STATE-OF-THE-ART PAPER

Stress Echocardiography
Current Methodology and Clinical Applications

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Stress echocardiography is commonly employed for the clinical management of known or suspected coronary artery disease. This review discusses the accuracy of the technique, which is equivalent to that of competing imaging techniques, as well as its overall role in patient management. The utilization of stress echocardiographic modalities in clinical presentations, such as chest pain, congestive heart failure, and valvular heart disease, and preoperative risk assessment, as well as determining myocardial viability, are discussed. (J Am Coll Cardiol 2005;45:1739–47) © 2005 by the American College of Cardiology Foundation

Stress echocardiography was introduced in 1979 and has developed into a versatile technique for identifying patients with coronary artery disease (CAD) and determining prognosis. The rationale for its use is that cardiovascular stress will result in ischemia, which in turn is manifested as a regional wall motion abnormality (WMA) distal to an obstructive coronary lesion (Fig. 1). In addition to its role in CAD, stress echocardiography can be used to assess the severity of valvular heart disease and for detection of occult pulmonary hypertension.

STRESS ECHOCARDIOGRAPHY METHODOLOGY

Either physical or pharmacologic stress can be used (Table 1). The choice of exercise (treadmill vs. bicycle) has become a matter of laboratory choice and patient acceptability. With treadmill exercise, only post-exercise imaging is available. This results in the possibility of WMA resolving rapidly and hence a false-negative study. This effect is most likely with milder or single-vessel stenosis. Bicycle exercise has the advantage of imaging the heart at peak exercise. This may result in detection of a greater extent of ischemia and in a theoretical increase in sensitivity. If post-treadmill imaging is utilized, it is imperative that imaging be completed within 45 to 60 s to avoid resolution of stress-induced WMA.

For patients incapable of adequate physical exercise, pharmacologic stress can be substituted. The most commonly employed agents are dobutamine and dipyridamole (or adenosine). Based on a number of factors, including cost, dobutamine has been the preferred agent in the U.S. Combinations of dobutamine and dipyridamole have been used to simultaneously increase myocardial oxygen demand and accentuate flow discrepancy. Pacing stress, using either a temporary transvenous catheter, an implanted pacemaker, or transesophageal atrial pacing, is also an alternative to exercise.

For patients capable of exercise, in whom the question is the presence or absence of CAD, or for evaluation of dyspnea and fatigue, exercise is preferred to pharmacologic testing because it allows a link to be drawn between physical activity and provokable abnormalities. Similarly, while the response of pulmonary artery pressures (measured from the tricuspid regurgitation jet) to exercise has been validated, the same conclusion cannot be made when using pharmacologic stress. Table 2 outlines the commonly employed stress echocardiographic methodologies that should be considered as primary, alternative, or not recommended depending on the clinical question to be addressed.

ANALYSIS OF STRESS ECHOCARDIOGRAMS

Analysis of stress echocardiograms is one of the more challenging aspects of echocardiography, and it should only be undertaken by individuals with appropriate training and experience (1). There are several levels of complexity with which wall motion can be analyzed. These include a simple qualitative assessment of normal versus abnormal qualitative descriptors of regional wall motion as normal, hypokinetic, akinetic, or dyskinetic, generation of a wall motion score, and quantitative techniques such as ventricular volumes, ejection fraction, chordal, and area shrinkage. The most commonly employed scheme is simply to describe segments as normal, hypokinetic, akinetic, or dyskinetic and to calculate a wall motion score.

A wall motion score index is a unit-less number that is directly proportional to the severity and extent of WMA. For its calculation, each left ventricular (LV) segment is given a score of one to four (normal, hypokinetic, akinetic, or dyskinetic, respectively). The wall motion score is calculated as the sum of individual scores divided by the number of scored segments. A separate score can be calculated for the left anterior descending coronary artery (LAD) and posterior circulation. In addition to analysis of standard images, other technology can be brought to bear for evalu-

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Abbreviations and Acronyms
CAD  = coronary artery disease
DSE  = dobutamine stress echocardiography
ECG  = electrocardiogram
LAD  = left anterior descending coronary artery
LV   = left ventricle/ventricular
WMA  = wall motion abnormality
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Table 1. Stress Echocardiography Methods

Exercise
Post-treadmill exercise
Supine bicycle
Upright bicycle
Pharmacologic
Dobutamine infusion (±atropine)
Dipyridamole (±atropine)
Adenosine (±atropine)
Combined dobutamine−dipyridamole
Other
Transesophageal atrial pacing
Transvenous pacing (temporary or permanent)
Ergonovine*
Hyperventilation*
Cold pressor

*For provocation of coronary vasospasm.

ation of stress echocardiograms. Doppler tissue imaging has recently been used for quantitation of myocardial mechanics at rest and with stress, with most studies suggesting it is more sensitive than visual analysis alone (2). Finally, using Doppler methods, strain or strain rate can be calculated. Preliminary studies have suggested that strain rate imaging is even more sensitive than Doppler tissue velocity or displacement for detecting myocardial ischemia (3). These techniques have not yet seen widespread utilization in routine clinical laboratories.

When undertaken with exercise, the validity of the ST-segment response to stress is identical to that seen with routine treadmill testing; however, the electrocardiographic (ECG) response during dobutamine or vasodilator stress

provides less information. With exercise echocardiography, the hemodynamic response to stress has the same clinical implications as it does during routine treadmill testing. The hemodynamic response to vasodilator stress does not provide diagnostic or prognostic information. During dobutamine stress echocardiography (DSE), occasional patients have a paradoxical decrease in blood pressure. Hypotension
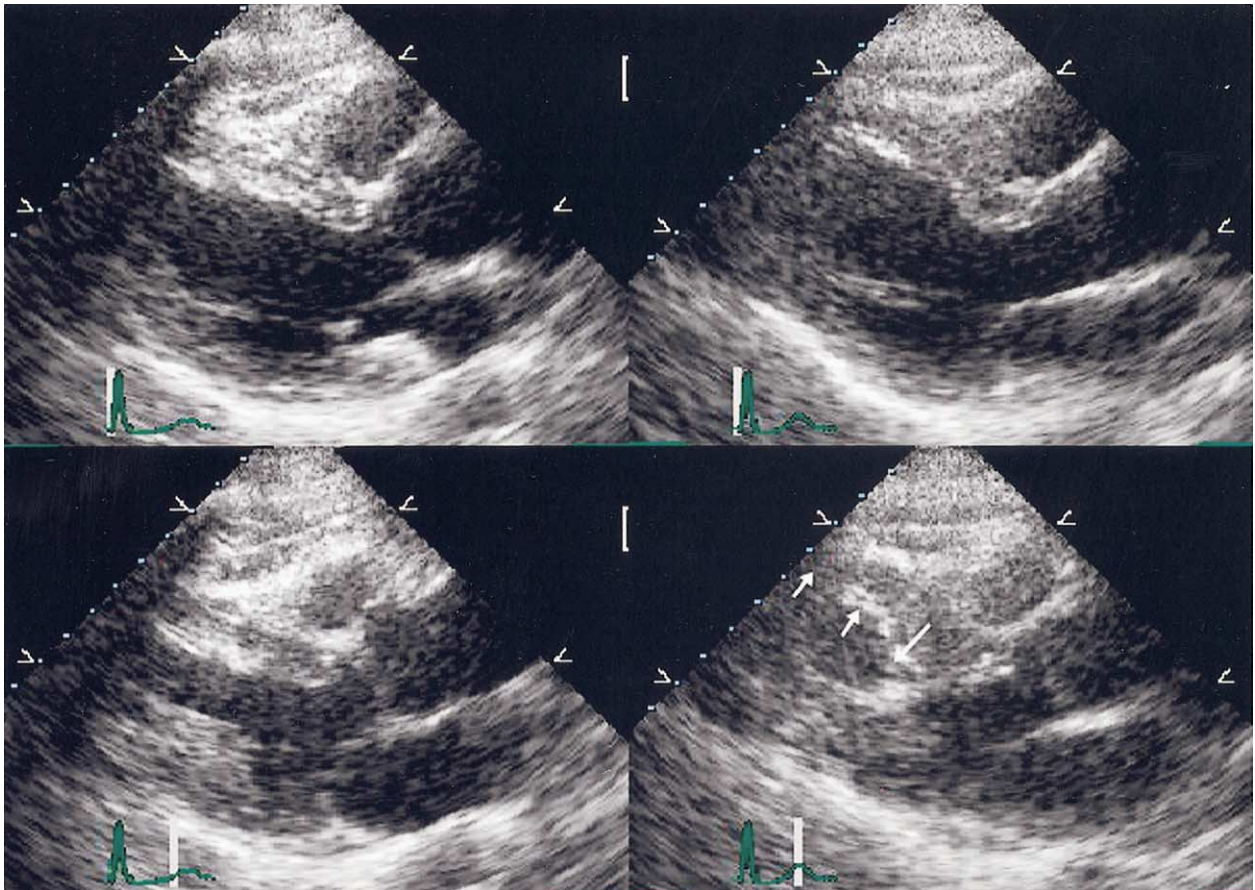

Figure 1. Parasternal long-axis echocardiogram recorded at rest **(left)** and immediately after exercise **(right)** in a patient with stenosis of the left anterior descending coronary artery. Diastolic frames are on the **top**, and systolic frames are on the **bottom**. At rest, notice the normal contraction of the septum and posterior wall. Immediately after exercise, the proximal septum has normal contractility **(downward pointing arrow)**, and there is dyskinesia of the distal ventricular septum **(upward pointing arrows)**.

Table 2. Role of Stress Echocardiography in Clinical Decision-Making

	TME	Bike	DSE
Chest pain evaluation	+	+	±
Post-MI risk	+	+	+
Viability	−	±	+
Dyspnea/fatigue	+	+	−
Preoperative risk assessment*	±	±	+
Valvular disease	−	+	−
Pulmonary hypertension	−	+	−

*For noncardiac surgery.

+ = preferred technique; ± = alternate technique, if preferred method not feasible; − = not recommended, lack of data to support use; DSE = dobutamine stress echocardiography; MI = myocardial infarction; TME = treadmill exercise time.

noted during DSE is not necessarily a manifestation of severe ischemia, as it is with exercise. Dobutamine-induced hypotension may be due to myocardial ischemia (usually multivessel), provocation of dynamic outflow tract obstruction, or a hyperdynamic ventricle with a small cavity size and a low stroke volume.

Because the accuracy of stress echocardiography is critically dependent on evaluation of myocardial thickening and endocardial motion, it is essential that all myocardial segments be adequately visualized. Utilization of tissue harmonic imaging has greatly enhanced the ability to identify and analyze wall segments. Intravenous contrast for LV cavity opacification also improves endocardial border definition and may salvage an otherwise suboptimal study.

ROLE OF STRESS ECHOCARDIOGRAPHY IN CAD

The most common uses of stress echocardiography are for the diagnosis of CAD and for determining prognosis. The diagnosis of CAD is based on detection of either a resting or inducible WMA. The implications of rest WMA are that a previous infarction has occurred or that there is sufficient ischemia at rest to render systolic function abnormal. If WMA is provoked at the time of stress, this implies the presence of obstructive CAD. To simply establish the diagnosis of CAD, a qualitative assessment generally suffices. Calculation of a wall motion score adds a semiquantitative element to this assessment, which may be valuable either for prognosis, serial studies, or risk stratification with respect to the amount of myocardium in jeopardy.

The accuracy of exercise echocardiography (Table 3) has been examined in numerous studies (4–16). Sensitivity has ranged from a low of 71% (13) to a high of 97% (5). As the threshold level of WMA required to define a positive study has varied, there has been the expected inverse relationship between sensitivity and specificity, with specificity ranging from 64% (5) in the studies reporting the highest sensitivity to over 90% (13) in studies with lower sensitivity. As with all other imaging modalities, the sensitivity for detection of patients with single-vessel disease has been lower (59% to 94%) than sensitivity for detection of patients with multivessel disease (85% to 100%). Although the sensitivity for identifying patients with multivessel disease is high, it is not

Table 3. Selected Studies Outlining the Accuracy of Exercise Echocardiography*

Author (Ref.)	Year	Exercise	Significant CAD	Total No. of Patients	Sensitivity (%)	Sensitivity for 1-VD (%)	Sensitivity for MVD (%)	Specificity (%)	PPV (%)	NPV (%)	Overall Accuracy (%)
Armstrong et al. (4)	1987	TME	50%	123	88	81	93	86	97	61	88
Crouse et al. (5)	1991	TME	50%	228	97	92	100	64	90	87	89
Marwick et al. (6)	1992	TME	50%	150	84	79	96	86	95	63	85
Quinones et al. (7)	1992	TME	50%	112	74	59	89	88	96	51	78
Hecht et al. (8)	1993	SBE	50%	180	93	84	100	86	95	79	91
Roger et al. (9)	1994	TME	50%	150	91	—	—	—	—	—	—
Beleslin et al. (10)	1994	TME	50%	136	88	88	91	82	97	50	88
Roger et al. (11)	1995	TME	50%	127	88	—	—	72	93	60	—
Marwick et al. (12)	1995	TME	50%	161	80	75	85	81	71	91	81
Marwick et al. (13)	1995	TME	>50%	147	71	63	80	91	85	81	82
Luotolahti et al. (14)	1996	UBE	50%	118	94	94	93	70	97	50	92
Roger et al. (15)	1997	TME	50%	340	78	—	—	41	79	40	69

*Modified with permission from the American College of Cardiology Foundation and American Heart Association (2).

1-VD = single vessel disease; CAD = coronary artery disease; MVD = multivessel disease; NPV = negative predictive value; PPV = positive predictive value; SBE = supine bicycle exercise; TME = treadmill exercise; UBE = upright bicycle exercise.

uncommon to understate the number of diseased vessels. This phenomenon occurs when a test is stopped for an indication such as angina or ST-segment depression. In this instance, the study will be discontinued when the most critical lesion becomes unmasked, and less severe stenoses may go undetected. Because decreased sensitivity is generally balanced by increased specificity, overall accuracy has been relatively high (69% to 92%). A similar level of accuracy with many of the same limitations has been noted for DSE (Table 4) (17–22).

Complicating sensitivity analysis is the definition of "significant" stenosis. As with all other diagnostic imaging modalities, sensitivity is greatest when significant stenosis is defined as a threshold of ≥70% diameter narrowing and falls when significant stenosis is defined as ≥50% diameter narrowing.

There are several situations in which the accuracy of stress echocardiography will be adversely impacted, compared with an angiographic standard. These include the presence of cardiomyopathy, microvascular disease, an acute hypertensive response to stress, and significant LV hypertrophy, especially the combination of increased wall thickness with normal or small chamber sizes (concentric remodeling). In the latter situation, wall stress is reduced, and the likelihood of a false-negative result is increased.

Specific accuracy for identification of coronary lesions in the LAD, versus that in the posterior circulation (right and circumflex coronary artery), has been investigated in several studies. Although the overall accuracy for detecting patients with coronary disease has been equivalent, the ability to precisely identify an obstruction in the LAD has exceeded that for the posterior circulation. The underlying basis for this phenomenon probably relates to the greater ease with which the LAD territory is visualized versus the occasional problematic visualization of the posterior endocardium, as well as the greater amount of myocardium perfused by the anterior circulation. Additionally, because of the overlap between the right coronary artery and circumflex coronary artery territories, precise separation of these territories has been problematic.

Technical factors that adversely impact accuracy include any procedural complexity which delays imaging, as well as suboptimal image quality. As with all other forms of stress testing, a low level of physical stress, resulting in a suboptimal cardiovascular workload, will result in a reduction in sensitivity for detecting CAD. The degree to which a suboptimal heart rate impacts the accuracy of pharmacologic stress is less clear. Vasodilator stress does not rely on increasing cardiovascular workload, and thus traditional measures of cardiovascular workload may have little relevance. Dobutamine increases the heart rate and blood pressure and has a primary impact on contractility, which also drives myocardial oxygen demand, all of which mimic the effects of exercise. As such, a "suboptimal" heart rate response to dobutamine, if seen in the presence of a hyperdynamic response, may not confer as great a decre-

Table 4. Selected Studies Outlining the Accuracy of Dobutamine Echocardiography*

Author (Ref.)	Year	Stress Method (Dobutamine Dose Range, μg/kg/min)	Significant CAD	Total No. of Patients	Sensitivity (%)	Sensitivity for 1-VD (%)	Sensitivity for MVD (%)	Specificity (%)	PPV (%)	NPV (%)	Overall Accuracy (%)
Segar et al. (17)	1992	DSE (5–30)	50%	88	95	—	—	82	94	86	92
Marcovitz et al. (18)	1992	DSE (5–30)	50%	141	96	95	98	66	91	84	89
McNeill et al. (19)	1992	DASE (10–40)	50%	80	70	—	—	88	89	67	78
Marwick et al. (20)	1993	DSE (5–40)	50%	217	72	66	77	83	89	61	76
Previtali et al. (21)	1993	DSE (5–40)	50%	80	79	63	91	83	92	61	80
Takeuchi et al. (22)	1993	DSE (5–30)	50%	120	85	73	97	93	95	80	88

*Modified with permission from the American College of Cardiology Foundation and American Heart Association (2).
DASE = dobutamine-atropine stress echocardiography; DSE = dobutamine stress echocardiography; other abbreviations as in Table 3.

ment in accuracy as a similar reduction in heart rate with physical stress. If desired, the heart rate can be augmented by the use of atropine either at peak dobutamine dose or often at intermediate stages (typically 20 μg/kg/min).

The accuracy of stress echocardiography has been compared with competing diagnostic techniques. When stress echocardiography is compared directly with radionuclide scintigraphy, using laboratories of equivalent proficiency, there is general parity in accuracy for the techniques (7). A recent meta-analysis suggested virtually identical sensitivity for stress echocardiographic and radionuclide techniques, with a higher specificity noted with stress echocardiography (23). The relative advantages of radionuclide scintigraphy include the ease with which data can be quantified and hence used for serial studies. Relative advantages of stress echocardiography include its versatility and ability to evaluate all other forms of cardiac disease simultaneously.

Finally, the validation studies of stress echocardiography are subjected to the same issues of referral and test verification bias as other techniques. The combination of referral and verification bias typically leads to an overstatement of sensitivity in early studies. After adjustment for referral and verification bias, sensitivities typically are lower and specificity higher in the unselected general population than reported in the initial verification cohorts (15).

USE OF STRESS ECHOCARDIOGRAPHY IN CARDIAC RISK STRATIFICATION

Patients with known or suspected CAD. The information gleaned from regional and global ventricular function at peak exercise is a powerful predictor of subsequent cardiac events and is additive to clinical variables, exercise duration, ECG changes, and resting ventricular function (24–26). This prognostic power was demonstrated in various clinical subsets, including hypertension and diabetes mellitus, and is irrespective of age or gender. An exercise wall motion score index >1.4 or exercise ejection fraction <50% portends a significantly worse prognosis. This prognostic cut-off is similar to that of a radionuclide perfusion defect size of >15% (24). Results of exercise echocardiography have been combined with the Duke treadmill score and can further stratify cardiac risk events (25). It is important to note that while ventricular function at peak exercise is the most powerful independent index for prognosis, ischemic ST-segment depression and exercise duration also remain important prognostic indicators. A risk index combining echocardiographic and exercise variables was recently validated and further improved the risk stratification of exercise echocardiography, particularly its negative predictive value for cardiac events (Fig. 2) (27). The rate of spontaneous cardiac events in individuals with a normal exercise echocardiogram and good exercise tolerance is usually <1% per year (24–27). Exercise echocardiography is cost-effective
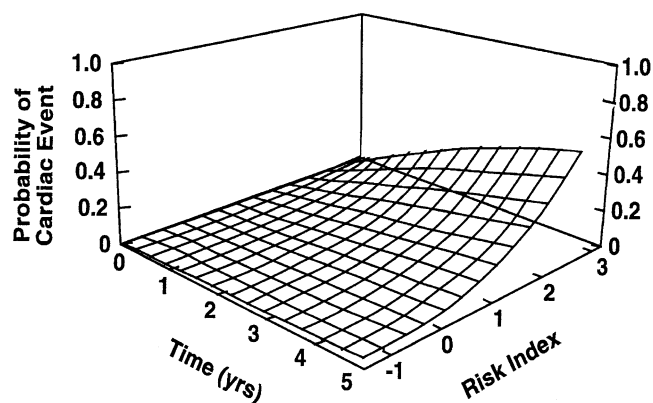

Figure 2. Three-dimensional model of probability of a cardiac event over the ensuing five years after exercise echocardiography versus risk index, derived from the exercise wall motion score index (ExWMSI), occurrence of ischemic ST-segment change at maximal exercise (STΔ = 0 or 1), and treadmill exercise time (on Bruce protocol, in min). Reproduced from Mazur et al. (27), with permission.

compared with exercise electrocardiography in the management of patients with suspected or known CAD (28).

Similar to exercise echocardiography, pharmacologic stress with either dobutamine or dipyridamole has been shown to have significant prognostic power (29–32). A greater extent of WMA, dilation of the LV at maximal stress, and a low threshold at which ischemia develops all predict a worse outcome. A normal dobutamine stress echocardiogram carries a low spontaneous cardiovascular event rate (usually <1.5%/year), although total mortality may be as high as 8% per year (29–32). This may reflect differences in population characteristics and underlying medical conditions.

Post-acute myocardial infarction prognosis. Identification of high-risk patients after an acute myocardial infarction is possible by using clinical features such as recurrent post-infarction angina, older age, heart failure, and cardiogenic shock. Absence of these clinical characteristics, however, does not necessarily predict a low subsequent risk. Evaluation of cardiac markers, LV ejection fraction, ventricular dysrhythmias, and identification of residual or remote myocardial ischemia improve risk stratification. With stress echocardiography, the presence of residual or remote ischemia is detected as stress-induced WMA. After infarction, worsening ventricular function with stress confers a worse prognosis. The majority of studies have involved pharmacologic stress. This is particularly relevant in the era of thrombolytic therapy and percutaneous interventions, as pharmacologic stress testing allows the concomitant evaluation of myocardial viability at a low stress level, as well as the threshold and extent of ischemia at higher stress levels. The extent of rest WMAs, inducible ischemia, and nonviability all imply a worse prognosis (33–35).

Preoperative risk assessment. Cardiac risk assessment before major noncardiac surgery is an important clinical challenge. The most important clinical predictors of cardiac death and nonfatal myocardial infarction are previous in-

Table 5. Assessment of Myocardial Viability With Stress Echocardiography

Resting Function	Low Dose	Maximal Stress	Type of Response	Interpretation	Likelihood for Recovery of Function
Abnormal	Improvement	Worse than low dose	Biphasic	Viable, ischemic	Very high
Abnormal	Worse than rest or no change	Worse than rest or low dose	Worsening	Viable, ischemic	Medium
Abnormal	Improved	Further or continued improvement	Sustained improvement	Viable, nonischemic	Low
Abnormal	No change	No change	No change	Nonviable	Low

farction, angina, heart failure, and diabetes mellitus. Patients with one or more of these risk factors generally warrant further risk assessment. Because the majority of patients being evaluated for major surgical procedures, especially vascular, cannot adequately exercise, pharmacologic stress testing is preferred. Dobutamine stress testing has been shown to improve risk stratification of patients before vascular or nonvascular surgery (36–38). A low ischemic threshold during stress testing—at a heart rate <70% of the age-predicted maximal heart rate—is the strongest predictor of cardiac events. Based on recent meta-analyses, the prognostic power of stress echocardiography is similar to or exceeds that seen with radionuclide testing (39,40). Beta-blocker therapy has been shown to reduce perioperative cardiac events in patients undergoing major noncardiac surgery. Of interest is that in patients receiving beta-blockers, DSE was also beneficial in further risk stratification, particularly in individuals who had three or more clinical risk factors (38).

ROLE OF STRESS ECHOCARDIOGRAPHY IN MYOCARDIAL VIABILITY

Chronic systolic ventricular dysfunction does not necessarily imply irreversible myocardial injury. Indicators of myocardial viability have included contractile reserve to inotropic stimulation and preserved myocardial thickness, as well as intact myocardial perfusion and metabolism. Several studies have shown the utility of DSE in the evaluation of myocardial viability. Incremental infusion of dobutamine elicits an augmentation of regional function in dysfunctional segments that is predictive of recovery of function after revascularization (41,42). The use of high-dose in addition to low-dose dobutamine unmasks differences in contractile reserve, with significant implications for both recovery of function after revascularization and prognosis. Dysfunctional myocardium shows one of four responses to dobutamine: 1) biphasic response: augmentation at a low dose followed by deterioration at a higher dose; 2) sustained improvement: improvement in function at a low dose that persists or further improves at higher doses; 3) worsening of function, without contractile reserve; and 4) no change in function (Table 5). Sensitivity for recovery of function ranges between 74% and 88%, with a specificity between 73% and 87% (42). A biphasic response confers the highest predictive value for recovery of function after revascularization. A combination of the types of re-

sponses to dobutamine (e.g., any contractile reserve) increases the sensitivity of DSE with a slight decrease in specificity for predicting recovery of function. Studies that have compared determination of viability with DSE and radionuclide studies have shown slightly higher sensitivity and lower specificity for radionuclide techniques (42,43).

Myocardial thickness also is an indicator of myocardial viability. Myocardium that is thin (≤6 mm) has a very low likelihood of viability and recovery of function after revascularization (negative predictive value of 93%). A combination of contractile reserve during DSE and preserved myocardial thickness (>6 mm) yields the best diagnostic accuracy for echocardiography in predicting recovery of function (44).

Observational data suggest that dysfunctional, viable myocardium that is not revascularized is a predictor of further ischemic events and higher overall mortality. Recent studies using DSE have demonstrated a very poor prognosis in individuals with depressed ventricular function who have no evidence of myocardial viability, irrespective of whether or not they underwent revascularization (Fig. 3). In patients with myocardial viability who do not undergo revascularization, prognosis was equally poor. Similar to data from radionuclide or positron emission tomography, the best prognosis was observed in patients
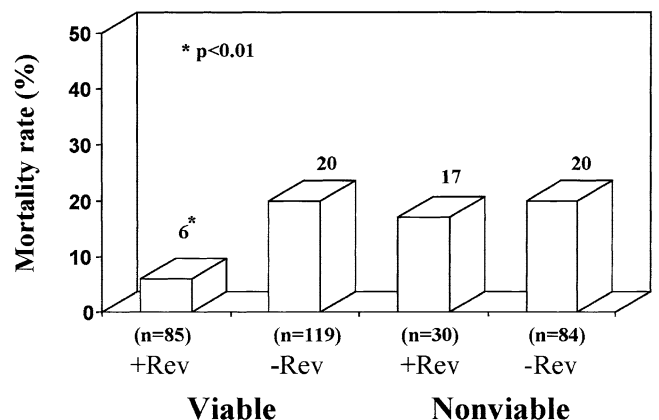
Figure 3. Dobutamine stress echocardiography (DSE) in ischemic left ventricular (LV) dysfunction impact on survival. Mortality rates at a mean follow-up of 18 ± 10 months in patients with chronic LV dysfunction, grouped by the presence of viability by DSE and by whether or not patients underwent revascularization (+Rev and −Rev, respectively). *p = 0.01 vs. others. Modified from Afridi et al. (45), and reproduced with permission.
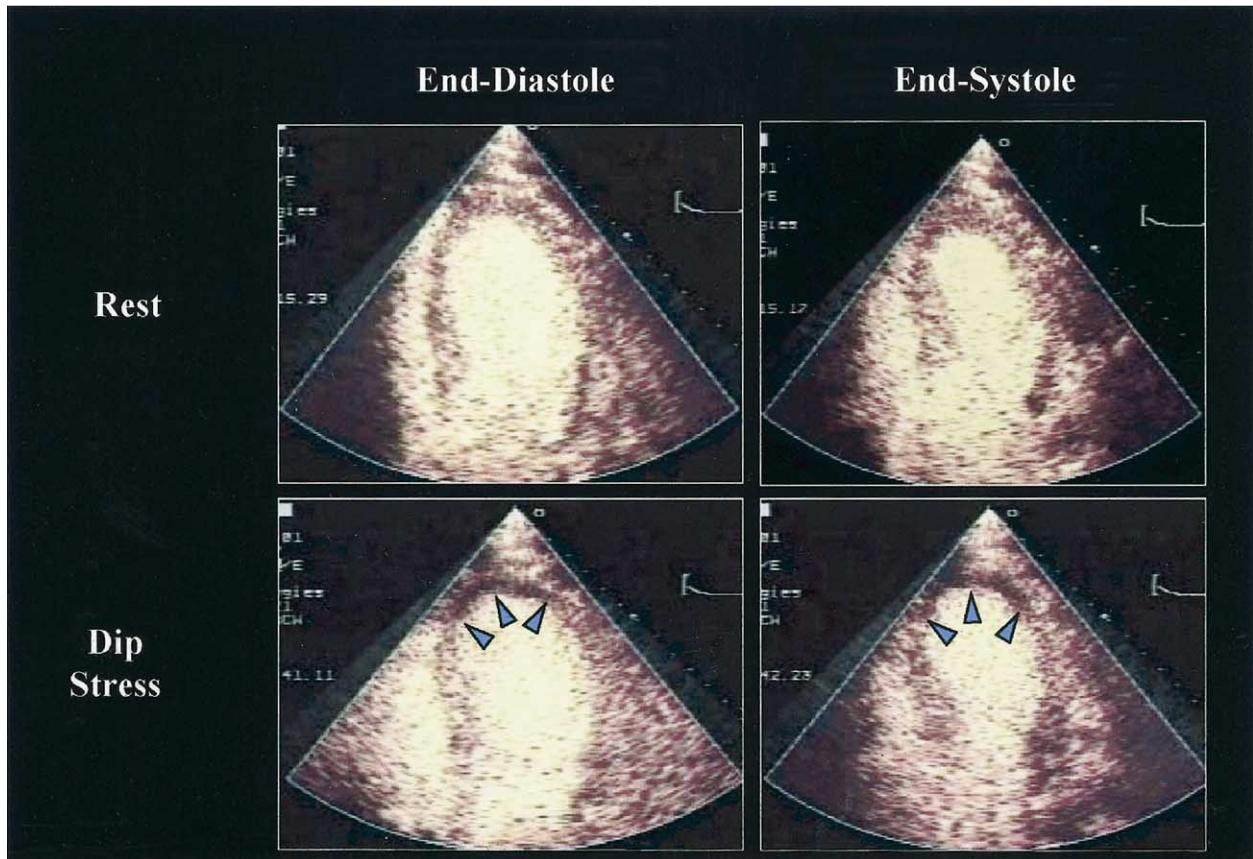
Figure 4. Dipyridamole (Dip) stress contrast echocardiography using real-time perfusion imaging at a low mechanical index, showing images at end diastole and end systole in a patient with significant stenosis of the left anterior descending coronary artery. Note the perfusion defect that developed in the apex **(highlighted by arrows)** and the corresponding wall motion abnormality.

with evidence of myocardial viability who underwent revascularization (42,45).

USE OF STRESS ECHOCARDIOGRAPHY IN NONISCHEMIC HEART DISEASE

Stress Doppler techniques allow a unique application of stress echocardiography in valvular heart disease and other entities, such as hypertrophic cardiomyopathy and pulmonary hypertension. The majority of patients with valvular stenosis have a conclusive evaluation based on a resting echocardiogram and Doppler examination. In patients with unexplained symptoms and what appears to be, at most, moderate mitral stenosis at rest, a hemodynamic re-evaluation with exercise is beneficial (46). An exercise echocardiogram—usually with a bicycle study—can provide re-evaluation of valvular gradients during exertion and simultaneous determination of pulmonary artery pressure from the tricuspid regurgitation jet. In patients with apparent severe aortic stenosis and depression of ventricular function, the reduction in blood flow may exaggerate the reduction in orifice area of the stenotic valve (47). In these instances, DSE plays a

significant role in re-evaluating valvular hemodynamics and contractile reserve.

NEW DEVELOPMENTS IN STRESS ECHOCARDIOGRAPHY

Real-time three-dimensional (3D) imaging. Technological advances in transducer and computer technology have allowed the recent introduction of real-time 3D echocardiography. A real-time 3D volume set can be acquired within one to four cardiac cycles. Subsequent analysis allows multiple tomographic interrogations off-line, thus avoiding foreshortening of the ventricle and possibly improving accuracy. Similar to two-dimensional echocardiography, contrast echocardiography can be used for enhancement of endocardial border definition and possibly for myocardial perfusion. Initial studies with 3D echocardiography during pharmacologic stress have been encouraging (48).
Evaluation of simultaneous myocardial perfusion with contrast echocardiography. The past decade has seen significant advances in the field of myocardial contrast echocardiography: with the development of microbubbles that traverse the pulmonary circulation, enhance LV border delineation, and evaluate myocardial perfusion (49,50). Because of the sensitivity of the microbubbles to ultrasound

energy, either intermittent imaging or low-power imaging (low mechanical index) is necessary to preserve microbubbles while imaging (Fig. 4). Initial studies have demonstrated the feasibility of such techniques to image myocardial perfusion in combination with either vasodilator stress, DSE, or exercise (51,52). Current limitations of the technique include attenuation in the cardiac base and variability of regional perfusion parameters. Large-scale trials are currently under way to evaluate the accuracy of stress myocardial contrast echocardiography in comparison with radionuclide perfusion techniques and angiography.

FUTURE DIRECTIONS

Future developments in stress echocardiography are aimed at refinements of the methodology and quantitative techniques to further improve accuracy, decrease subjectivity, and increase reproducibility of interpretation. These potential enhancements include the incorporation of tissue Doppler, myocardial strain, and strain rate imaging, contrast echocardiography, and 3D imaging. Further advances in myocardial contrast echocardiography would allow the simultaneous evaluation of myocardial regional function and perfusion—an ultimate goal of noninvasive physiologic evaluation of CAD.

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REFERENCES

1. Quinones MA, Douglas PS, Foster E, 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.
2. Pasquet A, Yamada E, Armstrong G, Beachler L, Marwick TH. Influence of dobutamine or exercise stress on the results of pulsed-wave Doppler assessment of myocardial velocity. Am Heart J 1999;138:753–8.
3. Voigt JU, Exner B, Schmiedehausen K, et al. Strain-rate imaging during dobutamine stress echocardiography provides objective evidence of inducible ischemia. Circulation 2003;107:2120–6.
4. Armstrong WF, O'Donnell J, Ryan T, Feigenbaum H. Effect of prior myocardial infarction and extent and location of coronary disease on accuracy of exercise echocardiography. J Am Coll Cardiol 1987;10:531–8.
5. Crouse LJ, Harbrecht JJ, Vacek JL, Rosamond TL, Kramer PH. Exercise echocardiography as a screening test for coronary artery disease and correlation with coronary arteriography. Am J Cardiol 1991;67:1213–8.
6. Marwick TH, Nemec JJ, Pashkow FJ, Stewart WJ, Salcedo EE. Accuracy and limitations of exercise echocardiography in a routine clinical setting. J Am Coll Cardiol 1992;19:74–81.
7. Quinones MA, Verani MS, Haichin RM, Mahmarian JJ, Suarez J, Zoghbi WA. Exercise echocardiography versus ^{201}Tl single-photon emission computed tomography in evaluation of coronary artery disease: analysis of 292 patients. Circulation 1992;85:1026–31.
8. Hecht HS, DeBord L, Shaw R, et al. Digital supine bicycle stress echocardiography: a new technique for evaluating coronary artery disease. J Am Coll Cardiol 1993;21:950–6.

9. Roger VL, Pellikka PA, Oh JK, Bailey KR, Tajik AJ. Identification of multivessel coronary artery disease by exercise echocardiography. J Am Coll Cardiol 1994;24:109–14.
10. Beleslin BD, Ostojic M, Stepanovic J, et al. Stress echocardiography in the detection of myocardial ischemia: head-to-head comparison of exercise, dobutamine, and dipyridamole tests. Circulation 1994;90:1168–76.
11. Roger VL, Pellikka PA, Oh JK, Miller FA, Seward JB, Tajik AJ. Stress echocardiography. Part I. Exercise echocardiography: techniques, implementation, clinical applications, and correlations. Mayo Clin Proc 1995;70:5–15.
12. Marwick TH, Anderson T, Williams MJ, 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.
13. Marwick TH, Torelli J, Harjai K, et al. Influence of left ventricular hypertrophy on detection of coronary artery disease using exercise echocardiography. J Am Coll Cardiol 1995;26:1180–6.
14. Luotolahti TH, Torelli J, Hartiala J. Exercise echocardiography in the diagnosis of coronary artery disease. Ann Med 1996;28:73–7.
15. 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. Circulation 1997;95:405–10.
16. Badruddin SM, Ahmad A, Mickelson J, et al. Supine bicycle versus post-treadmill exercise echocardiography in the detection of myocardial ischemia: a randomized single-blind cross-over trial. J Am Coll Cardiol 1999;33:1485–90.
17. Segar DS, Brown SE, Sawada SG, Ryan T, Feigenbaum H. Dobutamine stress echocardiography: correlation with coronary lesion severity as determined by quantitative angiography. J Am Coll Cardiol 1992;19:1197–202.
18. Marcovitz PA, Armstrong WF. Accuracy of dobutamine stress echocardiography in detecting coronary artery disease. Am J Cardiol 1992;69:1269–73.
19. McNeill AJ, Fioretti PM, el-Said SM, et al. Enhanced sensitivity for detection of coronary artery disease by addition of atropine to dobutamine stress echocardiography. Am J Cardiol 1992;70:41–6.
20. Marwick T, D'Hondt AM, Baudhuin T, 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.
21. Previtali M, Lanzarini L, Fetiveau R, et al. Comparison of dobutamine stress echocardiography, dipyridamole stress echocardiography and exercise stress testing for diagnosis of coronary artery disease. Am J Cardiol 1993;72:865–70.
22. Takeuchi M, Araki M, Nakashima Y, Kuroiwa A. Comparison of dobutamine stress echocardiography and stress thallium-201 single-photon emission computed tomography for detecting coronary artery disease. J Am Soc Echocardiogr 1993;6:593–602.
23. Fleischmann KE, Hunink MG, Kuntz KM, et al. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. JAMA 1998;280:913–20.
24. Olmos LI, Dakik H, Gordon R, et al. Long-term prognostic value of exercise echocardiography compared with exercise ^{201}Tl, ECG, and clinical variables in patients evaluated for coronary artery disease. Circulation 1998;98:2679–86.
25. Marwick TH, Case C, Vasey C, Allen S, Short L, Thomas JD. Prediction of mortality by exercise echocardiography: a strategy for combination with the Duke treadmill score. Circulation 2001;103:2566–71.
26. McCully RB, Roger VL, Mahoney DW, et al. Outcome after normal exercise echocardiography and predictors of subsequent cardiac events: follow-up of 1,325 patients. J Am Coll Cardiol 1998;31:144–9.
27. Mazur W, Rivera JM, Khoury AF, et al. Prognostic value of exercise echocardiography: validation of a new risk index combining echocardiographic, treadmill, and exercise electrocardiographic parameters. J Am Soc Echocardiogr 2003;16:318–25.
28. Marwick TH, Shaw L, Case C, Vasey C, Thomas JD. Clinical and economic impact of exercise electrocardiography and exercise echocardiography in clinical practice. Eur Heart J 2003;24:1153–63.
29. Chuah SC, Pellikka PA, Roger VL, McCully RB, Seward JB. Role of dobutamine stress echocardiography in predicting outcome in 860 patients with known or suspected coronary artery disease. Circulation 1998;97:1474–80.

30. Marwick TH, Case C, Sawada S, et al. Prediction of mortality using dobutamine echocardiography. J Am Coll Cardiol 2001;37:754–60.

31. 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.

32. Geleijnse ML, Elhendy A, van Domburg RT, 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.

33. Carlos ME, Smart SC, Wynsen JC, Sagar KB. Dobutamine stress echocardiography for risk stratification after myocardial infarction. Circulation 1997;95:1402–10.

34. Picano E, Sicari R, Landi P, et al. Prognostic value of myocardial viability in medically treated patients with global left ventricular dysfunction early after an acute uncomplicated myocardial infarction: a dobutamine stress echocardiographic study. Circulation 1998;98:1078–84.

35. Sicari R, Landi P, Picano E, et al. Exercise-electrocardiography and/or pharmacological stress echocardiography for non-invasive risk stratification early after uncomplicated myocardial infarction: a prospective international large scale multicentre study. Eur Heart J 2002;23:1030–7.

36. Poldermans D, Arnese M, Fioretti PM, et al. Improved cardiac risk stratification in major vascular surgery with dobutamine-atropine stress echocardiography. J Am Coll Cardiol 1995;26:648–53.

37. Das MK, Pellikka PA, Mahoney DW, et al. Assessment of cardiac risk before nonvascular surgery: dobutamine stress echocardiography in 530 patients. J Am Coll Cardiol 2000;35:1647–53.

38. Boersma E, Poldermans D, Bax JJ, et al. Predictors of cardiac events after major vascular surgery: role of clinical characteristics, dobutamine echocardiography, and beta-blocker therapy. JAMA 2001;285:1865–73.

39. Shaw LJ, Eagle KA, Gersh BJ, Miller DD. 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.

40. Kertai MD, Boersma E, Bax JJ, et al. A meta-analysis comparing the prognostic accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. Heart 2003;89:1327–34.

41. Afridi I, Kleiman NS, Raizner AE, Zoghbi WA. Dobutamine echocardiography in myocardial hibernation: optimal dose and accuracy in predicting recovery of ventricular function after coronary angioplasty. Circulation 1995;91:663–70.

42. Bax JJ, Poldermans D, Elhendy A, Boersma E, Rahimtoola SH. Sensitivity, specificity, and predictive accuracies of various noninvasive techniques for detecting hibernating myocardium. Curr Probl Cardiol 2001;26:141–86.

43. Qureshi U, Nagueh SF, Afridi I, et al. Dobutamine echocardiography and quantitative rest-redistribution ^{201}Tl tomography in myocardial hibernation: relation of contractile reserve to ^{201}Tl uptake and comparative prediction of recovery of function. Circulation 1997;95:626–35.

44. Cwajg JM, Cwajg E, Nagueh SF, et al. End-diastolic wall thickness as a predictor of recovery of function in myocardial hibernation: relation to rest-redistribution T1-201 tomography and dobutamine stress echocardiography. J Am Coll Cardiol 2000;35:1152–61.

45. Afridi I, Grayburn PA, Panza JA, Oh JK, Zoghbi WA, Marwick TH. 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.

46. Aviles RJ, Nishimura RA, Pellikka PA, Andreen KM, Holmes DR Jr. Utility of stress Doppler echocardiography in patients undergoing percutaneous mitral balloon valvotomy. J Am Soc Echocardiogr 2001;14:676–81.

47. Nishimura RA, Grantham JA, Connolly HM, Schaff HV, Higano ST, Holmes DR Jr. 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.

48. Ahmad M, Xie T, McCulloch M, Abreo G, Runge M. Real-time three-dimensional dobutamine stress echocardiography in assessment stress echocardiography in assessment of ischemia: comparison with two-dimensional dobutamine stress echocardiography. J Am Coll Cardiol 2001;37:1303–9.

49. Kaul S, Ito H. Microvasculature in acute myocardial ischemia. Part I: evolving concepts in pathophysiology, diagnosis, and treatment. Circulation 2004;109:146–9.

50. Kaul S, Ito H. Microvasculature in acute myocardial ischemia. Part II: evolving concepts in pathophysiology, diagnosis, and treatment. Circulation 2004;109:310–5.

51. Shimoni S, Zoghbi WA, Xie F, et al. Real-time assessment of myocardial perfusion and wall motion during bicycle and treadmill exercise echocardiography: comparison with single photon emission computed tomography. J Am Coll Cardiol 2001;37:741–7.

52. Kaul S, Senior R, Dittrich H, Raval U, Khattar R, Lahiri A. Detection of coronary artery disease with myocardial contrast echocardiography: comparison with ^{99m}Tc-sestamibi single-photon emission computed tomography. Circulation 1997;96:785–92.

APPENDIX

For accompanying videos, please see the June 7, 2005, issue of *JACC* at www.onlinejacc.org.