

GUIDELINES AND STANDARDS

American Society of Echocardiography Recommendations for Performance, Interpretation, and Application of Stress Echocardiography

Patricia A. Pellikka, MD, Sherif F. Nagueh, MD, Abdou A. Elhendy, MD, PhD,
Cathryn A. Kuehl, RDCS, and Stephen G. Sawada, MD, Rochester, Minnesota; Houston,
Texas; Marshfield, Wisconsin; and Indianapolis, Indiana

TABLE OF CONTENTS

Methodology.....	1021
Imaging Equipment and Technique.....	1021
Stress Testing Methods.....	1022
Training Requirements and Maintenance of Competency.....	1023
Image Interpretation.....	1024
Table 1. Normal and Ischemic Responses for Various Modalities of Stress.....	1025
Quantitative Analysis Methods.....	1025
Accuracy.....	1026
False-negative Studies.....	1026
False-positive Studies.....	1027
Assessment of Myocardial Viability.....	1027
Assessment of Patients With Dyspnea, Pulmonary Hypertension, and Valvular Heart Disease.....	1028
Dyspnea.....	1028
Pulmonary Hypertension.....	1029
Mitral Valve Disease.....	1029
Aortic Valve Disease.....	1029
Evaluation of Prosthetic Valves.....	1030
Stress Echocardiography for Risk Stratification.....	1030
Table 2. Summary of Studies Evaluating the Value of Stress Echocardiography in Predicting Outcome.....	1031
Table 3. Stress Echocardiography Predictors of Risk.....	1032
Women.....	1032
After Acute Myocardial Infarction.....	1032
Elderly.....	1033
Patients With Diabetes Mellitus.....	1033
Before Noncardiac Surgery.....	1033
After Coronary Revascularization.....	1033
Patients With Angina.....	1033
Comparison With Radionuclide Imaging.....	1033
Recent and Future Developments.....	1034
Strain and Strain Rate Echocardiography.....	1034
Three-Dimensional Echocardiography.....	1034
Myocardial Contrast Perfusion Imaging.....	1034
Summary.....	1034
References.....	1034

Advances since the 1998 publication of the Recommendations for Performance and Interpretation of Stress Echocardiography¹ include improvements in imaging equipment, refinements in stress testing protocols and standards for image interpretation, and important progress toward quantitative analysis. Moreover, the roles of stress echocardiography for cardiac risk stratification and for assessment of myocardial viability are now well documented. Specific recommendations and main points are identified in bold.

METHODOLOGY

Imaging Equipment and Technique

Digital acquisition of images has evolved from the days of stand-alone computers that digitized analog video signals to the current era in which ultrasound systems have direct digital output.² This has resulted in significant improvements in image quality. Many ultrasound systems have software to permit acquisition and side-by-side display of baseline and stress images. However, transfer of images to a computer workstation for offline analysis is preferred as the ultrasound equipment can be continuously used for imaging. Network systems with large archiving capacity allow retrieval of serial stress examinations. Digital image acquisition permits review of multiple cardiac cycles with stress, which maximizes accuracy of interpretation. Videotape recordings are recommended as a backup.

Advances in imaging technology have improved endocardial border visualization and increased the

From the ^aDivision of Cardiovascular Diseases and Internal Medicine, Mayo Clinic and Foundation; ^bMethodist DeBakey Heart Center, Houston (S.F.N.); ^cMarshfield Clinic (A.A.E.); and ^dIndiana University School of Medicine (S.G.S.).

Reprint requests: Patricia A. Pellikka, MD, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (E-mail: pellikka.patricia@mayo.edu).

0894-7317/\$32.00

Copyright 2007 by the American Society of Echocardiography.

doi:10.1016/j.echo.2007.07.003

feasibility of imaging. **Tissue harmonic imaging should be used for stress echocardiography imaging.** This reduces near-field artifact, improves resolution, enhances myocardial signals, and is superior to fundamental imaging for endocardial border visualization.³ The improvement in endocardial visualization achieved with harmonic imaging has decreased interobserver variability and improved the sensitivity of stress echocardiography.^{4,5}

The availability of intravenous contrast agents for left ventricular (LV) opacification represents another advance. When used in conjunction with harmonic imaging, contrast agents increase the number of interpretable LV wall segments, improve the accuracy of less experienced readers, enhance diagnostic confidence, and reduce the need for additional noninvasive tests because of equivocal noncontrast stress examinations.^{6,9} Opacification of the LV cavity with contrast agents also improves the potential for quantitative assessment of studies. **Contrast should be used when two or more segments are not well visualized.** With experience and well-defined protocols, contrast stress echocardiography has been shown to be time-efficient.¹⁰

The baseline echocardiogram performed at the time of stress echocardiography should include a screening assessment of ventricular function, chamber sizes, wall-motion thicknesses, aortic root, and valves unless this assessment has already been performed. This examination permits recognition of causes of cardiac symptoms in addition to ischemic heart disease, including pericardial effusion, hypertrophic cardiomyopathy, aortic dissection, and valvular heart disease.

Stress Testing Methods

Exercise stress testing. For patients who are capable of performing an exercise test, exercise stress rather than pharmacologic stress is recommended, as the exercise capacity is an important predictor of outcome. Either treadmill or bicycle exercise may be used for exercise stress. Symptom-limited exercise according to a standardized protocol in which the workload is gradually increased in stages is recommended. The Bruce protocol is most commonly used for treadmill exercise echocardiography and the expected exercise level for a given age and sex can be expressed as functional aerobic capacity.¹¹ Imaging is performed at rest and immediately after completion of exercise.¹² Bicycle stress echocardiography can be performed with either supine or upright ergometry; an advantage is that imaging can be performed during exercise. With a commonly used supine bicycle protocol, imaging is performed at baseline, at an initial workload of 25

W, at peak stress, and in recovery. The workload is increased at increments of 25 W every 2 or 3 minutes.¹³ A higher initial workload may be appropriate for a younger patient.

Both types of exercise examinations provide valuable information for detection of ischemic heart disease and assessment of valvular heart disease. The workload and maximum heart rate achieved tend to be higher with treadmill exercise; exercise blood pressure is higher with supine bicycle exercise. If assessment of regional wall motion is the only objective, treadmill exercise is usually used. If additional Doppler information is desired, bicycle exercise offers the advantage that Doppler information, in addition to assessment of regional wall motion, can be evaluated during exercise.¹⁴

Pharmacologic stress testing. In patients who cannot exercise, dobutamine and vasodilator stress are alternatives. **Although vasodilators may have advantages for assessment of myocardial perfusion, dobutamine is preferred when the test is based on assessment of regional wall motion. A graded dobutamine infusion starting at 5 $\mu\text{g}/\text{kg}/\text{min}$ and increasing at 3-minute intervals to 10, 20, 30, and 40 $\mu\text{g}/\text{kg}/\text{min}$ is the standard for dobutamine stress testing.**^{15,16} **The inclusion of low-dose stages facilitates recognition of viability and ischemia in segments with abnormal function at rest, even if viability assessment is not the main objective of the test.** End points are achievement of target heart rate (defined as 85% of the age-predicted maximum heart rate), new or worsening wall-motion abnormalities of moderate degree, significant arrhythmias, hypotension, severe hypertension, and intolerable symptoms. **Atropine, in divided doses of 0.25 to 0.5 mg to a total of 2.0 mg, should be used as needed to achieve target heart rate.** Atropine increases the sensitivity of dobutamine echocardiography in patients receiving beta-blockers and in those with single-vessel disease.¹⁷ The minimum cumulative dose needed to achieve the desired heart rate effect should be used to avoid the rare complication of central nervous system toxicity. Protocols using atropine in early stages of the test, and accelerated dobutamine administration, have been shown to be safe and to reduce infusion times.^{18,19} Patients given atropine at the 30- $\mu\text{g}/\text{kg}/\text{min}$ stage reached target heart rate more quickly using lower doses of dobutamine and with fewer side effects. A beta-blocker may be administered to reverse the side effects of dobutamine.²⁰ Administration of beta-blockers at peak stress or during recovery may increase test sensitivity.²¹

Both dobutamine and exercise echocardiography result in a marked increase of heart rate. The increment in systolic blood pressure is much less with dobutamine compared with exercise. For both

techniques, the induction of ischemia is related to an increase in myocardial oxygen demand. Among patients with normal dobutamine stress echocardiography results, the subgroup in whom target heart rate is not achieved has a higher cardiac event rate.²² Achievement of target rate is an important goal of testing and consideration should be given to holding beta-blocker therapy on the day of testing until after the test. However, in a patient with known coronary artery disease (CAD), continuation of beta-blocker therapy may be preferred, depending on the clinical objectives of the test, which may include assessing adequacy of therapy. Side effects (palpitations, nausea, headache, chills, urinary urgency, and anxiety) are usually well tolerated, without the need for test termination. The most common cardiovascular side effects are angina, hypotension, and cardiac arrhythmias. Severe, symptomatic hypotension necessitating test termination occurs only rarely. Frequent premature atrial or ventricular contractions occur in about 10% of patients and supraventricular or ventricular tachycardias each occur in about 4% of patients. Ventricular tachycardias are usually non-sustained and more frequently encountered in patients with a history of ventricular arrhythmias or baseline wall-motion abnormalities. On the basis of combined diagnostic and safety reports on dobutamine stress echocardiography, it is estimated that ventricular fibrillation or myocardial infarction occurs in 1 of 2000 studies. Dobutamine stress echocardiography can safely be performed in patients with LV dysfunction,²³ aortic²⁴ and cerebral²⁵ aneurysms, and implantable cardioverter defibrillators.²⁶ Dobutamine stress echocardiography can safely and efficiently be performed under supervision by registered nurses.²⁷

Vasodilator stress testing may be performed with adenosine or dipyridamole.²⁸ Atropine is routinely used with vasodilator stress to enhance test sensitivity. The addition of handgrip at peak infusion enhances sensitivity. Vasodilator stress echocardiography usually produces a mild to moderate increase in heart rate and a mild decrease in blood pressure. The safety of high-dose (up to 0.84 mg/kg over 10 minutes) dipyridamole echocardiography tests has been documented. Significant side effects and minor but limiting side effects occur in about 1%. Major adverse reactions have included cardiac asystole, myocardial infarction, and sustained ventricular tachycardia. Hypotension and/or bradycardia may occur, but can be treated with aminophylline.²⁹ The duration of action of adenosine is shorter than dipyridamole. Adenosine stress is used to assess myocardial perfusion with contrast echocardiography, but it has not been widely used as a clinical tool. Both adenosine and dipyridamole are contraindicated in patients with reactive airway obstruction or significant conduction defects.

Pacing stress testing. In patients with a permanent pacemaker, stress testing can be achieved by increasing the pacing rate until the target heart rate is reached. This technique can be used with or without dobutamine. Recent studies have shown a good accuracy of this technique in identifying CAD³⁰ and in predicting outcome.³¹

Transesophageal atrial pacing stress echocardiography is an efficient alternative for the detection of CAD in patients unable to exercise.³² The catheter may be placed orally or nasally after topical anesthesia. The cardiac pacing and recording catheter (housed in a 10F sheath) is advanced by having the patient swallow while in the left lateral decubitus position. Pacing is initiated at 10/min above the patient's baseline heart rate starting at the lowest current that provides stable atrial capture (approximately 10 mA). The pacing protocol consists of 2-minute stages with the paced heart rate being increased to levels of 85% and 100%, respectively, for prepeak and peak stress information.³³ Images are obtained at rest, the first stage, and prepeak and peak heart rate. Wenckebach second-degree heart block may occur, necessitating atropine administration. Termination of the stress test occurs with achievement of age-predicted maximal heart rate, new or worsening moderate regional wall-motion abnormalities, greater than 2-mm horizontal or downsloping S-T depression, or presence of intolerable symptoms, including moderate angina. The advantage of pacing is the rapid restoration of baseline conditions and heart rate on discontinuation of the atrial stimulus; this avoids a prolonged state of ischemia.³³ Side effects, except for mild atrial arrhythmogenicity, are uncommon.

Training Requirements and Maintenance of Competency

Interpretation of stress echocardiography 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-II training and specific additional training in stress echocardiography have responsibility for supervision and interpretation of stress echocardiograms. To achieve the minimum level of competence for independent interpretation, training should include interpretation of at least 100 stress echocardiograms under the supervision of an echocardiographer with level-III training and expertise in stress echocardiography.³⁴ To maintain competence, it is recommended that physicians interpret a minimum of 100 stress echocardiograms per year, in addition to participation in relevant continuing medical education. It is recommended that sonographers perform a minimum of 100 stress echocardiograms per year to maintain an appropriate level of skill.³⁵ These

recommendations refer to routine stress echocardiograms for evaluation of CAD and not highly specialized studies such as evaluation of valvular disease or myocardial viability, for which more experience and higher volumes may be required for maintenance of skills.

IMAGE INTERPRETATION

Visual assessment of endocardial excursion and wall thickening is used for analysis of stress echocardiograms. The 2005 American Society of Echocardiography (ASE) recommendations suggested that either a 16- or 17-segment model of the LV may be used.³⁶ The 17-segment model includes an "apical cap," a segment beyond the level that the LV cavity is seen. The 17-segment model is recommended if myocardial perfusion is evaluated or if echocardiography is compared with another imaging modality. **Function in each segment is graded at rest and with stress as normal or hyperdynamic, hypokinetic, akinetic, dyskinetic, or aneurysmal. Images from low or intermediate stages of dobutamine infusion or bicycle exercise should be compared with peak stress images to maximize the sensitivity for detection of coronary disease.**³⁷

The timing of wall motion and thickening should also be assessed. Ischemia delays both the onset of contraction and relaxation and slows the velocity of contraction in addition to decreasing the maximum amplitude of contraction. "Hypokinesis" can refer to delay in the velocity or onset of contraction ("tardokinesis") and reduction in the maximum amplitude of contraction. The routine use of digital technology enables assessment of abnormalities in the timing of contraction (asynchrony). Differences in the onset of contraction and relaxation of ischemic segments compared with normal segments may range from less than 50 to more than 100 milliseconds.^{38,39} The frame rates used in current ultrasound systems have the necessary temporal resolution to permit visual recognition of asynchrony by the trained observer.^{40,41} Although assessment of asynchrony is most accurate using a high temporal resolution technique such as M-mode echocardiography, incorporation of visual assessment of the timing of contraction contributes to improved interobserver agreement.⁴² Work stations used for analysis of stress echocardiograms enable the interpreter to compare the timing of segmental contraction on a frame-by-frame basis and allow the interpreter to limit review to early systole where ischemia-induced reduction in the speed of contraction may be best appreciated.^{43,44}

A normal stress echocardiogram result is defined as normal LV wall motion at rest and with stress. Resting wall-motion abnormalities, un-

changed with stress, are classified as "fixed" and most often represent regions of prior infarction. Patients with fixed wall-motion abnormalities and no inducible ischemia should not be considered as having a normal study result. **Abnormal study findings include those with fixed wall-motion abnormalities or new or worsening abnormalities indicative of ischemia. In addition to the evaluation of segmental function, the global LV response to stress should be assessed. Stress-induced changes in LV shape, cavity size, and global contractility have been shown to indicate the presence or absence of ischemia.**^{45,46}

Although evaluation of right ventricular (RV) systolic function is often omitted, RV free wall asynergy or lack of increase in tricuspid annular plane excursion during dobutamine stress are indicators of right coronary or multivessel disease.^{47,48}

The modality of stress and details of the stress test itself should be considered in the interpretation of normal and ischemic responses to stress. **The report must include not only the baseline and stress assessment of systolic function and segmental wall motion, but the protocol used, the exercise time or dose of pharmacologic agent used, the maximum heart rate achieved, whether the level of stress was adequate, the blood pressure response, the reason for test termination, any cardiac symptoms during the test, and electrocardiographic (ECG) changes or significant arrhythmias.** In the presence of similar extents of CAD, stress-induced decrease in ejection fraction (EF) or increase in end-systolic cavity size are more commonly seen with exercise than with dobutamine stress.⁴⁶ Table 1 lists several modalities of stress and the general responses of regional and global function that are seen in healthy individuals and in those with obstructive coronary disease.^{32,33,46,49-59} The responses are described for individuals with normal regional and global systolic function in the resting state. An interpretive scheme for those with resting regional wall-motion abnormalities is described in the section on myocardial viability.

With modalities in which imaging is performed at various stages of stress, such as dobutamine stress echocardiography or supine bicycle stress echocardiography, images from each stage of stress should be reviewed to determine the heart rate and stage at which ischemia first occurs. This information is useful in perioperative risk stratification,^{60,61} as ischemia occurring at a low heart rate identifies patients at highest risk of a perioperative event. Ischemic threshold, calculated as the heart rate at which ischemia first occurs, divided by 220 minus the patient's age, multiplied by 100, has been shown to

Table 1 Normal and ischemic responses for various modalities of stress

Stress method	Regional		Global	
	Normal response	Ischemic response	Normal response	Ischemic response
Treadmill	Postexercise increase in function compared with rest	Postexercise decrease in function compared with rest	Decrease in ESV, increase in EF	Increase in ESV, decrease in EF in multivessel or L main disease
Supine bicycle	Peak exercise increase in function compared with rest	Peak exercise decrease in function compared with rest	Decrease in ESV, increase in EF	Increase in ESV and decrease in EF in multivessel or L main disease
Dobutamine	Increase in function, velocity of contraction compared with rest and usually with low dose	Decrease in function, velocity of contraction compared with low dose; may be less compared with rest	Greater decrease in ESV, marked increase in EF	Often same as normal response; infrequently, ischemia produces decreased EF; cavity dilatation rarely occurs
Vasodilator	Increase in function compared with rest	Decrease in function compared with rest	Decrease in ESV, increase in EF	Often same as normal response; occasionally, ischemia produces decreased EF; cavity dilatation rarely occurs
Atrial pacing	No change or increase in function compared with rest	Decrease in function compared with rest	Decrease in ESV, no change in EF	No change or increase in ESV, decrease in EF

EF, Ejection fraction; ESV, end-systolic volume; L, left.

correlate with the number of stenosed vessels and with the EF response to exercise.⁶²

Quantitative Analysis Methods

Visual assessment of LV wall thickening and motion remains the standard method of interpretation of stress echocardiography but is subject to interobserver and interinstitutional variability.⁶³ Very good reproducibility has been demonstrated in a clinical setting by those with training and experience.^{64,65} Quantitative methods of analysis have been investigated in an effort to improve the reproducibility of interpretation and enhance detection of coronary disease, particularly by less experienced physicians.

Doppler assessment of global systolic and diastolic function, automated endocardial border detection using integrated backscatter, tissue Doppler assessment of displacement, velocity, strain, and strain rate have shown promise as clinically useful, quantitative methods for detection of ischemia. Doppler assessment of global diastolic function by analysis of mitral inflow patterns is difficult at high heart rates achieved during stress; assessment of aortic systolic flow during stress lacks sensitivity.

The use of integrated backscatter to identify the blood-endocardial interface is promising as an automated method for detection of ischemia during dobutamine stress. Using this technique, in which

border detection may be enhanced by contrast opacification of the ventricular cavity, endocardial motion in successive frames throughout the cardiac cycle can be color encoded to permit assessment of the timing and location of regional abnormalities in systolic and diastolic function.^{66,67}

Doppler tissue imaging enables assessment of high amplitude, low velocity signals from myocardium. Tissue velocities are assessed along the long axis of the heart using apical views. Displacement, strain, and strain rate can be derived from assessment of tissue velocities. Tissue velocity imaging with dobutamine stress has shown comparable accuracy with wall-motion assessment by experts in both single and multicenter trials.^{68,69} Tissue velocity imaging also improves the reproducibility and accuracy of less experienced readers.⁷⁰ Because of the normal base to apex gradient in velocities, detection of coronary disease requires derivation of normal values for different myocardial segments. Strain (measuring myocardial shortening or lengthening) and strain rate (measuring the rate of shortening or lengthening) provide better assessment of myocardial contraction and relaxation than displacement or tissue velocities, which are more subject to tethering and translational motion. Postsystolic shortening, time to onset of regional relaxation, and reduction in peak systolic strain and strain rate have

been shown to be accurate markers of ischemia in experimental⁷¹ and early clinical⁷²⁻⁷⁵ studies.

Adequate quality 2-dimensional (2D) images are a prerequisite to successful quantitative analysis, even using Doppler-based techniques. Like all Doppler-derived parameters, tissue velocities, strain, and strain rate are influenced by the angle of interrogation so that off-axis apical images may result in calculation errors. Recently introduced 2D echocardiographic methods for assessment of strain and strain rate eliminate the angle dependency of these Doppler-based techniques.⁷⁶ In the future, quantitative methods may serve as an adjunct to expert visual assessment of wall motion. **The widespread use of quantitative methods will require further validation and simplification of analysis techniques.**

ACCURACY

The 1998 ASE document on stress echocardiography reported an average sensitivity of 88% (1265/1445) and average specificity of 83% (465/563) for stress echocardiography for the detection of coronary artery stenosis (generally >50% diameter stenosis by angiography), based on data pooled from available studies. Since then, additional studies evaluating the accuracy of stress echocardiography have been performed, often in comparison with alternative imaging modalities. **Studies comparing the accuracy of nuclear perfusion imaging and stress echocardiography in the same patient population have shown that the tests have similar sensitivities for the detection of CAD, but stress echocardiography has higher specificity.**⁷⁷⁻⁸¹ In a pooled analysis of 18 studies in 1304 patients who underwent exercise or pharmacologic stress echocardiography in conjunction with thallium or technetium-labeled radioisotope imaging, sensitivity and specificity were 80% and 86% for echocardiography. Corresponding values were 84% and 77% for myocardial perfusion imaging, respectively.⁷⁹

In the current era, the specificity of all noninvasive imaging tests will be reduced by test verification bias.⁸² A diminishing number of patients with normal or negative noninvasive examinations are subjected to angiography leading to reduction in the apparent specificity of the noninvasive method when angiography is used as the reference standard. **The comparatively high specificity of stress echocardiography contributes to its use as a cost-effective diagnostic method, particularly in populations in which alternative stress testing methods have higher false-positive rates.**

False-negative Studies

With few exceptions, the causes of false-negative studies are not unique to stress echocardiography

but are also seen with other noninvasive methods. Suboptimal stress is a primary cause of false-negative studies.⁸³ An adequate level of stress is frequently defined as achievement of 85% or more of the patient's age-predicted maximal heart rate for exercise or dobutamine stress and/or a rate-pressure product of 20,000 or more for exercise testing. Although these thresholds are not well validated, the importance of increasing heart rate and rate-pressure product is well supported by the linear relationship between myocardial oxygen consumption and these hemodynamic parameters. Inadequate exercise capacity and the use of beta-blockers are two common causes of inadequate stress. Pharmacologic stress and atrial pacing are suggested alternatives in those who cannot exercise. Of the nonexercise methods, the highest heart rates and sensitivity may be achieved with atrial pacing.^{33,84} The use of atropine substantially enhances the sensitivity of dobutamine stress in the setting of beta-blockade¹⁷ and may be required to overcome Wenckebach heart block during atrial pacing.³²

The results of small comparative studies of treadmill and supine bicycle exercise echocardiography suggest that imaging during peak exercise may permit detection of ischemic wall-motion abnormalities in some cases when posttreadmill exercise imaging produces negative findings.^{85,86} However, workloads achieved are usually higher with treadmill exercise, partially offsetting the advantage of peak exercise imaging.

As with other forms of stress testing, false-negative stress echocardiographic examination results are also more common in patients with single-vessel disease or disease of the left circumflex artery because of the smaller amount of myocardium supplied.⁸⁷ Supine bicycle exercise test has higher sensitivity for detection of left circumflex disease.^{88,89} Routine use of apical long-axis views may also decrease false-negative study results in those with left circumflex disease.

Detection of ischemia is more difficult in patients with concentric remodeling, characterized by small LV cavity volume and increased relative wall thickness.⁹⁰ False-negative studies in patients with concentric remodeling may be more common with dobutamine stress than with other methods. The prominent global hyperkinesis and reduction of diastolic and systolic volumes that occur with dobutamine stress (Table 1) may make detection of isolated wall-motion abnormalities more challenging. In addition, in patients with concentric remodeling, dobutamine may lower wall stress and myocardial oxygen consumption, reducing the frequency of induction of ischemia.⁹¹ Finally, the hyperdynamic state accompanying significant aortic or mitral regurgitation may make detection of ischemia more difficult.⁹²

False-positive Studies

False-positive stress echocardiogram findings can be attributed to induction of ischemia in the absence of epicardial coronary obstruction, or to nonischemic causes of abnormal wall-motion responses to stress.⁹³ Abnormalities in regional function with stress can occur in the absence of epicardial coronary artery obstruction if myocardial perfusion reserve is inadequate to meet myocardial oxygen demand. Examples include global or regional LV dysfunction in the case of hypertensive response to stress⁹⁴ or apical hypokinesis or other wall-motion abnormalities in the case of hypertrophic cardiomyopathy with or without dynamic LV outflow tract obstruction.⁹⁵ Myocardial perfusion reserve can be reduced in cardiac disorders with microvascular involvement, including patients with LV hypertrophy, syndrome X, diabetes mellitus, myocarditis, and idiopathic cardiomyopathy. Epicardial coronary spasm may cause ischemia in the absence of fixed, obstructive disease; spasm has been reported with both exercise and dobutamine stress.

Wall-motion responses to exercise may be abnormal in patients with hypertension or underlying cardiomyopathy in the absence of ischemia. Exercise may result in worsening of regional and global systolic function in myopathic ventricles. Abnormal global responses to stress are common in patients with long-standing hypertension.^{96,97} The abnormal wall-motion response of some patients with long-standing hypertension may be a result of underlying cardiomyopathy even in the absence of LV hypertrophy or depression of resting systolic function.^{98,99}

The effects of tethering on the assessment of regional wall motion can lead to false-positive studies. The absence of radial motion of the mitral annulus can lead to a reduction in motion of adjacent basal inferior and basal inferoseptal segments by the tethering effect of the stationary annulus.⁹³ This effect can be more pronounced in patients with annulus calcification and previous mitral valve replacement.

Abnormal ventricular septal motion related to left bundle branch block, RV pacing, and post-open heart surgery can sometimes be confused with ischemia-induced abnormalities. In these situations, abnormal septal motion is usually present at rest. Difficulty in determining the presence of ischemia may occur if worsening of these abnormalities occurs during stress. Assessment of wall thickening and the recognition that ischemia-induced wall-motion abnormalities should follow a typical coronary distribution pattern may help to distinguish septal dyssynchrony from ischemia.¹⁰⁰⁻¹⁰² In addition, septal dyssynchrony may result in worsening of septal perfusion and wall thickening at high heart rates in the absence of coronary obstruction.

ASSESSMENT OF MYOCARDIAL VIABILITY

Stress echocardiography has emerged as an important modality for the assessment of patients with CAD and LV systolic dysfunction. Multicenter studies have shown worse outcome when viable myocardium was identified by stress echocardiography but the patient was not revascularized.^{103,104} Viable myocardium refers to reversible dysfunctional myocardium resulting from CAD. However, the determination of contractile reserve in patients with nonischemic cardiomyopathy can also provide useful information as to myocardial recovery of function¹⁰⁵ and likelihood of response to beta-blocker therapy.¹⁰⁶

Reversible myocardial dysfunction in the setting of chronic CAD has been referred to as "hibernating myocardium." Earlier descriptions of this entity emphasized the presence of a match between the decrease in myocardial perfusion and the presence of regional dysfunction. However, more recent studies have shown that contractility may be reduced despite the presence of normal or only moderately reduced myocardial perfusion at rest. This suggests that repetitive episodes of myocardial ischemia are a cause of chronic dysfunction. In myocardium with reduced perfusion at rest, structural and functional changes that can occur include interstitial fibrosis, glycogen accumulation, loss of contractile proteins, cellular remodeling, higher calcium sensitivity of myocyte contractility, and attenuation of beta-receptor signaling.¹⁰⁷⁻¹¹⁰ With delay in revascularization, these myocardial changes may progress to a more advanced stage with a lower likelihood of functional recovery.¹¹¹

Most stress echocardiography protocols are centered on the detection of contractile reserve and have used inotropic stimulation with dobutamine. However, other modalities of stress echocardiography have been applied, including exercise, postpremature ventricular contraction stimulation, enoximone, and low-dose dipyridamole.

In comparison with the assessment of viability using nuclear perfusion tracers or contract echocardiography, a lower extent of interstitial fibrosis and greater percentage of viable myocytes are needed for the detection of contractile reserve by dobutamine echocardiography.¹⁰⁷ This probably accounts for the higher sensitivity but lower specificity of myocardial perfusion imaging compared with dobutamine echocardiography in the detection of viable myocardium.

Both low- and high-dose protocols have been shown to be useful for detection of viability. Earlier studies examined low-dose dobutamine, whereas other investigators emphasized the importance of reaching at least 85% of target heart rate in an attempt to uncover the presence of ischemia. Wall thickness should be assessed on the resting echocardiographic images. Segments that are thinned (≤ 0.5 or 0.6 cm) and bright (likely a result of advanced fibrosis) rarely recov-

er.^{112,113} It is also useful to examine the mitral inflow pattern, particularly in patients who have received adequate medical therapy at the time of imaging. A pattern of restrictive LV filling is associated with few viable segments and a low likelihood of functional recovery after revascularization.¹¹⁴ Baseline imaging should include assessment for the presence of significant valvular disease that may alter surgical plans. After adequate baseline data have been obtained, dobutamine infusion is begun.

An initial infusion of dobutamine at 2.5 $\mu\text{g}/\text{kg}/\text{min}$, with gradual increase to 5, 7.5, 10, and 20 $\mu\text{g}/\text{kg}/\text{min}$, is frequently used.¹¹⁵ Because many of these patients have multivessel disease, moderate to severely depressed LV systolic function, and an arrhythmogenic substrate, vigilant monitoring is indicated. The absence of functional improvement in akinetic segments would then trigger termination of the test, because this response signifies a very low likelihood of functional recovery in these segments. The presence of worsening of function in hypokinetic segments should likewise trigger termination of the infusion. Alternatively, functional improvement in the absence of untoward side effects would lead to an escalation of the drip rate to 40 $\mu\text{g}/\text{kg}/\text{min}$ and, if needed, atropine injection. The advantage of the higher dose dobutamine is the potential to elicit ischemia. Dysfunctional myocardium responds to dobutamine in one of 4 ways that are most likely to be appreciated when the response to both high and low doses of dobutamine are considered. These responses include biphasic response (augmentation at a low dose followed by deterioration at a higher dose), sustained improvement (improvement in function at a low dose without deterioration at higher doses), worsening of function, and no change in function.

The sensitivity of dobutamine echocardiography in predicting functional recovery (which varies depending on the protocol used) ranges from 71% to 97%, with a specificity ranging from 63% to 95%.¹¹⁶ **The highest sensitivity for detection of viability is noted when improvement at low-dose dobutamine echocardiography is considered; highest specificity is achieved when a biphasic response occurs.**¹¹⁷ Patients with a large area of viable myocardium (>25% of LV) have a high likelihood of improvement in EF and a better outcome after revascularization compared with patients with less or no contractile reserve.¹¹⁸ **Although presence of viability has been defined in various ways, it is recommended that improvement by at least one grade in two or more segments be demonstrated.** A substantial amount of viable myocardium detected by low-dose dobutamine echocardiography has been shown to prevent ongoing remodeling after revascularization and to be associated with persistent improvement of heart failure

symptoms and a lower incidence of cardiac events.¹¹⁹

Additional echocardiographic methods used to identify viable myocardium have included assessment of the microcirculation with contrast echocardiography, and myocardial tissue characterization using integrated backscatter. For both approaches, data are acquired at baseline and with vasodilators or dobutamine infusion. In the future, quantitative methods for analysis of regional function may improve viability assessment. Preliminary studies suggest that assessment of strain rate and strain can enhance detection of viable myocardium.¹²⁰⁻¹²²

ASSESSMENT OF PATIENTS WITH DYSPNEA, PULMONARY HYPERTENSION, AND VALVULAR HEART DISEASE

Dyspnea

Stress echocardiography is useful for the evaluation of patients with dyspnea of possible cardiac origin.¹²³ In addition to data on the presence, severity, and extent of myocardial ischemia, LV and left atrial volumes, EF, presence of LV hypertrophy and/or valvular disease, a baseline echocardiogram can identify the presence of pulmonary hypertension or abnormal LV relaxation and elevated filling pressures. In some cases, the diagnosis of a cardiac origin can be ascertained by the findings of the baseline resting images and stress testing may not be needed. Exercise using a supine bike is the recommended modality as it allows the acquisition of Doppler recordings during exercise. Doppler assessment of the mitral inflow velocities should be assessed at rest, during exercise, and in recovery when the E and A velocities are no longer fused. Doppler recordings should be acquired at a sweep speed of 100 mm/s. The ratio of mitral E (peak early diastolic velocity) to mitral annulus early diastolic velocity (e') can be used to estimate LV filling pressures at rest and exercise. Healthy individuals will show a similar increase in mitral E and annular e' , such that the ratio has no or only minimal change with exercise.¹²⁴ Patients with impaired LV relaxation develop an increase in LV filling pressures with exercise as a result of tachycardia and the abbreviated diastolic filling period. Accordingly, mitral peak E velocity increases. However, given the minimal effect of preload on annular e' in the presence of impaired relaxation, annular e' remains reduced. Therefore, E/ e' ratio increases with exercise in patients with diastolic dysfunction.^{125,126} This approach has been validated against invasive measurements for identifying an elevated exercise mean LV diastolic pressure.¹²⁶ Limitations to the above methodology include atrial fibrillation, tech-

nically challenging imaging windows, and limited validation. Furthermore, it remains to be seen how abnormalities in regional function influence the accuracy of a single site measurement of e' .

Pulmonary Hypertension

Transthoracic Doppler echocardiography permits a reliable estimation of pulmonary artery pressures, detection of cardiac causes of pulmonary hypertension, and changes in RV and LV volumes and function with the disease and its treatment.¹²⁷ Exercise may be useful in patients with pulmonary hypertension to gain insight into RV and LV function^{128,129} and the changes in stroke volume with exercise.¹³⁰ Some patients with a normal pulmonary artery pressure at rest have marked increase with exercise; the prognostic significance of this has not been defined. The normal response to exercise has been assessed in healthy individuals and in young male athletes.¹³¹ Highly trained male athletes have been found to have a Doppler-derived pulmonary artery systolic pressure as high as 60 mm Hg with exercise.¹³¹ There are also published reports about the use of exercise echocardiography in detecting asymptomatic gene carriers of familial primary pulmonary hypertension,¹³ and identifying patients susceptible to high-altitude pulmonary edema.¹³²

Mitral Valve Disease

In patients with mitral valve disease, exercise testing may provide insights regarding exertional symptoms disproportionate to resting hemodynamics.¹³³ It is also useful in patients with severe lesions but no symptoms; exercise-induced increase in pulmonary artery systolic pressure to greater than 60 mm Hg may be considered an indication for mitral valve surgery (class IIA indication in 2006 American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines for the Management of Patients with Valvular Heart Disease).¹³⁴ Most of the published studies used a supine bike protocol for image acquisition. Mitral inflow is recorded with pulsed wave Doppler (for mitral regurgitation) and continuous wave Doppler (for mitral stenosis), along with recording of tricuspid regurgitation velocity by continuous wave Doppler at rest and during exercise.

For patients with mitral stenosis, stress Doppler echocardiography is indicated in asymptomatic patients with significant lesions based on hemodynamic calculations obtained at rest, and for patients with symptoms disproportionate to resting Doppler hemodynamics (class I indication).¹³⁴ At baseline and with stress, transmitral pressure gradient and tricuspid regurgitation velocity are obtained by continuous wave Doppler using the modified Bernoulli equation. With

proper alignment of the ultrasound beam with transmitral flow, accurate Doppler-derived gradients can be obtained at rest and with exercise and correlate well with invasively derived measurements.¹³⁵ In sedentary patients, exercise-induced dyspnea, along with an increase in mean transmitral pressure gradient to greater than 15 mm Hg and pulmonary artery systolic pressure to greater than 60 mm Hg, identifies patients with hemodynamically significant lesions that may benefit from percutaneous valvotomy if anatomy is suitable and mitral regurgitation is mild or less.^{134,136} When exercise results in only minimal changes in transmitral pressure gradient but a marked increase in pulmonary artery systolic pressure occurs, further evaluation for underlying lung disease is indicated. In patients unable to exercise, dobutamine stress may be used.^{137,138}

Evaluation of mitral regurgitation is possible with quantitative and semiquantitative color Doppler methods.^{14,139} Exercise echocardiography has been used to uncover the presence of severe mitral regurgitation with exercise in patients with rheumatic mitral valve disease and only mild mitral stenosis and regurgitation at rest.¹⁴⁰ Likewise, exercise echocardiography is of value in identifying hemodynamically significant dynamic mitral regurgitation in patients with LV systolic dysfunction. In some patients, dynamic mitral regurgitation can account for acute pulmonary edema and predicts poor outcome.¹⁴¹ For patients with severe mitral regurgitation and normal EF at rest, stress echocardiography can detect the presence of reduced LV contractile reserve.¹⁴²

Aortic Valve Disease

Dobutamine echocardiography is indicated in the diagnostic evaluation of patients with LV systolic dysfunction and low-gradient aortic stenosis, defined as Doppler-derived aortic valve area less than 1.0 cm² and mean gradient less than 30 mm Hg.¹³⁴ In these patients, dobutamine is used to assess both the severity of aortic stenosis and the presence of LV contractile reserve.^{143,144} The infusion begins at 5 µg/kg/min and is increased at 5-minute intervals to 10 and 20 µg/kg/min.

Dobutamine results in a larger increase of mean pressure than transvalvular flow in patients with severe aortic stenosis. Accordingly, aortic valve area remains abnormally low indicating true aortic stenosis. On the other hand, dobutamine infusion results in larger increments of flow rate and valve area in patients with "functional" aortic stenosis, which is primarily a result of reduced flow rate. In a recent study, calculation of projected effective orifice area improved the diagnostic accuracy of dobutamine echocardiography in identifying patients with true

aortic stenosis, with surgical inspection used as the gold standard.¹⁴⁵ Dobutamine echocardiography provides important prognostic information in patients with LV systolic dysfunction and aortic stenosis, as surgery with aortic valve replacement appears to improve outcome for most patients with LV contractile reserve. In contrast, surgery is associated with high mortality in the absence of contractile reserve.¹⁴⁶

For patients with chronic aortic regurgitation, exercise testing may be considered to evaluate functional capacity when symptoms are questionable, or before participation in athletic activities (class IIA indications).¹³⁴ Likewise, useful prognostic information may be obtained before surgery in patients with LV dysfunction (class IIB indication).¹³⁴ This is supported by a number of studies with radionuclide angiography showing abnormal EF (and change in EF) with exercise in asymptomatic patients with aortic regurgitation. However, the incremental value of exercise data to LV dimensions and EF at rest is unclear. Stress echocardiography is not indicated in clearly symptomatic patients with severe aortic regurgitation or patients with depressed EF who should be referred for surgery without stress testing.

Evaluation of Prosthetic Valves

Stress echocardiography has been applied to the assessment of transvalvular gradients and flow in prosthetic aortic valves. The majority of reports used dobutamine¹⁴⁷⁻¹⁴⁹ but a few examined changes in valvular hemodynamics with exercise.¹⁴⁹

Although stress echocardiography has the potential to assess ventricular and prosthetic valvular function in symptomatic patients with equivocal findings at rest, the interpretation of Doppler gradients can be challenging given their dependence not only on flow rate but the type and size of the prosthetic valve. Additional data are needed to characterize normal responses for various prostheses.

STRESS ECHOCARDIOGRAPHY FOR RISK STRATIFICATION

Stress echocardiography is a useful technique for the risk stratification of patients with known or suspected CAD. This has been well documented in numerous large studies in which follow-up was obtained in consecutive patients referred for clinically indicated stress echocardiography. **These studies have documented the prognostic use of the test in patients with various pretest probabilities of disease, symptoms, known CAD, prior coronary artery revascularization, or prior myocardial infarction and in asymptomatic patients with risk factors for CAD.** The prognostic value of

the test has been shown to be maintained in patients with good exercise capacity,¹⁵⁰ and for those with reduced exercise capacity.¹⁵¹ **Table 2** summarizes major studies that reported the prognostic use of stress echocardiography in patients with known or suspected CAD.¹⁵²⁻¹⁵⁴ **Table 3** shows predictors of outcome found in these and other studies. Stress echocardiography has been shown to provide incremental prognostic value for predicting overall mortality, cardiac mortality, and composite cardiac end points in patients with known or suspected CAD, after adjustment for risk factors and stress test parameters.

A normal exercise echocardiogram result is associated with an annual event rate of cardiac death and nonfatal myocardial infarction of less than 1%, equivalent to that of an age- and sex-matched population. These patients do not require further diagnostic evaluation unless there is a change in clinical status.^{155,156} **Patients with a normal pharmacologic stress echocardiogram result have a slightly higher event rate.**²² **This may be explained by the higher risk status of patients who are unable to perform exercise stress test, as this group tends to be older with more comorbidities.**

Ischemia was shown in many studies to be associated with incremental risk of mortality and cardiac events. **Patients with extensive stress-induced abnormalities in a multivessel distribution are at a high risk of mortality and cardiac events.** In these patients, coronary angiography and subsequent myocardial revascularization may be justified, with particular consideration of symptomatic status, functional capacity, and resting LV function. An exercise wall-motion score index greater than 1.4 or exercise EF less than 50% portends a significantly worse prognosis. Results of stress echocardiography have been combined with the Duke treadmill score and clinical and stress test variables including age, sex, symptoms, exercise tolerance, rate-pressure product, and severity of wall-motion abnormalities.¹⁵⁷⁻¹⁵⁹

Baseline LV function expressed as wall-motion score index or EF remains a powerful predictor of future events. **Patients with resting LV dysfunction but no inducible myocardial ischemia have an intermediate risk, whereas patients with resting LV dysfunction and new wall-motion abnormalities have the greatest risk for death and cardiac events.**

Table 3 summarizes stress echocardiography test results characterizing patients at increased risk. **In addition to baseline LV dysfunction, variables associated with adverse outcome include extensive ischemia,^{65,160-162} poor EF response or failure to reduce end-systolic volume with exercise,¹⁵⁰ wall-motion abnormalities in mul-**

Table 2 Summary of studies evaluating the value of stress echocardiography in predicting outcome

Author	No. of patients	Patient characteristics	Stress type	Mean or median follow-up, y	End point	Echocardiographic predictors
Arruda-Olson et al 2002 ¹⁶¹	5798	Known or suspected CAD	Exercise	3.2	Cardiac death/MI	Exercise WMSI
Marwick et al 2001 ¹⁵⁹	5375	Known or suspected CAD	Exercise	5.5	All deaths	Extent of resting WMA; extent of ischemia
Biagini et al 2005 ¹⁶²	3381	Known or suspected CAD	Dobutamine	7	Cardiac death/MI	Resting WMA, ischemia
Marwick et al 2001 ¹⁶⁰	3156	Known or suspected CAD	Dobutamine	3.8	Cardiac death	Resting WMA, ischemia
Chuah et al 1998 ⁶⁵	860	Known or suspected CAD	Dobutamine	2	Cardiac death/MI	Stress WMA; end-systolic volume response
Shaw et al 2005 ¹⁷³	11,132	Known or suspected CAD	Exercise or dobutamine	5	Cardiac death	Extent of resting WMA; extent of ischemia
Sicari et al 2003 ¹⁵²	7333	Known or suspected CAD	Dipyridamole or dobutamine	2.6	Cardiac death/MI	Resting EF, change in WMSI
Tsutsui et al 2005 ¹⁵³	788	Known or suspected CAD	Dobutamine myocardial contrast perfusion	1.7	Death/MI	Contrast perfusion defects
Bergeron et al 2004 ¹²³	3260	Chest pain or dyspnea	Exercise	3.1	Mortality/morbidity	Change in WMSI
Elhendy et al 2001 ¹⁶³	563	Diabetes	Exercise	3	Cardiac death/MI	EF, extent of ischemia
Sozzi et al 2003 ¹⁸⁷	396	Diabetes	Dobutamine	3	Cardiac death/MI	EF, extent of ischemia
Marwick et al 2002 ¹⁸⁸	937	Diabetes	Exercise or dobutamine	3.9	All deaths	Extent of resting WMA; extent of ischemia
Chaowalit et al 2006 ¹⁸⁶	2349	Diabetes	Dobutamine	5.4	Mortality/morbidity (MI, late coronary revascularization)	Extent of ischemia and failure to reach target heart rate
Arruda et al 2001 ¹⁸⁴	2632	Elderly (≥ 65 y)	Exercise	2.9	Cardiac death/MI	Changes of EF and end-systolic volume
Biagini et al 2005 ¹⁸⁵	1434	Elderly (>65 y)	Dobutamine	6.5	Cardiac death/MI	Resting WMA, ischemia
Carlos et al 1997 ¹⁷⁸	214	Acute MI	Dobutamine	1.4	Cardiac death, MI, arrhythmias, heart failure	Resting WMSI; remote abnormalities
Elhendy et al 2005 ¹⁸³	528	Heart failure	Dobutamine	3.2	Cardiac death	Resting EF, ischemia
Elhendy et al 2003 ¹⁵⁴	483	LVH by echocardiographic criteria	Exercise	3	Cardiac death/MI	Resting WMSI, EF response
Arruda et al 2001 ¹⁹⁸	718	Previous CABG	Exercise	2.9	Cardiac death/MI	Changes of EF and end-systolic volume
Bountiouko et al 2004 ¹⁹⁹	331	Previous CABG or PCI	Dobutamine	2	Cardiac death/MI/late revascularization	Ischemia
Biagini et al 2005 ³¹	136	Pacemaker recipients	Pacing	3.5	Cardiac death	Ischemia
Das et al 2000 ⁶¹	530	Before nonvascular surgery	Dobutamine	Hospital stay	Cardiac death/MI	Ischemic threshold
Poldermans et al 1997 ¹⁹³	360	Before vascular surgery	Dobutamine	1.6	Perioperative and late cardiac events	Ischemia
Sicari et al 1999 ¹⁹¹	509	Before vascular surgery	Dipyridamole	Hospital stay	Death, MI, unstable angina	Ischemia

CABG, Coronary artery bypass grafting; CAD, coronary artery disease; EF, ejection fraction; LVH, left ventricular hypertrophy; MI, myocardial infarction; PCI, percutaneous intervention; WMA, wall-motion abnormalities; WMSI, wall-motion score index.

Table 3 Stress echocardiography predictors of risk

Very low risk* MI, cardiac events < 1%/y	Low risk* MI, cardiac death < 2%/y	Factors increasing risk† →	High risk‡ RR ≥ 4-fold over low risk
Normal exercise echocardiogram result with good exercise ca- pacity 7 METs men 5 METs women	Normal pharmacologic stress echocardiogram result with adequate stress, defined as achievement of HR ≥ 85% age-predicted maximum for dobutamine stress, and low to intermediate pretest probability of CAD	Increasing age Male sex Diabetes High pretest probability History of dyspnea or CHF History of myocardial infar- ction Limited exercise capacity Inability to exercise Stress ECG with ischemia Rest WMA LV hypertrophy Stress echocardiography with ischemia Reduced baseline EF No change or increase ESV with stress§ No change or decrease EF with stress§ Increasing wall-motion score with stress	Extensive rest WMA (4-5 segments of LV) Baseline EF < 40% Extensive ischemia (4-5 segments of LV) Multivessel ischemia Rest WMA and remote ischemia Low ischemic threshold Ischemia with 0.56 mg/kg dipyridamole or 20 µg/ kg/min dobutamine or based on heart rate// Ischemic WMA, no change or decrease in exercise EF§

CAD, Coronary artery disease; CHF, congestive heart failure; ECG, electrocardiogram; EF, ejection fraction; ESV, end-systolic volume; HR, heart rate; LV, left ventricular; METs, metabolic equivalents; MI, myocardial infarction; WMA, wall-motion abnormalities.

*High pretest probability of CAD, poor exercise capacity or low rate-pressure product, increased age, angina during stress, LV hypertrophy, history of infarction, history of CHF, and anti-ischemic therapy are factors known to increase risk in patients with normal stress echocardiogram results.

†The degree to which each factor increases risk is variable.

‡Cut-off values for high-risk group are approximate values derived from available studies. Studies have shown that increased rest and low- and peak-dose wall-motion scores can identify individuals at high risk, especially those with reduced global LV function, but threshold values used to define patients at high risk have been variable (eg, peak exercise scores range from 1.4 to > 1.7).

§For treadmill and dobutamine stress.

//Low ischemic threshold based on HR for dobutamine stress has been defined in various studies as ischemia with HR < 60% of age-predicted maximum, HR < 70% of age-predicted maximum, or at HR < 120/min.

tivessel distribution,¹⁶³ a low ischemic threshold,⁶¹ LV hypertrophy,¹⁵⁵ and location of wall-motion abnormalities in left anterior descending coronary artery distribution.¹⁶⁴ Akinosis becoming dyskinesis is associated with more extensive LV dysfunction, absence of reversible perfusion defects,¹⁶⁵ and very low probability of regional improvement after revascularization.¹⁶⁶ In the presence of concomitant anti-ischemic therapy, a positive test result is more prognostically malignant, and a negative test result less prognostically benign.¹⁶⁷

The prognostic use of stress echocardiography has been established in specific patient groups including those with hypertension,^{168,169} electronic pacemaker,³¹ left bundle branch block,¹⁷⁰ LV dysfunction,¹⁷¹ and atrial fibrillation.¹⁷² Use in other groups is described below.

Women

The prognostic value of stress echocardiography is well established in both men and women.^{161,162,173-175} Although some studies have reported a higher incidence of cardiac events in men than in women after

a normal study, the magnitude of risk associated with stress echocardiographic abnormalities is independent of sex.^{161,162}

After Acute Myocardial Infarction

Resting LV function is a major determinant of prognosis after myocardial infarction. **Stress echocardiography can be performed safely early after myocardial infarction and provides not only assessment of global and regional ventricular function, but can detect the presence and extent of residual myocardial ischemia.**¹⁷⁶ Several studies have confirmed that the extent of residual ischemia is related to adverse cardiac outcomes in this setting and provides information incremental to that obtained by exercise ECG¹⁷⁷ or angiography.¹⁷⁸⁻¹⁸¹ The incremental prognostic value of stress echocardiography is preserved in patients with abnormal LV function.¹⁸² In patients with heart failure and low EF because of ischemic cardiomyopathy, myocardial ischemia during dobutamine stress echocardiography was predictive of cardiac death, especially among patients who did not undergo coronary revascularization.¹⁸³

Elderly

Exercise echocardiography has been demonstrated to be a useful noninvasive tool for the evaluation of CAD in the elderly. The addition of stress echocardiographic variables that reflect not only the presence, but extent, of ischemia (in particular LV end-systolic volume response and exercise EF) to clinical, exercise ECG data and resting echocardiographic data has improved the prediction of cardiac events and all-cause mortality.¹⁸⁴ **Pharmacologic stress echocardiography can independently predict mortality among elderly patients unable to exercise.**¹⁸⁵ Patients with both resting and stress-induced wall-motion abnormalities were at highest risk of cardiac events.

Patients with Diabetes Mellitus

Exercise echocardiography is effective for cardiac risk stratification of patients with diabetes mellitus. Approximately one of 3 patients with multivessel distribution of exercise wall-motion abnormalities will experience cardiac death or myocardial infarction during the 3 years after the stress test.¹⁶³ Many patients with diabetes are unable to undergo an exercise stress test because of the higher prevalence of peripheral vascular disease and neuropathy. Such patients generally represent a higher-risk population than those who are able to undergo exercise stress testing. Dobutamine stress echocardiography was shown to provide independent prognostic information.¹⁸⁶⁻¹⁸⁸

Before Noncardiac Surgery

Cardiac risk factors and stress tests help to identify patients at high risk before major vascular surgery, identifying those who will benefit from coronary revascularization or pharmacologic (beta-blocker) therapy.¹⁸⁹ Pharmacologic stress echocardiography has been shown to be a powerful tool for cardiac risk stratification before vascular¹⁹⁰⁻¹⁹³ and nonvascular⁶¹ surgery. Test results provided better risk stratification than that which can be gained from clinical indices.⁶¹ Extensive ischemia (≥ 3 -5 segments) has a strong independent prognostic impact and may identify patients who would benefit most from revascularization before noncardiac surgery. Ischemia occurring at less than 60% of age-predicted maximal heart rate identifies patients at highest risk.⁶¹ In a recent meta-analysis comparing 6 noninvasive techniques for preoperative risk stratification before vascular surgery, pharmacologic stress tests had a higher overall sensitivity and specificity than the other tests. **For preoperative risk stratification, dobutamine stress echocardiography had a similar sensitivity to myocardial perfusion scintigraphy and a higher specificity and a better overall predictive accuracy.**^{190,194} In patients at clinically intermediate and high risk receiving beta-blockers, dobutamine stress echocardiography

can help identify those in whom surgery can still be performed and those in whom cardiac revascularization should be considered.¹⁸⁹

After Coronary Revascularization

Stress echocardiography can localize restenosis or graft occlusion, detect native unvascularized CAD, and assess adequacy of revascularization.^{194,196} Positive stress echocardiography after coronary angioplasty identifies patients at high risk for recurrence of angina.¹⁹⁷ Ischemia by stress echocardiography was incrementally predictive of cardiac events.^{198,199} In patients with previous coronary artery bypass grafting, the addition of the exercise echocardiographic variables, abnormal LV end-systolic volume response and exercise EF, to the clinical, resting echocardiographic, and exercise ECG model provided incremental information in predicting cardiac events.¹⁹⁸ However, routine use of stress testing in asymptomatic patients early after revascularization is not indicated.

Patients with Angina

The specificity of the symptom, angina, for the detection of underlying CAD is limited. Inducible ischemia during stress echocardiography was observed in only approximately 50% of patients with angina. In patients with stable angina, a normal stress echocardiogram finding identifies patients at low risk of cardiac events. In patients with CAD, angina is a poor predictor of the amount of myocardial ischemia. **In patients with angina, stress echocardiography can provide objective evidence of myocardial ischemia and determine the extent of myocardium at risk²⁰⁰ and has been shown to be useful for risk stratification.**²⁰¹

Comparison with Radionuclide Imaging

The annual cardiac event rate of less than 1% after a normal stress echocardiogram result is comparable with the event rate after a normal stress radionuclide imaging result reported in the current American Society of Nuclear Cardiology (ASNC)/ACC/AHA guidelines and in a recent meta-analysis.^{202,203} **Both wall-motion score index for stress echocardiography and summed stress score used in radionuclide imaging have been shown to be directly associated with the incidence of cardiac events during follow-up. Studies comparing stress echocardiography with radionuclide imaging in the same population^{204,205} and several meta-analyses^{190,194,203} have demonstrated comparable prognostic use.** In a study of 301 patients who underwent simultaneous dobutamine stress echocardiography and sestamibi single photon emission computed tomography (SPECT) radionuclide imaging and were followed up for a mean of 7 years, the annual cardiac death rate was 0.7% after a normal SPECT result and 0.6% after a

normal stress echocardiogram result. Abnormalities with either technique were equally predictive of cardiac death and composite end points.²⁰⁶ The prognosis and cost-effectiveness of exercise echocardiography versus SPECT imaging were compared in large numbers of stable patients at intermediate risk with chest pain. The risk-adjusted 3-year death or myocardial infarction rates classified by extent of ischemia were similar. A strategy based on cost-effectiveness supported the use of echocardiography in patients at low risk with suspected CAD and SPECT imaging in those at higher risk.²⁰⁷ **Advantages of stress echocardiography include shorter imaging time, lack of ionizing radiation, portability, immediate availability of the results, lower cost, and availability of ancillary information about chamber sizes and function, valves, pericardial effusion, aortic root disease, and wall thicknesses.**

RECENT AND FUTURE DEVELOPMENTS

Strain and Strain Rate Echocardiography

As discussed, strain and strain rate imaging using Doppler and 2D echocardiography-based techniques permit quantification of regional function with stress.⁷²⁻⁷⁵ Further modifications in protocols and software will enhance application of these techniques to clinical practice.

Three-dimensional Echocardiography

Real-time 3-dimensional echocardiography using matrix-array transducers allows rapid acquisition of a 3-dimensional data set with stress. This data set can be sliced to permit visualization of multiple 2D views of the LV, allowing assessment of function in segments of myocardium that are not routinely seen with 2D scanners. The ability to obtain multiple 2D views permits exact matching of baseline and stress views, which may be important for detection of limited wall-motion abnormalities. The feasibility of real-time 3-dimensional stress echocardiography has been documented.²⁰⁸⁻²¹⁰ Continued improvements in image quality will likely result in increased use of this method.

Myocardial Contrast Perfusion Imaging

The onset of ischemic wall-motion abnormalities is preceded by development of regional disparities in coronary perfusion that can be assessed by contrast agents. Thus, use of contrast agents to assess myocardial perfusion during vasodilator stress may improve the sensitivity of stress echocardiography.²¹¹ Both real-time (low energy) and triggered (high energy) imaging techniques have been shown to be useful for detection of coronary stenosis. The timing of contrast replenishment of a vascular bed has been found to be a useful indicator of the degree of coronary stenosis.²¹²

Myocardial contrast perfusion imaging may have greater sensitivity than wall-motion analysis.^{213,214} However, the specificity of contrast perfusion imaging may be lower than for wall-motion analysis.

SUMMARY

Stress echocardiography is a well-validated tool for detection and assessment of CAD. Its prognostic value has been well documented in multiple large studies, which have demonstrated its role for preoperative risk stratification before noncardiac surgery, recovery of function of viable myocardium, and identification of patients at increased risk of cardiac events and death. The test is less expensive than other stress imaging modalities, providing accuracy for detection of CAD and prognostic information equivalent to SPECT perfusion imaging. Moreover, it has great versatility, permitting assessment of valvular and pericardial abnormalities, chamber sizes, and wall thicknesses.

The authors appreciate the thoughtful review of this manuscript by Harvey Feigenbaum, MD, Editor-in-Chief, *Journal of the American Society of Echocardiography*.

REFERENCES

1. Armstrong W, Pellikka P, Ryan T, Crouse L, Zoghbi W, Stress Echocardiography Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. Stress echocardiography: recommendations for performance and interpretation of stress echocardiography. *J Am Soc Echocardiogr* 1998;11:97-104.
2. Feigenbaum H. Digital recording, display, and storage of echocardiograms. *J Am Soc Echocardiogr* 1988;1:378-83.
3. Skolnick D, Sawada S, Feigenbaum H, Segar D. Enhanced endocardial visualization with noncontrast harmonic imaging during stress echocardiography. *J Am Soc Echocardiogr* 1999;12:559-63.
4. Franke A, Hoffman R, Kuhl H. Non-contrast second harmonic imaging improves interobserver agreement and accuracy of dobutamine stress echocardiography in patients with impaired image quality. *Heart* 2000;83:133-40.
5. Sozi F, Poldermans D, Bax J. Second harmonic imaging improves sensitivity of dobutamine stress echocardiography for the diagnosis of coronary artery disease. *Am Heart J* 2001;142:153-9.
6. Rainbird A, Mulvagh S, Oh J, McCully R, Klarich K, Shub C, et al. Contrast dobutamine stress echocardiography: clinical practice assessment in 300 consecutive patients. *J Am Soc Echocardiogr* 2001;14:378-85.
7. Vlassak I, Rubin D, Odabashian J. Contrast and harmonic imaging improves the accuracy and efficiency of novice readers for dobutamine stress echocardiography. *Echocardiography* 2002;19:483-8.
8. Dolan M, Riad K, El-Shafei A. Effect of intravenous contrast for left ventricular opacification and border definition on sensitivity and specificity of dobutamine stress echocardiography compared with coronary angiography in technically difficult patients. *Am Heart J* 2001;142:908-15.

9. Thanigaraji S, Nease R, Schechtman K, Wade R, Loslo S, Perez J. Use of contrast for image enhancement during stress echocardiography is cost-effective and reduces additional diagnostic testing. *Am J Cardiol* 2001;87:1430-2.
10. Castello R, Bella J, Rovner A, Swan J, Smith J, Shaw J. Efficacy and time-efficiency of "sonographer-driven" contrast echocardiography protocol in a high-volume echocardiography laboratory. *Am Heart J* 2003;145:535-41.
11. Bruce R, Kusumi F, Hosmer D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. *Am Heart J* 1973;85:546-62.
12. Roger V, Pellikka P, Oh J, Miller FJ, Seward J, Tajik A. Stress echocardiography, part I: exercise echocardiography; techniques, implementation, clinical applications, and correlations [see comments]. *Mayo Clin Proc* 1995;70:5-15.
13. Grunig E, Janssen B, Mereles D, Barth U, Borst M, Vogt I, et al. Abnormal pulmonary artery pressure response in asymptomatic carriers of primary pulmonary hypertension gene. *Circulation* 2000;102:1145-50.
14. Modesto K, Rainbird A, Klarich K, Mahoney D, Chandrasekaran K, Pellikka P. Comparison of supine bicycle exercise and treadmill exercise Doppler echocardiography in evaluation of patients with coronary artery disease. *Am J Cardiol* 2003;91:1245-8.
15. Sawada S, Segar D, Ryan T, Brown S, Dohan A, Williams R, et al. Echocardiographic detection of coronary artery disease during dobutamine infusion. *Circulation* 1991;83:1605-14.
16. Mathias W Jr, Arruda A, Santos F, Arruda A, Mattos E, Osorio A, et al. Safety of dobutamine-atropine stress echocardiography: a prospective experience of 4,033 consecutive studies. *J Am Soc Echocardiogr* 1999;12:785-91.
17. Ling L, Pellikka P, Mahoney D, Oh J, McCully R, Roger V, et al. Atropine augmentation in dobutamine stress echocardiography: role and incremental value in a clinical practice setting. *J Am Coll Cardiol* 1996;28:551-7.
18. Lewandowski T, Armstrong W, Bach D. Reduced test time by early identification of patients requiring atropine during dobutamine stress echocardiography. *J Am Soc Echocardiogr* 1998;11:236-43.
19. Burger A, Notarianni M, Aronson D. Safety and efficacy of an accelerated dobutamine stress echocardiography protocol in the evaluation of coronary artery disease. *Am J Cardiol* 2000;86:825-9.
20. Pellikka P, Roger V, Oh J, Miller F Jr, Seward J, Tajik A. Stress echocardiography, part II: dobutamine stress echocardiography; techniques, implementation, clinical applications, and correlations [see comments]. *Mayo Clin Proc* 1995;70:16-27.
21. Karagiannis S, Bax J, Elhendy A, Feringa H, Cookinos D, van Domburg R, et al. Enhanced sensitivity of dobutamine stress echocardiography by observing wall motion abnormalities during the recovery phase after acute beta blocker administration. *Am J Cardiol* 2006;97:462-5.
22. Chaowalit N, McCully R, Callahan M, Mookadam F, Bailey K, Pellikka P. Outcomes after normal dobutamine stress echocardiography and predictors of adverse events: long-term follow-up of 3014 patients. *Eur Heart J* 2006;27:3039-44.
23. Cornel J, Balk A, Boersma E, Maat A, Elhendy A, Arnese M, et al. Safety and feasibility of dobutamine-atropine stress echocardiography in patients with ischemic left ventricular dysfunction. *J Am Soc Echocardiogr* 1996;9:27-32.
24. Pellikka P, Roger V, Oh J, Seward J, Tajik A. Safety of performing dobutamine stress echocardiography in patients with abdominal aortic aneurysm >4 cm in diameter. *Am J Cardiol* 1996;77:413-6.
25. Takhtehchian D, Novaro G, Barnett G, Griffin B, Pellikka P. Safety of dobutamine stress echocardiography in patients with unruptured intracranial aneurysms. *J Am Soc Echocardiogr* 2002;15:1401-4.
26. Elhendy A, Windle J, Porter T. Safety and feasibility of dobutamine stress echocardiography in patients with implantable cardioverter defibrillators. *Am J Cardiol* 2003;92:475-7.
27. Bremer M, Monahan K, Stussy V, Miller F Jr, Seward J, Pellikka P. Safety of dobutamine stress echocardiography supervised by registered nurse sonographers. *J Am Soc Echocardiogr* 1998;11:601-5.
28. Picano E, Lattanzi F. Dipyridamole echocardiography: a new diagnostic window on coronary artery disease. *Circulation* 1991;83:III19-26.
29. Picano E, Marini C, Pirelli S, Maffei S, Bolognese L, Chiriatti G, et al. Safety of intravenous high-dose dipyridamole echocardiography: the echo-Persantine international cooperative study group. *Am J Cardiol* 1992;70:252-8.
30. Picano E, Alaimo A, Chubuchny V, Polonska E, Baldo V, Baldini U, et al. Noninvasive pacemaker stress echocardiography for diagnosis of coronary artery disease: a multicenter study. *J Am Coll Cardiol* 2002;40:1305-10.
31. Biagini E, Schinkel A, Elhendy A, Bax J, Rizzello V, van Domburg R, et al. Pacemaker stress echocardiography predicts cardiac events in patients with permanent pacemaker. *Am J Med* 2005;118:1381-6.
32. Lee C, Pellikka P, McCully R, Mahoney D, Seward J. Non exercise stress transthoracic echocardiography: transesophageal atrial pacing versus dobutamine stress. *J Am Coll Cardiol* 1999;33:506-11.
33. Rainbird A, Pellikka P, Stussy V, Mahoney D, Seward J. A rapid stress-testing protocol for the detection of coronary artery disease: comparison of two-stage transesophageal atrial pacing stress echocardiography with dobutamine stress echocardiography. *J Am Coll Cardiol* 2000;36:1659-63.
34. Quinones M, Douglas P, Foster E, Gorcsan J, Lewis J, Pearlman A, et al. ACC/AHA clinical competence statement on echocardiography: a report of the American College of Cardiology/American Heart Association/American College of Physicians-American Society of Internal Medicine task force on clinical competence. *J Am Coll Cardiol* 2003;41:687-708.
35. Bierig S, Ehler D, Knoll M, Waggoner A. American Society of Echocardiography minimum standards for the cardiac sonographer: a position paper. *J Am Soc Echocardiogr* 2006;19:471-4.
36. Lang R, Bierig M, Devereux R, Flachskampf F, Foster E, Pellikka P, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's guidelines and standards committee and the chamber quantification writing group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18:1440-63.
37. Senior R, Lahiri A. Enhanced detection of myocardial ischemia by stress dobutamine echocardiography utilizing the "biphasic" response of wall thickening during low and high dose dobutamine infusion. *J Am Coll Cardiol* 1995;26:26-32.

38. Tyberg J, Parmley W, Sonnenblick E. In-vitro studies of myocardial asynchrony and regional hypoxia. *Circ Res* 1969; 25:569-79.
39. Pislaru C, Belohlavek M, Bae R, Abraham T, Greenleaf F, Seward J. Regional asynchrony during acute myocardial ischemia quantified by ultrasound strain rate imaging. *J Am Coll Cardiol* 2001;37:1141-8.
40. Sutherland G, Kukulski T, Kvitting J, D'hooge J, Arnold M, Brandt E. Quantitation of left-ventricular asynergy by cardiac ultrasound. *Am J Cardiol* 2000;86:4-9G.
41. Kvitting J, Wigstrom L, Strotmann J, Sutherland G. How accurate is visual assessment of synchronicity in myocardial motion? An in vitro study with computer simulated regional delay in myocardial motion: clinical implications for rest and stress echocardiography studies. *J Am Soc Echocardiogr* 1999;12:698-705.
42. Hoffmann R, Marwick T, Poldermans D, Lethen H, Ciani R, van der Meer P. Refinements in stress echocardiographic techniques improve inter-institutional agreement in interpretation of dobutamine stress echocardiograms. *Eur Heart J* 2002;23:821-9.
43. Johnson L, Ellis K, Schmidt D, Weiss M, Cannon P. Volume ejected in early systole: a sensitive index of left ventricular performance in coronary artery disease. *Circulation* 1975;52:1075-83.
44. Holman B, Wynne J, Idoine J, Neill J. Disruption in the temporal sequence of regional ventricular contraction, I: characteristics and incidence in coronary artery disease. *Circulation* 1980;61:1075-83.
45. Arsenault M, Crete M, Bergeron S. Left ventricular shape assessment: a new simple diagnostic tool in stress echocardiography. *J Am Soc Echocardiogr* 2002;15:1321-5.
46. Attenhofer C, Pellikka P, Oh J, Roger V, Sohn D, Seward J. Comparison of ischemic response during exercise and dobutamine echocardiography in patients with left main coronary artery disease. *J Am Coll Cardiol* 1996;27:1171-7.
47. Roman S, Vilacosta J, Rollan M, Castillo J, Alonso J, Duran J, et al. Right ventricular asynergy during dobutamine-atropine echocardiography. *J Am Coll Cardiol* 1997;30:430-5.
48. O'Sullivan C, Duncan A, Daly C, Li W, Oldershaw P, Henein M. Dobutamine stress-induced ischemic right ventricular dysfunction and its relation to cardiac output in patients with three-vessel coronary artery disease with angina-like symptoms. *Am J Cardiol* 2005;62:622-7.
49. Carstensen S, Ali S, Stensgaard-Hansen F, Toft J, Haunso S, Kelbaek H. Dobutamine-atropine stress echocardiography in asymptomatic healthy individuals: the relativity of stress-induced hyperkinesia. *Circulation* 1995;92:3453-63.
50. Coletta C, Galati A, Ricci R, Sestili A, Guagnozzi G, Re F, et al. Prognostic value of left ventricular volume response during dobutamine stress echocardiography. *Eur Heart J* 1997; 18:1599-605.
51. Olson C, Porter T, Deligonul U, Xie F, Anderson J. Prognostic value of left ventricular volume response during dobutamine stress echocardiography. *J Am Coll Cardiol* 1994; 24:1268-73.
52. Anselmi M, Golia G, Marino P, Vitolo A, Rossi A, Caraffi G, et al. Comparison of left ventricular function and volumes during transesophageal atrial pacing combined with two dimensional echocardiography in patients with syndrome X, atherosclerotic coronary artery disease, and normal subjects. *Am J Cardiol* 1997;80:1261-5.
53. Labovitz A, Pearson A, Chaitman B. Doppler and two-dimensional echocardiographic assessment of left ventricular function before and after intravenous dipyridamole stress testing for detection of coronary artery disease. *Am J Cardiol* 1988;62:1180-5.
54. Sochor H, Pachinger O, Ogris E, Probst P, Kaindl F. Radionuclide imaging after coronary vasodilation: myocardial scintigraphy with thallium-201 and radionuclide angiography after administration of dipyridamole. *Eur Heart J* 1984;5: 500-9.
55. Klein H, Ninio R, Eliyahu S, Bakst A, Levi A, Dean H. Effects of the dipyridamole test on left ventricular function in coronary artery disease. *Am J Cardiol* 1992;69:482-8.
56. Ginzton L, Conant R, Brizendine M, Lee F, Mena I, Laks M. Exercise subcostal two-dimensional echocardiography: a new method of segmental wall motion analysis. *Am J Cardiol* 1984;53:805-11.
57. Freeman M, Berman D, Staniloff H, Elkayam U, Maddahi J, Swan H. Comparison of upright and supine bicycle exercise in the detection and evaluation of extent of coronary artery disease by equilibrium radionuclide ventriculography. *Am Heart J* 1981;102:182-9.
58. Zwehl W, Gueret P, Meerbaum S, Holt D, Corday E. Quantitative two dimensional echocardiography during bicycle exercise in normal subjects. *Am J Cardiol* 1981;47:866-73.
59. Poliner L, Dehmer G, Lewis S, Parkey R, Blomqvist C, Willerson J. Left ventricular performance in normal subjects: a comparison of the responses to exercise in the upright and supine positions. *Circulation* 1980;62:528-34.
60. Poldermans D, Arnese M, Fioretti P, Salustri A, Boersma E, Thomson I, et al. Improved cardiac risk stratification in major vascular surgery with dobutamine-atropine stress echocardiography. *J Am Coll Cardiol* 1995;26:648-53.
61. Das M, Pellikka P, Mahoney D, Roger V, Oh J, McCully R, et al. Assessment of cardiac risk before nonvascular surgery: dobutamine stress echocardiography in 530 patients. *J Am Coll Cardiol* 2000;35:1647-53.
62. Panza J, Curiel R, Laurienzo J, Quyyumi A, Dilsizian V. Relation between ischemic threshold measured during dobutamine stress echocardiography and known indices of poor prognosis in patients with coronary artery disease. *Circulation* 1995;92:2095-101.
63. Hoffmann R, Lethen H, Marwick T, Arnese M, Fioretti P, Pingitore A, et al. Analysis of interinstitutional observer agreement in interpretation of dobutamine stress echocardiograms. *J Am Coll Cardiol* 1996;27:330-6.
64. Anand D, Theodosiadis I, Senior R. Improved interpretation of dobutamine stress echocardiography following 4 months of systematic training in patients following acute myocardial infarction. *Eur J Echocardiogr* 2004;5:12-7.
65. Chuah S, Pellikka P, Roger V, McCully R, Seward J. Role of dobutamine stress echocardiography in predicting outcome in 860 patients with known or suspected coronary artery disease. *Circulation* 1998;97:1474-80.
66. Lang R, Vignon P, Weinert L, Bednarz J, Korcarz C, Sandelski J, et al. Echocardiographic quantification of regional left ventricular wall motion with color kinesis. *Circulation* 1996; 93:1877-85.
67. Mor-Avi V, Vignon P, Koch R. 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;95:2082-97.
68. Cain P, Baglin T, Case C, Spicer D, Short L, Marwick T. Application of tissue Doppler to interpretation of dobut-

- amine echocardiography and comparison with quantitative coronary angiography. *Am Coll Cardiol* 2001;87:525-31.
69. Madler C, Payne N, Wilkenschoff U. Non-invasive diagnosis of coronary artery disease by quantitative stress echocardiography: optimal diagnostic models using off-line tissue Doppler in the MYDISE study. *Eur Heart J* 2003;24:1587-94.
 70. Fathi R, Cain P, Nakatani S, Yu H, Marwick T. Effect of tissue Doppler on the accuracy of novice and expert interpreters of dobutamine echocardiography. *Am J Cardiol* 2001;88:400-5.
 71. Pislaru R, Bruce P, Anagnostopoulos L, Allen J, Seward C, Pellikka J, et al. Ultrasound strain imaging of altered myocardial stiffness: stunned versus infarcted reperfused myocardium. *Circulation* 2004;109:2905-10.
 72. Abraham T, Belohlavek M, Thomson H, Pislaru C, Khandheria B, Randolph G, et al. Time to onset of regional relaxation: feasibility, variability and utility of a novel index of regional myocardial function by strain rate imaging. *J Am Coll Cardiol* 2002;39:1531-7.
 73. Voigt J, Nixdorff U, Bogdan R, Exner B, Schmiedehausen K, Platsch G, et al. Comparison of deformation imaging and velocity imaging for detecting regional inducible ischemia during dobutamine stress echocardiography. *Eur Heart J* 2004;25:1517-25.
 74. Merli E, Sutherland G. Can we quantify ischemia during dobutamine stress echocardiography in clinical practice? *Eur Heart J* 2004;25:1477-9.
 75. Yip G, Khandheria B, Belohlavek M. Strain echocardiography tracks dobutamine-induced decrease in regional myocardial perfusion in nonocclusive coronary stenosis. *J Am Coll Cardiol* 2004;44:1664-71.
 76. Marwick T. Measurement of strain and strain rate by echocardiography: ready for prime time? *J Am Coll Cardiol* 2006;47:1313-27.
 77. Quinones M, Verani M, Haichin R, Mahmarian J, Suarez J, Zog W. Exercise echocardiography versus 201Tl single-photon emission computed tomography in evaluation of coronary artery disease: analysis of 292 patients. *Circulation* 1992;85:1217-8.
 78. Fleischmann K, Hunink M, Kuntz K, Douglas P. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. *JAMA* 1998;280:913-20.
 79. Schinkel A, Bax J, Geleijnse M, Boersma E, Elhendy A, Roelandt J, et al. Noninvasive evaluation of ischemic heart disease: myocardial perfusion imaging or stress echocardiography? *Eur Heart J* 2003;24:789-800.
 80. Smart S, Bhatia A, Hellman R, Stoiber T, Krasnow A, Collier D. Dobutamine-atropine stress echocardiography and dipyridamole sestamibi scintigraphy for the detection of coronary artery disease: limitations and concordance. *J Am Coll Cardiol* 2000;36:1265-73.
 81. Marwick T, D'Hondt A, Baudhuin T, Willemart B, Wijns W, Detry J, et al. Optimal use of dobutamine stress for the detection and evaluation of coronary artery disease: combination with echocardiography or scintigraphy, or both? *J Am Coll Cardiol* 1993;22:159-67.
 82. Roger VL, Pellikka PA, Bell MR, Chow CW, Bailey KR, Seward JB. Sex and test verification bias: impact on the diagnostic value of exercise echocardiography [see comments]. *Circulation* 1997;95:405-10.
 83. McNeill A, Fioretti P, el-Said S, Salustri A, Forster T, Roelandt J. Enhanced sensitivity for detection of coronary artery disease by addition of atropine to dobutamine stress echocardiography. *Am J Cardiol* 1992;70:41-6.
 84. Schroder K, Voller H, Dingerkus H, Munzberg H, Dissman R, Linderer T. Comparison of the diagnostic potential of four echocardiographic stress tests shortly after acute myocardial infarction: submaximal exercise, transesophageal atrial pacing, dipyridamole, and dobutamine-atropine. *Am J Cardiol* 1996;77:909-14.
 85. Dagianti A, Penco M, Bandiera A, Sgorbini L, Fedele F. Clinical application of exercise stress echocardiography: supine bicycle or treadmill? *Am J Cardiol* 1998;81:62-7G.
 86. Badruddin S, Ahmad A, Mickelson J, et al. Supine bicycle versus post-treadmill exercise echocardiography in the detection of myocardial ischemia: a randomized single-blind crossover trial. *J Am Coll Cardiol* 1999;33:1485-90.
 87. Ryan T, Segar D, Sawada S, et al. Detection of coronary artery disease with upright bicycle exercise echocardiography. *J Am Soc Echocardiogr* 1993;6:186-97.
 88. Hecht H, DeBord L, Shaw R, Dunlap R, Ryan C, Stertzer S, et al. Usefulness of supine bicycle stress echocardiography for detection of restenosis after percutaneous transluminal coronary angioplasty. *Am J Cardiol* 1993;71:293-6.
 89. Hecht H, DeBord L, Sotomayor N, Shaw R, Dunlap R, Ryan C. Supine bicycle stress echocardiography: peak exercise imaging is superior to postexercise imaging. *J Am Soc Echocardiogr* 1993;6:265-71.
 90. Smart S, Knickelbine T, Malik F, Sagar K. 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;101:258-63.
 91. Yuda S, Khoury V, Marwick T. Influence of wall stress and left ventricular geometry on the accuracy of dobutamine stress echocardiography. *J Am Coll Cardiol* 2002;40:1311-9.
 92. Wahi S, Marwick T. Aortic regurgitation reduces the accuracy of exercise echocardiography for diagnosis of coronary artery disease. *J Am Soc Echocardiogr* 1999;12:967-73.
 93. Bach D, Muller D, Gros B, Armstrong W. False positive dobutamine stress echocardiograms: characterization of clinical, echocardiographic and angiographic findings. *J Am Coll Cardiol* 1994;24:928-33.
 94. Ha J, Juracan E, Mahoney D, Oh J, Shub C, Seward J, et al. Hypertensive response to exercise: a potential cause for new wall motion abnormality in the absence of coronary artery disease. *J Am Coll Cardiol* 2002;39:323-7.
 95. Okeie K, Shimizu M, Yoshio H, Ino H, Yamaguchi M, Matsuyama T, et al. Left ventricular systolic dysfunction during exercise and dobutamine stress in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2000;36:856-63.
 96. Miller D, Ruddy T, Zusman R, Okada R, Strauss H, Kanarek D. Left ventricular ejection fraction response during exercise in asymptomatic systemic hypertension. *Am J Cardiol* 1987;59:409-13.
 97. Schulman D, Tugoen J, Flores A, Dianzumba S, Reichek N. Left ventricular ejection fraction during supine and upright exercise in patients with systemic hypertension and its relation to peak filling rate. *Am J Cardiol* 1995;76:61-5.
 98. Melin J, Wijns W, Pouleur H, Robert A, Nannan M, DeCoster P, et al. Ejection fraction response to upright exercise in hypertension: relation to loading conditions and to contractility. *Int J Cardiol* 1987;17:37-49.

99. Mottram P, Haluska B, Yuda S, Leano R, Marwick T. Patients with a hypertensive response to exercise have impaired systolic function without diastolic dysfunction or left ventricular hypertrophy. *J Am Coll Cardiol* 2004;43:848-53.
100. Mairese G, Marwick T, Arnese M, Vanoverschelde J, Cornel J, Detry J. Improved identification of coronary artery disease in patients with left bundle branch block by use of dobutamine stress echocardiography and comparison with myocardial perfusion tomography. *Am J Cardiol* 1995;76:321-5.
101. Tandogan I, Yetkin E, Yanik A, Ulusoy F, Temizhan A, Cehreli S. Comparison of thallium 201 exercise SPECT and dobutamine stress echocardiography for diagnosis of coronary artery disease in patients with left bundle branch block. *Int J Cardiovasc Imaging* 2001;17:339-45.
102. Geleijnse M, Vigna C, Kasprzak J, Rambaldi R, Salvatori M, Elhendy A, et al. Usefulness and limitations of dobutamine-atropine stress echocardiography for the diagnosis of coronary artery disease in patients with left bundle branch block. *Eur Heart J* 2000;21:1666-73.
103. Afridi I, Grayburn P, Panza J, Oh J, Zoghbi W. Myocardial viability during dobutamine echocardiography predicts survival in patients with coronary artery disease and severe left ventricular systolic dysfunction. *J Am Coll Cardiol* 1998;32:921-6.
104. Meluzin J, Cerny J, Frelich M, Stetka F, Spinarova L, Popelova J, et al. Prognostic value of the amount of dysfunctional but viable myocardium in revascularized patients with coronary artery disease and left ventricular dysfunction: investigators of this multicenter study. *J Am Coll Cardiol* 1998;32:912-20.
105. Naqvi T, Goel R, Forrester J, Siegel R. Myocardial contractile reserve on dobutamine echocardiography predicts late spontaneous improvement in cardiac function in patients with recent onset idiopathic dilated cardiomyopathy. *J Am Coll Cardiol* 1999;34:1537-44.
106. Eichhorn E, Grayburn P, Mayer S, St John Sutton M, Appleton C, Plehn J, et al. Myocardial contractile reserve by dobutamine stress echocardiography predicts improvement in ejection fraction with beta-blockade in patients with heart failure: the beta-blocker evaluation of survival trial (BEST). *Circulation* 2003;108:2336-41.
107. Nagueh S, Mikati I, Weilbaecher D, Reardon M, Al-Zaghrini G, Cacela D, et al. Relation of the contractile reserve of hibernating myocardium to myocardial structure in humans. *Circulation* 1999;100:490-6.
108. Elsasser A, Schlepper M, Klovekorn W, Cai W, Zimmerman R. Hibernating myocardium: an incomplete adaptation to ischemia. *Circulation* 1997;96:2920-31.
109. Bito V, Heinzel F, Weidemann. Cellular mechanisms of contractile dysfunction in hibernating myocardium. *Circ Res* 2004;94:794-801.
110. Iyer V, Canty J. Regional desensitization of beta-adrenergic receptor signaling in swine with chronic hibernating myocardium. *Circ Res* 2005;97:789-95.
111. Schwarz E, Schoendube F, Schmiedtke S, Schultz G, Buell U. Prolonged myocardial hibernation exacerbates cardiomyocyte degeneration and impairs recovery of function after revascularization. *J Am Coll Cardiol* 1998;31:1018-26.
112. Cwajg J, Cwajg E, Nagueh D, He Z, Qureshi U, Olmos L. End-diastolic wall thickness as a predictor of recovery of function in myocardial hibernation: relation to rest-redistribution Tl-201 tomography and dobutamine stress echocardiography. *J Am Coll Cardiol* 2000;35:1152-61.
113. Biagini E, Galema T, Schinkel A, Vletter W, Roelandt J, Ten Cate F. Myocardial wall thickness predicts recovery of contractile function after primary coronary intervention for acute myocardial infarction. *J Am Coll Cardiol* 2004;43:1489-93.
114. Yong Y, Nagueh S, Shimoni S, Shan K, He Z, Reardon M. Deceleration time in ischemic cardiomyopathy: relation to echocardiographic and scintigraphic indices of myocardial viability and functional recovery after revascularization. *Circulation* 2001;103:1232-7.
115. Ling L, Christian T, Mulvagh S, Klarich K, Hauser M, Nishimura R, et al. Determining myocardial viability in chronic ischemic left ventricular dysfunction: a prospective comparison of rest-redistribution thallium 201 single-photon emission computed tomography, nitroglycerin-dobutamine echocardiography, and intracoronary myocardial contrast echocardiography. *Am Heart J* 2006;151:882-9.
116. Senior R, Lahiri A. Role of dobutamine echocardiography in detection of myocardial viability for predicting outcome after revascularization in ischemic cardiomyopathy. *J Am Soc Echocardiogr* 2001;14:240-8.
117. Afridi I, Kleiman N, Raizner A, Zoghbi W. Dobutamine echocardiography in myocardial hibernation: optimal dose and accuracy in predicting recovery of ventricular function after coronary angioplasty. *Circulation* 1995;91.
118. Bax J, Poldermans D, Elhendy A. Improvement of left ventricular ejection fraction, heart failure symptoms and prognosis after revascularization in patients with chronic coronary artery disease and viable myocardium detected by dobutamine stress echocardiography. *J Am Coll Cardiol* 1999;34:163-9.
119. Rizzello V, Poldermans D, Boersma E. Opposite patterns of left ventricular remodeling after coronary revascularization in patients with ischemic cardiomyopathy: role of myocardial viability. *Circulation* 2004;110:2383-8.
120. Hoffmann R, Altiok E, Nowak B, Heussen N, Kuhl H, Kaiser H, et al. Strain rate measurement by Doppler echocardiography allows improved assessment of myocardial viability in patients with depressed left ventricular function. *J Am Coll Cardiol* 2002;39:443-9.
121. Hoffmann R, Altiok E, Nowak B, Kuhl H, Kaiser H, Buell U, et al. Strain rate analysis allows detection of differences in diastolic function between viable and nonviable myocardial segments. *J Am Soc Echocardiogr* 2005;18:330-5.
122. Zhang Y, Chan A, Yu C, Yip G, Fung J, Lam W, et al. Strain rate imaging differentiates transmural from non-transmural myocardial infarction: a validation study using delayed-enhancement magnetic resonance imaging. *J Am Coll Cardiol* 2005;46:864-71.
123. Bergeron S, Ommen S, Bailey K, Oh J, McCully R, Pellikka P. Exercise echocardiographic findings and outcome of patients referred for evaluation of dyspnea. *J Am Coll Cardiol* 2004;43:2242-6.
124. Ha J, Lulic F, Bailey K, Pellikka P, Seward J, Tajik A, et al. Effects of treadmill exercise on mitral inflow and annular velocities in healthy adults. *Am J Cardiol* 2003;91:114-5.
125. Ha J, Pellikka P, Oh J, Ommen S, Stussy V, Bailey K, et al. Diastolic stress echocardiography: a novel noninvasive diagnostic test for diastolic dysfunction using supine bicycle exercise Doppler echocardiography. *J Am Soc Echocardiogr* 2005;18:63-8.
126. Burgess M, Jenkins C, Sharman J, Marwick T. Diastolic stress echocardiography: hemodynamic validation and clinical

- cal significance of estimation of ventricular filling pressure with exercise. *J Am Coll Cardiol* 2006;47:1891-900.
127. Galie N, Torbicki A, Barst R, Darteville P, Haworth S, Higenbottam T, et al. Guidelines on diagnosis and treatment of pulmonary arterial hypertension: the task force on diagnosis and treatment of pulmonary arterial hypertension of the European Society of Cardiology. *Eur Heart J* 2004;25:2243-78.
 128. Himelman R, Stulbarg M, Kircher B, Lee E, Kee L, Dean N, et al. Noninvasive evaluation of pulmonary artery pressure during exercise by saline-enhanced Doppler echocardiography in chronic pulmonary disease. *Circulation* 1989;79:863-71.
 129. Nootens M, Wolfkiel C, Chomka E, Rich S. Understanding right and left ventricular systolic function and interactions at rest and with exercise in primary pulmonary hypertension. *Am J Cardiol* 1995;75:374-7.
 130. Holverda S, Gan C, Marcus J, Postmus P, Boonstra A, Vonk-Noordegraaf A. Impaired stroke volume response to exercise in pulmonary arterial hypertension. *J Am Coll Cardiol* 2006;47:1732-3.
 131. Bossone E, Rubenfire M, Bach D, Ricciardi M, Armstrong W. Range of tricuspid regurgitation velocity at rest and during exercise in normal adult men: implications for the diagnosis of pulmonary hypertension. *J Am Coll Cardiol* 1999;33:1662-6.
 132. Grunig E, Mereles D, Hildebrandt W, Swenson E, Kubler W, Kuecherer H, et al. Stress Doppler echocardiography for identification of susceptibility to high altitude pulmonary edema. *J Am Coll Cardiol* 2000;35:980-7.
 133. Wu W, Aziz G, Sadaniantz A. The use of stress echocardiography in the assessment of mitral valvular disease. *Echocardiography* 2004;21:451-8.
 134. Bonow R, Carabello B, Chatterjee K, de Leon A, Faxon D, Freed M, et al. ACC/AHA guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (writing committee to revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *J Am Coll Cardiol* 2006;48:e1-148.
 135. Voelker W, Jaksch R, Dittman H, Schmitt A, Maiuser M, Karsch K. Validation of continuous-wave Doppler measurement of mitral valve gradients during exercise: a simultaneous Doppler-catheter study. *Eur Heart J* 1989;10:737-46.
 136. Aviles R, Nishimura R, Pellikka P, Andreen K, Holmes D. Utility of stress Doppler echocardiography in patients undergoing percutaneous mitral balloon valve valvotomy. *J Am Soc Echocardiogr* 2001;14:676-81.
 137. Hecker S, Zabalgoitia M, Ashline P, Oneschuk L, O'Rourke R, Herrera C. Comparison of exercise and dobutamine stress echocardiography in assessing mitral stenosis. *Am J Cardiol* 1997;80:1374-7.
 138. Mohan J, Patel A, Passey R, Gupta D, Kumar M, Arora R, et al. Is the mitral valve area flow-dependent in mitral stenosis? A dobutamine stress echocardiographic study. *J Am Coll Cardiol* 2002;40:1809-15.
 139. Zoghbi W, Enriquez-Sarano M, Foster E, Grayburn P, Kraft C, Levine R, et al. American Society of Echocardiography: recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr* 2003;16:777-802.
 140. Tischler M, Battle R, Saha M, Niggel J, LeWinter M. Observations suggesting a high incidence of exercise-induced severe mitral regurgitation in patients with mild rheumatic mitral valve disease at rest. *J Am Coll Cardiol* 1995;25:128-33.
 141. Pierard L, Lancellotti P. The role of ischemic mitral regurgitation in the pathogenesis of acute pulmonary edema. *N Engl J Med* 2004;351:1627-34.
 142. Leung D, Griffin B, Stewart W, Cosgrove D, Thomas J, Marwick T. Left ventricular function after valve repair for chronic mitral regurgitation: predictive value of preoperative assessment of contractile reserve by exercise echocardiography. *J Am Coll Cardiol* 1996;28:1198-205.
 143. deFilippi C, Willett D, Brickner M, Appleton C, Yancy C, Eichhorn E, et al. Usefulness of dobutamine echocardiography in distinguishing severe from nonsevere valvular aortic stenosis in patients with depressed left ventricular function and low transvalvular gradients. *Am J Cardiol* 1995;75:191-4.
 144. Nishimura R, Grantham J, Connolly H, Schaff H, Higano S, Holmes D. Low-output, low-gradient aortic stenosis in patients with depressed left ventricular systolic function: the clinical utility of the dobutamine challenge in the catheterization laboratory. *Circulation* 2002;106:809-13.
 145. Blais C, Burwash I, Mundigler G, Dumesnil J, Loho N, Rader F, et al. Projected valve area at normal flow rate improves the assessment of stenosis severity in patients with low-flow, low-gradient aortic stenosis: the multicenter TOPAS (truly or pseudo-severe aortic stenosis) study. *Circulation* 2006;113:711-21.
 146. Monin J, Quere J, Monchi M, Petit H, Baleynaud S, Chauvel C, et al. Low-gradient aortic stenosis; operative risk stratification and predictors for long-term outcome: a multicenter study using dobutamine stress hemodynamics. *Circulation* 2003;108:319-24.
 147. Zabalgoitia M, Kopec K, Abochamh D, Oneschuk L, Herrera C, O'Rourke R. Usefulness of dobutamine echocardiography in the hemodynamic assessment of mechanical prostheses in the aortic valve position. *Am J Cardiol* 1997;80:523-6.
 148. Izzat M, Birdi I, Wilde P, Bryan A, Angelini G. Evaluation of the hemodynamic performance of small CarboMedics aortic prostheses using dobutamine-stress Doppler echocardiography. *Ann Thorac Surg* 1995;60:104-52.
 149. Zabalgoitia M, Kopec K, Oneschuk L, Linn W, Herrera C, O'Rourke R. Use of dobutamine stress echocardiography in assessing mechanical aortic prostheses: comparison with exercise echocardiography. *J Heart Valve Dis* 1997;6:253-7.
 150. McCully R, Roger V, Mahoney D, Burger K, Click R, Seward J, et al. Outcome after abnormal exercise echocardiography for patients with good exercise capacity: prognostic importance of the extent and severity of exercise-related left ventricular dysfunction. *J Am Coll Cardiol* 2002;39:1345-52.
 151. McCully R, Roger V, Ommen S, Mahoney D, Burger K, Freeman W, et al. Outcomes of patients with reduced exercise capacity at time of exercise echocardiography. *Mayo Clin Proc* 2004;79:750-7.
 152. Sicari R, Pasanisi E, Venneri L, Landi P, Cortigiani L, Picano E. Stress echo results predict mortality: a large-scale multicenter prospective international study. *J Am Coll Cardiol* 2003;41:589-95.
 153. Tsutsui J, Elhendy A, Anderson J, Zie F, McGrain A, Porter T. Prognostic value of dobutamine stress myocardial contrast perfusion echocardiography. *Circulation* 2005;112:1440-50.

154. Elhendy A, Modesto K, Mahoney D, Khandheria B, Seward J, Pellikka P. Prediction of mortality in patients with left ventricular hypertrophy by clinical, exercise stress, and echocardiographic data. *J Am Coll Cardiol* 2003;41:129-35.
155. McCully R, Roger V, Mahoney D, Karon B, Oh J, Miller FJ, 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.
156. Sawada S, Ryan T, Conley M, Corya B. Prognostic value of a normal exercise echocardiogram. *Am Heart J* 1990;120:49-55.
157. Elhendy A, Mahoney D, McCully R, Seward J, Burger K, Pellikka P. Use of scoring model combining clinical, exercise test, and echocardiographic data to predict mortality in patients with known or suspected coronary artery disease. *Am J Cardiol* 2004;93:1223-8.
158. Marwick T, Case C, Poldermans D, Boersma E, Bax J, Sawada S, et al. A clinical and echocardiographic score for assigning risk of major events after dobutamine echocardiograms. *J Am Coll Cardiol* 2004;43:2102-7.
159. Marwick T, Case C, Vasey C, Allen S, Short L, Thomas J. Prediction of mortality by exercise echocardiography: a strategy for combination with the Duke treadmill score. *Circulation* 2001;103:2566-71.
160. Marwick T, Case C, Sawada S. Prediction of mortality using dobutamine echocardiography. *J Am Coll Cardiol* 2001;37:754-60.
161. Arruda-Olson A, Juracan E, Mahoney D, McCully R, Roger V, Pellikka P. Prognostic value of exercise echocardiography in 5,798 patients: is there a gender difference? *J Am Coll Cardiol* 2002;39:625-31.
162. Biagini E, Elhendy A, Bax J, Rizzello V, Schinkel A, van Domburg R, et al. Seven-year follow-up after dobutamine stress echocardiography: impact of gender on prognosis. *J Am Coll Cardiol* 2005;45:93-7.
163. Elhendy A, Arruda A, Mahoney D, Pellikka P. Prognostic stratification of diabetic patients by exercise echocardiography. *J Am Coll Cardiol* 2001;37:1551-7.
164. Elhendy A, Mahoney D, Khandheria B, Paterick T, Burger K, Pellikka P. Prognostic significance of the location of wall motion abnormalities during exercise echocardiography. *J Am Coll Cardiol* 2002;40:1623-9.
165. Elhendy A, Cornel J, Roelandt J, van Domburg R, Nierop P, Geleynse MS, et al. Relation between contractile response of akinetic segments during dobutamine stress echocardiography and myocardial ischemia assessed by simultaneous thallium-201 single-photon emission computed tomography. *Am J Cardiol* 1996;77:955-9.
166. Elhendy A, Cornel J, Roelandt J, Van Domburg R, Fioretti P. Akinesis becoming dyskinesis during dobutamine stress echocardiography: a predictor of poor functional recovery after surgical revascularization. *Chest* 1996;110:155-8.
167. Sicari R, Cortigiani L, Bigi R, Landi P, Raciti M, Picano E, et al. Prognostic value of pharmacologic stress echocardiography is affected by concomitant antiischemic therapy at the time of testing. *Circulation* 2004;109:2428-31.
168. Marwick T, Case C, Sawada S, Vasey C, Thomas J. Prediction of outcomes in hypertensive patients with suspected coronary disease. *Hypertension* 2002;39:1113-8.
169. Cortigiani L, Coletta C, Bigi R. Clinical, exercise electrocardiographic, and pharmacologic stress echocardiographic findings for risk stratification of hypertensive patients with chest pain. *Am J Cardiol* 2003;91:941-5.
170. Cortigiani L, Picano E, Vigna C, Lattanzi F, Coletta C, Mariotti E, et al. Prognostic value of pharmacologic stress echocardiography in patients with left bundle branch block. *Am J Med* 2001;110:361-9.
171. Smart S, Dionisopoulos P, Knickelbine T. Dobutamine-atropine stress echocardiography for risk stratification in patients with chronic left ventricular dysfunction. *J Am Coll Cardiol* 1999;33:512-21.
172. Poldermans D, Bax J, Elhendy A, Sozzi F, Boersma E, Thomson I, et al. Long-term prognostic value of dobutamine stress echocardiography in patients with atrial fibrillation. *Chest* 2001;119:144-9.
173. Shaw L, Vasey C, Sawada S, Rimmerman C, Marwick T. Impact of gender on risk stratification by exercise and dobutamine stress echocardiography: long-term mortality in 4234 women and 6898 men. *Eur Heart J* 2005;26:447-56.
174. Marwick T, Anderson T, Williams M, Haluska B, Melin J, Pashkow F, et al. Exercise echocardiography is an accurate and cost-efficient technique for detection of coronary artery disease in women. *J Am Coll Cardiol* 1995;26:335-41.
175. Elhendy A, Geleijnse M, van Domburg R. Gender differences in the accuracy of dobutamine stress echocardiography for the diagnosis of coronary artery disease. *Am J Cardiol* 1997;80:1414-8.
176. Smart S, Knickelbine T, Stoiber T, Carlos M, Wynsen J, Sagar K. Safety and accuracy of dobutamine-atropine stress echocardiography for the detection of residual stenosis of the infarct-related artery and multivessel disease during the first week after acute myocardial infarction. *Circulation* 1997;95:1394-401.
177. Desideri A, Fioretti P, Cortigiani L, Trocino G, Astarita C, Gregori D, et al. Pre-discharge stress echocardiography and exercise ECG for risk stratification after uncomplicated acute myocardial infarction: results of the COSTAMI-II (cost of strategies after myocardial infarction) trial. *Heart* 2005;91:146-51.
178. Carlos M, Smart S, Wynsen J, Sagar K. Dobutamine stress echocardiography for risk stratification after myocardial infarction. *Circulation* 1997;95:1402-10.
179. Sicari R, Landi P, Picano E, Pirelli S, Chiaranda G, Previtali M, et al. Exercise-electrocardiography and/or pharmacological stress echocardiography for non-invasive risk stratification early after uncomplicated myocardial infarction: a prospective international large scale multicenter study. *Eur Heart J* 2002;23:1030-7.
180. Greco C, Salustri A, Seccareccia F, Ciavatti M, Biferali F, Valtorta C, et al. Prognostic value of dobutamine echocardiography early after uncomplicated acute myocardial infarction: a comparison with exercise echocardiography. *J Am Coll Cardiol* 1997;29:261-7.
181. Ryan T, Armstrong W, O'Donnell J, Feigenbaum H. Risk stratification after acute myocardial infarction by means of exercise two-dimensional echocardiography. *Am Heart J* 1987;114:1305-15.
182. Williams M, Obadashian J, Lauer M. Prognostic value of dobutamine echocardiography in patients with left ventricular dysfunction. *J Am Coll Cardiol* 1996;27:132-9.
183. Elhendy A, Sozzi F, van Domburg R, Bax J, Schinkel A, Roelandt J, et al. Effect of myocardial ischemia during dobutamine stress echocardiography on cardiac mortality in patients with heart failure secondary to ischemic cardiomyopathy. *Am J Cardiol* 2005;96:469-73.
184. Arruda A, Das F, Roger R, Klarich J, Mahoney A, Pellikka J. Prognostic value of exercise echocardiography in 2,632 patients \geq 65 years of age. *J Am Coll Cardiol* 2001;37:1036-41.
185. Biagini E, Elhendy A, Schinkel A, Rizzello V, Bax J, Sozzi F, et al. Long-term prediction of mortality in elderly persons by

- dobutamine stress echocardiography. *J Gerontol A Biol Sci Med Sci* 2005;60:1333-8.
186. Chaowalit N, Arruda A, McCully R, Bailey K, Pelikka P. Dobutamine stress echocardiography in patients with diabetes mellitus: enhanced prognostic prediction using a simple risk score. *J Am Coll Cardiol* 2006;47:1029-36.
187. Sozzi F, Elhendy A, Roelandt J. Prognostic value of dobutamine stress echocardiography in patients with diabetes. *Diabetes Care* 2003;26:1074-8.
188. Marwick T, Case C, Sawada S, Vasey C, Short L, Lauer M. Use of stress echocardiography to predict mortality in patients with diabetes and known or suspected coronary artery disease. *Diabetes Care* 2002;25:1042-8.
189. Boersma E, Poldermans D, Bax J, Steyerberg E, Thomson I, Banga J, et al. Predictors of cardiac events after major vascular surgery: role of clinical characteristics, dobutamine echocardiography, and beta-blocker therapy. *J Am Med Assoc* 2001;285:1865-73.
190. Shaw L, Eagle K, Gersh B, Miller D. Meta-analysis of intravenous dipyridamole-thallium-201 imaging (1985 to 1994) and dobutamine echocardiography (1991 to 1994) for risk stratification before vascular surgery. *J Am Coll Cardiol* 1996;27:787-98.
191. Sicari R, Ripoli A, Picano E, Djordjevic-Dikic A, Di Giovanbattista R, Minardi G, et al. Perioperative prognostic value of dipyridamole echocardiography in vascular surgery: a large-scale multicenter study in 509 patients; EPIC (echo Persantine international cooperative) study group. *Circulation* 1999;100:269-74.
192. Poldermans D, Fioretti P, Forster T, Thomson I. Dobutamine stress echocardiography for assessment of perioperative cardiac risk in patients undergoing major vascular surgery. *Circulation* 1993;87:1506-12.
193. Poldermans D, Arnese M, Fioretti P, Boersma E, Thomson I, Rambaldi R, et al. Sustained prognostic value of dobutamine stress echocardiography for late cardiac events after major non-cardiac vascular surgery. *Circulation* 1997;95:53-8.
194. Kertai M, Boersma E, Bax J. A meta-analysis comparing the prognostic accuracy of six diagnostic rests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. *Heart* 2003;89:1327-34.
195. Elhendy A, Geleijnse M, Roelandt J, Cornel J, van Domburg R, El-Rafae M, et al. Assessment of patients after coronary artery bypass grafting by dobutamine stress echocardiography. *Am J Cardiol* 1996;77:1234-6.
196. Kafka H, Leach A, Fitzgibbon G. Exercise echocardiography after coronary artery bypass surgery: correlation with coronary angiography. *J Am Coll Cardiol* 1995;25:1019-23.
197. Dagianti A, Rosanio S, Penco M, Dagianti A, Sciomer S, Tocchi M, et al. Clinical and prognostic usefulness of supine bicycle exercise echocardiography in the functional evaluation of patients undergoing elective percutaneous transluminal coronary angioplasty. *Circulation* 1997;95:1176-84.
198. Arruda A, McCully R, Oh J, Mahoney D, Seward J, Pelikka P. Prognostic value of exercise echocardiography in patients after coronary artery bypass surgery. *Am J Cardiol* 2001;87:1069-73.
199. Bountiokos M, Elhendy A, van Domburg R, Schinkel A, Bax J, Krenning B, et al. Prognostic value of dobutamine stress echocardiography in patients with previous coronary revascularization. *Heart* 2004;90:1031-5.
200. Elhendy A, Mahoney D, Burger K, McCully R, Pelikka P. Prognostic value of exercise echocardiography in patients with classic angina pectoris. *Am J Cardiol* 2004;94:559-63.
201. Biagini E, Elhendy A, Schinkel A, Bax J, Vittoria R, van Domburg R, et al. Risk stratification of patients with classic angina pectoris and no history of coronary artery disease by dobutamine stress echocardiography. *J Am Coll Cardiol* 2005;46:730-2.
202. Klocke F, Baird M, Lorell B, Bateman T, Messer J, Berman D, et al. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging—executive summary: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (ACC/AHA/ASNC committee to revise the 1995 guidelines for the clinical use of cardiac radionuclide imaging). *J Am Coll Cardiol* 2003;42:1318-33.
203. Metz L, Beattie M, Hom R, Redberg R, Grady D, Fleischmann K. The prognostic value of normal exercise myocardial perfusion imaging and exercise echocardiography: a meta-analysis. *J Am Coll Cardiol* 2007;49:227-37.
204. Geleijnse M, Elhendy A, van Domburg R, Cornel J, Rambaldi R, Salustri A, et al. Cardiac imaging for risk stratification with dobutamine-atropine stress testing in patients with chest pain: echocardiography, perfusion scintigraphy, or both? *Circulation* 1997;96:137-47.
205. Olmos L, Dakik H, Gordon R, Dunn J, Verani M, Quinones M, et al. Long-term prognostic value of exercise echocardiography compared with exercise 201TI, ECG, and clinical variables in patients evaluated for coronary artery disease. *Circulation* 1998;98:2679-86.
206. Schinkel A, Bax J, Elhendy A, van Domburg R, Valkema R, Vourvouri E, et al. Long-term prognostic value of dobutamine stress echocardiography compared with myocardial perfusion scanning in patients unable to perform exercise tests. *Am J Med* 2004;117:1-9.
207. Shaw L, Marwick T, Berman D, Sawada S, Heller G, Vasey C, et al. Incremental cost-effectiveness of exercise echocardiography vs SPECT imaging for evaluation of stable chest pain. *Eur Heart J* 2006;27:2448-58.
208. Ahmad M, Tianrong X, McCulloch M, Abreo G, Runge M. Real-time three-dimensional dobutamine stress echocardiography in assessment of ischemia: comparison with two-dimensional dobutamine stress echocardiography. *J Am Coll Cardiol* 2001;37:1303-8.
209. Sugeng L, Weinert L, Lang R. Left ventricular assessment using real-time three dimensional echocardiography. *Heart* 2003;89:29-36.
210. Yang H, Pelikka P, McCully R, Oh J, Kukuzke J, Khandheria B, et al. Role of biplane and biplane echocardiographically guided 3-dimensional echocardiography during dobutamine stress echocardiography. *J Am Soc Echocardiogr* 2006;19:1136-43.
211. Wei K, Ragosta M, Thorpe J, Coggins M, Moos S, Kaul S. Noninvasive quantification of coronary blood flow reserve in humans using myocardial contrast echocardiography. *Circulation* 2001;103:2560-5.
212. Masugata H, Lafitte S, Peters B, Strachan G, DeMaria A. Comparison of real-time and intermittent triggered myocardial contrast echocardiography for quantification of coronary stenosis severity and transmural perfusion gradient. *Circulation* 2001;104:1550-6.
213. Moir S, Haluska B, Jenkins C, Fathi R, Marwick T. Incremental benefit of myocardial contrast to combine dipyridamole-exercise stress echocardiography for the assessment of coronary artery disease. *Circulation* 2004;110:1108-13.
214. Elhendy A, O'Leary E, Xie F, Mcgrain A, Anderson J, Porter T. Comparative accuracy of real-time myocardial contrast perfusion imaging and wall motion analysis during dobutamine stress echocardiography for the diagnosis of coronary artery disease. *J Am Coll Cardiol* 2004;44:2185-91.

stress echocardiography. 4. echocardiography recommendations. 4. recommendations performance. 4. society echocardiography. 4. american society. 4. echocardiography. 2. stress. 1. application. 1. american. 1.Â Please type a message to the paper's authors to explain your need for the paper. Paper: American Society of Echocardiography recommendations for performance, interpretation, and application of stress echocardiography. To: Patricia A Pellikka, Sherif F Nagueh, Abdou A Elhendy, Cathryn A Kuehl, Stephen G Sawada, From (Name): E-mail: Only shared with authors of paper. Please enter a personalized message to the authors. More detailed explanations for your need are more likely to get a response. Send Request. Load Form Load Form. American Society of Echocardiography Recommendations for Performance, Interpretation, and Application of Stress Echocardiography. Pellikka PA, Nagueh SF, Elhendy AA, Kuehl CA, Sawada SG. J Am Soc Echocardiogr 2015, 20:1021-1041.Â The clinical use of stress echocardiography in non-ischaemic heart disease: recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, Edvardsen T, Garbi M, Ha JW, Kane GC, Kreeger J, Mertens L, Pibarot P, Picano E, Ryan T, Tsutsui JM, Varga A. Eur Heart J Cardiovasc Imaging. ASE Recommendations for Performance, Interpretation and Application of Stress Echocardiography, JASE, September 2007. Guidelines for Performing a Comprehensive Epicardial Echocardiography Examination: Recommendations of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists, JASE, April 2007. 3D Echocardiography: A Review of the Current Status and Future Directions, JASE, March 2007.Â American Society of Echocardiography and Society of Cardiovascular Anesthesiologists Task Force Guidelines for Training in Perioperative Echocardiography, JASE, June 2002. Hand-carried Ultrasound Device: Recommendations Regarding New Technology, JASE, April 2002.