Stress echocardiography in special groups: in women, in left bundle branch block, in hypertension and after heart transplantation

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The non-invasive diagnosis of coronary artery disease by exercise electrocardiography is less accurate in women than in men, with a high rate of false-positive results in women. In contrast, recent studies have demonstrated that stress echocardiography in women is more accurate than exercise echocardiography and that the significantly higher specificity of stress electrocardiography may have the benefit of avoiding unnecessary angiography in women.

Exercise-induced changes in the electrocardiogram are non-diagnostic in the presence of left bundle branch block or basal ST changes. In these patients, stress echocardiography can be used instead of conventional scintigraphy for the detection of coronary artery disease, but further echocardiographic studies are needed to confirm the promising results.

Exercise electrocardiography and exercise echocardiography have been reported to be disappointing in the early detection of cardiac allograft vasculopathy after heart transplantation, and dobutamine stress echocardiography overestimates the incidence of angiographic evidence of cardiac allograft vasculopathy. However, compared to intravascular ultrasound imaging, dobutamine stress echocardiography seems to be a suitable non-invasive method for detecting cardiac allograft vasculopathy.

Key Words: Stress echocardiography, coronary artery disease.

Introduction

The non-invasive detection of myocardial ischaemia in patients with coronary artery disease remains an important clinical problem. Numerous methods have been introduced to induce ischaemia, such as exercise testing, pharmacological stress testing using dipyridamole or dobutamine, and atrial pacing. Ischaemia may be detected using the electrocardiogram, the perfusion scan or the echocardiogram, and in recent years, stress echocardiography has become a widely available and relatively cheap method for detecting myocardial ischaemia.

The goal of this paper is to provide an overview of the diagnostic value of stress echocardiography in the detection of coronary artery disease in women, in patients with left bundle branch block or left ventricular hypertrophy and after heart transplantation.

Stress echocardiography in women

The non-invasive diagnosis of coronary artery disease is less accurate in women than in men with a high rate of false-positive exercise electrocardiographies in women with angiographically normal epicardial coronary arteries. The reasons for these differences are uncertain. In the review recently published by Douglas and Ginsburg, recommendations are given for the use of diagnostic tests in women with chest pain. Before diagnostic testing, patients should be clinically stratified into low, moderate or high probability groups for coronary artery disease according to symptoms, age and cardiovascular risk factors. In women with a low probability of coronary artery disease, further non-invasive testing should be avoided because of the high rate of false-positive results. However, women in the highest risk group should undergo exercise electrocardiography and the threshold for coronary angiography should be low, because such women are unlikely to have false-positive results. In actual practice, most women will belong in the moderate risk group, which must be evaluated further, but the non-invasive test for this group is still uncertain.

In recent years interest has grown in the use of stress echo for the detection of coronary artery disease in women. Sawada et al., Williams et al. and Marwick et al. investigated the diagnostic value of exercise electrocardiography and exercise echocardiography. The results were compared with the presence or absence of...
Figure 1 Specificities of exercise electrocardiography and exercise echocardiography in women for the detection of coronary artery disease. □, (n=57) Sawada, J Am Coll Cardiol 1989; 14: 1440; △, (n=70) Williams, Am J Cardiol 1994; 74: 435; ●, (n=161) Marwick, J Am Coll Cardiol 1995; 26: 335.

Figure 2 Sensitivities of exercise electrocardiography and exercise echocardiography in women for the detection of coronary artery disease. Symbols as for Fig. 1.

50% diameter stenosis at angiography (Figs 1 and 2). In all three studies, the specificities (ranging from 80% to 86%) and sensitivities (ranging from 81% to 88%) of exercise echocardiography were superior to exercise electrocardiography (specificity ranging from 51% to 78% and sensitivity ranging from 47% to 77%) in the detection of coronary artery disease.

Masini et al. using dipyridamole echocardiography in women reported a sensitivity of 79% and a specificity of 93%[7]. The significantly higher specificity of stress echocardiography may enable avoiding unnecessary angiography in women presenting with chest pain.

Sawada et al. determined the relative diagnostic value of exercise echocardiography when exercise electrocardiography was not helpful[8]. They compared the results from patients with a non-diagnostic or a diagnostic stress electrocardiogram, but there were no significant differences in sensitivity, specificity or accuracy between the two groups. The results support the conclusion that stress echocardiography may be useful as an additional test in this subgroup of patients.

Atypical chest pain is more common in women than in men, because of the higher prevalence among women of mitral valve prolapse, coronary artery spasm and syndrome X[2,3]. Therefore the nature of chest pain is less predictive of coronary artery disease in women than in men. Sawada et al. compared the stress echo findings in women with atypical and typical chest pain for coronary artery disease[4]. They found that stress echocardiography has a similar diagnostic accuracy in women with atypical chest pain or angina.

Bach and coworkers studied the clinical, echocardiographic and angiographic findings of patients who had a positive dobutamine stress echo, but no critical stenosis[8]. In this study, false-positive results occurred predominantly in women (21%) in comparison to men (5%). Picano et al. also investigated the value of dipyridamole echocardiography in the detection of coronary artery disease in women and men[9]. However, they found no difference in sensitivity or specificity between the two groups.

Marwick et al. calculated the accuracy and rate of angiography of seven different strategies for the diagnosis of coronary heart disease in women[6]. For this review, two strategies commonly used in the diagnosis of coronary heart disease were selected. The first strategy was based on the initial performance of exercise electrocardiogram in all women. Exercise echo was only carried out in patients with a non-diagnostic electrocardiogram and angiography was recommended for all patients with a positive electrocardiogram or a positive echo test. This led to an angiogram being carried out in 51% of patients, of which an unacceptably high 44% were inappropriate. The rate of false-negative results was 14%. Strategy II involved stepwise progression of the exercise electrocardiogram for all patients, with stress echo limited to patients with a positive or non-diagnostic exercise electrocardiogram. Angiography was reserved only for women with a positive stress echo. This strategy led to a lower rate of angiography (31%), a correspondingly lower rate of inappropriate angiography (26%) with a small increase in false-negative results (22%) in comparison to strategy I. Based on these data, Marwick speculated that the use of stress echocardiography as an initial test in all women with chest pain is the most cost-effective approach, achieving diagnostic accuracy similar to that of thallium but at a lower cost per patient.

In conclusion: stress echocardiography in women is more specific in the detection of coronary artery disease than exercise electrocardiography and is a helpful guide in women with atypical chest pain or with a non-diagnostic electrocardiogram. However, despite the greater specificity of exercise echocardiography, the rate of false-positive results in women seems to be higher than in men.
Stress echocardiography in patients with left bundle branch block

Septal wall motion abnormalities with delayed contraction of the septum are well known in patients with left bundle branch block; however, myocardial thickening remains nearly normal in the absence of coronary artery disease. Therefore, an ischaemic response cannot be identified by wall motion analysis, but may be identified by stress-induced wall thickening impairment, including failure to improve wall thickening relative to the hyperkinetic response to maximal stress. Using these criteria Mairesse et al. found a sensitivity of 80% in the detection of coronary artery disease but the specificity of 72% was only moderate[10]. Two important limitations of the study should be considered: first the small number of patients and second the inclusion of patients with previous myocardial infarction. Therefore studies in a larger population of patients are needed. However, it is of interest that there were no differences as regards sensitivity and specificity in left anterior descending, circumflex or right coronary artery disease. In contrast, thallium scintigraphy is associated with a significantly higher rate of false-positive results in the perfusion bed of the left anterior descending artery compared to circumflex or right coronary artery disease[11].

Stress echocardiography in patients with arterial hypertension

The accurate diagnosis of obstructive epicardial coronary artery disease in hypertensive patients is important since the prevalence of the disease is higher in this group than in normotensive patients. Senior et al. investigated the value of dobutamine stress echo in hypertensive patients without electrocardiographic evidence of left ventricular hypertrophy and/or basal ST-T changes[12]. The exercise electrocardiogram and the dobutamine echo results of 43 patients were compared with angiographically proven epicardial coronary artery disease. Sensitivity, specificity and positive and negative predictive values were significantly lower in the exercise electrocardiogram in comparison to dobutamine stress echo. Even when patients with echocardiographic signs of left ventricular hypertrophy were excluded, exercise electrocardiography was a poor predictor of coronary artery disease. In addition, the diagnostic accuracy of dipyridamole echocardiography was also markedly superior to exercise electrocardiography in patients with hypertension, and the accuracy of exercise echocardiography also exceeded that of exercise electrocardiography (85% vs 60%) in patients with left ventricular hypertrophy[10,13].

In conclusion, dobutamine, dipyridamole and exercise stress echocardiography are superior to exercise electrocardiography in the diagnosis of epicardial coronary artery disease in hypertensive patients or in patients with known or clinically suspected left ventricular hypertrophy. However, the small number of patients investigated so far is a major limitation and further studies are needed to confirm the promising results.

A subgroup with a high prevalence for hypertension and left ventricular hypertrophy are patients with end-stage renal disease. In these patients screening for coronary artery disease is an important aspect of preoperative risk evaluation and patient selection for transplantation. However, exercise testing in patients with end-stage renal disease is of limited value because many patients do not attain an adequate workload. Reis and coworkers evaluated the diagnostic accuracy of dobutamine stress echo in the detection of coronary artery disease and its usefulness for cardiac risk stratification in 97 patients[14]. Hypertension and diabetes mellitus were the most prevalent primary causes of renal failure. Due to the effects of long-term diabetes mellitus, many patients had either no or only atypical chest pain. In this subgroup of patients, dobutamine stress echo was an excellent test for the detection of coronary artery disease, with a sensitivity of 95%, a specificity of 86% and an accuracy of 90%[14,15]. In addition, during a mean follow-up period of 12 months, Reis et al. demonstrated that a normal dobutamine stress echo would identify a very low risk population for future cardiac events[14]. However, inducible ischaemia on dobutamine stress echo was a poor predictor of cardiac events in the follow-up period. Bates and coworkers recently published contradictory results[15]. They found that a positive dobutamine stress echo is a good predictor for cardiac events in patients with juvenile insulin-dependent diabetes mellitus who are being considered for kidney and or pancreas transplantation.

The results in patients with end-stage renal disease suggest that dobutamine stress echo accurately identifies patients with coronary artery disease. But a positive stress test is only moderately capable of predicting cardiac events, probably due to the rapid progression of the disease in these patients and the inability of any stress test to predict coronary plaque rupture.

Stress echocardiography in patients after heart transplantation

After heart transplantation, cardiac allograft vasculopathy is one of the leading causes of mortality and retransplantation. The presentation of the disease is often silent, resulting in delayed diagnosis. Therefore an ideal screening test for the heart transplantation population should focus on the detection of minimal coronary artery disease. Exercise electrocardiography and thallium scintigraphy have been reported to be disappointing or conflicting in the early detection of coronary artery disease after transplantation[16]. Today, coronary angiography or intravascular ultrasound imaging are the established techniques for the detection of cardiac allograft vasculopathy. However, because of its invasiveness these techniques are unattractive.
In recent years interest has grown in the use of stress echo for the assessment of patients with suspected cardiac allograft vasculopathy. High-dose dipyridamole echocardiography was found to have little value in the detection of the early stages of cardiac allograft vasculopathy, but may identify severe coronary artery disease after transplantation.\(^1\) Studies using dobutamine stress echocardiography showed contradictory results in heart transplant recipients\(^{18-21}\). One explanation for the controversial results might be the diffuse nature of the disease in the early stage with angiographic lesions less than 50%. All echocardiographic stress tests were designed to detect lesions of more than 50% and theoretically it can be concluded that there is no indication for stress echocardiography in the detection of minimal coronary disease. In addition, the diffuse nature of the disease could result in a balanced ischaemia in severe cardiac allograft vasculopathy with no regional differences in contractility. On this assumption one would expect there to be a decrease in global left ventricular function on inotropic stimulation. However, Herregods and coworkers found no decrease in response in global left ventricular function to inotropic stimulation\(^{19}\).

Collings et al. from Stanford University performed exercise stress echo to detect cardiac allograft vasculopathy, whereas Akosah et al. and Derumeaux et al. examined the value of dobutamine stress echo\(^{18,21}\). In all these studies angiography was regarded as the definitive procedure in which a qualitative grading system was used with regard to local lesions more or less than 50% and the absence or presence of diffuse coronary irregularities (Fig. 3). Exercise stress echo could only identify an unacceptably low rate of patients with angiographic evidence of coronary artery disease (sensitivity 25%). However, dobutamine-induced wall motion abnormalities could be demonstrated in 86 or 95% of all patients with cardiac allograft vasculopathy\(^{18,21}\). The difference in sensitivity between exercise and dobutamine echo can partly be explained by the diminished increase in heart rate during physical exercise in patients after heart transplantation. In addition, the chronotropic response of the denervated heart to adrenergic stimulation is increased which may allow a more easily provable myocardial ischaemia.

Studies using dobutamine echo in the diagnosis of cardiac allograft vasculopathy showed contradictory results for specificity (55% and 91%) in the detection of allograft vasculopathy (Fig. 4). In other words, the dobutamine-induced wall motion abnormality is only a moderate predictor for the presence of angiographic coronary artery disease in these patients. There are two possible explanations for the high rate of false-positive results. First: we cannot differentiate between whether a dobutamine-induced wall motion abnormality is related to altered myocardial function due to an ongoing or past rejection episode, or to true ischaemia caused by impaired perfusion. Secondly, wall motion abnormalities in patients with a normal angiogram may represent not a false-positive echo result but rather a false-negative angiographic result. It is well known that pathological and intracoronary ultrasound studies have demonstrated that angiography underestimates the occurrence and extent of cardiac allograft vasculopathy\(^{23,24}\).

The Munich group performed a dobutamine stress echo in 50 patients after heart transplantation and compared the results with the presence of cardiac vasculopathy using angiography or intravascular ultrasound imaging as the gold standard (Drs Spes and Angermann, personal communication). There was no difference in sensitivity whether they used angiography or intravascular ultrasound imaging as the gold standard (Drs Spes and Angermann, personal communication). There was no difference in sensitivity whether they used angiography or intravascular ultrasound (83% vs 79%). However, there was a significant difference in specificities (angiography 56% and intravascular ultrasound 87%). In other words, there are fewer false-positive results for stress echocardiography in the detection of coronary artery disease after transplantation, if the results are compared with intraluminal ultrasound imaging rather than with angiography.
In conclusion, stress echocardiography is unsuitable for the early detection of cardiac allograft vasculopathy, but identifies patients with severe cardiac allograft vasculopathy. Dobutamine stress echo overestimates the incidence of angiographic evidence of cardiac allograft vasculopathy, which can partly be explained by the known angiographic underestimation of the extent of the disease. The optimal monitoring for this disease still requires the use of intracoronary ultrasonography.

References