



February 2006

cardiac care provided in a **heartbeat**

Women and Heart Disease

Cardiovascular disease is the leading cause of death in Canadian women with coronary heart disease causing over 25,000 deaths annually. It was until recently, viewed as a disease of middle aged men, a concept unchanged from that of Heberden, who over 200 years ago in his paper to the Royal College of Physicians of London in July 1768 described “some account of the disorder of the breast”. In this he stated “males are most liable to this disease especially such as have past their fiftieth year. I have seen nearly a hundred people under this disorder, of which number there have been three women.”

In the seventies and eighties, all NIH trials excluded women, either deliberately or by accident. For example, in the CASS trial the upper limit of inclusion was 65. Eighty per cent of women have the initial clinical manifestation of heart disease after the age of 65; therefore, their representation in coronary artery bypass surgery was too few.

Let's look at the facts in women.

1. Cardiovascular disease is the leading cause of death in Canada and death from coronary heart disease is far greater than all the cancers combined.
2. It causes over 25,000 deaths annually.
3. The incident of heart disease between the age of 45 and 64 is 10%, and over the age of 65 it is 35%.
4. Fifty-one per cent of all fatal heart attacks occur in women.
5. One-third of women are post-menopausal and in this group the risk of coronary artery disease is high. As this percentage increases, heart disease becomes more common in women than in men.



What is most surprising is that given similar clinical presentation, less women go on for coronary angiography. Also, if there are similar clinical presentations with coronary angiographic findings, fewer women than men are referred for bypass surgery.

The natural history of coronary heart disease in women is:

1. Initial symptoms are ten years later in women.
2. The initial heart attack is twenty years later in women.
3. Coronary heart disease is more age dependent in women. For example, coronary morbidity from ages 75 – 84 is forty times the incidence as for ages 35-44. By the age of 80, the incident of coronary heart disease is equal in men and women.
4. Seventy percent of women present with angina as opposed to only thirty percent of men.

Angina is not as “benign” in women as was once believed. The Framingham study revealed that after five years follow-up in men, the incidence of serious coronary event was 34% as opposed to 14% in women. At fourteen years, it was 44% in men and 17% in women. The reason for this discrepancy is that an older women subset who have a poorer prognosis were totally overlooked.

It was in the CASS registry that the Framingham “benign” nature of angina was clarified. The diagnosis of angina, especially in younger women should have been called chest pain. In 24,179 CASS patients undergoing coronary angiography in excellent medical centers for chest pain severe enough to merit bypass surgery consideration 50% of the women had normal coronary arteries while only 17% of the men had normal arteries.



In the older woman, whether the angina is atypical or typical, the number of positive angios were equal. Therefore, the pre-angiographic differentiation of non-cardiac from cardiac cause of chest pain is a problem. Therefore, it is not surprising that “benign” natural history for angina pectoris in women was noted in the Framingham study. It is highly likely that half of the women had no heart disease at all!

In the Mayo Clinic study, 80% of females and 71% of males were free from a heart attack on follow-up in confirmed coronary heart disease diagnosis. This gender difference is much less than that reported by the Framingham study. However, there are many reasons for these differences including non-invasive diagnostic error.

The non-invasive evaluation of chest pain is a problem in women. Chest pain is a fairly common symptom below the age of 65, but coronary heart disease is uncommon. For example, if you do angiography in young women with typical angina and a positive stress test, it appears that if they have more than two coronary risk factors, the angiography shows significance in more than half of the cases, but if there are less than two risk factors, the chance of significant coronary heart disease is less than two percent. (Recall that risk factors include family history, smoking, diabetes, high blood pressure and elevated blood cholesterol levels).

In fact, men over 40 years of age who complain of typical angina are found to have coronary artery disease upon cardiac catheterization almost 100% of the time. This is very different for women between the age of 40 and 49 who are found to have coronary heart disease only 60% of the time upon catheterization. The percentage does increase to 70% for women between the ages of 50 and 59, but there is also a higher percentage of women who have single vessel disease.

When we consider non-invasive stress testing, it has been found that if the pre-test probability of disease is low, the post test probability will depend on the amount of ST



depression seen during the test. (ST depression is the main change in a cardiogram that your team is watching for during a stress test). Therefore, especially in the case of young women, significant ST depression with symptoms is needed in order to stop the test and call it a positive one.

As usual, most non-invasive diagnostic stress tests were developed for the male population. The “Bruce” protocol, which is the test used most often was based on “Bruce” himself who was 6’3” tall. This makes the test too fast for women. (Any female patients who routinely walk with a husband who is much taller will understand the nature of this problem with the test). Also, women have a higher incidence of high blood pressure, mitral valve prolapse and left ventricular hypertrophy. These factors cause ECG changes which are seen prior to starting the actual stress test.

It is still important to remember that if the ECG is normal and a woman achieves an adequate workload, a negative test does exclude coronary artery disease. Also, if the resting ECG is normal, a positive test is of equal value in both sexes. However, if there are changes in the resting cardiogram, a thallium test is the next necessary step.

In general, although there have been considerable improvements made in non-invasive stress testing over the last five years, fewer women with positive stress tests are referred for angiography. The question becomes whether this is because of test unreliability, or is there a gender based referral bias?

One of the reasons for this difference in management has been that for a long time, doctors have believed that chest pain in women is not due to coronary heart disease. However, if this is the case, it is difficult to explain why anti-anginal medications are prescribed equally for men and women, and yet ten times more men are referred for angiography than women. Even after angiograph, if there is a high risk lesion, men and women have bypass surgery done equally, but in low to medium risk lesions, far more



men have bypass surgery done than women. Men are also twice as likely to undergo cardiac catheterization, and twice as likely to undergo coronary bypass surgery.

Thus the question becomes; is this a gender bias or is it appropriate therapy? Are there even enough data to really determine the appropriate indication and outcome for bypass in women?

The CASS registry as well as the MITI registry (one done in the '70's and one in the '80's) both show that the incidence of peri-operative and hospital mortality is higher in women than in men. What is the possible cause of this finding?

First, women are older when they get intervention than men. They have more unstable angina and a higher incidence of co-morbidity, i.e. diabetes and hypertension. This was found in both of the above studies. However, both studies determined that an unstable clinical presentation was a powerful adverse prognosis factor. As angiography and elective bypass surgery are more frequently deferred in women, then the more urgent nature of the female patients in the study may account for the higher rate of adverse outcomes. Although the success rate of angioplasty has improved, (based on data collected between the 1970's and data collected in 1985-86), women are still considered to be an independent risk factor.

Bell, et al. (1992), found that the higher in-hospital mortality rate is mainly due to the greater severity of disease and instability associated with the associated diabetes and hypertension. When age and co-morbidity were controlled, the long term prognosis was similar in both men and women. However, despite these similar outcomes, there were still more subsequent re-vascularization procedures done in men.

In terms of the medical therapy provided, the drugs are prescribed under the assumption that they will work as well in women as they have been reported to work in men.



HRT (Hormone Replacement Therapy) is not considered beneficial in reducing CAD (Coronary Artery Disease)

In summary;

1. Most research in cardiology has been based on men rather than women.
2. Women are less frequently investigated for coronary heart disease at all stages of investigation, based on similar clinical presentations.
3. Even when they are investigated and found to have significant coronary heart disease, women are less frequently referred for angioplasty or bypass surgery.
4. More than half of all fatal heart attacks occur in women.