual cycle and in response to estrogen therapy. Having noted the potential problems with ECG stress testing, this diagnostic modality still plays an important role in the non-invasive workup of women with suspected CAD. If the patient exercises to target heart rate and there are no significant ECG abnormalities, the test is very good at ruling out significant CAD. In order to increase the specificity for ruling out CAD, the Duke Treadmill Score (DTS) has been developed. This consists of a weighted score combining ST segment changes, treadmill time and exercise-induced chest pain. Combining the use of ECG stress testing with DTS increases the accuracy of diagnosing CAD in women.

Stress imaging studies include nuclear stress testing or echocardiographic stress testing. They provide increased sensitivity and specificity of the diagnosis, particularly in the setting of resting ECG abnormalities. Pharmacologic stress, using dipyridamole, adenosine or dobutamine can be performed with these stress-imaging modalities, adding to their usefulness in patients who cannot exercise adequately. These modalities also allow for the localization of and quantification of ischemia in patients with CAD.

Coronary angiography has been the gold standard for the diagnosis of significant CAD in both men and women. This procedure is associated with potential risks and relatively high costs. It should not be used routinely as an initial investigative modality, except in patients with acute coronary syndromes or with very high-risk profiles and/or unstable symptoms. Positive non-invasive tests, particularly those with evidence of critical or multivessel CAD, should lead physicians to consider coronary angiography to further define the extent and location of coronary artery stenoses.

The most important determinant of what type of testing, if any, is appropriate for a woman presenting with chest pain is the clinical probability of disease, as determined by stratifying the patient at low, intermediate or high risk for CAD.

Women with a low-probability profile should not undergo stress testing, as the likelihood of false-positive test results are greater than the likelihood of a true-positive result. Negative ECG stress testing in this group has a very high negative predictive value, however. Women with an intermediate-probability profile, who are able to exercise and who have a normal resting ECG, should undergo ECG stress testing as an appropriate initial test. The Duke Treadmill Score is recommended to increase specificity of the test. Stress imaging studies should be performed if the patient has a non-diagnostic ECG stress test, when there are baseline ECG abnormalities, or where the goal of the test is to localize and quantify ischemia. Women with a high probability of CAD should undergo stress testing with Duke Treadmill Score or coronary angiography, depending on their severity and stability of symptoms.

## Conclusion

Clinical evaluation of women presenting with chest pain is an important step in stratifying patients into low-, intermediate-, and high risk groups, and is useful in guiding further investigation. The combination of clinical assessment and non-invasive testing can define those women at very high and very low risk for future cardiac events. The appropriate use of non-invasive testing, along with improvements in test specificity can reduce unnecessary coronary angiography and provide accurate assessment of cardiac risk, thereby, providing a cost-effective approach to testing women with known or suspected CAD.

### Suggested readings

1. Isaac DL, Walling A: Section 6. In Brister SJ, Turek M (eds). *Canadian Cardiovascular Society Consensus Document Women and Ischemic Heart Disease*, Canadian Journal of Cardiology (in press).
2. Alexander KP, Shaw LJ, Shaw LK, et al: Value of exercise treadmill testing in women. *J Am Coll Cardiol* 1998 Nov; 32(6):1657-64.
3. Douglas PS, Ginsburg GS: The evaluation of chest pain in women. *N Engl J Med* 1996; 334(20):1311-5.
4. Cerquiera MD: Diagnostic testing strategies for coronary artery disease: Special issues related to gender. *Am J Cardiol* 1995; 75(11):52D-60D.

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Answer the questions in our quiz found on page 263 and send the response card to the University of Calgary for CME credits.