Value of Transesophageal Dobutamine Stress Echocardiography in Assessing Coronary Artery Disease

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The introduction of digital echocardiography has significantly enhanced our ability to select the best set of frames for analysis. However, despite the beneficial attributes of transthoracic dobutamine stress echocardiography, poor quality 2-dimensional images continue to be a significant limiting factor in patients with chest deformities, severe chronic obstructive lung disease, marked obesity, and previous chest surgery. Transesophageal echocardiography provides a new window to monitor left ventricular contractility without the interference of bone and air-filled structures of the thoracic cage. The transesophageal dobutamine stress test is a logical but poorly explored modality to image/stress the heart in certain patients with known or suspected myocardial ischemia. Overall sensitivity (≤85%) and specificity (≤95–100%) of transesophageal dobutamine stress echocardiography appear to be similar to that of previous transthoracic studies, although no direct comparison has been accomplished between transthoracic and transesophageal stress images. False negative transesophageal dobutamine stress echocardiography results have been described in patients with single-vessel disease in whom ischemic regions may not have been visualized throughout the entire study. False positive study results may be present in patients with hypertension and myocardial hypertrophy that may have signs and symptoms of myocardial ischemia in absence of obstructive disease of the epicardial coronary arteries, presumably related to either microvascular disease or impaired vasodilatory reserve. The proportion of patients with coronary artery disease who need a transesophageal examination for reliable assessment of echocardiographic response to stress varies depending on the operators' skills, the interpreters' experience, and the use of videotape or digitizing systems for image analysis. Although clinically useful in its present transthoracic and transesophageal form, a major limitation of dobutamine stress echocardiographic study is the subjective visual interpretation of endocardial motion and wall thickening, which is only semiquantitative. Color kinesis and tissue Doppler imaging (TDI) are 2 novel echocardiographic techniques that color code endocardial motion and myocardial velocity online and have the potential to objectively quantify regional left ventricular function. Quantitative standardization of transthoracic and transesophageal data interpretation, such as establishing endocardial motion by color kinesis or velocity thresholds by TDI for an abnormal segmental response to stress, has the potential to decrease interobserver variability and increase interinstitutional agreement.

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The sensitivity and specificity of transthoracic dobutamine stress testing in the evaluation of patients at risk for coronary artery disease (CAD) has been shown to equal other forms of noninvasive assessment of myocardial ischemia (MI).[1–3] Low-dose dobutamine echocardiography has also been proposed to identify dyssynergic but viable myocardium after a recent myocardial infarction and in chronic left ventricular dysfunction.[4,5]

Despite these beneficial attributes, although the introduction of digital echocardiography has significantly enhanced our ability to select the best set of frames for analysis, poor quality 2-dimensional images continue to be a significant limiting factor in patients with chest deformities, severe chronic obstructive lung disease, marked obesity, and previous chest surgery.

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Transesophageal echocardiography provides a new window to monitor left ventricular contractility without the interference of bone and air-filled structures of the thoracic cage.[6] The transesophageal dobutamine stress test is a logical and not well-explored modality to image/stress the heart in certain patients with known or suspected myocardial ischemia.

The purpose of the present study was to point out the clinical value of transesophageal dobutamine stress echocardiography in comparison with the conventional transthoracic approach and the potential of the new imaging modalities (color kinesis, tissue Doppler imaging [TDI]) in allowing a quantitative assessment of the test.

TRANSTHORACIC DOBUTAMINE STRESS ECHOCARDIOGRAPHY

Noninvasive assessment of patients with suspected CAD is most often performed by exercise electrocardiography. However, the limited sensitivity and specificity of this technique have led to its combination with planar or tomographic imaging to identify stress-

induced perfusion defects, or with 2-dimensional echocardiography to identify abnormalities of left ventricular wall motion that develop with the onset of ischemia.

An alternative is to combine echocardiography with nonexercise stress using atrial pacing or pharmacologic stress using dobutamine, dipyridamole, or adenosine.[7,8] There is evidence from animal experiments that dobutamine, a sympathomimetic agent with both positive chronotropic and inotropic effects, is the pharmacologic stress agent of choice for combination with imaging techniques that assess left ventricular systolic function, including echocardiography.

Dobutamine is a synthetic sympathomimetic amine that stimulates β_1, β_2 and α_1 receptors. As a result, there is a marked inotropic response (mediated by both α_1 and β_1 receptors), a modest chronotropic response (mediated by β_1 receptors), and a minor increase in systolic blood pressure (due to α_1- and β_1-mediated increase in cardiac output and relative stabile peripheral vasculature tonus, mediated by α_1 vasoconstriction and β_2 vasodilation). As a result of this augmentation of myocardial contractility, heart rate, left-ventricular pressure, and wall stress, more oxygen is required. Normally a dose-related increase in subepicardial and subendocardial blood flow occurs with myocardium supplied by normal coronary arteries. However, blood flow increases minimally with vascular beds supplied by significantly stenosed arteries, with most of the increase occurring within the subepicardium rather than the subendocardium.[7]

It has been shown that transthoracic dobutamine stress echocardiography has an overall sensitivity of 68–95% and a specificity of 64–100% for detection of angiographically defined CAD as assessed by either quantitative or visual estimates of stenosis.[8] To obtain a high degree of interobserver agreement, multiple views are necessary to visualize all segments of the left ventricle with high quality images. Competence of the observer in the interpretation of stress echocardiography is essential to reach high accuracy and thus a high interobserver agreement. It has been found that accuracy in the interpretation of stress echocardiograms is significantly higher for echocardiographers with a high level of experience with stress echocardiography.[9] However, for high interobserver agreement, there also needs to be homogeneity in the classification of a wall motion as being normal, hypokinetic, akinetic, or dyskinetic.[10,11] This applies especially to the classification of hypokinetic wall motion, which may range from slight to severe and where the cutoff from what is considered normal may vary between observers and institutions. Mild hypokinesia may be viewed as normal clinical variability at one institution and be considered pathologic at another.

TRANSESOPHAGEAL APPROACH

Transesophageal dobutamine stress echocardiography has been shown to be safe, feasible, and generally well tolerated by patients, with only few of the studies (1%) terminated because of patient discomfort.[12,13] Total time of transesophageal probe insertion is relatively short (≤15 minutes). Although transesophageal echocardiography is a semi-invasive technique that demands greater skills than the transthoracic examination, requires patient sedation, and imposes a small risk for serious complications, no major complications or side effects have been reported during the transesophageal stress test.

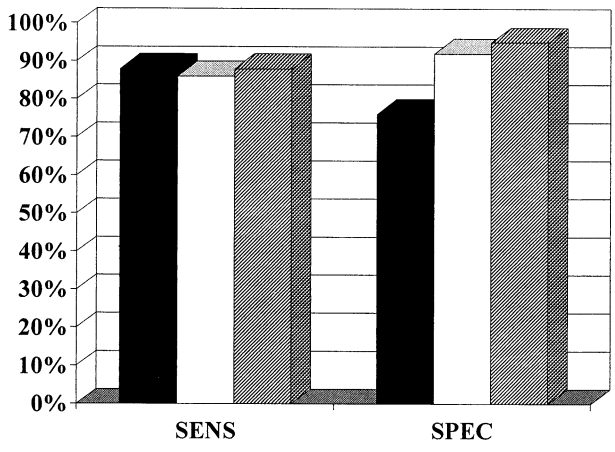

FIGURE 1. Comparative sensitivity (SENS) and specificity (SPEC) of thallium scintigraphy (*solid bars*), transesophageal dobutamine stress echocardiography (*open bars*), and transesophageal dobutamine stress echocardiography with tissue Doppler imaging (*hatched bars*) in patients undergoing coronary arteriography.[58]

Overall sensitivity (up to 85%) and specificity (≤95–100%) of transesophageal dobutamine stress echocardiography appear to be similar (Figure 1) to that of previous transthoracic studies,[13] although no direct comparison has been accomplished between transthoracic and transesophageal stress images. False negative transesophageal dobutamine stress echocardiography results have been described in patients with single-vessel disease in whom ischemic regions may not have been visualized throughout the entire study. False positive study results may be present in patients with hypertension and myocardial hypertrophy that may have signs and symptoms of myocardial ischemia in absence of obstructive disease of the epicardial coronary arteries, presumably related to either microvascular disease or impaired vasodilatory reserve.

Sensitivity and specificity for detection of disease in specific major coronary vessels may vary depending on percent lumen narrowing used to determine presence of coronary disease.[14] There is no universal agreement on the severity of stenosis that best reflects physiologic significance. The percent lumen narrowing has varied between ≥50% and ≥70% as indicative of obstructive CAD. Considering ≥50% stenosis as a marker, specificity of this technique up to 100% has been reported. Minimal lumen area or diameter obtained by quantitative angiography may be a more physiologic marker for severity of coronary artery lesions than percent diameter stenosis determined by visual estimation. Lesions with a minimal lumen diameter <1 mm are more likely to be physiologically

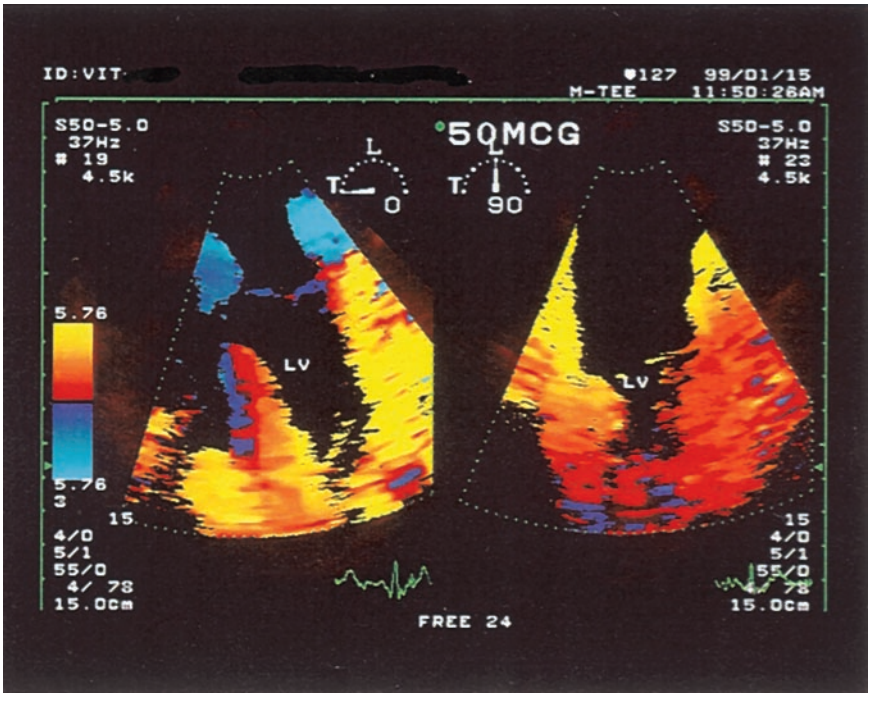

FIGURE 2. Tissue Doppler images from a patient with abnormal segments and abnormal velocity responses at peak dobutamine stress by transesophageal echocardiography. Abnormally low peak velocity response occurring at peak stress is color-coded as orange rather than yellow.

significant and to be correctly identified using either the transthoracic or transesophageal approach.[14]

The proportion of patients with CAD who need a transesophageal examination for reliable assessment of echocardiographic response to stress varies depending on the operators' skills, the interpreters' experience, and the use of videotape or digitizing systems for image analysis. In patients at our institution, up to 20% have inadequate transthoracic echocardiographic endocardial definition, even after the introduction of tissue harmonic imaging. The definition of suboptimal echocardiographic study is necessarily subjective and therefore variable among different laboratories. If visualization of <10 of 16 myocardial segments is considered suboptimal, a number of patients will have a suboptimal ultrasound examination; thus, defined but lower thresholds will render a lower proportion of suboptimal studies. Factors such as obesity, chronic obstructive pulmonary disease, advanced age, and previous cardiac surgery may interfere with an optimal echocardiographic examination and are not uncommon among patients with CAD. Prospective studies with transthoracic and transesophageal test performed in the same patients may be needed.

QUANTITATIVE ASSESSMENT

Although clinically useful in its present transthoracic and transesophageal form, a major limitation of dobutamine stress echocardiographic study is the subjective visual interpretation of endocardial motion and wall thickening, which is only semiquantitative. Color kinesis and TDI are 2 novel echocardiographic techniques that color code endocardial motion and myocardial velocity online and have the potential to objectively quantify regional left-ventricular function.

Acoustic quantification has been previously described and validated against a variety of techniques. Analysis of the tissue backscatter data identifies the border between blood and tissue and automatically tracks endocardial motion throughout the cardiac cycle. Color kinesis is a further extension of this technology, which defines endocardial motion by color encoding for inward and outward motion.[15–19]

Echocardiographic assessment of the timing of endocardial motion has been extremely difficult. The advent of automatic border detection allowed assessment of global left-ventricular area and volume changes throughout the cardiac cycle. The advantage of segmental analysis of color kinesis images is that it allows quantitation of the timing of endocardial excursion during both contraction and relaxation on a regional basis. The potential role of multiplane transesophageal echocardiography with the use of color kinesis during graded dobutamine infusion in screening patients for obstructive CAD has recently been shown.[20] The sensitivity of the test for the detection of CAD was 85% and the specificity 82%. The positive predictive value was 95%, the negative predictive value was 56%, and the overall accuracy was 85%. Thus dobutamine stress transesophageal echocardiography with color kinesis is a feasible and sensitive test for the detection of significant CAD and may be useful in a selected group of patients.

TDI is a modification of routine color flow Doppler

signal processing, bypassing the high-pass filter and inputting the comparatively lower frequency Doppler data from myocardial motion directly into the autocorrelator. Calculated velocity data are color-coded and superimposed on the conventional 2-dimensional images. It has been shown that quantitative evaluation of the segmental left-ventricular response to dobutamine stress can be accomplished by online color-coded tissue Doppler measures of endocardial velocity both by transthoracic and transesophageal approach (Figure 2).[21–24] Alterations in endocardial velocity induced by dobutamine stress from multiple segmental sizes can be serially assessed to quantify segmental function. With the exception of apical segments, the endocardial velocity response to peak stress is significantly blunted in abnormal hypokinetic or akinetic segments.

The ischemic cascade is a pathophysiologic continuum with segmental dysfunction due to myocardial ischemia occurring before either electrocardiographic changes or angina pectoris is manifest. This concept has served as the clinically useful basis of stress echocardiography to detect early signs of ischemia. Although dobutamine stress echocardiography has become widely utilized, variability in the visual interpretation of wall-motion assessment has been demonstrated in a recent multicenter study with interinstitutional agreement of only 73%. Quantitative standardization of transthoracic and transesophageal data interpretation, such as establishing endocardial motion by color kinesis or velocity thresholds by TDI for an abnormal segmental response to stress, has the potential to decrease interobserver variability and increase interinstitutional agreement.

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