Eur J Echocardiography (2002) **3,** 171–176
doi:10.1053/euje.2002.0160, available online at http://www.idealibrary.com on IDEAL®

REVIEW PAPER

Quantitative Techniques for Stress Echocardiography: Dream or Reality?

T. H. Marwick

University of Queensland, Australia

Stress echocardiography is now an everyday clinical tool. However, the substantial evidence base that supports its use is largely derived from expert centres, and concerns have been expressed about the performance of the test in less expert hands. A unifying feature of the problems of stress echocardiography is its subjective assessment. This review examines the consequences of qualitative interpretation and the benefits of developing a quantitative approach. Although no quantitative approach is in widespread clinical use, several alternative techniques are feasible, and this area warrants further study.
(Eur J Echocardiography 2002; 3: 171–176)

Key Words: stress echocardiography; interpretation; quantitation.

Is Quantitation an Important Goal for Stress Echocardiography?

Stress echocardiography is already an established tool that is used on an everyday basis for clinical decision-making. In large studies, the technique has been shown to have an accuracy averaging 80–85%, and these results are comparable with data obtained using other stress-imaging approaches[1]. Stress echocardiography may be used to assess the physiologic effects of cardiac disease, including the significance of stenoses, the functional significance of valvular lesions, and to predict myocardial viability. Finally, stress echocardiography is a valuable test for defining prognosis in chronic CAD, after myocardial infarction and in the stratification of risk before major non-cardiac surgery[2–4].

Nonetheless, stress echocardiography has a number of limitations (Table 1). The reliability and feasibility of stress echocardiography are very dependent on image quality, although this is less of a problem than previously, as image quality has been improved by the introduction of harmonic imaging as well as contrast echocardiography. However, attention to detail in image acquisition remains critically important; studies are uninterpretable if the same imaging planes are not compared before and after stress if insufficient endocardial detail is recorded, or if the LV is insufficiently visualized. Patients with small LV cavities pose a particular problem for the technique[5], perhaps because of loading considerations or because of the smaller endocardial circumference over which a wall motion abnormality can be detected.

Address correspondence to: Prof. T. Marwick, University Department of Medicine, Princess Alexandra Hospital, Brisbane, Qld 4102, Australia. Tel: +61-7-3240-5346; Fax: +61-7-3240-5399; E-mail: tmarwick@medicine.pa.uq.edu.au

Table 1. Limitations of stress echocardiography.

- Dependence on image quality
- Influence of LV cavity size
- Subjective interpretation;
  - Need for specific training
  - Discordance between observers
  - Problems with application as a follow-up tool
- Limitations of an ischaemia-based technique;
  - Diagnosis of single vessel CAD
  - Recognition of multivessel CAD
  - Recognition of ischaemia within areas of abnormal resting wall motion

1525-2167/02/030171+06 $35.00/0

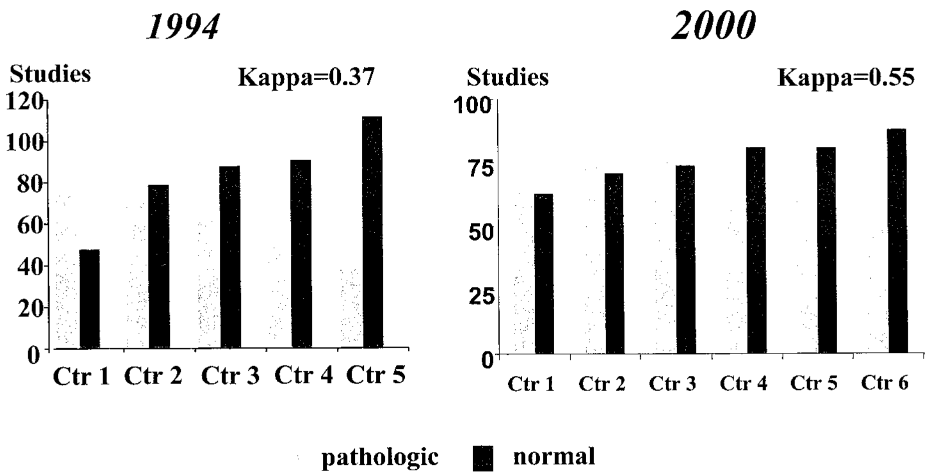

Figure 1. Number of positive and negative studies in a group of 150 studies interpreted by expert readers of stress echocardiograms in studies before (1994) and after (2000) the development of uniform reading criteria and technical advances including harmonic imaging[8,10].

A unifying feature of the problems of stress echocardiography is its subjective assessment. The development of regional dysfunction requires the presence of ischaemia, but mild ischaemia may be difficult to judge without a means of quantitation. The current subjective assessment may therefore pose a problem if tissue does not become sufficiently ischaemic to provoke clearly abnormal wall motion (e.g. insufficient stress), or the extent of ischaemia is small (e.g. mild single-vessel stenosis with collaterals or mild stenosis in the presence of a stenosis elsewhere causing limiting symptoms)[6]. Furthermore, if wall motion is abnormal at rest, the visual recognition of worsening wall motion may be difficult, posing problems for the distinction of ischaemia from scar[7].

However, the greatest problems with subjective assessment relate to the interpreter rather than the patient or ischaemic process. When the same studies are read by several experts, a significant proportion of interpretations are found to be discordant, especially when image quality is suboptimal, or when the extent of abnormality is small[8]. This problem has been reduced by the development of standard interpretive criteria, side-by-side digital display and improved imaging[9,10], but nonetheless remains as a significant issue (Fig. 1). To a large extent, it reflects the shortcomings of subjective evaluation of wall motion — each interpreter may have a different threshold for identifying wall motion as abnormal, and therefore read with various degrees of 'aggressiveness'. Finally, the use of subjective evaluation means that even proficient echocardiographers require special training in order to become expert in stress echocardiography[11] (Fig. 2). Many clinicians performing stress echocardiograms have not had the opportunity of significant training. Less expert interpreters may not achieve the same results as those of expert readers, which are recorded as the existing literature on stress echocardiography.

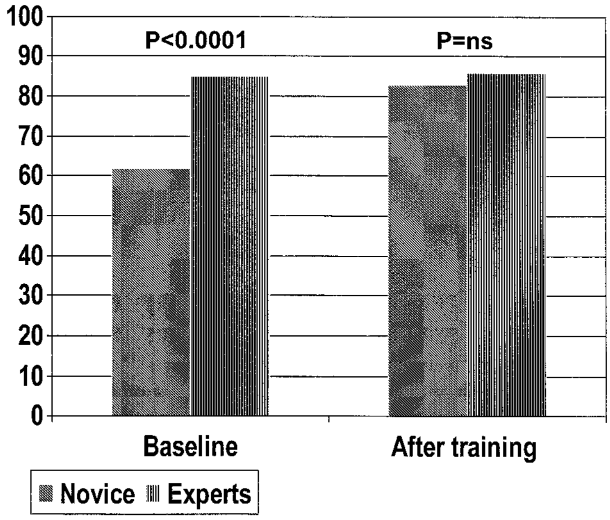

Figure 2. The importance of the learning curve to the correct interpretation of stress echocardiograms, illustrated in the performance of 'novice' and expert stress echocardiographers before and after a training period during which 100 studies were reviewed.

The development of a truly quantitative approach could overcome each of these limitations. A quantitative approach might be more sensitive than visual assessment. If a particular threshold of wall motion or velocity could be identified, there would be little opportunity for variation in interpretation between reviewers, and the difference between a highly trained and less highly trained observer would be reduced. However, such an approach would need to satisfy several criteria in order to be useful (Table 2).

Table 2. Criteria for a quantitative approach to stress echocardiography.

- Feasibility in most patients (i.e. not dependent on perfect image quality)
- Obtainable with minimal disruption/incremental time to standard imaging
- Limited increment in interpretation time
- Consistent between and within observers
- Limited test retest variation
- Definable normal range suitable for most candidates

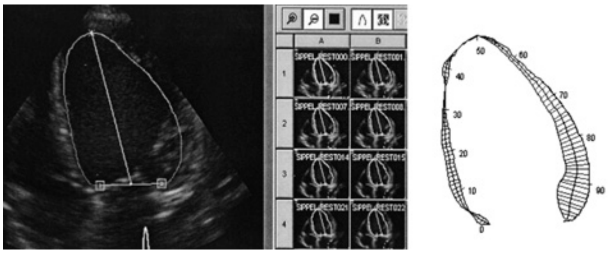

Figure 3. Automated edge-detection software may be used to outline the endocardial border (left frame), which can be stored for each frame (centre), and the distance between end-diastolic and end-systolic images may be measured using the centreline approach.

Approaches to Quantitation of Stress Echocardiography

Regional LV function may be quantified in either the radial (short axis) or longitudinal (base–apex) dimensions, using various tools (Table 3). In general, the process of quantifying regional function has proven to be very challenging, especially in combination with exercise echocardiography[12]. However, there are currently two approaches that appear feasible on a routine clinical basis — an approach that is based on measuring endocardial motion from two-dimensional images, and one that depends on measurement of myocardial velocity (or a derivative of this) using tissue Doppler.

Wall Motion Tracking and Measurement Techniques

The simplest means of gathering regional wall thickening data involves the use of M-mode ultrasound. Unfortunately, this technique is constrained by the limited numbers of segments and angle-dependence of standard M-mode imaging. Anatomic M-mode images can be reconstructed for high frame-rate 2D imaging[13], and circumvents the angle-dependence limitations, but the clinical benefit of this approach is not well defined.

The initial approaches to quantitation of regional function during 2D imaging were based on the centreline approach[12], initially developed for contrast ventriculography. While these studies generated quite favourable results, there are three major limitations to this approach during echocardiography. First, the technique is dependent on tracing the endocardial border, which is not always clearly visualized, and this process may be quite time-consuming. Second, the timing of systole and diastole are not necessarily homogeneous throughout the left ventricle, implying that high frame rates and tracing multiple frames may be necessary to define the extremes of excursion. Third, translational movement of the heart many influence the apparent excursion, and this may either produce false positive or false negatives interpretations, depending on the direction of motion of the heart relative to the ischaemic territory.

Several recent developments have alleviated some of these limitations. Image quality has been significantly improved by harmonic imaging, and can be improved further using contrast echocardiography. Sophisticated edge detection mechanisms have been developed which allow the endocardial border to be accurately traced with minimal guidance from the interpreter (Fig. 3). Acoustic quantification techniques use an alternative approach to optimizing the delineation of the border, based upon the difference in backscatter between blood and myocardium. This ‘color kinesis’ technique is based on colour coding of the magnitude and timing of endocardial motion, superimposed as a colour overlay on the two-dimensional echocardiographic image[14]. The magnitude and timing of regional endocardial excursion can be expressed by combining colour pixels in each segment as stacked histograms, and normal ranges have been defined (Fig. 4). Using these normal ranges, the diagnostic variability between echocardiographic interpretation of wall motion and automated interpretation was similar to that between interpretation of wall motion by two experienced readers[15].

Some clinical experience has been developed using colour kinesis during stress echocardiography. In a study of 20 patients, segmental analysis with colour kinesis correlated with wall motion abnormalities in 36

Table 3. Techniques for the quantitation of regional LV function.

	Radial	Longitudinal
Displacement	Standard M-mode	Annular M-mode tissue tracking
Thickening	Anatomical M-mode acoustic quantification	
Velocity	Velocity from displacement longitudinal velocity	Tissue Doppler velocity
Velocity gradient	Tissue Doppler gradient	Strain
Timing	Tissue Doppler	Tissue Doppler

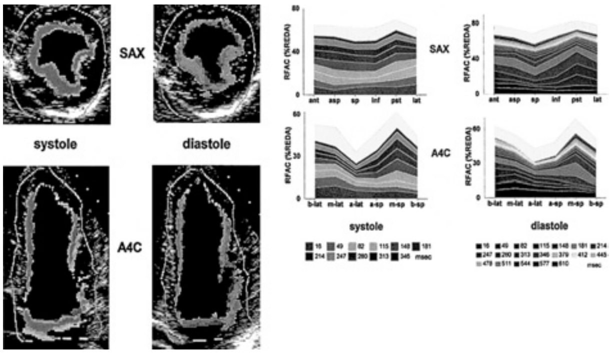

Figure 4. Colour kinesis images in a normal ventricle, showing colour outlining of each successive frame in the four-chamber view. Normal ranges of excursion have been developed and are expressed in the histogram on the right. Modified from reference [16].

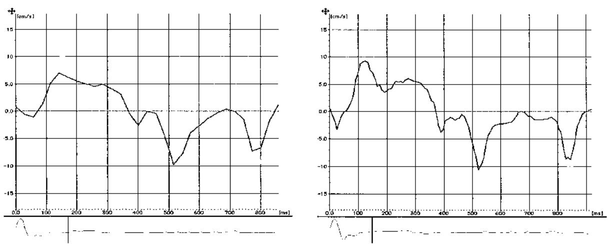

Figure 5. Tissue Doppler velocity spectra at low (35 frames/s) and high frame-rate (110 frames/s), showing the dependence of accurate peak systolic (S) and diastolic (E and A) wave velocity and timing measurements on a high sampling rate.

of 38 segments, and were found in the absence of abnormal wall motion in five of 322 segments[16]. Subsequent work[17] showed the automated colour kinesis approach correlated more closely with standard interpretation than did the interpretations of inexperienced reviewers. In a subgroup of 16 patients who underwent coronary angiography, the CK images differentiated between normal and abnormal wall motion more accurately than standard interpretation by experts (accuracy 93% vs 82%). However, measurements varied by 10–20% in the apical views, and adequate images were not obtainable in all patients. The dependence of this technique on very good image quality remains a significant limitation, which may be addressed by contrast echocardiography.

Tissue Doppler Approaches

Tissue Doppler is an extension of the Doppler principle, used widely to measure bloodflow, whereby modifications to Doppler sampling enable the quantification of tissue motion[18]. Myocardial Doppler may be used to measure velocity, timing, velocity gradients, and left ventricular strain, the latter two relating to differential velocity between different segments of tissue. Generally, the most feasible approach for combination with stress testing has been colour tissue Doppler, because data may be processed off-line, thus minimizing the disruption of the standard study. However, it is critically important that colour data are obtained at sufficient frame rate to enable accurate resolution of the different peaks of the velocity profile (Fig. 5). Tissue Doppler has two unique aspects — first, a high signal-to-noise ratio and second, the ability to interrogate the longitudinal (base–apex) function of the left ventricle, which has hitherto been largely ignored[19].

Both experimental and clinical studies have indicated that tissue velocity decreases in the presence of ischaemia[20,21]. The initial applications of tissue Doppler to stress echocardiography indicated that tissue velocity correlated with regional wall motion scoring[22]. The velocity of normal tissue generally doubles in response to maximal stress, while this velocity increment is blunted in ischaemic tissue. Scar tissue has a lower velocity at rest, and enjoys a small velocity increment, because of tethering of adjacent tissue. Because of variations in resting velocity, the most robust measurement has been the peak velocity at peak stress. Subsequent studies showed that tissue velocity correlated with independent markers of ischaemia such as SPECT myocardial perfusion imaging[23].

Recent work has focused on the application of tissue Doppler techniques to the diagnosis of coronary disease, using simple velocity cutoffs or more sophisticated modelling approaches. The variation of velocity in the normal heart mandates the use of site-specific normal ranges[24]. Definition of normal velocities is difficult at rest because they are influenced by age, heart-rate and loading, at peak stress. However, most normal patients

Table 4. Comparison of studies of tissue Doppler with stress echocardiography.

Favourable	Unfavourable
Feasible	Works in most patients but not all
Supplement to wall motion scoring rather than replacement	Concordance mandates positioning sample volume in same location
Simple	Image quality problem
	Automated peak detection not robust yet
	Diagnosis of CAD, not ischaemia
	Apical velocities close to zero

develop similar velocities at peak stress, and only the extremes of age, haemodynamics and volumes exert important effects on normal velocities[25]. Thus, the application of velocity cut-offs to independent patient groups has shown a high sensitivity and specificity for the angiographic diagnosis of coronary disease, comparable to that attainable by an expert observer[26]. More importantly, an increment of accuracy can be obtained by use of these techniques by less expert readers[27]. The results of the European study are yet to be published, but preliminary presentations suggest that the accuracy of a more complex approach, taking into account age and stress variables, actually exceeds that of an expert interpreter.

Despite several advantages, tissue Doppler has a number of disadvantages (Table 4). The apex is relatively fixed and velocities are so low at this site that exogenous noise limits the feasibility of apical measurements. The current application of peak myocardial velocity to stress echocardiography is likely to be superseded by more sophisticated tissue Doppler techniques, including strain and strain-rate imaging[28]. The reason for this is that tissue Doppler measures velocity of a segment relative to the transducer, so that in addition to measuring muscle thickening, the results are influenced by translation and rotation of the heart, as well as tethering of adjacent segments. Thus, normal adjacent tissue may augment the velocity of ischaemic segments, while abnormal tissue may reduce the velocity of normal segments. Nonetheless, despite these limitations, the tissue Doppler approaches appear more feasible than alternative approaches to the quantitation of regional function — less dependent on good image quality, and with higher intra- and inter-observer reproducibility.

Conclusions

The difficulties posed by imaging the heart during tachycardia, image quality issues related to hyperventilation, and translational movement are among a number of obstacles limiting the ability to quantify stress echocardiography. Indeed, to paraphrase Boswell, what is remarkable about the progress made so far is not so much whether it is superior to standard interpretation, but that it has been achieved at all. However, given the shortcomings of the existing subjective approach, this field warrants further attention.

Acknowledgement

Supported in part by the National Health and Medical Research Council of Australia.

References

[1] Fleischmann KE, Hunink MG, Kuntz KM, Douglas PS. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. *JAMA* 1998; **280:** 913–920.

[2] Krivokapich J, Child JS, Walter DO, Garfinkel A. Prognostic value of dobutamine stress echocardiography in predicting cardiac events in patients with known or suspected coronary artery disease. *J Am Coll Cardiol* 1999; **33:** 708–716.

[3] Picano E, Lattanzi F, Sicari R *et al.* Role of stress echocardiography in risk stratification early after an acute myocardial infarction. EPIC (Echo Persantin International Cooperative) and EDIC (Echo Dobutamine International Cooperative) Study Groups. *Eur Heart J* 1997; **18** (Suppl D): D78–D85.

[4] Poldermans D, Arnese M, Fioretti PM *et al.* Sustained prognostic value of dobutamine stress echocardiography for late cardiac events after major noncardiac vascular surgery. *Circulation* 1997; **95:** 53–58.

[5] Smart SC, Knickelbine T, Malik F, Sagar KB. Dobutamine-atropine stress echocardiography for the detection of coronary artery disease in patients with left ventricular hypertrophy. Importance of chamber size and systolic wall stress. *Circulation* 2000; **101:** 258–263.

[6] O'Keefe JH, Jr., Barnhart CS, Bateman TM. Comparison of stress echocardiography and stress myocardial perfusion scintigraphy for diagnosing coronary artery disease and assessing its severity. *Am J Cardiol* 1995; **75:** 25D–34D.

[7] Quinones MA, Verani MS, Haichin RM, Mahmarian JJ, Suarez J, Zoghbi WA. Exercise echocardiography versus 201Tl single-photon emission computed tomography in evaluation of coronary artery disease. Analysis of 292 patients. *Circulation* 1992; **85:** 1026–1031.

[8] Hoffmann R, Lethen H, Marwick T *et al.* Analysis of interinstitutional observer agreement in interpretation of dobutamine stress echocardiograms. *J Am Coll Cardiol* 1996; **27:** 330–336.

[9] Hoffmann R, Lethen H, Marwick T *et al.* Standardized guidelines for the interpretation of dobutamine echocardiography reduce interinstitutional variance in interpretation. *Am J Cardiol* 1998; **82:** 1520–1524.

[10] Hoffmann R, Poldermans D, van der Meer P *et al.* The maturing of stress echocardiography: Improved intercentre agreement in interpretation of dobutamine stress echocardiograms using new techniques. *Eur Heart J* 2001 (in press).

[11] Picano E, Lattanzi F, Orlandini A, Marini C, L'Abbate A. Stress echocardiography and the human factor: the importance of being expert. *J Am Coll Cardiol* 1991; **17:** 666–669.

[12] Ginzton LE, Conant R, Brizendine M, Thigpen T, Laks MM. Quantitative analysis of segmental wall motion during maximal upright dynamic exercise: variability in normal adults. *Circulation* 1986; **73:** 268–275.

[13] Chan J, Wahi SCP, Marwick TH. Anatomical M-mode: A novel technique for the quantitative evaluation of regional wall motion analysis during stress echocardiography. *Int J Card Imaging* 2000; **16:** 247–255.

[14] Bednarz J, Vignon P, Mor-Avi VV *et al.* Color kinesis: principles of operation and technical guidelines. *Echocardiography* 1998; **15:** 21–34.

[15] Lang RM, Vignon P, Weinert L *et al.* Echocardiographic quantification of regional left ventricular wall motion with color kinesis. *Circulation* 1996; **93:** 1877–1885.

[16] Mor-Avi V, Vignon P, Koch R *et al.* Segmental analysis of color kinesis images: new method for quantification of the magnitude and timing of endocardial motion during left ventricular systole and diastole. *Circulation* 1997; **95:** 2082–2097.

[17] Koch R, Lang RM, Garcia MJ *et al.* Objective evaluation of regional left ventricular wall motion during dobutamine stress echocardiographic studies using segmental analysis of color kinesis images. *J Am Coll Cardiol* 1999; **34:** 409–419.

[18] Hatle L, Sutherland GR. Regional myocardial function — a new approach. *Eur Heart J* 2000; **21:** 1337–1357.

[19] Henein MY, Gibson DG. Long axis function in disease. *Heart* 1999; **81:** 229–231.

[20] Bach DS, Armstrong WF, Donovan CL, Muller DW. Quantitative Doppler tissue imaging for assessment of regional myocardial velocities during transient ischemia and reperfusion. *Am Heart J* 1996; **132:** 721–725.

[21] Gorcsan J, III, Strum DP, Mandarino WA, Pinsky MR. Color-coded tissue Doppler assessment of the effects of acute ischemia on regional left ventricular function: comparison with sonomicrometry. *J Am Soc Echocardiogr* 2001; **14:** 335–342.

[22] Pasquet A, Armstrong G, Beachler L, Lauer MS, Marwick TH. Analysis of segmental myocardial Doppler velocity as a quantitative adjunct to exercise echocardiography. *J Am Soc Echocardiogr* 1999; **12:** 901–912.

[23] Pasquet A, Armstrong G, Rimmerman CM, Marwick TH. Correlation of myocardial Doppler velocity response to exercise with independent evidence of myocardial ischemia by dual isotope single photon emission computed tomography. *Am J Cardiol* 2000; **85:** 536–542.

[24] Wilkenshoff UM, Sovany A, Wigstrom L *et al*. Regional mean systolic myocardial velocity estimation by real-time color Doppler myocardial imaging: a new technique for quantifying regional systolic function. *J Am Soc Echocardiogr* 1998; **11:** 682–692.

[25] Cain P, Napier S, Haluska B, Short L, Marwick TH. Influence of left ventricular size and hemodynamics on the systolic longitudinal myocardial Doppler velocity response to stress. *Am Heart J* 2002; **143:** 169–175.

[26] Cain P, Baglin T, Case C, Spicer D, Short L, Marwick TH. Application of tissue Doppler to interpretation of dobutamine echocardiography: comparison with quantitative coronary angiography. *Am J Cardiol* 2001; **87:** 525–531.

[27] Fathi RB, Cain P, Nakatani S, Yu H, Marwick TH. Effect of tissue Doppler on the accuracy of novice and expert interpreters of dobutamine echocardiography. *Am J Cardiol* 2001; **88:** 400–405.

[28] Pislaru C, Belohlavek M, Bae RY, Abraham TP, Greenleaf JF, Seward JB. Regional asynchrony during acute myocardial ischemia quantified by ultrasound strain rate imaging. *J Am Coll Cardiol* 2001; **37:** 1141–1148.