Advances since the 1998 publication of the Recommendations for Performance and Interpretation of Stress Echocardiography 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. 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...
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. The improvement in endocardial visualization achieved with harmonic imaging has decreased interobserver variability and improved the sensitivity of stress echocardiography.

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. 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.

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. Imaging is performed at rest and immediately after completion of exercise. 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. 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.

**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 μg/kg/min and increasing at 3-minute intervals to 10, 20, 30, and 40 μg/kg/min is the standard for dobutamine stress testing. 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. 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. Patients given atropine at the 30-μg/kg/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. Administration of beta-blockers at peak stress or during recovery may increase test sensitivity.

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 dysfunct,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

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.23 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.47

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, unchanged 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.57,58

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.56 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
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

**Table 1 Normal and ischemic responses for various modalities of stress**

<table>
<thead>
<tr>
<th>Stress method</th>
<th>Regional</th>
<th>Global</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal response</strong></td>
<td><strong>Ischemic response</strong></td>
<td><strong>Normal response</strong></td>
</tr>
<tr>
<td>Treadmill</td>
<td>Postexercise increase in function compared with rest</td>
<td>Postexercise decrease in function compared with rest</td>
</tr>
<tr>
<td>Supine bicycle</td>
<td>Peak exercise increase in function compared with rest</td>
<td>Peak exercise decrease in function compared with rest</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>Increase in function, velocity of contraction compared with rest and usually with low dose</td>
<td>Decrease in function, velocity of contraction compared with low dose; may be less compared with rest</td>
</tr>
<tr>
<td>Vasodilator</td>
<td>Increase in function compared with rest</td>
<td>Decrease in function compared with rest</td>
</tr>
<tr>
<td>Atrial pacing</td>
<td>No change or increase in function compared with rest</td>
<td>Decrease in function compared with rest</td>
</tr>
</tbody>
</table>

EF, Ejection fraction; ESV, end-systolic volume; L, left.
been shown to be accurate markers of ischemia in experimental\textsuperscript{71} and early clinical\textsuperscript{72-75} 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{79}

In the current era, the specificity of all noninvasive imaging tests will be reduced by test verification bias.\textsuperscript{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.\textsuperscript{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.\textsuperscript{33,84} The use of atropine substantially enhances the sensitivity of dobutamine stress in the setting of beta-blockade\textsuperscript{17} and may be required to overcome Wenckebach heart block during atrial pacing.\textsuperscript{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.\textsuperscript{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.\textsuperscript{87} Supine bicycle exercise test has higher sensitivity for detection of left circumflex disease.\textsuperscript{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.\textsuperscript{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.\textsuperscript{91} Finally, the hyperdynamic state accompanying significant aortic or mitral regurgitation may make detection of ischemia more difficult.\textsuperscript{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.95 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.95 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 dysynchrony from ischemia.100-102 In addition, septal dysynchrony 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, post-premeasure ventricular contraction stimulation, enoximone, and low-dose dipyridamole.

In comparison with the assessment of viability using nuclear perfusion tracers or contrast 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-
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. 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 μg/kg/min, with gradual increase to 5, 7.5, 10, and 20 μg/kg/min, is frequently used. 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 μg/kg/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%. 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 μg/kg/min, with gradual increase to 5, 7.5, 10, and 20 μg/kg/min, is frequently used. 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 μg/kg/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%. 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. 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. 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.

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.

**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. 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. 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. This approach has been validated against invasive measurements for identifying an elevated exercise mean LV diastolic pressure. Limitations to the above methodology include atrial fibrillation, tech-
chnically 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. Exercise may be useful in patients with pulmonary hypertension to gain insight into RV and LV function and the changes in stroke volume with exercise. 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. Highly trained male athletes have been found to have a Doppler-derived pulmonary artery systolic pressure as high as 60 mm Hg with exercise. There are also published reports about the use of exercise echocardiography in detecting asymptomatic gene carriers of familial primary pulmonary hypertension, and identifying patients susceptible to high-altitude pulmonary edema.

**Mitral Valve Disease**

In patients with mitral valve disease, exercise testing may provide insights regarding exertional symptoms disproportionate to resting hemodynamics. 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). 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). At baseline and with stress, transmural 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. In sedentary patients, exercise-induced dyspnea, along with an increase in mean transmural 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. When exercise results in only minimal changes in transmural 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.

Evaluation of mitral regurgitation is possible with quantitative and semiquantitative color Doppler methods. 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. 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. For patients with severe mitral regurgitation and normal EF at rest, stress echocardiography can detect the presence of reduced LV contractile reserve.

**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. In these patients, dobutamine is used to assess both the severity of aortic stenosis and the presence of LV contractile reserve. 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.
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 IIB 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 endpoints 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,155,160-162 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

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of patients</th>
<th>Patient characteristics</th>
<th>Stress type</th>
<th>Mean or median follow up, y</th>
<th>End point</th>
<th>Echocardiographic predictors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arruda-Olson et al 2002(^{161})</td>
<td>5798</td>
<td>Known or suspected CAD</td>
<td>Exercise</td>
<td>3.2</td>
<td>Cardiac death/MI</td>
<td>Exercise WMSI</td>
</tr>
<tr>
<td>Marwick et al 2001(^{159})</td>
<td>5375</td>
<td>Known or suspected CAD</td>
<td>Exercise</td>
<td>5.5</td>
<td>All deaths</td>
<td>Extent of resting WMA; extent of ischemia</td>
</tr>
<tr>
<td>Biagini et al 2005(^{162})</td>
<td>3381</td>
<td>Known or suspected CAD</td>
<td>Dobutamine</td>
<td>7</td>
<td>Cardiac death/MI</td>
<td>Resting WMA, ischemia</td>
</tr>
<tr>
<td>Marwick et al 2001(^{160})</td>
<td>3156</td>
<td>Known or suspected CAD</td>
<td>Dobutamine</td>
<td>3.8</td>
<td>Cardiac death</td>
<td>Resting WMA, ischemia</td>
</tr>
<tr>
<td>Chuah et al 1998(^{66})</td>
<td>860</td>
<td>Known or suspected CAD</td>
<td>Dobutamine</td>
<td>2</td>
<td>Cardiac death/MI</td>
<td>Stress WMA; end-systolic volume response</td>
</tr>
<tr>
<td>Shaw et al 2005(^{173})</td>
<td>11,132</td>
<td>Known or suspected CAD</td>
<td>Exercise or dobutamine</td>
<td>5</td>
<td>Cardiac death</td>
<td>Extent of resting WMA; extent of ischemia</td>
</tr>
<tr>
<td>Sicari et al 2003(^{152})</td>
<td>7333</td>
<td>Known or suspected CAD</td>
<td>Dipyridamole or dobutamine</td>
<td>2.6</td>
<td>Cardiac death/MI</td>
<td>Resting EF, change in WMSI</td>
</tr>
<tr>
<td>Tsutsui et al 2005(^{153})</td>
<td>788</td>
<td>Known or suspected CAD</td>
<td>Dobutamine myocardial contrast perfusion</td>
<td>1.7</td>
<td>Death/MI</td>
<td>Contrast perfusion defects</td>
</tr>
<tr>
<td>Bergeron et al 2004(^{123})</td>
<td>3260</td>
<td>Chest pain or dyspnea</td>
<td>Exercise</td>
<td>3.1</td>
<td>Mortality/morbidity</td>
<td>Change in WMSI</td>
</tr>
<tr>
<td>Elhendy et al 2001(^{163})</td>
<td>563</td>
<td>Diabetes</td>
<td>Exercise</td>
<td>3</td>
<td>Cardiac death/MI</td>
<td>EF, extent of ischemia</td>
</tr>
<tr>
<td>Sozzi et al 2003(^{187})</td>
<td>396</td>
<td>Diabetes</td>
<td>Dobutamine</td>
<td>3</td>
<td>Cardiac death/MI</td>
<td>EF, extent of ischemia</td>
</tr>
<tr>
<td>Marwick et al 2002(^{188})</td>
<td>937</td>
<td>Diabetes</td>
<td>Exercise or dobutamine</td>
<td>3.9</td>
<td>All deaths</td>
<td>Extent of resting WMA; extent of ischemia</td>
</tr>
<tr>
<td>Chaowalit et al 2006(^{186})</td>
<td>2349</td>
<td>Diabetes</td>
<td>Dobutamine</td>
<td>5.4</td>
<td>Mortality/morbidity (MI, late coronary revascularization)</td>
<td>Extent of ischemia and failure to reach target heart rate</td>
</tr>
<tr>
<td>Arruda et al 2001(^{184})</td>
<td>2632</td>
<td>Elderly (≥65 y)</td>
<td>Exercise</td>
<td>2.9</td>
<td>Cardiac death/MI</td>
<td>Changes of EF and end-systolic volume</td>
</tr>
<tr>
<td>Biagini et al 2005(^{185})</td>
<td>1434</td>
<td>Elderly (≥65 y)</td>
<td>Dobutamine</td>
<td>6.5</td>
<td>Cardiac death/MI</td>
<td>Resting WMA, ischemia</td>
</tr>
<tr>
<td>Carlos et al 1997(^{178})</td>
<td>214</td>
<td>Acute MI</td>
<td>Dobutamine</td>
<td>1.4</td>
<td>Cardiac death, MI, arrhythmias, heart failure</td>
<td>Resting WMSI; remote abnormalities</td>
</tr>
<tr>
<td>Elhendy et al 2005(^{183})</td>
<td>528</td>
<td>Heart failure</td>
<td>Dobutamine</td>
<td>3.2</td>
<td>Cardiac death</td>
<td>Resting EF, ischemia</td>
</tr>
<tr>
<td>Elhendy et al 2003(^{182})</td>
<td>483</td>
<td>LVH by echocardiographic criteria</td>
<td>Exercise</td>
<td>3</td>
<td>Cardiac death/MI</td>
<td>Resting WMSI, EF response</td>
</tr>
<tr>
<td>Arruda et al 2001(^{198})</td>
<td>718</td>
<td>Previous CABG</td>
<td>Exercise</td>
<td>2.9</td>
<td>Cardiac death/MI</td>
<td>Changes of EF and end-systolic volume</td>
</tr>
<tr>
<td>Bountioutko et al 2004(^{199})</td>
<td>331</td>
<td>Previous CABG or PCI</td>
<td>Dobutamine</td>
<td>2</td>
<td>Cardiac death/MI/late revascularization</td>
<td>Ischemia</td>
</tr>
<tr>
<td>Biagini et al 2005(^{31})</td>
<td>136</td>
<td>Pacemaker recipients</td>
<td>Pacing</td>
<td>3.5</td>
<td>Cardiac death</td>
<td>Ischemia</td>
</tr>
<tr>
<td>Das et al 2000(^{61})</td>
<td>530</td>
<td>Before nonvascular surgery</td>
<td>Dobutamine</td>
<td>Hospital stay</td>
<td>Cardiac death/MI</td>
<td>Ischemia threshold</td>
</tr>
<tr>
<td>Poldermans et al 1997(^{193})</td>
<td>360</td>
<td>Before vascular surgery</td>
<td>Dobutamine</td>
<td>1.6</td>
<td>Perioperative and late cardiac events</td>
<td>Ischemia</td>
</tr>
<tr>
<td>Sicari et al 1999(^{191})</td>
<td>509</td>
<td>Before vascular surgery</td>
<td>Dipyridamole</td>
<td>Hospital stay</td>
<td>Death, MI, unstable angina</td>
<td>Ischemia</td>
</tr>
</tbody>
</table>

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.
the magnitude of risk associated with stress echocardiographic abnormalities is independent of sex.\textsuperscript{161,162}

After Acute Myocardial Infarction

Resting LV function is a major determinant of prognosis after myocardial infarction.\textsuperscript{163} \textbf{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.}\textsuperscript{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 ECG\textsuperscript{177} or angiography.\textsuperscript{178} The incremental prognostic value of stress echocardiography is preserved in patients with abnormal LV function.\textsuperscript{162} 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.\textsuperscript{183}

### Table 3 Stress echocardiography predictors of risk

<table>
<thead>
<tr>
<th>Very low risk* MI, cardiac events</th>
<th>Low risk* MI, cardiac death</th>
<th>Factors increasing risk‡</th>
<th>High risk‡ RR ≥ 4-fold over low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal exercise echocardiogram</td>
<td></td>
<td></td>
<td>Extensive rest WMA (4−5 segments of LV)</td>
</tr>
<tr>
<td>result with good exercise capacity</td>
<td></td>
<td></td>
<td>Baseline EF &lt; 40%</td>
</tr>
<tr>
<td>7 METs men</td>
<td></td>
<td></td>
<td>Extensive ischemia (4−5 segments of LV)</td>
</tr>
<tr>
<td>5 METs women</td>
<td></td>
<td></td>
<td>Multivessel ischemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rest WMA and remote ischemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low ischemic threshold</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ischemia with 0.56 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>dipyridamole or 20 µg/</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>kg/min dobutamine or based on heart rate/</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ischemia WMA, no change or decrease in exercise EF$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{*}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.

\textsuperscript{†}The degree to which each factor increases risk is variable.

\textsuperscript{$}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).

\textsuperscript{§}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.
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. Pharmacologic stress echocardiography can independently predict mortality among elderly patients unable to exercise. 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. 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.

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. Pharmacologic stress echocardiography has been shown to be a powerful tool for cardiac risk stratification before vascular and nonvascular surgery. Test results provided better risk stratification than that which can be gained from clinical indices. 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. In 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. 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.

After Coronary Revascularization

Stress echocardiography can localize restenosis or graft occlusion, detect native unvascularized CAD, and assess adequacy of revascularization. Positive stress echocardiography after coronary angioplasty identifies patients at high risk for recurrence of angina. Ischemia by stress echocardiography was incrementally predictive of cardiac events. 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. 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 risk, and has been shown to be useful for risk stratification.

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. 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 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. 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. 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. 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. 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. 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. Myocardial contrast perfusion imaging may have greater sensitivity than wall-motion analysis. 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**


40. Sutherland G, Kukulski T, Krüting J, D’hooge J, Arnold M, Brandt E. Quantitation of left ventricular asynchrony by cardiac ultrasound. Am J Cardiol 2000;86:4-9G.


68. Cain P, Baglin T, Case C, Spicer D, Short L, Marwick T. Application of tissue Doppler to interpretation of dobut-


The Journal of the American Society of Echocardiography (JASE) brings physicians and sonographers peer-reviewed original investigations and state-of-the-art review articles that cover conventional clinical applications of cardiovascular ultrasound, as well as newer techniques with emerging clinical applications. These include three-dimensional echocardiography, strain and strain rate methods for evaluating cardiac mechanics and interventional applications. Benefits to authors We also provide many author benefits, such as free PDFs, a liberal copyright policy, special discounts on Elsevier publications. "Guidelines for Performance, Interpretation, and Application of Stress Echocardiography in Ischemic Heart Disease: From the American Society of Echocardiography." J Am Soc Echocardiogr. 2020 Jan;33(1):1-41.e8 Klein AL, Abbara S, Agler DA, et al. "American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography." J Am Soc Echocardiogr. 2013;26:965-1012.e15.