Women's Health Issues and Nuclear Medicine, Part I: Women and Heart Disease

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Objective: This is the first article of a four-part series on women's health issues and nuclear medicine. This article will review women and heart disease. After reading this article the technologist will be able to: (a) compare and contrast the differences in diagnosing coronary artery disease between men and women; (b) explain the importance of radionuclide myocardial perfusion imaging in diagnosing and stratifying risk of coronary artery disease in women; and (c) list and explain the technical challenges of imaging women's hearts.

Key Words: coronary artery disease; radionuclide myocardial perfusion imaging; technetium-99m-sestamibi; thallium-201


Many Americans have the misconception that cardiovascular heart disease is a man's disease. In reality, cardiovascular heart disease is the single largest cause of death in American women (1). Cardiovascular disease claims the lives of more than 500,000 women annually, compared with all forms of cancer, which are responsible for the deaths of 250,000 women per year (1). Statistics have shown that 1 in 9 women between the ages of 45 and 64 y have some form of heart or blood vessel disease and this number increases to 1 in 3 women after age 65 (1). Since 1984, the total number of deaths due to cardiovascular disease in women annually has been greater than in men (2).

Distinct differences between coronary artery disease in men and in women have been recognized. Women average approximately 10 y older than men at the initial onset of coronary artery disease and are approximately 20 y older at the occurrence of myocardial infarction (3). This difference in age is thought to be due to the protective effects of estrogen in women. However, as women approach menopause their incidence of coronary artery disease increases and continues to do so with age.

Although women and men share similar cardiac risk factors, the profiles for men and women tend to differ. Women have a greater risk of developing hypertension at an earlier age, and by age 75 the prevalence is greater in women compared to men (1).

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Diabetes is more common among women than men at all ages. Although cholesterol levels are lower in women before menopause, after menopause their levels are higher compared to men at similar ages (4,5). Obesity, physical inactivity and tobacco use also have been associated with an increased risk of heart disease in women (4,6,7).

DIAGNOSING CORONARY ARTERY DISEASE IN WOMEN

Diagnosing coronary artery disease in women continues to be a challenge for physicians. Women often experience symptoms that are different from men. Classic or typical symptoms for coronary artery disease have been based on what men experience and, until recently, the majority of research in coronary artery disease has been directed towards men (8).

Women more often than men experience chest pain as an initial symptom rather than myocardial infarction or cardiac death. Historically, however, chest pain has not been perceived to be of great prognostic value in women. This is based on follow-up reports from the Framingham study, which stated that although women develop symptoms more often than men, they progress less often to myocardial infarction (3). The Coronary Artery Surgery Study (CASS) found that of the 2810 women referred for coronary angiography for the evaluation of chest pain, 50% had no significant obstructive coronary artery disease (9).

Although chest pain is not considered to be of great prognostic value in women, it still remains the most common symptom reported by women with coronary artery disease. The Myocardial Infarction Triage and Intervention (MITI) Project reported that nearly 90% of women who suffered a myocardial infarction experienced chest pain as the initial symptom similar to men (10). It also reported, however, that women who suffered a myocardial infarction were significantly more likely than men to present with symptoms considered to be atypical, such as upper abdominal pain, dyspnea, nausea or fatigue.

Classifying the symptoms that women present with to angina, probable angina or nonspecific chest pain may help increase the prognostic value of these symptoms (8). Results of the CASS study showed that women with classical angina had a 71% chance of obstructive disease by coronary angiography.
while those with probable angina had only a 36% chance of disease (9). Women who are considered to have nonspecific chest pain syndromes rarely are found to have any obstructive coronary artery disease by coronary angiography (5).

Health care professionals need to understand the differences in symptoms which women may present with and that symptoms, even those perceived to be atypical or possibly noncardiac in origin, should be evaluated with some type of diagnostic procedure. A recent review of the evaluation of chest pain syndromes in women suggested that it is possible to risk stratify women for coronary artery disease and use diagnostic procedures more informatively and effectively (11).

**NONINVASIVE EVALUATION OF CORONARY ARTERY DISEASE IN WOMEN**

Several noninvasive procedures have been studied to evaluate their role in diagnosing coronary artery disease in women including: cardiac fluoroscopy, exercise tolerance testing (ETT), exercise myocardial perfusion scintigraphy and stress echocardiography (12–16). Although exercise tolerance testing is the most commonly used procedure for evaluating chest pain syndromes, several studies have shown a lower sensitivity and specificity in women compared with men (17–21). This is probably due to the gender differences in the prevalence and extent of disease, as well as the inability of women to achieve an adequate heart rate response (22). Combined with exercise or pharmacologic stress testing, however, radionuclide myocardial perfusion imaging is considered to be one of the most important noninvasive modalities for detecting coronary artery disease in women.

**RADIONUCLIDE MYOCARDIAL PERFUSION IMAGING**

Exercise myocardial perfusion imaging has been reported to show increased sensitivity and specificity for detecting coronary artery disease over standard exercise treadmill testing alone for both men and women (12,23–27). There also has been an increase of sensitivity and specificity when performing SPECT myocardial perfusion imaging as compared to planar imaging (28–29).

As mentioned earlier, women are sometimes unable to achieve an adequate heart rate response with exercise testing alone. This may be due to the advanced age at which women experience the onset of symptoms, resulting in a diminished exercise capacity. For this reason, pharmacologic stress myocardial perfusion imaging has been found to be useful in women to achieve higher diagnostic accuracy than exercise testing alone (30).

**Technical Challenges**

One of the most common problems when performing SPECT myocardial perfusion imaging in women is a false-positive study due to breast attenuation artifact (31–34). This generally appears as a localized area of decreased photon activity because of the differential in counts due to attenuation and is most commonly seen as a fixed perfusion defect (Fig. 1). The artifacts vary in appearance because of differences in size, shape and density of breast tissue (32). Physicians always should review the unprocessed planar projection data before interpreting a SPECT study to identify breast attenuation.

When performing myocardial perfusion imaging on women it is important to have similar positioning of the breast tissue for both the stress and rest acquisitions. It is recommended that women not wear brassieres during the acquisition because they may position the breast tissue more anteriorly and increase the amount of attenuation. However, if the patient wears a brassiere during the first acquisition, she should wear one during the second acquisition to maintain consistency.

Some laboratories use breast binders, which flatten the breast against the chest wall, or breast markers, which outline the breast tissue, to aide in recognizing and reducing breast attenuation artifacts. Both of these techniques may be helpful but require more precise and identical positioning of the breast during the stress and rest images, which may not always be possible (32).

Recent developments, such as 99mTc-labeled myocardial perfusion imaging agents as well as ECG gated SPECT imaging, have helped improve image quality and specificity when performing myocardial perfusion imaging in women (35). Technetium-99m-labeled agents offer a higher energy window (140 keV versus 80 keV) and shorter half-life (6 h versus 73 h) over 201Tl. These characteristics result in a larger amount of activity administered for the same radiation exposure to the patient resulting in better count statistics. This increase in count statistics allows gated SPECT imaging to be performed. The
addition of gated SPECT imaging has improved the differentiation of scar versus attenuation artifacts when fixed defects are present and has increased diagnostic accuracy (36).

A study performed by Taillefer et al. directly compared the sensitivity and specificity of 201Tl, 99mTc-sestamibi perfusion and 99mTc-sestamibi gated SPECT imaging for detecting coronary artery disease in women (37). They concluded that 201Tl SPECT and 99mTc-sestamibi SPECT perfusion had similar sensitivities. However, 99mTc-sestamibi showed a significantly higher specificity, which was even further enhanced with gated SPECT imaging.

Attenuation correction is another proposed application that may offer assistance in the future for distinguishing between true perfusion defects and artifacts. This application has not been fully evaluated and will require more extensive clinical validation.

Other problems that may affect myocardial perfusion imaging in women are the high prevalence of single- versus multivessel disease in premenopausal women and the smaller chamber size of the left ventricle. These factors may have an effect on diagnostic accuracy (12,29,30,38,39).

**Prognostic Value of Radionuclide Myocardial Perfusion Imaging**

Myocardial perfusion imaging has been proven over the years to be a strong indicator of patient prognosis (40,41). Study results have reported a strong correlation between abnormal images and an increased risk of future cardiac events, while normal images have a low risk for future cardiac events. Although previous studies were performed on predominantly male populations, there have been several studies recently published evaluating the prognostic value of myocardial perfusion imaging in women (42–45). The results of these studies indicate that myocardial perfusion imaging is a strong predictor of patient prognosis in both genders (35).

**CONCLUSION**

Coronary artery disease is the number one cause of death in women in the U.S. Only recently has research been performed to evaluate the differences that exist among men and women with this disease. It has been established that women present with symptoms at an older age and their symptoms are often considered to be atypical in nature. This has made diagnosis in women more difficult.

Nuclear medicine has an important role in assisting with the diagnosis of coronary artery disease in women. Radionuclide myocardial perfusion imaging is considered one of the most important diagnostic procedures for women. It offers a high degree of diagnostic accuracy and is a strong indicator for patient prognosis. It is important for technologists to understand the differences between women and men to achieve optimal image quality for both genders.

**REFERENCES**


