Exercise Cross-sectional Echocardiography in Ischemic Heart Disease

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SUMMARY We performed cross-sectional echocardiograms at rest, during supine bicycle exercise, and after sublingual nitroglycerin administration in 28 patients suspected of having ischemic heart disease. Technically adequate exercise cross-sectional echocardiograms were obtained in 20 patients (71%). Ten patients had new areas of reversible segmental dysynergy, and all 10 had significant stenoses of coronary arteries supplying areas of the heart corresponding to the location of reversible dysynergy. Six of these 10 patients also underwent exercise thallium-201 perfusion scanning, and all six had reversible perfusion defects in the area that demonstrated reversible dysynergy on exercise cross-sectional echocardiography. At least two of the remaining 10 patients who did not have reversible segmental dysynergy on exercise cross-sectional echocardiography probably experienced myocardial ischemia that we did not detect. We conclude that exercise cross-sectional echocardiography is technically difficult but feasible. The mechanical consequences of exercise-induced regional myocardial ischemia can be detected noninvasively by real-time, two-dimensional, cross-sectional echocardiography.

Regional left ventricular dysfunction is a hallmark of ischemic heart disease. Segmental left ventricular contraction abnormalities occur within a few seconds after onset of acute myocardial infarction, and appear transiently during episodes of reversible myocardial ischemia. Noninvasive detection of these mechanical consequences of myocardial ischemia and infarction should improve our ability to diagnose and enhance our understanding of coronary heart disease.

Cross-sectional echocardiography provides real-time, two-dimensional tomographic images of the heart. The procedure is being used more frequently in cardiac diagnosis, and has been useful in detecting abnormal left ventricular wall motion during and after acute myocardial infarction. Although we have observed transient segmental left ventricular dysynergy during episodes of variant angina, cross-sectional echocardiography has not been widely used to detect wall motion abnormalities dueing exercise-induced angina pectoris. This study was undertaken to determine the feasibility of detecting areas of transient left ventricular dysynergy with cross-sectional echocardiography during exercise-induced myocardial ischemia.

Materials and Methods

Patient Population

We studied 28 patients who underwent cardiac catheterization for clinical evaluation of suspected ischemic heart disease. All patients had experienced...
chest pain that was considered consistent with angina pectoris or myocardial infarction. Patients who had unstable or resting angina, recent myocardial infarction, advanced congestive heart failure or physical infirmity precluding leg exercise were excluded. All 28 patients were male. Their average age was 48 years (range 25–67 years). The resting scalar 12-lead ECGs showed prior myocardial infarction in eight patients and was normal in eight patients. Twelve patients had nonspecific ST-segment and T-wave changes.

Echocardiographic Technique

Cross-sectional echocardiograms were performed at rest, during supine bicycle exercise and after sublingual nitroglycerin using a 30° mechanical sector scanner (Smith Kline Instruments, Sunnyvale, California). The ultrasound transducer was handheld on each patient’s chest. Initially, multiple echocardiographic views of the heart were obtained at rest using all available acoustic windows. We tried to visualize the heart from apical and subxiphoid transducer positions and several sites along the left sternal border, including 1) long axis at the base of the ventricle, 2) long axis at the apex of the ventricle, 3) short axis at the mitral valve level, 4) short axis at the papillary muscle level, 5) short axis at the cardiac apex, 6) apical four-chamber view, 7) apical two-chamber view, and 8) subxiphoid view. During exercise new areas of abnormal wall motion were initially identified by rapidly manipulating the ultrasound transducer through these positions, recording the images continuously in real time. Having established an optimal transducer position for observing any abnormal wall motion that occurred with exercise, the transducer was held stationary during the final stage of exercise and throughout the recovery period.

Nitroglycerin 0.4 mg was administered sublingually to all patients immediately on termination of exercise to relieve discomfort and to assist in unmasking reversible dysynergy. Cross-sectional echocardiograms were recorded on videotape for later analysis by two observers who had no knowledge of other clinical findings. The two observers independently reviewed the cross-sectional echocardiograms and reached a consensus on the grading of each study. In reviewing the videotapes in real-time, slow-motion and single-frame formats, wall motion in nine regions of the heart (fig. 1) was visually analyzed in a qualitative fashion similar to that previously used for interpreting resting cross-sectional echocardiograms. Overall motion of the left ventricle was assessed; segments of abnormal wall motion were identified by comparing motion of adjacent segments of the heart to one another. Motion patterns of the individual segments of the heart were thus described as normal, hypokinetic, akinetic or dyskinetic for each period of the examination — rest, exercise and after nitroglycerin recovery.

Exercise Protocol

Exercise was performed in the supine or slight left lateral position using a bicycle ergometer (Warren E. Collins, Braintree, Massachusetts) mounted to the foot of a sturdy hospital bed (fig. 2). Exercise was performed at a constant work load of 10 kg-m/sec until the patient’s symptom-limiting end point was reached, or until 85% of the age-predicted maximum heart rate was achieved. Nitroglycerin 0.4 mg was given to all patients immediately on termination of exercise. Unipolar electrocardiographic lead V₆ and blood pressure were monitored throughout the stress and recovery periods.

Catheterization and Treadmill Testing

Cardiac catheterization was performed within 1 week of exercise cross-sectional echocardiography in all patients using either the Sones or Judkins technique. The coronary arteries were visualized in multiple projections. Left ventriculography was routinely performed in the right anterior oblique projection. Left anterior oblique views and ventriculography during exercise were not available. Cardiac catheterization data were analyzed in standard clinical fashion without knowledge of the cross-sectional echocardiographic findings.

A separate treadmill exercise test was performed within 1 week of exercise cross-sectional echocardiography in 25 of the 28 patients selected for study. Using a modified Balke protocol, unipolar electrocardiographic lead V₆ and lead II were monitored for ST-segment changes. The ECG was considered positive if a normal resting ST-segment showed greater than 1 mm depression 80 m/sec beyond the J junction during or immediately after exercise.

In 23 of 25 patients who underwent treadmill exercise testing, thallium-201 was injected as a bolus of 1.5 mCi 30–45 seconds before maximum stress. Radio-
nuclide imaging was performed in multiple projections within 25 minutes of exercise termination, and repeated after 3–4 hours rest. Areas of transient myocardial ischemia were identified by independent observers as perfusion defects present on exercise scintigraphic images, but not on resting examinations. A normal thallium image was defined as the absence of localized perfusion defects.

Results

Technical Feasibility

Technically adequate exercise cross-sectional echocardiograms were obtained in 20 of the 28 patients (71%). Cross-sectional echocardiograms were technically unsatisfactory at rest and during exercise in three patients. Five patients were adequately examined in the resting state, but cross-sectional echocardiograms performed during exercise were technically unsuitable for interpretation.

In general, many cross-sectional echocardiograms performed during exercise were not as high in quality as studies performed at rest, but were sufficient to be diagnostic. The major technical limitation during exercise appeared to be hyperventilation rather than motion of the chest wall. Commonly, standard echocardiographic views obtained from parasternal transducer positions were difficult to record continuously during exercise due to interposition of the lung between the heart and chest wall. Technically adequate parasternal visualization of the heart was accomplished in only 11 of the 28 patients (39%). However, the acoustic window located at the cardiac apex remained readily accessible during exercise in 19 of the 20 patients whose echocardiograms were considered technically acceptable. In many instances, apical views were more readily obtained during exercise than at rest due to increased prominence of the apical impulse during exercise. When available, the subxiphoid acoustic window was particularly well suited to the performance of high-quality cross-sectional echocardiograms during exercise. However, we could get adequate subxiphoid studies in only eight patients. Because of these limitations in the


FIGURE 3. Diastolic and systolic frames of short-axis cross-sectional echocardiograms at the level of the chorda tendinea. (top) During exercise-induced angina pectoris the anterolateral wall of the ventricle became akinetic. (bottom) After nitroglycerin, wall motion returned to normal.
availability of acoustic windows during exercise, the cardiac apex and inferior wall of the heart were the areas most easily visualized. The anterior wall, particularly at the base of the heart, was the most difficult area to examine during exercise because of the limitations of parasternal acoustic windows.

The constant bicycle work load of 10 kg-m/sec was well tolerated. Exercise produced either symptoms or 85% of the age-predicted maximal heart rate within 5 minutes in all patients. Symptoms and electrocardiographic changes that occurred during supine exercise were similar to those that occurred during separate treadmill exercise testing, although supine exercise was generally terminated at a slightly lower maximal heart rate.

Of the 20 patients in whom we obtained technically adequate cross-sectional echocardiograms, 10 had new segmental wall motion abnormalities during exercise. Eight of these 10 patients had typical angina pectoris during the exercise test. Chest pain and abnormal wall motion persisted for 1–3 minutes after termination of exercise and nitroglycerin administration. Particularly helpful in the qualitative detection and verification of transient regional wall motion abnormalities was the real-time visualization of wall motion immediately after cessation of exercise. Areas of abnormal wall motion that had not been detected at rest could be seen to normalize gradually during this recovery period. In some instances, segments of the left ventricle that had moved abnormally during exercise appeared to return to normal and then to contract more vigorously than at rest. This spectrum of wall motion as observed in real time over 3–4 minutes, ranging from dyskinesia to normal to hyperkinesis, was convincing in the detection of transient wall motion abnormalities.

Figure 3 displays still frames selected from the exercise and postnitroglycerin cross-sectional echocardiograms of a patient who had 75% obstructive lesions of the left anterior descending and circumflex coronary arteries. The resting left ventriculogram was normal, as were multiple cross-sectional echocardiographic views of the left ventricle obtained immediately before exercise. However, during exercise, a few seconds before onset of the patient’s typical angina pectoris, an area in the anterolateral wall of the left ventricle became akinetic. Figure 3A shows short-axis systolic and diastolic images of the mid-left ventricle at the level of the chordae tendineae obtained at peak exercise. As illustrated on the line diagram, the anterolateral wall of the ventricle is akinetic. Figure 3B shows short-axis systolic and diastolic images of the same area shortly after exercise termination and nitroglycerin administration. Chest pain had resolved. Wall motion returned to normal.

Figure 4 illustrates cross-sectional echocardiograms from a patient who had total occlusion of the left anterior descending coronary artery and 90% occlu-
TABLE 1. Results of Exercise Cross-Sectional Echocardiography, Cardiac Catheterization and Thallium-201/Electrocardiographic Treadmill Testing

<table>
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<th>Pt no.</th>
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Abbreviations: CSE = cross-sectional echocardiogram; RCA = right coronary artery; LAD = left anterior descending coronary artery; LCCA = left circumflex coronary artery; LMCA = left main coronary artery.

sion of both the left circumflex and right coronary arteries. Resting left ventriculography and cross-sectional echocardiography both showed dyskinesis of the anterior and apical segments of the heart. During exercise (fig. 4A), the inferior wall of the heart became akinetic simultaneous with onset of typical angina pectoris. Repeat exercise cross-sectional echocardiograms performed in this patient after saphenous vein coronary artery bypass grafting (fig. 4B) showed normal motion of the inferior wall at a higher heart rate-blood pressure product than preoperatively. The anteroapical segment remained dyskinetic both at rest and during exercise on preoperative and postoperative examinations.

Comparison of Exercise Echocardiography to Catheterization and Treadmill Testing

The results of exercise cross-sectional echocardiography, cardiac catheterization and thallium-201/electrocardiographic treadmill testing are summarized in Table 1 for the 20 patients with technically adequate exercise echocardiograms. Areas of abnormal wall motion described under “exercise cross-sectional echocardiography” are areas that displayed different motion during exercise than at rest. In no case did resting segmental wall motion abnormalities disappear during exercise; these areas are listed only in the resting cross-sectional echocardiography column.

Similarly, areas of perfusion abnormality listed under exercise thallium are areas that were present immediately after exercise but appeared to be reperfused on resting images.

Transient Segmental Dysynergy During Exercise

We saw an abnormality in left ventricular wall motion during exercise cross-sectional echocardiography that had not been observed at rest in 10 patients. All 10 patients had significant coronary stenoses (> 50% luminal obstruction) in the vessel supplying the area of the heart in which we saw exercise wall motion abnormalities. In seven of these patients, the left ventriculogram showed wall motion abnormalities consistent with the resting cross-sectional echocardiogram, but did not show the abnormalities induced during exercise cross-sectional echocardiography. In three patients, the left ventriculogram, which was performed without exercise, showed areas of segmental dysynergy similar to those during exercise cross-sectional echocardiography. Two of these three required nitroglycerin for chest pain during the catheterization procedure. Abnormal wall motion observed on left ventriculography in these patients may not be representative of the basal state.

Six of these 10 patients had thallium-201 myocardial perfusion treadmill exercise tests. Radionuclide imaging immediately after exercise showed defects
TABLE 1. (Continued)

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<tr>
<th>Exercise ST segment</th>
<th>Left ventriculogram</th>
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<th>LCCA</th>
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that appeared reperfused after rest in all six patients. In each case, these ischemic areas corresponded in location to the areas of exercise-induced wall motion abnormality seen on cross-sectional echocardiography. Resting thallium-201 perfusion defects correlated with the location of dysnergy on resting cross-sectional echocardiography in three patients. One patient had an inferior wall resting perfusion defect, but diffuse hypokinesis on resting echocardiography. One patient had a normal resting thallium-201 perfusion scan, but generalized hypokinesis and inferior akinesis on resting echocardiography.

A positive ST-segment response was seen during treadmill exercise testing in four of the nine patients who had transient dysnergy on exercise cross-sectional echocardiography. Three had nondiagnostic ST-segment changes and two had negative exercise ECGs.

Abnormal Resting Wall Motion

Five patients had abnormal left ventricular wall motion on resting cross-sectional echocardiography, but no new areas of segmental dysnergy appeared during exercise. Two of these five appeared to have nonischemic cardiomyopathies. Both cross-sectional echocardiography and left ventriculography showed generalized hypokinesis. No coronary stenoses were present and thallium-201 imaging showed no segmental perfusion defects.

Three patients had significant coronary disease and segmental dysynergy at rest that did not appear to change during exercise cross-sectional echocardiography. Two had negative thallium-201 exercise tests. One patient appeared to have inferior ischemia on thallium imaging, but an area of infroapical dyskinesis seen on resting cross-sectional echocardiography did not appear to change during exercise. This case may represent a false-negative exercise cross-sectional echocardiogram for ischemic change or a false-positive thallium-201 exercise test.

Normal Resting and Exercise
Cross-sectional Echocardiograms

No abnormalities were noted on either resting or exercise cross-sectional echocardiograms in five patients. Three of these patients also appeared normal by catheterization and treadmill testing. One patient had an isolated stenosis of the midportion of the left anterior descending coronary artery, but no evidence of ischemia on thallium-201/ECG exercise testing. This patient had a false-negative exercise cross-sectional echocardiogram for the presence of coronary disease, but probably did not have myocardial ischemia. Finally, one patient who had a normal exercise cross-sectional echocardiogram did have significant coronary stenoses, an abnormal resting left ventriculogram, and a positive thallium-201 exercise test. On the cross-sectional echocardiogram, this patient had abnormalities in the motion of the anterior wall that were not appreciated on initial data analysis. This
examination represents a false-negative test due to observer error.

Discussion

One of the earliest manifestations of insufficient myocardial blood flow is an alteration in contractility. In a classic study, Tennant and Wiggers showed that acute coronary ligation produced systolic expansion of the resulting ischemic myocardial segment. Subsequently, ischemic contractile abnormalities have been shown to occur in humans as well as animals using a wide variety of techniques, including cineangiography, epicardial dimension gauges, strain gauges, sonomicrometers, and reflected ultrasound. The mechanical results of myocardial ischemia appear within seconds after onset of ischemia, and disappear rapidly when ischemia is reversed. Ventricular dysnergy causes congestive heart failure, may be involved in the production of arrhythmias and is clearly related to survival of patients with ischemic heart disease.

Clinically, ischemic heart disease frequently presents as angina of effort due to a relative imbalance between myocardial oxygen demand and the ability of a narrowed coronary artery to maintain adequate blood flow. Left ventricular cineangiography and gated left ventricular radionuclide blood pool scans have been performed during exercise in patients with ischemic heart disease. New areas of exercise-induced segmental dysnergy that were not present on resting ventriculograms have correlated well with the location of significant coronary artery stenoses. Similarly, gated radionuclide ventriculography performed during exercise has shown that reversible segmental dysnergy occurs during transient myocardial ischemia. Global left ventricular ejection fraction also decreases during exercise-induced ischemia.

M-mode echocardiograms have been performed during angina pectoris induced by handgrip stress and bicycle exercise. These studies have demonstrated diminished amplitude of wall motion and velocity of circumferential shortening, reduced myocardial thickening or systolic thinning, depressed ejection fractions and reduced left ventricular posterior wall diastolic velocity in response to myocardial ischemia. Although M-mode echocardiography provides extremely good temporal resolution of cardiac motion within its thin interrogating beam, this technique is hampered by its lack of true spatial orientation. It is not possible to examine the entire left ventricle with M-mode echocardiography due to the absence of lateral resolution.

Cross-sectional echocardiography provides real-time, two-dimensional tomographic images of the heart. Cardiac motion can be visualized in the lateral as well as axial dimension. In this study, we performed cross-sectional echocardiograms at rest, during supine bicycle exercise and after nitroglycerin administration in 28 patients suspected of having ischemic heart disease. Although we had technical problems in performing cross-sectional echocardiography during exercise, adequate studies were obtained in 20 patients (71%). This incidence of technically adequate examinations is not markedly different from our overall rate of success in cross-sectional echocardiograms at rest, which is approximately 85% in our population of middle-aged and older men, many of whom have chronic obstructive pulmonary disease.

Our success rate in recording technically adequate cross-sectional echocardiograms during exercise is higher than that reported for M-mode echocardiography. This is probably due to the superior spatial orientation of cross-sectional echocardiography, particularly as this relates to the ability to use the apical acoustic window. Because cross-sectional echocardiography allows visualization of the shape of the left ventricle in two dimensions, recognition of cardiac structures is less dependent than M-mode echocardiography on relative transducer positions and valvular motion patterns. The characteristic shape of ventricular structures, such as the cardiac apex and the papillary muscles, allows them to be used as landmarks for standardization of cross-sectional echocardiographic images. These landmarks are not as readily apparent on the M-mode echocardiography. The apical acoustic window was particularly useful during exercise cross-sectional echocardiography because, unlike the parasternal acoustic windows, this area was readily accessible during exercise. Development of wide-angle sector scanners with increased depth of field may allow better use of the apical acoustic window than did the 30° mechanical sector scanner used in this study. The increased field of view provided by wide-angle scanners should also allow easier and more precise identification of an area of segmental dysnergy during the relatively short period of exercise induced ischemia.

Of the 20 patients in whom technically adequate cross-sectional echocardiograms were obtained, 10 patients demonstrated segments of reversible dysnergy during exercise. Each of these patients had significant stenosis in coronary arteries supplying corresponding areas of the left ventricle. A similar area of the heart appeared ischemic in all six who underwent thallium-201 treadmill exercise testing. Reversible areas of dysnergy were not seen on exercise cross-sectional echocardiography in the other 10 patients. Five of these patients had significant coronary lesions; two of these five probably had ischemia that was not detected on exercise cross-sectional echocardiography. Although this series is small, and correlative studies were not performed simultaneously, it appears that the presence of reversible dysnergy on exercise cross-sectional echocardiography is a specific finding of myocardial ischemia. Exercise cross-sectional echocardiography was not sensitive in detecting coronary disease per se. In addition, two patients probably had ischemia that was not detected.

Cross-sectional echocardiography has several advantages over other diagnostic techniques capable of detecting regional wall motion abnormalities during exercise. Compared with cineangiography, cross-sectional echocardiography is noninvasive, easily repeatable, and relatively inexpensive. The physiologic
effects of injected contrast media are avoided, and a large number of cardiac cycles can be evaluated in real time throughout the exercise test. In addition, cross-sectional echocardiography provides spatially oriented tomographic images of the interior structures of the heart themselves, not silhouette images of contrast media. Although use of wide-angle sector scanners will increase the amount of the ventricle examined at any one time, the tomographic nature of the cross-sectional echocardiographic technique does not permit visualization of the entire ventricle at once. Thus, the ability to locate an area of transient segmental dysnergy depends on rapid manipulation of the ultrasound transducer through multiple planes of interrogation to examine the whole ventricle during ischemia. Abnormalities in wall motion must be skillfully and rapidly recognized during the relatively brief period of ischemia to obtain an adequate examination. Considerable technical expertise is necessary. Intraobserver variation in both the performance and interpretation of exercise cross-sectional echocardiograms has not been determined.

Radionuclide blood-pool imaging during exercise shares many of the advantages of cross-sectional echocardiography compared with cineangiography. In addition, radionuclide studies, unlike echocardiography, can be performed in almost all patients, and the global left ventricular ejection fraction can be measured without regard to left ventricular internal geometry. However, cross-sectional echocardiography may prove to be superior to radionuclide imaging for evaluating regional wall motion because it can provide continuous, direct, real-time images of the interior structures of the heart.

M-mode echocardiography has been useful in examining not only the rate and amplitude of wall motion during ischemia, but also in measuring systolic myocardial thickening properties. M-mode echocardiography is hampered, however, by its lack of lateral resolution and spatial orientation. In this preliminary study, the interpretation of cross-sectional echocardiograms was limited to a qualitative analysis of regional wall motion similar to that generally used in interpreting angiograms. However, quantitative data similar to that obtained from M-mode echocardiography can be obtained from high-quality cross-sectional echocardiograms, with the additional advantages of lateral resolution and spatial orientation. More quantitative indices of myocardial thickening have been used to interpret resting cross-sectional echocardiograms, and may increase the yield of exercise cross-sectional echocardiography if technically adequate images are obtained. In addition, it should be possible to quantitate the size of an ischemic myocardial segment from spatially oriented real time cross-sectional echocardiographic images. However, precise definition of the endocardial and epicardial surfaces throughout the ventricle may be difficult during exercise.

We conclude that exercise cross-sectional echocardiography is feasible and that transient wall motion abnormalities that correspond to areas of myocardial ischemia can be detected. This technique expands the usefulness of resting cross-sectional echocardiography, and may improve our understanding of ischemic heart disease.

Acknowledgment

The authors thank Dr. Clifford Hallam, Dr. William Bauman, Dr. Abe Friedman, Norman Howard, Linda Doyle and Dee Chimento for their help in this study.

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Comparative Value of Eight M-Mode Echocardiographic Formulas for Determining Left Ventricular Stroke Volume

A Correlative Study with Thermodilution and Left Ventricular Single-plane Cineangiography

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SUMMARY Sixty-six consecutive patients without left ventricular volume overload, significant arrhythmia or significant pericardial effusion were examined by M-mode echocardiography immediately before diagnostic left- and right-heart catheterization. Using various echocardiographic measurements, left ventricular stroke volume (SV) was calculated according to eight different echocardiographic formulas (SVE) that have been proposed previously. At catheterization SV was also determined by thermodilution (SVT) and by single-plane left ventricular cineangiography in the right anterior oblique projection (SVA).

When comparing SVE with SVT, the four formulas developed to calculate mitral or aortic flow failed ($r = 0.10$ to $0.54$). As expected, poor correlations ($r = 0.22$ to $0.47$) were also found when formulas used to calculate ventricular volumes from the ventricular diameter or SV from the change in diameter (left ventricular formulas) were used in coronary patients with grossly asymmetrical ventricular contraction patterns. When the use of the left ventricular formulas was confined to patients with symmetrical or almost symmetrical contraction, two formulas yielded favorable correlations of $r = 0.84$, $SEE = 12.7$ ml and $r = 0.86$, $SEE = 12.2$ ml, respectively. These correlations were comparable to the correlation between our two invasive reference techniques ($r = 0.81$; $SEE = 12.2$ ml). The comparison between SVE and SVA confirmed the results of the thermodilution study, though the correlations were generally weaker.

We conclude that the formula of Teichholz et al., which was the best of all tested formulas, may be used to obtain a clinically useful estimate of SV in patients in whom symmetrical or almost symmetrical left ventricular contraction can be anticipated.

SEVERAL RESEARCHERS have attempted to determine left ventricular stroke volume (SV) from M-mode echocardiographic recordings. Initially the changes in left ventricular dimension have been used to measure SV,¹⁵ but more recently there has been increasing interest in trying to determine mitral and aortic valve flow from the echocardiogram.⁶⁻¹⁴ However, the use of several formulas in the same patient may yield grossly different measurements, so obviously these formulas cannot be used interchangeably, and it is not clear if any of them allows reasonably accurate SV determination.⁵⁻¹⁶

The present study was designed to assess the comparative value of eight formulas that have been proposed for echocardiographic SV determination (SVE). Two generally accepted invasive methods (thermodilution and single-plane left ventricular cineangiography) were chosen as reference methods.
Exercise cross-sectional echocardiography in ischemic heart disease.
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Circulation. 1979;60:1300-1308
doi: 10.1161/01.CIR.60.6.1300
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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