Stress Echocardiography: Recommendations for Performance and Interpretation of Stress Echocardiography

Stress Echocardiography Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography: William F. Armstrong, MD, Chair, Patricia A. Pellikka, MD, Thomas Ryan, MD, Linda Crouse, MD, and William A. Zoghbi, MD

Cardiovascular stress testing remains the mainstay of provocative evaluation for patients with known or suspected coronary artery disease. Stress echocardiography has become a valuable means of cardiovascular stress testing. It plays a crucial role in the initial detection of coronary disease, in determining prognosis, and in therapeutic decision making. The purpose of this document is to outline the recommended methodology for stress echocardiography with respect to personnel and equipment as well as the clinical use of this recently developed technique. Specific limitations will also be discussed. (J Am Soc Echocardiogr 1998;11:97-104.)

There are significant limitations to reliance on the symptomatic and electrocardiographic responses to cardiovascular stress. The rationale for stress echocardiography is that if a patient with coronary artery disease exercises or the cardiovascular system is otherwise stressed, ischemia will be induced in the region subtended by a critically stenosed coronary artery. This will be manifest as an abnormality of cardiac function, which can be detected with echocardiographic imaging. Various forms of imaging have been shown to enhance the clinical utility of cardiovascular stress testing. Echocardiographic imaging provides several distinct advantages compared to other imaging methods. These benefits include accurate tomographic imaging of virtually all myocardial regions, the absence of any associated risk, the versatility of the examination, and the relatively lower cost compared with competing technologies. It can be used in conjunction with multiple forms of cardiovascular stress (Table 1).

Table 1 Stress echocardiography: methods

Exercise	Treadmill
	Supine bicycle
	Upright bicycle
	Isometric**
Pharmacologic	Dipyridamole
	Adenosine
	Dobutamine
	Ergonovine†
	Arbutamine
Other	Atrial pacing - direct
	Atrial pacing - esophageal
	Cold pressor**
	Mental stress**
	Hyperventilation†

†For evaluation of suspected coronary vasospasm; **clinical utility uncertain.

METHODOLOGY

Imaging Techniques and Equipment

For the diagnosis of coronary artery disease, stress echocardiograms are performed in conjunction with two dimensional echocardiographic imaging. Doppler flow profiles, which reflect global parameters of either systolic or diastolic function, can be employed but are less useful clinically. Doppler stress echocardiography may be of clinical use in evaluating patients with valvular heart disease to determine valve gradients and areas or the degree of regurgitation with stress. Tricuspid insufficiency velocities can be used for calculation of right ventricular systolic pressure. Detection of stress-related increases in pulmonary artery pressures can provide valuable insights as to the physiological significance of a wide range of conditions including valvular disease, primary myocardial disease, pulmonary hypertension, and ischemic cardiomyopathy.

Required Equipment

Because analysis of wall motion abnormalities is difficult in the presence of poor quality images, it is essential that high-quality two-dimensional echocardiographic equipment be used to optimize visualization of the endocardial

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border. Use of digital frame grabbers and split or "quad-screen" displays allows side-by-side comparison of rest and stress images and is the current standard for performance of stress echocardiograms. These systems facilitate detection of subtle wall motion abnormalities and are recommended for all laboratories undertaking stress echocardiography.

When performing stress echocardiograms it is essential that practitioners record and capture multiple views to ensure visualization of left ventricular segments supplied by each of the three major coronary distributions. In the majority of cases this is most consistently accomplished through the recording and digitizing of the parasternal long and short axis and apical four- and two-chamber views. Subcostal, apical long-axis, or additional short-axis views can be substituted when necessary or when more appropriate for visualization of specific anatomy. Digital capture and replay can be performed at capture rates ranging from 17 to 100 msec intervals. For the majority of examinations, 50 msec intervals are recommended for capture and playback. However with HR >140 beats/min, acquisition may be enhanced with 33 msec capture intervals. The number of cells captured can vary from eight per cardiac cycle, which captures only systole, to capture of the entire cardiac cycle. No clinical advantage to either scheme has been demonstrated.

As with other forms of stress testing, standard electrocardiographic and blood pressure monitoring is also performed. This may provide ancillary diagnostic and prognostic information during exercise studies. Electrocardiographic monitoring has limited diagnostic value during pharmacologic stress.

Personnel Required

Stress echocardiography is one of the more difficult techniques employed in cardiac ultrasound laboratories, both from the standpoint of the sonographer and the physician-interpreter. It should be performed only in laboratories staffed by persons who have substantial experience in the evaluation of patients with ischemic heart disease and in analysis of wall motion abnormalities. The examination should be performed by a skilled sonographer on a patient who is monitored by appropriate medical personnel. The personnel requirements and the level of monitoring required will vary with local standards of care and the type of stress being employed. Interpretation of stress echocardiograms requires extensive experience in echocardiography and should be performed only by physicians with specific training in the technique. It is recommended that only echocardiographers with at least Level 2 training and specific additional training in stress echocardiography have responsibility for supervision and interpretation of stress echocardiograms. The levels of training required have recently been outlined by the ACC/AHA committee on training in cardiovascular disease and also by a subcommittee of the American Society of Echocardiography. In addition to Level 2 training, supervised overreading of at least 100 stress echocardiograms is required to attain the minimum level of competence for independent interpretation. The Committee on Physician Training and Education of the American Society of Echocardiography recommends that physicians interpret a minimum of 15 stress echocardiograms per month to maintain interpretational skills. It is recommended that sonographers perform a minimum of 10 stress echocardiograms per month to maintain an appropriate level of skill. These recommendations refer to routine stress echocardiograms for evaluation of coronary artery disease and not highly specialized studies such as evaluation of valvular disease or myocardial viability, for which substantially more experience and higher volumes may be required for maintenance of skills.

Exercise Echocardiography

The forms of exercise that have seen most widespread acceptance in conjunction with echocardiography have been either posttreadmill imaging or upright or supine bicycle ergometry. If echocardiography is combined with treadmill exercise, imaging takes place immediately prior to exercise and is repeated immediately following symptom-limited exercise. Because ischemia-induced wall motion abnormalities may resolve quickly, postexercise imaging should be accomplished within 60 to 90 seconds of termination of exercise. With appropriate training and experience, success rates in excess of 95% should be attained.

Alternatively, patients can be stressed with either supine or upright bicycle exercise. This has the advantage of allowing imaging at incremental levels of stress including peak exercise. While treadmill exercise echocardiography is terminated at traditional endpoints such as attainment of target heart rates and cardiovascular symptoms, bicycle exercise provides additional echocardiographic endpoints because it allows on-line visualization of wall motion. It is recommended that exercise echocardiography with on-line monitoring during bicycle stress be terminated at traditional endpoints as well as at the time of development of wall motion abnormalities corresponding to two or more coronary territories, or wall motion abnormalities associated with ventricular dilation and/or global reduction of systolic function. The application of these echocardiographic end-points may require the presence of a physician-echocardiographer to monitor the test. Supine and upright bicycle exercise appear to have equivalent degrees of accuracy. Supine bicycle ergometry has the specific advantage of allowing Doppler interrogation of mitral-, tricuspid-, and aortic-valve flows during exercise. While not specifically pertaining to the diagnosis of coronary disease, analysis of these flow profiles can provide valuable physiologic information regarding the severity of valvular lesions as well as evaluation of pulmonary hypertension.

Nonexercise Stress

Two-dimensional echocardiography combined with pharmacologic stress is useful in patients unable to exercise.

Graded dobutamine infusion (5 to 40 μg/kg/min in 3-minute stages) increases myocardial oxygen demand in a fashion analogous to staged exercise. Contractility, heart rate, and systolic blood pressure are all increased. An advantage of dobutamine is that it has a rapid onset and cessation of action, and its effects can be reversed by β blocker administration. In patients who have an "inadequate" heart rate response to dobutamine, atropine can be used to increase heart rate. Atropine should be used at the minimum effective dose (typically ≤1.0 mg) and administered in 0.25 mg increments every 60 seconds until the desired heart rate response is seen. The effect on accuracy is not fully established but appears beneficial.

During dobutamine echocardiography, images are typically recorded at baseline and in the final minute of each stage of infusion. Currently available digital imaging software is configured for capture of four different time points. It is recommended that baseline and peak images always be captured for digital comparison. Based on clinical necessity and laboratory preference the remaining two images may be a combination of low stress, intermediate stress, postatropine images or recovery images. Dobutamine stress echocardiography, like bicycle echocardiography, allows on-line monitoring of ventricular function. Termination of the test should occur at both traditional end-points and for development of major wall motion abnormalities with systolic dysfunction as described for bicycle exercise.

Regional redistribution of coronary blood flow can be achieved by infusion of dipyridamole or adenosine. Simultaneous two-dimensional echocardiography permits determination of regional wall motion abnormalities resulting from diminished flow distal to coronary stenoses. The currently recommended protocol for dipyridamole echocardiography includes continuous electrocardiographic and echocardiographic monitoring during a two-stage infusion. The first stage consists of 0.56 mg/kg dipyridamole over 4 minutes. Monitoring continues for 4 minutes. If there is no adverse effect, clinical or echocardiographic end-point occurs, and an additional 0.28 mg/kg is infused over 2 minutes. As with dobutamine, atropine can be used to increase heart rate. Typically, imaging is performed continuously, and if digital capturing is used, images are captured at baseline, at the termination of phase one, termination of phase two, and at recovery. As in the case of dobutamine, atropine can be added after the second stage to increase heart rate and improve sensitivity. Aminophylline (240 mg; IV) should be available for immediate use in case of an adverse dipyridamole-related event. Adenosine can be used in a similar manner and is typically infused at a maximum dose of 140 mg/kg/min during imaging.

Stress Doppler Techniques

Stress Doppler examinations should be tailored to specific clinical questions. Areas in which stress Doppler can provide incremental data required for decision making include patients with aortic stenosis and reduced left ventricular function, mitral stenosis with only moderate gradients, and patients with symptoms out of proportion to the documented severity of valvular disease at rest. Left ventricular volumes and ejection fraction as well as transvalvular pressure gradients can be followed during stress, and pulmonary artery pressures can be derived from the velocity of a tricuspid regurgitation jet at rest and with stress. The technique for stress Doppler can range from an evaluation of mitral valve gradients after limited exercise such as leg lifts to a formal approach with a recumbent bicycle and graded exercise protocols as are employed for coronary disease. It should be noted that direct evaluation of the degree of regurgitation may be problematic at high heart rates using color flow imaging. Determination of stenotic gradients across mitral, aortic, and dynamic obstructions can be accurately determined during stress using standard imaging windows.

The evaluation of patients with aortic stenosis requires specific attention to detail. Patients with symptomatic aortic stenosis who have clinically significant mean resting gradients (>50 mm Hg) should not be stressed unless specific overriding clinical concerns exist. Dobutamine stress echocardiography with calculation of ejection fraction, aortic valve gradient, area, and resistance may be valuable and provide critical clinical data in patients with marginally significant (typically ≤40 mm Hg peak) gradients at rest and concurrent left ventricular dysfunction. These studies may allow appropriate identification of patients with left ventricular dysfunction due to aortic stenosis and those with primary left ventricular dysfunction and coincidental, insignificant aortic stenosis.

Contraindications to Stress Echocardiography

While there are no contraindications or side effects associated with exercise echocardiography, other than those well known to be associated with physical exercise, pharmacologic stress echocardiography has the side effects and contraindications of the underlying pharmacologic stressor. It should be recognized that the "relative contraindications" such as hypertrophic cardiomyopathy or critical aortic stenosis are readily identified from the baseline echocardiogram and, as such, a built-in safeguard exists against the inappropriate stressing of patients with these entities. In clinical experience significant side effects with either dobutamine stress echocardiography or dipyridamole stress echocardiography have been infrequent and have been confined to transient arrhythmias and hemodynamic abnormalities that resolve rapidly after cessation of the infusion. Minor side effects of chest pain, headache, and nausea occur infrequently during dipyridamole infusion. Major complications of myocardial infarction, death and bronchospasm, have been rarely seen. Aminophylline infusion quickly terminates most of the reported side effects resulting from dipyridamole infusion. Because of its short half-life, adenosine-related adverse effects are short-lived.

There are several patient subsets in whom pharmacologic stress testing could be considered contraindicated. This would include patients with high-grade heart block or severe obstructive lung disease who are being considered for dipyridamole or adenosine echocardiography, and patients with unstable ventricular arrhythmias, who are being considered for dobutamine stress echocardiography. Persons with unstable ischemic syndromes or those who require intravenous nitrates for control of pain probably are

Table 2 Classification and clinical implications of stress echo responses

		Rest	Stress	Implication	Clinical situation
I	Normal	Normal	Hyperdynamic	no CAD, no ischemia	normal subject without CAD
II	Ischemic	Normal	Abnormal	CAD present, ischemia induced	CAD, no prior MI
III	Fixed	Abnormal	Stable	CAD present, no inducible ischemia	prior MI, single-vessel disease
IV	Mixed	Abnormal	New additional abnormality	CAD present, additional areas are ischemic	prior MI, multivessel disease

not candidates for any form of stress testing, pharmacologic or otherwise, whether monitored with echocardiographic techniques or radionuclide imaging.

Analysis Techniques

The manner in which stress echocardiograms are analyzed is dependent on prevailing local preferences and the need for detailed investigational data versus clinical data. Stress echocardiograms can be analyzed on several planes of complexity, which range from a qualitative assessment of segmental wall motion in response to stress to highly detailed schemes for quantitative analysis. The algorithm commonly used for detection of ischemia is shown in Table 2. For greater accuracy, a segmental evaluation of wall motion using the 16-segment model is recommended. Classification of wall motion as normal, hyperdynamic, hypokinetic, akinetic, or dyskinetic should be based on an evaluation of endocardial motion and degree of wall thickening. It is recommended that segmental wall motion be assessed using the 16-segment model recommended by the ASE. Calculation of a wall motion score provides a semiquantitative approach which facilitates serial comparison. In addition to an assessment of wall motion abnormalities, the effects of stress on cardiac chamber sizes and overall systolic function can be evaluated by calculation of ventricular volumes and ejection fraction.

Characterization of stress echocardiograms into strata of abnormality is feasible and may provide prognostic information. This can be accomplished using a comparison of the rest and stress images as outlined in Table 2. Calculation of wall motion scores is recommended for studies which are part of serial follow-up, before and after interventions, as part of prognostic evaluations prior to noncardiac surgery, and as part of risk stratification following myocardial infarction. Calculation of chamber volumes and ejection fraction is recommended when stress echocardiography is performed in patients with concurrent valvular heart disease or cardiomyopathy and for all patients in whom a component of congestive heart failure is suspected. Calculation of diastolic and systolic volumes and ejection fraction may also be of incremental value in patients with suspected coronary artery disease but in whom no distinct regional wall motion abnormality is apparent.

There are several areas that remain problematic and for which a firm consensus regarding the implications of stress echocardiographic responses remains to be defined. These areas of controversy include the behavior of myocardial segments adjacent to baseline abnormal segments and the role that tethering can play in producing systolic abnormalities during stress. In addition, atypical responses such as paradoxical improvement from an abnormal baseline remain problematic.

ACCURACY (Tables 3 and 4)

The accuracy of stress echocardiographic techniques has been established in numerous laboratories; it is superior to that of exercise electrocardiography alone and equivalent to that obtained with radionuclide perfusion techniques. Accuracy is independent of patient age or gender. For the overall detection of patients with coronary artery disease, sensitivity ranges from 72% to 97% depending on lesion severity (i.e., percent diameter stenosis) and the extent of coronary artery disease. Specificity has ranged from 64% to 100%. Stress echocardiography adds independent and incremental information to clinical and exercise test variables for identifying multivessel coronary artery disease. As with other imaging methods, sensitivity is less for the detection of single-vessel disease and greater for detection of multivessel disease.

Whereas stress echocardiography is an accurate technique for identification of patients with coronary disease, it is not essential for evaluation of all patients. Table 5 outlines different clinical situations in which routine treadmill, exercise echocardiography, or pharmacologic stress echocardiography are either preferred, optional, or not recommended. In individuals with typical symptoms and who have a normal resting electrocardiogram, routine treadmill exercise may suffice. In females most studies have suggested that exercise echocardiography is superior to standard exercise electrocardiography both in terms of sensitivity and specificity. For this reason, it may be preferred over routine treadmill exercise testing especially in female patients with atypical symptoms. When anatomic information is essential, as in the case of concurrent valvular disease, the combination of

Table 3 Accuracy of exercise echocardiography for detection of coronary artery disease

Author	Year	Stress type	Total* pts.	Sensitivity All	Sensitivity SV	Sensitivity MV	Specificity	No. MI	Sensitivity All	Sensitivity SV	Sensitivity MV
Limacher[1]	1983	TME	77	51/56 91%	7/11 64%	44/45 98%	15/17 88%	40	19/24 79%	3/7 43%	16/17 94%
Armstrong[4]	1987	TME	123	89/101 87%	34/42 81%	55/59 93%	19/22 86%	73	40/51 78%	21/29 72%	19/22 86%
Crouse[6]	1991	TME	228	167/172 97%	61/66 92%	106/106 100%	34/53 64%				
Marwick[7]	1992	TME	179[A]	96/114 84%	46/60 77%	50/54 93%	58/65[A] 89%	124	47/59 80%	23/34 68%	24/25 96%
Quinones[8]	1992	TME	112	64/85 75%	24/41 58%	40/45 89%	23/26 88%				
Sawada[5]	1989	TME UBE	57[B]	24/28 86%	15/17 88%	9/11 82%	25/29 86%				
Hecht[10]	1993	SBE	180	128/137 93%	46/55 84%	82/82 100%	37/43 86%	 100	91/100 91%	 N/A	 N/A
Marangelli[27]	1994	TME	80	42/47 89%	13/17 76%	29/30 97%	30/33 91%	80	42/47 89%	13/17 76%	29/30 97%
Ryan[9]	1993	UBE	309	192/211 91%	73/85 86%	120/126 95%	76/98 78%	183	76/92 83%	34/46 74%	40/46 87%
Roger[11]	1994	TME	150	106/117 91%							

A, Includes, normal, noncatheterized patients; *B*, all women; *TME*, echocardiographic imaging posttreadmill exercise; *UBE*, upright bicycle ergometry; *SV*, single-vessel; *MV*, multivessel; *SBE*, supine bicycle ergometry; *number of patients in study with success rates 84%-100%.

Table 4 Accuracy of pharmacologic stress echocardiography for detection of coronary artery disease

Author	Year	Stress type	Total pts.	Sensitivity All	Sensitivity SV	Sensitivity MV	Specificity	No. MI	Sensitivity All	Sensitivity SV	Sensitivity MV
Picano[15]	1986	Dipy	103[A]	53/72[C] 74%	12/24 50%	41/48 85%	31/31[A] 100%				
Zoghbi[20]	1991	Ad	73	46/54[C] 85%	24/30 80%	22/24 92%	17/19 92%	 35	12/20 60%	3/9 33%	9/11 82%
Sawada[18]	1991	Dob	103	N/A	N/A	N/A	17/20 85%	55	31/35 89%	17/21 81%	14/14 100%
Marcovitz[21]	1992	Dob	141	105/109 96%	59/62 95%	36/37 97%	21/32 66%	53	26/30 87%		
Marwick E[23]	1993	Dob	217	102/142 72%	45/68 66%	57/74 77%	62/75 83%	217	102/142 72%	45/68 66%	57/74 77%

A, Includes, normal, noncatheterized patients; *B*, all women; *C*, CAD >70%; *TME*, echocardiographic imaging posttreadmill exercise; *UB*, upright bicycle ergometry; *SV*, single-vessel; *MV*, multivessel; *Dipy*, dipyridamole; *Dob*, dobutamine; *Ad*, adenosine.

exercise electrocardiography with exercise echocardiography is probably cost-effective and the preferred approach. For individuals incapable of exercise, substitution of pharmacologic stress is necessary. Because of the inadequate accuracy of electrocardiographic and symptomatic responses during pharmacologic stress, concurrent imaging is essential.

PROGNOSTIC IMPLICATIONS

In addition to the diagnosis of coronary artery disease, stress echocardiography has shown substantial value as a prognostic tool. Available data suggest a benign prognosis in patients following normal exercise echocardiography and an adverse prognosis of new inducible wall motion abnormalities in the convalescent period following myocardial infarction. Several studies have addressed the role of pharmacologic stress echocardiography for preoperative risk assessment prior to noncardiac surgery. Dobutamine stress echocardiography has been the most commonly employed methodology. These studies demonstrate a benign prognosis for individuals without inducible ischemia and a substantially higher event rate for individuals with inducible ischemia. The

Table 5 Clinical situations and recommended echocardiographic techniques

	Typical Chest Pain							
	NI EKG, can exercise	Abn EKG, can exercise	Cannot exercise	Atypical Sx	Preop risk	Viability	Suspected PHT 1° or secondary	Valvular disease
Routine TME	P	NR	NR	NR	O	NR	NR	NR
Exercise echo	O	P	NR	P	O	NR	P	P
Pharmacologic stress echo	NR	NR	P	O	P	P	O	O
Stress Doppler	NR	NR	NR	NR	NR	NR	P	P

NR, Not recommended; *P,* preferred; *O,* optional.

prognostic power of dobutamine stress echocardiography is equivalent to or exceeds that reported with dipyridamole thallium scintigraphy for preoperative risk assessment.

Several new applications and observations have also been proposed for stress echocardiography. The one most actively investigated at this time is an assessment of myocardial viability in patients with chronic ischemic syndromes. Numerous studies have demonstrated that by using the response of the myocardium to low-dose dobutamine stimulation, prediction of eventual recovery of function can be obtained with a degree of accuracy equivalent to that seen with positron emission tomography.

CONCLUSIONS

Stress echocardiography is an accurate, versatile, and clinically valuable technique for evaluating patients with known or suspected ischemic heart disease. It is accurate for detection of both patients with coronary disease and individual stenoses. In experienced hands, accuracy is equivalent to that of more established radionuclide techniques. Recent developments in the field suggest a promising role for assessment of prognosis and myocardial viability.

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