Exercise Echocardiography: Detection of Wall Motion Abnormalities During Ischemia

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SUMMARY To assess the feasibility of detecting wall motion abnormalities with echocardiography during exercise-induced ischemia, we performed echocardiograms on 13 patients with angiographically documented coronary artery disease at rest and during supine bicycle exercise at increasing work loads until angina or ischemic electrocardiographic changes appeared. We analyzed echocardiographic indices of regional left ventricular function in these patients and 11 age- and heart rate-matched normal volunteers. In the 13 patients, 22 of 25 echocardiographically defined wall segments (13 septa, nine posterior left ventricular walls) were supplied by coronary arteries with $\geq 70\%$ stenosis and were compared with the corresponding 22 segments from the 11 normals. Mean systolic septal thickening increased in the 22 segments of normals from $56 \pm 3\%$ (SEM) at rest to $77 \pm 7\%$ in exercise ($p < 0.01$) while in the patients' 22 wall segments supplied by stenotic vessels the mean value fell during peak exercise from $59 \pm 6$ to $35 \pm 3\%$ ($p < 0.005$). Mean systolic posterior left ventricular wall thickening rose similarly in normals from $89 \pm 9$ to $115 \pm 8\%$ ($p < 0.005$) but fell during peak exercise from $75 \pm 9$ to $54 \pm 9\%$ ($p < 0.01$) in the patients' nine abnormally perfused segments. Maximal velocity of diastolic wall thinning rose from rest to exercise in the septa and posterior left ventricular walls of normals from $5.5 \pm 0.3$ to $7.7 \pm 0.6$ cm/sec ($p < 0.005$) and from $8.4 \pm 0.8$ to $11.8 \pm 1.2$ cm/sec ($p < 0.001$), respectively. In patients, these same indices fell at peak exercise from $5.9 \pm 0.5$ to $4.3 \pm 0.4$ cm/sec ($p < 0.05$) and from $8.3 \pm 1.2$ to $6.2 \pm 1.4$ cm/sec ($p < 0.005$ vs normals in exercise), respectively. The percent systolic change in left ventricular internal diameter increased from rest to exercise in normals from $38 \pm 2$ to $44 \pm 2\%$ ($p < 0.001$), but fell in patients during peak exercise from $35 \pm 2$ to $28 \pm 2\%$ ($p < 0.001$).

Exercise echocardiography appears in these patients to be sensitive in detecting wall motion abnormalities during exercise-induced ischemia, and may be applicable in patients in whom exercise electrocardiography is equivocal, or where the functional significance of a coronary arterial lesion is uncertain.

IN PATIENTS WITH coronary artery disease the function of the regions of myocardium supplied by a stenosed artery depends on the balance between oxygen demand of the muscle and the limited capacity of the narrowed artery to increase its delivery of oxygenated blood. In the absence of previous infarction or ongoing ischemia, many patients with even severely stenosed coronary arteries have normal ventricular function at rest. During exercise, however, as myocardial oxygen demands increase, flow through the stenosed artery can increase only to a certain level; beyond that level, the supplied myocardium becomes ischemic.

Studies in animals indicate that regional left ventricular wall motion and thickening decrease dramatically within seconds after the onset of ischemia. Although decreases in regional endocardial motion and global function have been demonstrated during exercise-induced ischemia by cineventriculography and radionuclide techniques, accurate measurement of the time course of changes in wall thickness is not possible with these methods. Changes in wall thickness may be more independent of translational movement of the heart than are changes in endocardial motion relative to an arbitrary reference point. In addition, recent studies have shown that areas of the left ventricular endocardium that move poorly on a resting ventriculogram may contain normal myocardium histologically. A technique that examines regional indices of thickening and thinning might give a more accurate and objective assessment of viability. Accordingly, we assessed the accuracy of echocardiography in detecting and localizing abnormalities in regional left ventricular wall thickening and thinning during exercise-induced ischemia in a group of patients with coronary artery disease.

Methods

Study Population

Eighty-three persons were examined initially by M-mode echocardiography at rest. The normal subjects were derived from two sources: 1) volunteers age-matched to the patient population who had no historical, physical, electrocardiographic, or echocardiographic findings suggestive of disease in the cardiovascular system and negative stress ECGs; and 2) individuals with chest pain of uncertain etiology referred to The Johns Hopkins Hospital for coronary...
Table 1. Study Population

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51 ± 8

96 ± 16

*ECG positive if 1 mm or more J point depression with planar or downsloping ST segment 1 mm or more depressed 80 msec after J point.

Abbreviations: HR = heart rate; EF = ejection fraction; LAD = left anterior descending; PD = posterior descending.

arteriography who had no evidence of cardiac disease or coronary artery spasm at catheterization. The patients had angiographically documented significant coronary artery disease (≥ 70% stenosis of one or more coronary arteries) and were exercised within 2 weeks of coronary arteriography.

High-quality resting echocardiograms in which both sides of the septum and posterior left ventricular wall were seen continuously throughout the cardiac cycle were obtained on 54 persons who, after giving informed consent, exercised according to the protocol below. Echocardiograms of similar quality during exercise were obtained on 24 of these (eight normal volunteers, three persons with chest pain of uncertain etiology and normal coronary arteriograms and left ventriculograms, and 13 patients with documented coronary artery disease) and form the basis for this report. The first four patients studied were consecutive patients with angiographically documented coronary artery disease who had high-quality resting echocardiograms. Two of these had a history of myocardial infarction. Subsequently, patients who were chosen had no history of myocardial infarction, normal left ventriculograms and at least one coronary artery with ≥ 70% stenosis. Details of the study population are given in table 1. The 13 patients with coronary artery disease had a mean age of 51 ± 8 years and exercised until typical angina or ischemic ECG changes appeared. Ischemic ECG changes were defined at ≥ 1 mm planar ST depression for at least 80 msec. Because of the severity of the coronary disease in the patient population and propranolol therapy in four, the mean maximal heart rate was 96 ± 16 beats/min. The average duration of exercise in this group was 5.3 minutes (range 3-8 min). The 11 normal volunteers had a mean age of 53 ± 9 years and exercised to exhaustion. Values of echocardiographic indices in the normals were selected at pre-exhaustion heart rates to match the maximal rates achieved by the patients with coronary artery disease, with a mean rate of 101 ± 13 beats/min. The average duration of exercise until exhaustion in the normals was 8.2 minutes (range 6-12 min); the average duration of exercise at which pre-exhaustion measurements were selected was 3.5 minutes (range 3-7 min).

Exercise Echocardiography

Patients and normal volunteers exercised on a mechanically-braked bicycle ergometer (Monark, model 850) while lying on a foam rubber wedge in a 20° semi-supine or slightly left-lateral decubitus posi-
tion. A graded exercise protocol was followed with patients pedalling at 18 km/hr at a work load of 300 kpm/min for the first 3 minutes. Thereafter the work load was increased by 300 kpm/min every 3 minutes, with speed held constant. Twelve-lead electrocardiograms (with V₅ and/or V₆ in the third left intercostal space so as to allow room for the echocardiographic transducer) and M-mode echocardiograms (Smith-Kline Ekoline 20A ultrasonoscope with a 2.25 MHz internally focused transducer interfaced with a Honeywell-1856 Visicorder strip chart recorder set at a paper speed of 100 mm/sec) were recorded at rest, during every minute of exercise, and every minute for 5 minutes thereafter.

The echocardiographic transducer was hand-held, without the need for special equipment, in the standard left parasternal location in the fourth intercostal space and aimed along the left ventricular minor axis just inferior to the mitral valve leaflets.

The right and left sides of the interventricular septum and the endocardial and epicardial surfaces of the posterior left ventricular wall were digitized by manual tracking on a magnetic digitizing board (Digi-grid, Computer Equipment Corp) throughout several cardiac cycles at rest and during every minute of exercise and the post-exercise recovery period. The thickness of both walls was measured from leading edge to leading edge in the usual manner. The person performing digitization was blinded to the results of coronary angiography. Indices of regional function were calculated by computer from the digitized data according to the following formulas:

\[
\% \text{systolic wall thickening (}\%\Delta T) = \frac{\text{end-systolic thickness} - \text{end-diastolic thickness}}{\text{end-diastolic thickness}} \times 100
\]

\[
\% \text{systolic change of diameter (}\%\Delta D) = \frac{\text{end-diastolic diameter} - \text{end-systolic diameter}}{\text{end-diastolic diameter}} \times 100
\]

End-diastolic measurements were taken at the onset of the QRS complex; end-systolic measurements were made at the greatest wall thickness or smallest ventricular diameter. The maximum velocities of wall thickening in systole (VT), of wall thinning in diastole (VTH), of decrease of diameter in systole (max dD/dt) and of increase of diameter in diastole (max − dD/dt) were calculated using a 5-point numerical differentiation equation. The derivative was computed for each digitized point (one every 2.5 msec), after which the derivatives were smoothed by taking an 11-point average.

Data were tested for statistical significance by the paired or unpaired t test, as appropriate, and 2 × 2 chi square analysis with Yates’ continuity correction. We examined the reproducibility of our digitizing technique by analysis of variance between eight repeat digitizations of the same in-exercise cardiac cycle by a single observer and between eight independent digitizations of the same cycle by each of two observers (table 2). There were no significant differences between independent digitizations by the same observer or between observers with the exception of a small (5%) difference in the means of %ΔD between the two observers. These data are comparable to those of Gibson and co-workers,10, 11 who demonstrated the reproducibility of digitizing resting M-mode echocardiograms and the validity of such measurements in reference to digitized cineventriculograms.

Results

Wall Thickening

One patient had single vessel coronary artery disease with near-total obstruction of the proximal left anterior descending coronary artery (table 1, patient 1). Examination of sample beats from his exercise echocardiogram allows an internal comparison between an abnormally perfused segment and a normally perfused one in the same patient at the same time (fig. 1). At rest, the systolic thickening of the septum and posterior wall are equal. During exercise, after the onset of ischemia, however, septal systolic thickening decreases, while posterior wall thickening increases. Mean percent change in ventricular diameter (%ΔD) for seven cardiac cycles at rest was 42% and fell slightly to 38% for three cycles during ischemia.

Figure 2 shows sample beats at rest and exercise in a normal person at similar heart rates to the beats shown in figure 1. At rest, the %ΔT of the septum and posterior wall are also equal. During exercise systolic thickening of both walls increases equally. Systolic thickening is the increase in wall thickness from end-diastole, expressed as a percent of end-diastolic thickness, and is an index of segmental function. Figure 3 shows the mean %ΔT in systole of the septum and posterior wall for several beats at rest, in early exercise, and after the development of ischemia in patient 1. The %ΔT of both segments is similar at rest and increases early in exercise, from 76 ± 6 to 83 ± 4% (mean ± SEM) in the septum and from 71 ± 5 to 101 ± 9% in the posterior wall. When ischemia develops, however, septal thickening falls to 38 ± 12%, while the posterior wall maintains the rate-related rise in segmental thickening, to 102 ± 10%.

The values at rest and in exercise for percent of regional wall thickening in all the patients compared with the normal volunteers are shown in figure 4. Panels A and B are a comparison of segmental thickening of the septum (%ΔTs) and posterior wall (%ΔTp) in patients with ≥70% stenosis of the artery supplying that wall, with the same indices in normals. The septum is supplied by the left anterior descending coronary artery, which was ≥70% stenosed proximal to the first septal perforator in all 13 patients. The posterior wall is supplied by the posterior descending coronary artery, a branch of the right coronary artery in a right-dominant circulation and of the left cir-
cumflex coronary artery in a left-dominant circulation. The proximal posterior descending, or the vessel giving rise to it, was stenosed ≥ 70% in nine of our 13 patients. In the remaining four patients the posterior walls were supplied by arteries with ≤ 30% stenosis. While it is possible that some segments perfused by an artery with a significant (≥ 70%) stenosis received adequate collateral flow from another artery during exercise, we considered all segments perfused by such a stenosed artery to be at risk for inadequate perfusion during exercise-induced ischemia.

The mean values for %ΔTs and %ΔTp at rest were similar in patients and normals. In exercise the mean %ΔTs of the normals rose significantly, from 56 ± 3 to 77 ± 7% (p < 0.01) while the mean for patients with coronary disease fell from 59 ± 6 to 35 ± 3%
CHEST WALL

RV

SEPTUM

LV

POSTERIOR WALL

REST (HR=60)

EXERCISE (HR=110)

FIGURE 2. Echocardiograms at rest (left) and exercise (right) in a normal person. The scale and paper speed (100 mm/sec) are the same for both. Systolic thickening of both walls is the same at rest and increases in exercise.

(\(p < 0.005\)). Only one of the 13 patients' values overlapped the range of values for the normals, and the mean value for patients in exercise was significantly lower than the mean for normals in exercise (\(p < 0.001\)). Similarly, in exercise, normals showed a significant rise in mean \(\%\Delta T_p\) from 89 ± 9 to 115 ± 8% (\(p < 0.005\)), while the mean for patients with coronary disease fell from 75 ± 9 to 54 ± 9% (\(p < 0.01\)), a value significantly below that for normals in exercise (\(p < 0.001\)).

The regional wall thickening data were also analyzed looking at the change in \(\%\Delta T\) from rest to exercise. The 11 normal volunteers had a total of 22 wall segments with normal perfusion. The 13 patients with coronary disease had a total of 22 segments with abnormal perfusion: 13 septa and nine posterior left ventricular walls were supplied by a coronary artery with \(\geq 70\%\) stenosis. Figure 5 shows the change in \(\%\Delta T\) from rest to exercise. Twenty-one of the 22 segments in normal volunteers thickened the same or more at exercise than at rest. In contrast, \(\%\Delta T\) fell from rest to exercise in 19 of 22 segments in the patients with coronary artery disease. By chi square analysis these differences were highly significant (\(\chi^2 = 26.5, p < 0.001\)). This suggests that, in our patients, a fall in \(\%\Delta T\) in a given segment predicts significant stenosis of the coronary artery perfusing that segment.

In order to determine if changes in wall thickening occurred before clinical signs of ischemia in the patients with coronary artery disease, we compared the values for \(\%\Delta T\) at rest with \(\%\Delta T\) during the minute before the onset of angina or ischemic ECG changes (pre-ischemic \(\%\Delta T\)). Both \%\(\Delta T_s\) and \%\(\Delta T_p\) fell insignificantly, from 59 ± 6 to 47 ± 5% in the septum and from 75 ± 9 to 64 ± 9% in the posterior wall.

The maximum velocities of thickening of the septum (\(VT_s\)) and posterior wall (\(VT_p\)) increased significantly from rest to exercise in normals (table 3). The mean \(VT_s\) for patients fell significantly in exercise.

FIGURE 3. Mean percent segmental thickening for several beats at rest, in early exercise, and at peak exercise with the onset of ischemia in the same patient as figure 1. Segmental thickening increases in both septum and posterior wall early in exercise, but with ischemia in the septum, regional thickening falls markedly. Values represent mean ± SEM.
to a value significantly lower than the normals in exercise, while the mean VTP for patients did not change significantly.

Wall Thinning

Because abnormal relaxation may occur without abnormalities of systolic function in the presence of ischemia and persist for many minutes after occlusion to blood flow is relieved in experimental models, we examined a parameter which may, in part, reflect the rate of relaxation, the VTh. Panels A and B of figure 6 show mean rest and exercise values for the maximum velocity of septal and posterior wall thickening, VThs and VThp, respectively. The mean values at rest were similar for normals and patients. In exercise VThs increased from $5.5 \pm 0.3$ to $7.7 \pm 0.6$ cm/sec in the normal subjects, ($p < 0.005$) but fell in the ischemic segments from $5.9 \pm 0.5$ to $4.3 \pm 0.4$ cm/sec ($p < 0.05; p < 0.001$ vs normals in exercise). Similarly, during exercise VThp increased in normals from $8.4 \pm 0.8$ to $11.8 \pm 1.2$ cm/sec ($p < 0.001$) but fell in the patients from $8.3 \pm 1.2$ to $6.2 \pm 1.4$ cm/sec ($p < 0.005$ vs normals in exercise). This indicates that slower diastolic thinning, as well as decreased systolic thickening, occurs with ischemia.

We also compared rest with pre-ischemic VThs and VThp, but found no significant fall in either before the onset of clinical ischemia. At rest VThs and FThs were $5.9 \pm 0.5$ and $8.3 \pm 1.2$ cm/sec, respectively, and in exercise before ischemia were $5.8 \pm 0.4$ and $7.2 \pm 1.0$ cm/sec, respectively.

Cavity Dimension

Figure 7 shows the changes from rest to exercise for the %AD. In the normals there was a significant rise in
mean %AD from 38 ± 2 to 44 ± 2% (p < 0.001), and 10 of 11 individual volunteers showed increases. In contrast, 12 of 13 patients with coronary disease showed a fall in %AD at peak exercise, and only one exercise value in the ischemic group (patient 1, table 1, with single vessel disease) overlapped the normal range. The mean value for the coronary disease group did not differ significantly from the normals at rest but in exercise fell from 35 ± 2 to 28 ± 2% and was significantly below the value for the patients at rest (p < 0.001) and the normals in exercise (p < 0.0005). The fall of %AD in exercise and the value at peak exercise thus appear sensitive in detecting ischemia in the presence of significant disease of the coronary arteries perfusing the septum and posterior left ventricular wall. During the minute before the onset of angina or ischemic ECG changes there was also a significant fall in %AD: mean %AD fell from 35 ± 2% at rest to 31 ± 2% in this period before clinical signs of ischemia (p < 0.01).

Max dD/dt, increased from rest to exercise in normals, but not in patients (table 3). The same table also shows that max - dD/dt increased significantly from rest to exercise in normals without changing significantly in patients. The pre-ischemic value of max - dD/dt, 14.5 ± 1.4 cm/sec, did not differ significantly from the resting or peak exercise values. However, the mean value of both parameters at peak exercise was significantly lower for patients than for normals.

**Discussion**

Tennant and Wiggers14 first recorded the rapid disappearance of systolic muscle shortening followed by systolic expansion that occurs after coronary occlusion in the dog. Other workers have described the regional dysfunction associated with ischemia in animal models by use of cinematography,18 strain gauges,1,16 epicardial dimension gauges,17,18

**TABLE 3. Velocity of Change in Thickness and Dimension During Rest and Exercise**

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*No significant difference between patients and normals in any resting values.
| p < 0.0005 vs normals in exercise.
| p < 0.05 vs normals in exercise.

Values represent mean ± SEM for 11 normals and 13 patients with the exception of VT, which is based on the nine patients who had ≥ 70% stenosis of the artery supplying the posterior wall.

Abbreviations: VT = maximum velocity of septal thickening in systole; VT = maximum velocity of posterior wall thickening in systole; Max dD/dt = maximum velocity of decrease of diameter in systole; Max -dD/dt = maximum velocity of increase of diameter in diastole.

**FIGURE 6. Maximum velocity of wall thinning in diastole at rest and exercise for patients with coronary artery disease (CAD) as compared to normals. Panel A, velocity of septal thinning; panel B, velocity of posterior wall thinning. All values are mean for group ± SEM. A highly significant difference between normals and patients developed in exercise for both parameters where none existed at rest. LAD = left anterior descending; PD = posterior descending.**
DETECTION OF ISCHEMIA BY EXERCISE ECHO/Mason et al. 57

**Figure 7.** The effect of exercise on systolic percent change in ventricular diameter (%ΔD) in normals and patients with coronary artery disease (CAD). The lines reflect changes in individuals and the large circles and triangles, the mean ± SEM. One CAD value for %ΔD overlaps the normal range.

Cineradiography of radiopaque markers, reflected ultrasound, and implanted ultrasonic crystals. These studies indicate that the deterioration of contractile function of the ventricle appears within seconds of coronary occlusion, before ST segment shifts. Changes in systolic myocardial thickening parallel deterioration in epicardial shortening. These mechanical alterations are rapidly reversible upon release of the stenosis, before ST segments return to baseline, although relaxation abnormalities may persist for almost an hour after a brief occlusion.

In humans, the resting echocardiogram in patients without previous infarction is a poor predictor of the presence of coronary disease. Ecocardiograms have been recorded during angina produced by handgrip stress and have demonstrated reduced wall motion amplitude, ejection fraction, and velocity of circumferential fiber shortening in some cases. Unfortunately, these abnormalities have only been seen in some patients in each group and all of them have had high-grade proximal disease. Furthermore, handgrip is frequently an inadequate stress for producing ischemia. Fogelman et al. recorded posterior wall endocardial echograms during handgrip or supine bicycle ergometer exercise in patients with ischemic heart disease. The patients he examined had slightly but significantly lower mean and maximal velocities of diastolic endocardial motion at rest than normal volunteers, but during exercise-induced angina these parameters fell markedly. The effect of exercise on wall thickening was not examined.

Cineventriculograms and gated blood pool scans have been performed during exercise in patients with ischemic heart disease. By exercise cineventriculography Sharma et al. demonstrated that the development of new areas of dyskinesis not present at rest correlated well with the location of coronary stenoses. Borer and colleagues, using radionuclide stress ventriculography, also demonstrated new areas of regional wall motion abnormality during exercise in segments perfused by an artery with > 50% stenosis. These workers also documented a fall in ejection fraction in most patients during exercise, as in the present study. Both regional and global cardiac function deteriorated in some patients in the absence of symptoms.

In this study we have examined changes in regional wall thickening and thinning and left ventricular cavity dimension during exercise using M-mode echocardiography. In our patients, a fall in segmental thickening during exercise appears to be a sensitive and predictive indicator of significant coronary artery disease (fig. 5), as %ΔT fell during exercise in only one of 22 normally perfused segments (5%), while this parameter fell in 19 of 22 abnormally perfused segments (86%). In a patient with one normally and another abnormally perfused wall (fig. 3), %ΔT rose initially in both segments during low levels of exercise; at the onset of ischemia, percent thickening fell only in the wall segment perfused by a stenosed artery, indicating that in the one patient examined with single vessel disease these changes correlated with coronary anatomy. Closer correlation with coronary anatomy must await further studies on patients with less severe or diffuse coronary disease.

Diastolic velocity of wall thickening falls in ischemic segments (fig. 6). This is consistent with earlier data of Vogel et al., showing a decrease in diastolic endocardial velocity during exercise-induced angina. Our patients' resting values did not differ from the normal controls. This may be because we used age-matched controls, while Vogel's controls were a young population. His patients may also have had more severe disease, as one had resting angina, and the mean heart rate achieved in exercise was lower for his patient population. The finding of slower diastolic thinning during ischemia may reflect delayed relaxation which has been described previously in man.

We found that a fall in %ΔD to less than 37% at peak exercise was a useful indicator of the presence of myocardial ischemia (fig. 5). The systolic change of left ventricular dimension measured echocardiographically will decrease if the systolic thickening of either septum or posterior wall decreases. These regions are usually perfused by the left anterior descending and right coronary arteries, respectively (or in a left-dominant circulation, by the circumflex). Thus, during ischemia, changes in the performance of these segments may result in deterioration of %ΔD. We also found that %ΔD fell significantly during exercise before the onset of ischemia recognizable by angina or electrocardiographic ST segment changes. This change was the earliest detectable sign of ischemia. None of the other parameters we measured showed a significant fall before the onset of angina or ischemic ECG changes. Nine of our 13 patients had

cineradiography of radiopaque markers, reflected ultrasound, and implanted ultrasonic crystals. These studies indicate that the deterioration of contractile function of the ventricle appears within seconds of coronary occlusion, before ST segment shifts. Changes in systolic myocardial thickening parallel deterioration in epicardial shortening. These mechanical alterations are rapidly reversible upon release of the stenosis, before ST segments return to baseline, although relaxation abnormalities may persist for almost an hour after a brief occlusion.

In humans, the resting echocardiogram in patients without previous infarction is a poor predictor of the presence of coronary disease. Ecocardiograms have been recorded during angina produced by handgrip stress and have demonstrated reduced wall motion amplitude, ejection fraction, and velocity of circumferential fiber shortening in some cases. Unfortunately, these abnormalities have only been seen in some patients in each group and all of them have had high-grade proximal disease. Furthermore, handgrip is frequently an inadequate stress for producing ischemia. Fogelman et al. recorded posterior wall endocardial echograms during handgrip or supine bicycle ergometer exercise in patients with ischemic heart disease. The patients he examined had slightly but significantly lower mean and maximal velocities of diastolic endocardial motion at rest than normal volunteers, but during exercise-induced angina these parameters fell markedly. The effect of exercise on wall thickening was not examined.

Cineventriculograms and gated blood pool scans have been performed during exercise in patients with ischemic heart disease. By exercise cineventriculography Sharma et al. demonstrated that the development of new areas of dyskinesis not present at rest correlated well with the location of coronary stenoses. Borer and colleagues, using radionuclide stress ventriculography, also demonstrated new areas of regional wall motion abnormality during exercise in segments perfused by an artery with > 50% stenosis. These workers also documented a fall in ejection fraction in most patients during exercise, as in the present study. Both regional and global cardiac function deteriorated in some patients in the absence of symptoms.

In this study we have examined changes in regional wall thickening and thinning and left ventricular cavity dimension during exercise using M-mode echocardiography. In our patients, a fall in segmental thickening during exercise appears to be a sensitive and predictive indicator of significant coronary artery disease (fig. 5), as %ΔT fell during exercise in only one of 22 normally perfused segments (5%), while this parameter fell in 19 of 22 abnormally perfused segments (86%). In a patient with one normally and another abnormally perfused wall (fig. 3), %ΔT rose initially in both segments during low levels of exercise; at the onset of ischemia, percent thickening fell only in the wall segment perfused by a stenosed artery, indicating that in the one patient examined with single vessel disease these changes correlated with coronary anatomy. Closer correlation with coronary anatomy must await further studies on patients with less severe or diffuse coronary disease.

Diastolic velocity of wall thickening falls in ischemic segments (fig. 6). This is consistent with earlier data of Fogelman et al., showing a decrease in diastolic endocardial velocity during exercise-induced angina. Our patients' resting values did not differ from the normal controls. This may be because we used age-matched controls, while Fogelman's controls were a young population. His patients may also have had more severe disease, as one had resting angina, and the mean heart rate achieved in exercise was lower for his patient population. The finding of slower diastolic thinning during ischemia may reflect delayed relaxation which has been described previously in man.

We found that a fall in %ΔD to less than 37% at peak exercise was a useful indicator of the presence of myocardial ischemia (fig. 5). The systolic change of left ventricular dimension measured echocardiographically will decrease if the systolic thickening of either septum or posterior wall decreases. These regions are usually perfused by the left anterior descending and right coronary arteries, respectively (or in a left-dominant circulation, by the circumflex). Thus, during ischemia, changes in the performance of these segments may result in deterioration of %ΔD. We also found that %ΔD fell significantly during exercise before the onset of ischemia recognizable by angina or electrocardiographic ST segment changes. This change was the earliest detectable sign of ischemia. None of the other parameters we measured showed a significant fall before the onset of angina or ischemic ECG changes. Nine of our 13 patients had
70% stenosis of the arteries supplying both the septum and posterior wall. The pre-ischemic fall in %ΔD may be a summation of the nonsignificant pre-ischemic decreases in %ΔTs and %ΔTp or an early echocardiographic index of regional ischemia. Since coronary disease frequently involves the left ventricle asymmetrically, resting or exercise-induced changes in wall motion in one or two areas may not reflect overall ventricular performance. The echocardiogram transects the left ventricle at two points along a single chord. Changes in %ΔD as well as Max dD/dt and Max – dD/dt measured echocardiographically during ischemia reflect changes in regional performance of the septum and posterolateral wall; such changes may falsely overestimate or underestimate changes in global ventricular performance because the anterolateral and apical regions are not examined.

A recent study has shown that Max – dD/dt increases early in exercise and at low heart rates in young normals. Our data agree with this finding in older normals but the patients with coronary artery disease showed no significant change in this parameter at similar heart rates. This lack of rise may also be an early sign of ischemia.

Most exercise protocols use upright exercise on a treadmill or bicycle. Patients with heart disease, however, reach higher heart rates and systolic blood pressures for a given level of oxygen consumption in the supine rather than the upright position. Furthermore, heart volume is larger in the supine position than upright. Consequently, for inducing angina, supine exercise may be preferable because greater heart rate, blood pressure and cavity size (and therefore wall stress) produce a higher oxygen demand. From a practical point of view, moreover, reproducible echocardiograms during exercise in a sitting position are very difficult to record, and we have had much better success in obtaining data during supine exercise.

Four of the coronary artery disease patients and two normals were taking propranolol at doses up to 320 mg/day at the time of exercise echocardiography. Although this drug causes resting bradycardia and may decrease resting ventricular function, it does not prevent exercise-induced increases in ventricular function in normals or exercise-induced deterioration of ventricular function or regional wall motion in patients with ischemic heart disease. All patients investigated on whom exercise echocardiograms were obtained developed ischemia with exercise, including the four on propranolol.

The greatest limitation of this technique is the difficulty in obtaining high quality echocardiograms during exercise. Of the 54 persons with good echocardiograms of both sides of the septum and posterior left ventricular wall at rest, echocardiograms of similar quality could be obtained during exercise in 24, or 44%. This compares favorably with other studies which have sought to record echoes of the septum and posterior wall continually throughout systole and diastole.

There are several advantages of exercise echocardiography in the evaluation of patients with ischemic heart disease. Echocardiography is the only technique widely available for measuring dynamic changes in wall thickness in different regions of the heart and is likely more independent of motion artifact than techniques which examine endocardial movement. Resting evaluation of regional endocardial motion correlates poorly with histological examination of the same regions. Therefore, measurement of regional thickening, thinning, and motion during exercise gives parameters of regional functional ability under conditions of high oxygen demand likely to precipitate ischemia. In this preliminary study an exercise-induced fall in thickening or minor axis shortening seemed sensitive for and predictive of ischemia in patients with high-grade proximal lesions. This technique may help assess the relative functional severity of different coronary stenoses in order to plan surgery or may reveal to the angiographer the functional significance of a lesion which may not have appeared severe. Further evidence of these applications must await studies on a larger group of patients with less severe coronary stenoses. In the presence of resting regional hypokinesis, echocardiography during exercise might detect improvement in regional function and localize a potentially viable wall segment similar to the effect of intervention-ventriculography. After coronary artery bypass surgery, exercise echocardiography may, as have radionuclide techniques, demonstrate improved performance during exercise of segments successfully reperfused. In the presence of disorders that make interpretation of the standard exercise test difficult, such as left bundle branch block, digitalis therapy, left ventricular hypertrophy, or ventricular pacing, echocardiography during exercise may be the only way of evaluating percent change in wall thickening, which should be unaffected by abnormal patterns of electrical depolarization or repolarization.

Compared with exercise cineangioography, echocardiography has the advantage of being noninvasive, easily repeatable, and inexpensive; it looks at a large number of cardiac cycles before, during, and after ischemia, and does not alter the function of that which it seeks to measure. Compared with stress radionuclide ventriculography, the technique reported here follows instantaneous events in each cardiac cycle rather than combining several cycles, imposes no radiation exposure, and evaluates changes in thickening as well as endocardial motion that gated blood pool scans do not assess. The yield of this type of investigation will be higher and the application more widespread when technical advances provide better resolution of echocardiographic signals and when other techniques become available for measuring regional thickening in man. With the extension of this methodology to two-dimensional echocardiography, most wall segments of the left ventricle will be accessible for similar analysis.
Acknowledgments

We acknowledge the assistance of Mrs. Sue Livengood and Dr. Charles G. K. Pawsey in the performance of these studies and Miss Spring Forsythe in the preparation of the manuscript.

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Circulation. 1979;59:50-59
doi: 10.1161/01.CIR.59.1.50
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1979 American Heart Association, Inc. All rights reserved.
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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