Fashioning a new approach to heart disease in women

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Implementation of new evidence-based guidelines is one of the most daunting tasks facing healthcare professionals today, and in order to meet this challenge we need to be well informed and to inform our patients. The Centers for Disease Control and Prevention National Ambulatory Medical Care Survey[1] showed that clinicians were missing opportunities to prevent heart disease, particularly in counselling women patients about exercise, nutrition and weight reduction. Recent years have seen the publication of several guidelines by the American Heart Association, American College of Cardiology, British Cardiac Society, European Cardiac Society and most recently the National Institute for Clinical Excellence. These will no doubt have a positive impact once incorporated into daily clinical practice though it is often difficult to challenge established practice. It is therefore incumbent upon us, as healthcare professionals, to review our practice constantly and to keep abreast of research and development in our field in order to maintain standards of good clinical care.

Prior to the 1990s cardiovascular disease was considered to be a man's disease. Few women (< 10%) were entered into clinical trials, resulting in few gender-specific data. This led to the under-recognition, under-diagnosis and under-treatment of women with heart disease. It became evident that heart disease in women was unique and that data from studies with a predominance of male subjects could not be extrapolated to women. Recognising this, the first gender-specific guidelines in preventative cardiology were published in 1999.[2]

Women present with heart disease a decade later than their male counterparts. The myth that endogenous oestrogen in pre-menopausal women provides them with cardioprotection has been challenged as studies have shown that heart disease in women is linearly proportional to increasing age without a sudden increase after menopause.[3] This correlates with data from the Heart and Estrogen/progestin Replacement Study (HERS) trial, which shows that despite improving serum lipid profiles, hormone replacement therapy (HRT) does not reduce coronary events in post-menopausal women and may confer an early increased risk of adverse cardiovascular outcomes.[4]

Coronary heart disease (CHD), which is the commonest form of heart disease in both sexes, is a major cause of death in women in developed nations. Two-thirds of women who die suddenly from fatal CHD have no previously recognised symptoms. Across all ages, one in six women in the UK and Europe and one in three women in the US die annually from heart disease; this exceeds the number of deaths in males and the next seven causes of death in women combined. To put this in perspective, women are 18 times more likely to die from heart disease than from breast cancer, although most women think that they will succumb to breast cancer.

Diagnosis of CHD in women is a challenge, particularly since this is perceived to be a man's disease and therefore not investigated sufficiently. Although most women present with typical chest pain, a greater proportion will present with atypical symptoms (fatigue, abdominal, neck and back pain or nausea) when compared to men. Preliminary results from the Euro Heart Survey, presented at the European Society of Cardiology in 2003, showed a higher than anticipated proportion of younger women (rather than mainly middle-aged and older women) with newly presenting stable angina. CHD is not just a disease of 'older' women. In the US, some 20,000 women younger than 65 years of age die annually from myocardial infarction (MI): 33% of these are under 55 years of age, whilst 36% of women aged 55–64 are disabled by the severity of their CHD.

The pathogenesis of CHD is similar in both sexes but cer-

tain risk factors have more emphasis in women. Most notably, diabetes confers a three- to seven-fold increased risk of CHD in women, at any age. The prognosis for diabetic women is worse than that for diabetic men, and once diabetic women have suffered an MI, their risk of re-infarction is doubled.

Other risk factors also show gender variance. The Heart Protection Study[5,6] showed that low levels of high-density lipoprotein cholesterol (HDL-C) (< 50 mg/dL; 1.3 mmol/L) are associated with an increased risk of heart disease in both older and younger women. This was found to be a stronger predictor of cardiovascular disease than total cholesterol or low-density lipoprotein cholesterol (LDL-C) levels in women. It has also been shown that elevated triglycerides are an independent risk factor for CHD mortality in women who have low HDL-C levels.[7] Therefore diabetes, low HDL and raised triglycerides are a greater risk for CHD in women. Smoking, family history and inflammation (raised C-reactive protein levels) are other risk factors with greater significance when present in women, whereas lipoprotein (a) is a stronger risk factor in men.

The Women's Ischemic Syndrome Evaluation (WISE) study[8] showed that atherosclerosis in women is of a more diffuse nature, with greater total compromised lumen, when compared to men. This may explain why women have unstable angina without overt obstructive coronary artery disease (MI) when compared with men.

However, when obstructive CHD does occur in women, the prognosis after MI is significantly worse. Data from the GUSTO IIb trial showed that women were more likely to suffer a non-ST elevation MI, and were hence not suitable for thrombolysis.[9] Data analysis from the WISE study showed that women presenting with acute coronary syndromes (ACS) to emergency departments were less likely to receive effective acute management, and often the diagnosis of cardiac ischaemia was overlooked. Yet the in-hospital and 30-day mortality of women following an acute MI was double the mortality in men. This dire scenario continues not only into the first year after an acute event, with a higher mortality in women (38% *vs.* 25%), but over the next six years more women will have a second acute coronary event, with a mortality of 35% *vs.* 18% in men, and more women will develop heart failure, 46% *vs.* 22% in men.

Based on age, risk factors and symptoms, therefore, the pre-test likelihood of CHD can be estimated. This is pivotal in choosing the appropriate diagnostic tool. Recently published NICE guidelines advocate the use of myocardial perfusion imaging as the initial investigation with the highest diagnostic accuracy in women with suspected CHD.[10] Myocardial perfusion imaging (MPI) has greater sensitivity (85% *vs.* 61%) and specificity (92% *vs.* 70%) than the exercise tolerance test (ETT) in women. It is therefore recommended that MPI should be the first line of investigation in all women with suspected CHD. MPI is a reliable and easily reproducible technique, which can readily be performed with pharmacological stress (rather than dynamic exercise): this may be useful in women who are poorly motivated, with a reduced exercise capacity.

Initially, non-invasive cardiac imaging was reserved for women with an intermediate-risk profile who had an abnormal resting ECG. However, cost-effective analyses have shown that it can be used successfully in middle-aged women at low and intermediate risk.[11]

There are gender-specific challenges to the performance of accurate MPI in women, such as breast attenuation artefact. This has largely been overcome by the use of technetium agents (brighter signal intensity) and gating (timing the acquisition of the images with the R-R interval of the ECG), resulting in fewer false-positive images. Whilst the sensitivity of thallium and Tc-99m images are comparable, there is a significant improvement in specificity of Tc-99m (92%) when compared to thallium (67%) images; and the use of Tc-99m reduced the false-positive rate by > 50%.[12]

MPI has the added advantage of providing incremental prognostic information. Pooled data from a recent meta-analysis of 7,500 women with normal scans showed an annual cardiac event rate of < 1% per annum for five years, even in women with a high pre-test likelihood of CHD. However, if there are significant myocardial perfusion defects on the SPECT scan images, then referral for early revascularisation is usually warranted. Prognosis can be gauged from the number, extent and depth of perfusion defects seen on the scan images.

'Fashioning a new approach to heart disease in women' is an educational and awareness workshop to be held at the National Heart and Lung Institute, Imperial College on 15th October 2004. It is designed to share knowledge from recent advances in the epidemiology, risk factors, diagnosis, prognosis and treatment of women with heart disease, and is aimed at cardiologists and all healthcare professionals involved in the care of women. There is no doubt that lifestyle changes and the treatment of risk factors have a significant impact on cardiovascular disease processes; but it is clear that there are significant differences in the management of women when compared to men, and that assumptions that the management is interchangeable between the sexes need to be revised. The challenge is to diagnose significant CHD accurately so that early risk factor reduction and revascularisation may be undertaken, before acute and fatal events occur. A combination of a major drive in preventative cardiology combined with the use of appropriate diagnostic techniques will play a major role in fashioning a new approach to coronary care in women.

Conflict of interest

None declared.

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