Stress echocardiography – current status

ROXY SENIOR, JOHN CHAMBERS

Abstract

Stress echocardiography has a high diagnostic accuracy for the detection of coronary disease. It is as effective as myocardial perfusion imaging for the stratification of risk in patients with coronary disease and can detect myocardial hibernation after myocardial infarction or in heart failure.

Key words: stress echocardiography, coronary disease.

Br J Cardiol 2007;**14**:90–7

Introduction

In the UK there is still an emphasis on coronary anatomy as currently assessed using coronary angiography, although a high-grade coronary lesion, for example, may cause no myocardial ischaemia in the presence of extensive collateral vessels. Functional imaging to show the physiological effect of any coronary stenosis is therefore an important part of the investigation of patients with stable symptoms although it is still grossly underused in the UK. Current workforce documents[1] suggest that six stress studies per 1,000 population each year should be performed, yet the number of centres offering a full service remains limited. This review discusses the evidence for the effectiveness of stress echocardiography.

What is stress echocardiography?

The hallmark of myocardial ischaemia during stress echocardiography is the occurrence of reduced systolic wall thickening. This precedes chest pain and ST-T wave changes, which makes stress echocardiography more sensitive than exercise treadmill electrocardiogram (ECG) testing. Rest and stress images are interpreted for global and regional left ventricular size, shape and function (figure 1). Stress echocardiography can identify the site of coronary stenoses. The total amount of myocardium in jeopardy predicts risk and prolonged persistence of a systolic wall thickening abnormality may also identify severe coronary artery disease.[2] Stress echocardiography can also predict the presence of myocardial hibernation.

Department of Cardiovascular Medicine, Northwick Park Hospital, Watford Hospital, Harrow, Middlesex, HA1 3UJ.
Roxy Senior, Consultant Cardiologist and Director of Cardiac Research, Department of Cardiovascular Medicine, Guy's and St Thomas Hospitals, London
John Chambers, Consultant Cardiologist, Guy's and St Thomas' Hospitals
Correspondence to: Dr R Senior
(E-mail: roxy.senior@virgin.net)

Evidence that stress echocardiography is effective

Diagnosis of coronary artery disease

The sensitivities for the detection of coronary artery disease are 85%, 80% and 78% for exercise, dobutamine and dipyridamole stress echocardiography, respectively, with corresponding specificities of 77%, 86% and 91%, respectively.[3,4] Stress echo-cardiography can also identify multi-vessel disease,[5,6] which is important since such patients have a poor outcome, even in the presence of normal left ventricular function.

Risk stratification

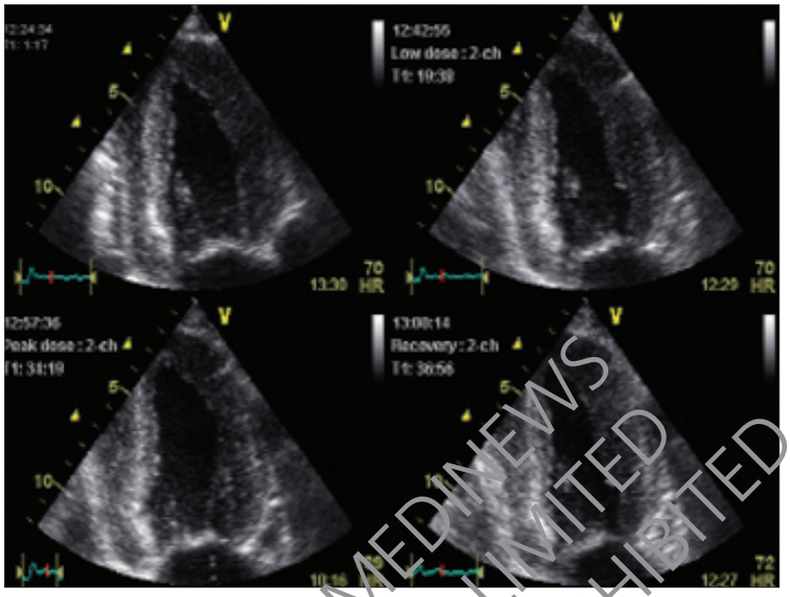
A normal stress echocardiograph gives an annual risk of 0.4–0.9% based on a total of 9,000 patients,[7-10] the same as for a normal stress myocardial perfusion scan.[11] This also holds true for patients with diabetes but the warranty period is less.[12] Thus, in patients with suspected coronary artery disease, a normal stress echocardiogram confers an excellent prognosis and coronary angiography can safely be avoided. By contrast, an abnormal stress echocardiogram is associated with a far higher risk of events, which is directly related to the extent of the wall motion abnormality in patients with[12] and without diabetes.[7]

In clinical practice, it is important whether a test provides incremental and independent information over and above clinical data. Information derived from exercise echocardiography[7] is incremental and independent of clinical data, Duke score and resting left ventricular function. In a study of 3,156 patients followed for nine years,[13] ischaemia and the extent of abnormal wall motion were independent predictors of cardiac death. Furthermore, the type of dobutamine response predicted outcome. Patients with resting left ventricular dysfunction and additional ischaemia had a worse outcome than those with ischaemia alone. In another study involving 7,333 patients[9] undergoing pharmacological stress echocardiography, an abnormal scan provided independent and incremental value over and above clinical data. In a subgroup of 4,037 patients who underwent coronary angiography without an intervention, the results of the coronary arteriogram did not add significant predictive power to the model.

Detection of hibernating myocardium

Hibernation implies myocardium which fails to contract normally but which may recover after revascularisation. It occurs in the presence of either repetitive stunning or a chronically sus-

Figure 1. Split-screen display of apical two-chamber views from a dobutamine stress echocardiogram. The images were recorded at end-systole at rest (below left), low-dose (below right), peak (bottom left) and recovery (bottom right). The apical and mid anterior segments are hypokinetic at peak. This is appreciated as a bulging of the left ventricle in these regions compared to the other panels



tained low level of blood flow, which is enough to repair 'wear and tear' but not enough to provide energy for contraction. It has been shown in non-randomised studies that revascularisation is effective in heart failure only in patients with hibernating myocardium.[14] The sensitivity and specificity of low-dose dobutamine echocardiography for predicting recovery of regional function following revascularisation is 84% and 81%, respectively, comparable to more expensive techniques (table 1).[15-17] Furthermore, revascularising myocardium designated as hibernating on dobutamine echocardiography improves survival.[16-19] Randomised trials are under way to address the relative benefit of revascularisation versus medical therapy in patients with hibernating myocardium.[20]

Table 1 Accuracy of imaging techniques for detection of myocardial viability

	N	Sensitivity (%)	Specificity (%)
^{18}F-FDG PET	332	88	73
^{201}TI reinjection	209	86	47
^{201}TI rest-redist	145	90	54
^{99m}TC MIBI	207	83	69
Dobutamine echo	448	84	81

Myocardial infarction

Despite thrombolysis, many patients are left with significant residual left ventricular dysfunction, either due to post-ischaemic stunning or myocardial necrosis. Post-ischaemic stunning implies a good prognosis as patients almost always recover left ventricular function in the absence of residual flow-limiting infarct-related artery stenosis. Echocardiography during low doses of dobutamine demonstrates increased contractility in these dysfunctional segments.

Several studies have confirmed the ability of dobutamine echocardiography to discriminate between stunned and necrotic myocardium after acute myocardial infarction[21,22] with similar sensitivity but higher specificity compared to radionuclide perfusion imaging.[11] Myocardial necrosis or a lack of dobutamine-induced contractile response is a more accurate marker of a poor prognosis[23] than angiography or clinical variables, with or without subsequent revascularisation.[24] Stress echocardiography can also stratify risk by demonstrating distant wall motion abnormalities implying multi-vessel disease.[23] Indeed, after revascularisation, the extent of non-viable myocardium[23,24] was the only predictor of cardiac events, while in the medically treated patients, both the extent of non-viable myocardium and stress echocardiographic indicators of non-viable myocardium and remote ischaemia were independent predictors of cardiac events.

Cost-effectiveness of stress echocardiography

Stress imaging has superior diagnostic and prognostic accuracy

Table 2 Risk stratification by exercise echocardiography and exercise electrocardiography

	Low risk	Intermediate risk	High risk
Exercise echocardiography	51%	27%	22%
Exercise electrocardiography	24%	51%	25%
p value	p<0.001	p<0.001	p=NS

to exercise electrocardiography, leading to fewer normal coronary angiograms and fewer coronary events. Thus, despite its higher initial cost, stress echocardiography is likely to be more cost-effective than exercise electrocardiography.

Marwick *et al*.[25] studied 7,656 patients undergoing exercise testing of whom half underwent stress echocardiography. Compared to exercise electrocardiography, stress echocardiography identified more patients as low risk and fewer as intermediate and high risk (table 2). Survival was greater in low- and intermediate-risk and less in high-risk patients and was better classified by stress echocardiography than exercise electrocardiography. Although initial procedural costs were greater, exercise echocardiography was associated with a greater incremental life-expectation (0–2 years) and a lower cost of additional diagnostic procedures when compared with exercise electrocardiography. Exercise echocardiography was therefore more cost-effective (€ 2,615/life year saved) than exercise electrocardiography. The authors further concluded that patients with symptoms who need non-invasive evaluation are less likely to undergo coronary angiography and hence revascularisation if a stress echocardiogram is performed in preference to exercise electrocardiography.

Similar results were obtained in a study of patients presenting with chest pain to an emergency department in the UK[26] and in patients with asymptomatic diabetes mellitus.[27]

Comparison with other imaging techniques?

Radionuclide single-photon-emission tomography (SPECT) has a slightly higher sensitivity than stress echocardiography and a lower specificity. In a meta-analysis[28] based on 44 studies in patients without prior acute myocardial infarction or otherwise known ischaemic heart disease, stress echocardiography had a sensitivity of 85% (95% CI, 83–87%) with a specificity of 77% (95% CI, 74–80%), while SPECT had a sensitivity of 87% (95% CI, 86–88%) with a specificity of 64% (95% CI, 60–68%). In a study by Nagel *et al*.,[29] cardiac magnetic resonance was found to be superior to echocardiography for the diagnosis of coronary artery disease but only in patients with suboptimal echocardiography imaging. Limitations in image quality, undoubtedly a problem in the past, have been largely solved by harmonic imaging, tissue Doppler techniques and contrast microbubbles together with advances in digital imaging and display.[30-4]

Echocardiography machines are universally available and relatively inexpensive while magnetic resonance and SPECT are expensive. Echocardiography does not involve ionising radiation and has the important advantage of being portable so that it can be taken to patients in emergency departments or coronary care units. All techniques require training. In the case of stress echocardiography, a training set of 100 studies is usually recommended since there are significant problems in artefact and interpretation. For example, interpreting isolated basal inferior and septal wall abnormalities often leads to increased false-positive scans. The development of stress echocardiography, as for all cardiac imaging, is seriously limited by a dearth of adequately trained cardiologists. National workforce planning suggest the need for 11–15 echocardiography consultants per million population but it remains rare for a hospital to employ a specialist in echocardiography. Table 3 outlines the indications and contraindications of stress echocardiography.

Table 3 Indications and contraindications to stress echocardiography

Indications

- Prediction of coronary disease in patients unsuitable for exercise testing (e.g. resting electrocardiographic changes, unable to walk), or at low risk of coronary disease (e.g. women)
- After coronary angiography to assess functional significance of an equivocal lesion, usually to decide on the need for intervention
- Risk stratification in known coronary disease (e.g. after myocardial infarction)
- To assess adequacy of revascularisation (e.g. before non-cardiac surgery)
- To determine the presence of viability in apparently infarcted myocardium
- To assess valve disease e.g. aortic stenosis with impaired left ventricle, moderate aortic stenosis and non-specific symptoms, moderate mitral regurgitation but severe breathlessness

Contraindications

These are similar to the contraindications to exercise stress testing and are relative rather than absolute.

- Early after admission with acute coronary syndrome
- Severe aortic stenosis (except for low gradient, low flow aortic stenosis)
- Severe aortic stenosis (except for low gradient, low flow aortic stenosis)
- Hypertrophic obstructive cardiomyopathy
- Significant dysrhythmia (e.g. ventricular tachycardia, uncontrolled atrial fibrillation)
- Acute intercurrent illness including hypokalaemia, uncontrolled hypertension, deep vein thrombosis or pulmonary embolism

In addition, dipyridamole/adenosine stress is contraindicated in patients with asthma and adenosine stress is contraindicated in patients with untreated heart block

The future of stress echocardiography

Myocardial perfusion imaging using ultrasound contrast agents

Key messages

- The sensitivity for the prediction of coronary disease on angiography is around 85% with a 90% specificity
- The sensitivity of low-dose dobutamine echocardiography for predicting recovery of regional function following revascularisation is 84% with an 81% specificity
- A normal stress echocardiogram is associated with an annual risk of coronary events of 0.4–0.9%
- Coronary angiography in patients with stable symptoms does not improve stratification provided by stress echocardiography

now allows simultaneous assessment of both function and perfusion,[35-37] with an improvement in diagnostic accuracy for the detection of coronary disease.[38] Accuracy is highest when myocardial perfusion is quantified[39,40] and measurement of myocardial velocities using Doppler tissue imaging allows an objective and reproducible assessment of myocardial wall motion.[31] Three-dimensional imaging is also expected to improve the detection of abnormalities of phase or thickening.

Conclusions

Clinical evidence involving more than 30,000 patients in multiple controlled trials has established stress echocardiography as an accurate, cost-effective non-invasive tool not only for the diagnosis of coronary artery disease but also for risk stratifying patients with known or suspected coronary disease and for detecting myocardial hibernation after myocardial infarction or in heart failure. It allows early discharge from accident and emergency departments or from the ward after myocardial infarction.

Conflict of interest

None declared.

References

1. British Cardiovascular Society. Workforce document on non-invasive cadiac imaging 2005. www.bcs.com
2. Tsoukas A, Ikonomidis I, Cokkinos P, Nihoyannopoulos P. Significance of persistent left ventricular dysfunction during recovery after dobutamine stress echocardiography. *J Am Coll Cardiol* 1997;**30**:621-6.
3. Beleslin BD, Osojic M. Djordjevic-Dikie A *et al*. Integrated evaluation of relation between coronary lesion features and stress echocardiography results: the importance of coronary lesion morphology. *J Am Coll Cardiol* 1999;**33**:717-26.
4. Marwick TH. Stress echocardiography. *Heart* 2003;**89**:113-18.
5. Roger VL, Pellikka PA, Oh JK, Bailey KR, Tajik AJ. Identification of multivessel coronary artery disease by exercise echocardiography. *J Am Coll Cardiol* 1994;**24**:109-14.
6. Senior R, Khattar R, Lahiri A. Value of dobutamine stress echocardiog-

Continued on page 97

Continued from page 94

raphy for the detection of multivessel coronary artery disease. *J Am Coll Cardiol* 1998;**81**:298-301.
7. Marwick TH, Case C, Vasey C, Allen S, Short L, Thomas JD. Prediction of mortality by exercise echocardiography. A strategy for combination with the Duke treadmill score. *Circulation* 2001;**29**:2566-71.
8. McCully RB, Roger VL, Mahoney DW *et al*. Outcome after normal exercise echocardiography and predictors of subsequent cardiac events: follow-up of 1,325 patients. *J Am Coll Cardiol* 1998;**31**:144-9.
9. Sicari R, Pasanisi E, Venneri L *et al*. Stress echo results predict mortality: a large-scale multicenter prospective international study. *J Am Coll Cardiol* 2003;**41**:589-95.
10. Chung G, Krishnamani R, Senior R. Prognostic value of normal stress echocardiogram in patients with suspected coronary artery disease – a British general hospital experience. *Int J Cardiol* 2004;**94**:181-6.
11. Geleijnse ML, Elhendy A. Can stress echocardiography compete with perfusion scintigraphy in the detection of coronary artery disease and cardiac risk assessment? *Eur J Echocardiography* 2000;**1**:12-21.
12. Elhendy A, Arruda AM, Mahoney *et al*. Prognostic stratification of diabetic patients by exercise echocardiography. *J Am Coll Cardiol* 2001; **37**:1551-7.
13. Marwick TH, Case C, Sawada S *et al*. Prediction of mortality using dobutamine echocardiography. *J Am Coll Cardiol* 2001;**37**:754-60.
14. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. *J Am Coll Cardiol* 2002;**39**:1151-8.
15. Bax JJ, Wijns W, Cornel JH *et al*. Accuracy of currently available techniques for prediction of functional recovery after revascularisation in patients with left ventricular dysfunction due to chronic disease: comparison of pooled data. *J Am Coll Cardiol* 1997;**30**:1451-60.
16. Senior R, Kaul S, Lahiri A. Myocardial viability on echocardiography predicts long term survival after revascularisation in patients with ischaemic congestive heart failure. *J Am Coll Cardiol* 1999;**33**:1848-54.
17. Afridi I, Grayburn PA, Panza JA *et al*. Myocardial viability during dobutamine echocardiography predicts survival in patients with coronary artery disease and severe left ventricular dysfunction. *J Am Coll Cardiol* 1998;**32**:921-6.
18. Senior R, Lahiri A, Kaul S. Effect of revascularisation on left ventricular remodelling in patients with heart failure from severe chronic ischaemic left ventricular dysfunction. *Am J Cardiol* 2001;**88**:624-9.
19. Meluzin J, Cerny J, Frelich M *et al*. Prognostic value of the amount of dysfunctional but viable myocardium in revascularisatized patients with coronary artery disease and left ventricular dysfunction. *J Am Coll Cardiol* 1998;**32**:912-20.
20. Cleland JG, Freemantle N, Ball SG *et al*. The heart failure revascularisation trial (HEART): rationale, design and methodology. *Eur J Heart Fail* 2003;**5**:295-303.
21. Pierard L, De Landsheere CM, Berthe C, Rigo P, Kulbertus HE. Identification of viable myocardium by echocardiography during dobutamine infusion in patients with myocardial infarction after thrombolytic therapy: comparison with positron emission tomography. *J Am Coll Cardiol* 1990;**15**:1021-31.
22. Barilla F, Gheorghiade M, Alam M *et al*. Low dose dobutamine in patients with acute myocardial infarction identifies viable but not contractile myocardium and predicts the magnitude of improvement in wall motion abnormalities in response to coronary revascularisation. *Am Heart J* 1991;**122**:1522-31.
23. Carlos ME, Smart SC, Wynsen JC, Sagar KB. Dobutamine stress echocardiography for risk stratification after myocardial infarction. *Circulation* 1997;**95**:1402-10.
24. Swinburn J, Senior R. Extent of non-viability, not ischaemia, predicts mortality after myocardial infarction. *Heart* 2004;**90**(suppl II): A35.
25. Marwick TH, Shaw L, Case C *et al*. Clinical and economic impact of exercise electrocardiography and exercise echocardiography in clinical practice. *Eur Heart J* 2003;**24**:1153-63.
26. Jeetley P, Burden L, Senior R. Superior risk stratification by stress echocardiography compared with exercise electrocardiography in troponin negative acute chest pain – a prospective randomised trial. *Heart* 2004;**90** (suppl II):A33.
27. Hayashino Y, Nagata-Kobayashi S, Morimoto T, Maeda K, Shimbo T, Fukui T. Cost-effectiveness of screening for coronary artery disease in asymptomatic patients with type 2 diabetes and additional atherogenic risk factors. *J Gen Int Med* 2004;**19**:1181-91.
28. Fleischmann KE, Hunink MGM, Kuntz KM *et al*. Exercise echocardiography or exercise SPECT imaging? *JAMA* 1998;**280**:913-20.
29. Nagel E, Lehmkuhl HB, Bocksch W *et al*. Noninvasive diagnosis of ischemia-induced wall motion abnormalities with the use of high-dose dobutamine stress MRI: comparison with dobutamine stress echocardiography. *Circulation* 1999;**99**:763-70.
30. Hoffmann R, Marwick TH, Poldermans D *et al*. Refinements in stress echocardiographic techniques improve inter-institutional agreement in interpretation of dobutamine stress echocardiograms. *Eur Heart J* 2002;**23**:821-9.
31. Mälder CF, Payne N, Wilkenshoff U *et al*. Non-invasive diagnosis of coronary artery disease by quantitative stress echocardiography. *Eur Heart J* 2003;**24**:1584-94.
32. Rainbird AJ, Mulvagh SL, McCully OJK *et al*. Contrast dobutamine stress echocardiography: clinical practice assessment in 300 consecutive patients. *J Am Soc Echocardiogr* 2001;**14**:378-85.
33. Anand DV, Theodosiadis D, Senior R. Improved interpretation of dobutamine stress echocardiography following 4 months of systematic training inpatients following acute myocardial infarction. *Eur J Echocardiogr* 2004;**5**:12-17.
34. Nanda NC, Kitzman DW, Dittrich HC *et al*. Imagent improves endocardial border delineation, inter-reader agreement, and the accuracy of segmental wall motion assessment. *Echocardiography* 2003;**20**:151-61.
35. Porter TR, Xie F, Silver M *et al*. Real-time perfusion imaging with low mechanical index pulse inversion Doppler imaging. *J Am Coll Cardiol* 2001;**37**:748-53.
36. Shimoni S, Zoghbi WA, Xie F. Real-time assessment of myocardial perfusion and wall motion during bicycle and treadmill exercise echocardiography: comparison with single photon emission computed tomography. *J Am Coll Cardiol* 2001;**37**:741-7.
37. Senior R, Lepper W, Pasquet A *et al*. Myocardial perfusion assessment in patients with medium probability of coronary artery disease and no prior myocardial infarction: comparison of myocardial contrast echocardiography with 99mTc-SPECT. *Am Heart J* 2004;**147**:1100-05.
38. Moir S, Haluska BA, Jenkins C *et al*. Myocardial contrast stress echocardiography for the assessment of coronary artery disease: incremental benefit of qualitative and quantitative approaches. *Circulation* 2004;**110**: 1108-13.
39. Peltier M, Vancraeynest D, Pasquet A. Assessment of the physiologic significance of coronary disease with dipyridamole real-time myocardial contrast echocardiography. Comparison with technetium-99m sestamibi single-photon emission computed tomography and quantitative coronary angiography. *J Am Coll Cardiol* 2004;**43**:257-64.
40. Janardhanan R, Senior R. Accuracy of dipyridamole myocardial contrast echocardiography for the detection of residual stenosis of the infarct-related artery and multivessel disease early after acute myocardial infarction. *J Am Coll Cardiol* 2004;**16**:2247-52.