Quantitative analysis of segmental wall motion during maximal upright dynamic exercise: variability in normal adults

Leonard E. Ginzton, M.D., Richard Conant, Ph.D., Marianne Brizendine, R.N., Timothy Thigpen, B.S., R.D.M.S. and Michael M. Laks, M.D.

ABSTRACT Twenty-five healthy adults underwent subcostal-view, four-chamber two-dimensional echocardiographic examination while upright at rest and at the peak of maximal bicycle exercise. The purpose of the study was to determine whether the variability in regional left ventricular endocardial motion, previously demonstrated to be present at rest, persisted at peak exercise. The rest and exercise end-diastolic and end-systolic endocardial contours were visually identified, digitized, and divided into 32 radial segments after realignment by the computer. At rest there was similar percent segmental area reduction for the septum (segments 1 to 12) (54 ± 4%, mean ± 1 SD), apex (segments 13 to 20) (67 ± 3%), and lateral wall (segments 21 to 32) (67 ± 8%). At peak exercise the percent area reduction increased significantly: septum 84 ± 5%, apex 88 ± 2%, lateral wall 83 ± 6% (p < .001 compared with rest for all areas). However, there was considerable variability in percent area reduction between different radial segments in the same individual. At rest the difference between minimal and maximal percent area reduction within the same individual was 49 ± 17 percentage units (range 21 to 83) and that at peak exercise was 32 ± 17 percentage units (range 0 to 66). It is concluded that, because the range of standard deviation of normal endocardial motion and the degree of variability between radial segments in the same healthy individual are significant, qualitatively determined "hypokinesis," as commonly assessed clinically, may be a normal event. However, segmental akinesis or dyskinesis, which occurred rarely at rest and never at peak exercise, must be considered abnormal events.


CLINICAL ANALYSIS of left ventricular segmental wall motion commonly involves the assumption that left ventricular endocardial motion, as assessed qualitatively, is symmetric and of uniform magnitude in all portions of the ventricle.1 Pathologic significance is frequently assigned to deviations from this expected symmetry of endocardial motion,2–5 especially if the "hypokinesis" is observed during exercise or similar stress.6–7 Recent quantitative cineangiographic,8–11 echocardiographic,12–19 and radionuclide20, 21 studies of segmental wall motion and thickening in normal adults at rest have revealed considerable variability in the magnitude and timing of maximal contraction in different segments of the left ventricle. However, the degree of variability in normal segmental wall motion during maximal exercise has not been studied. Therefore, it is not known whether the variability demonstrated at rest persists during exercise. If the variability were also present during exercise, the clinical significance of exercise-induced regional variations in segmental wall motion would require reassessment.

We have reported recently the use of subcostal-view, two-dimensional echocardiography performed during upright bicycle exercise.22, 23 This technique permits the acquisition of high-quality images of the left ventricle at all intensities of exercise and thereby allows the quantitative measurement of left ventricular endocardial motion during maximally tolerated exercise stress (figure 1). The purpose of this study was therefore to determine in normal adults (1) the magnitude of quantitative left ventricular endocardial motion during maximal upright bicycle exercise and (2) the degree of variability in segmental wall motion during exercise.
FIGURE 1. Subcostal four-chamber two-dimensional echocardiogram from a normal subject at rest (heart rate 64 beats/min) and at peak exercise (heart rate 185 beats/min). A, End-diastole at rest; B, end-systole at rest; C, end-diastole at peak exercise; D, end-systole at peak exercise. The electrocardiogram denotes the timing of the frame in the cardiac cycle. The endocardium is visualized at rest and exercise. The aortic and mitral valve planes were excluded from the area of analysis. AV = aortic valve; LA = left atrium; LV = left ventricle; MV = mitral valve.

Methods

Study population. Twenty-eight healthy adults were examined at rest for echocardiographic quality. In three subjects the subcostal view two-dimensional echocardiogram was of inadequate quality and these subjects were excluded. Thus, the final study population consisted of 25 healthy adults. Their mean (±SD) age was 22 ± 6 years with a range of 18 to 38 years. There were 17 men and eight women. No subject had any personal or family history of premature cardiovascular disease or hypertension. None was taking any medication and in all results of cardiac physical examination were normal. In addition, for all subjects a normal 12-lead electrocardiogram was obtained at rest and at the peak of maximal upright bicycle exercise.

Informed consent was obtained from all subjects according to a protocol approved July 27, 1982 by the Harbor-UCLA Medical Center Human Subjects Committee.

Exercise protocol. The subjects exercised in the upright position on a bicycle ergometer. Exercise was initiated at 0 kilopond-meters (kpm)/min and was increased by 75 kpm/min each minute until the subject was unable to continue further exercise. The subjects remained sitting upright on the bicycle during the recovery period, pedaling slowly without ergometer resistance for the first 1 to 2 min of recovery. Exercise was performed with continuous electrocardiographic monitoring. Blood pressure, heart rate, and a 12-lead electrocardiogram were obtained at rest, every 3 min during exercise, and at peak exercise.

Echocardiography. Two-dimensional echocardiograms were obtained with a wide-angle rotating transducer mechanical scanner (Advanced Technology Laboratories Mark 3) with a 3.0 MHz transducer and recorded on videotape (Panasonic NV 8200) at a frame rate of 25 frames/sec. The resting two-dimensional echocardiogram was obtained from the subcostal four-chamber view in subjects in the upright position just before the onset of exercise. The peak exercise echocardiogram was recorded from approximately 15 sec before the cessation of exercise until exercise was terminated (figure 1).

The following previously validated protocol was established to obtain high-quality, reproducible, subcostal-view two-dimensional echocardiograms in subjects at rest and during exercise. The handheld transducer was placed in the subcostal position, usually just to the left of the xiphoid process and
pressed gently but firmly inward and upward so that the ultrasound beam passed just below the xiphoid process. To improve the image quality the subject was instructed to sit “at attention” so that the trunk was extended and the shoulder girdle adducted. The subcostal four-chamber view was obtained by imaging the mitral valve leaflets and then rotating and angling the transducer to obtain the longest axis of the left ventricle while still visualizing the mitral valve. This ensured that the region of the apex was adequately visualized. The studies were done during held partial inspiration to minimize respiratory and body motion interference. All subjects were able to hold their breath for at least 1 to 2 sec even at peak exercise, which allowed three to seven cardiac cycles to be visualized. The Valsalva maneuver was carefully avoided. During the recording period the transducer was angled slightly from side to side to ensure that the longest left ventricular axis was visualized.

Identification of end-diastolic and end-systolic images. The videotapes recorded at rest and at peak exercise for each subject were analyzed in slow motion and frame by frame in both the forward and reverse mode. End-diastole was defined as the onset of the electrocardiographic QRS and end-systole was defined as the video frame demonstrating the smallest left ventricular cavity area just before mitral valve opening. End-diastolic and end-systolic frames were identified that showed the longest possible axis of the left ventricle and in which all, or nearly all, of the endocardial echoes could be identified on the single stop-frame image. The endocardial border was defined as the interface between the left ventricular cavity echoes and the myocardial echoes. The papillary muscles, if visualized, were considered to be within the left ventricular cavity.

Left ventricular wall motion analysis. The endocardial borders of the end-diastolic and end-diastolic images at rest and at peak exercise were identified and digitized (with the use of a 256 256 pixel matrix) by an XY sonic digitizer coupled to a minicomputer (figure 2). Vertical and horizontal calibrations were confirmed with a calibration phantom.

Segmental wall motion analysis was accomplished by the computer using the manually entered endocardial contours. To account for respiratory motion, the end-diastolic and end-systolic contours were realigned by the computer using the following method. The left ventricular long axes (mitral valve plane midpoint to the apex) of the diastolic and systolic contours were aligned and the midpoint of the mitral valve plane of the two contours were then superimposed. The center of area of the diastolic contour was identified by the computer, which then drew 32 equiangular radial segments (with the use of the center of area as the reference point) beginning at the base of the interventricular septum and proceeding clockwise along the septum to the apex and lateral wall and ending at the base of the lateral wall. Care was taken to exclude the mitral and aortic valve planes from the area of analysis. Percent area reduction for each of the 32 radial segments was then calculated by the computer. Percent segmental area reduction was calculated according to the following formula:

\[
\text{Percent area reduction} = \frac{(\text{End-diastolic area} - \text{end systolic area})}{\text{End-diastolic area}} \times 100
\]

Normal segmental wall motion was defined as inward systolic motion that was within the 95% confidence limits for that radial segment in the 25 normal subjects. Hypokinesis was defined as inward systolic motion that was less than the lower 95% confidence limit of percent area reduction for that radial segment. Akinetics was defined as no motion in the segment from end-diastole to end-systole. Dyskinesis was defined as outward systolic motion of the segments. The mean percent area reduction and the 95% confidence limits for each segment were established separately at rest and at peak exercise.

Statistical methods. Data are expressed as the mean ± 1 SD. Significance of changes in heart rate, systolic blood pressure, and ejection fraction were measured by the Student’s t test for paired observations. A p value less than .05 was considered significant. Individual segment-to-segment variability was tested using an F test for homogeneity of variance. The F test of homogeneity of variance was also used to evaluate interobserver variability.

Results

With maximal exercise the 25 normal subjects had a significant increase in heart rate (64 ± 10 to 187 ± 8 beats/min, p < .001) and peak systolic blood pressure (119 ± 16 to 184 ± 18 mm Hg, p < .001). Their mean two-dimensional echocardiographic left ventricular ejection fraction increased from 0.57 ± 0.08 at rest to 0.72 ± 0.06 at peak exercise (p < .001). Therefore, combining the inclusion criteria (subjects...
who were asymptomatic, had a negative family history, and a normal rest and exercise electrocardiogram) and the normal increase in ejection fraction with exercise, by Bayesian analysis each subject had a less than 2% likelihood of having coronary artery disease.24

The 32 left ventricular radial segments were subdivided into the interventricular septum (segments 1 to 12), the apex (segments 13 to 20), and the lateral wall (segments 21 to 32) for analysis (figure 2). At rest the percent area reductions in the three areas of the left ventricle were septum, 54 ± 4%; apex, 67 ± 3%; lateral wall, 67 ± 8% (figure 3, table 1). At peak exercise the mean percent area reduction in all areas increased significantly (septum, 84 ± 5%; apex, 88 ± 2%; lateral wall, 83 ± 6% (p < .001 compared with rest for all areas) (figure 4, table 1).

There was considerable variability, however, in percent area reduction between different radial segments in the same individual. At rest (figure 3), the difference between minimal and maximal percent area reduction within the same individual was 49 ± 17 percentage units (range 21 to 83) and that at peak exercise was 32 ± 17 percentage units (range 0 to 66; figure 4). The radial segments that demonstrated the extremes of variability were not localized to any one portion of the left ventricle but were scattered evenly throughout the septum, apex, and lateral wall both at rest and at peak exercise. However, at rest the mean difference between minimal and maximal percent area reduction was greater in the lateral region (31 ± 18%) than in the septum (22 ± 13%; p < .05); the apex (27 ± 14%) was not significantly different from the septum and lateral regions. At peak exercise the apex had significantly less variability (12 ± 11%) than the lateral wall (21 ± 15%; p < .05); the septum (20 ± 14%) was not different from the apex or lateral walls. At rest, one of the 800 radial segments analyzed was akinetic (0.1%) and 25 of the radial segments were hypokinetic (mean 1.0 ± 1.8 segments/subject), as defined in the Methods section. Hypokinesis, akinesis, or dyskinesis was not observed in any radial segment during peak exercise.

The F test for homogeneity of variance was used to address the question of whether the variability in percent area reduction between individual segments in the same subject could be explained simply by the intraobserver variability in tracing the contours. A p ≤ .05 indicates that the variance observed between different segments in that subject is significantly greater than the intraobserver variability. At rest 20 of the 25 subjects and at peak exercise 14 of the 25 had more variance in

**FIGURE 4.** Segmental left ventricular wall motion in a normal subject at peak exercise. The upper and lower curves are the 95% confidence limits for each segment derived from the peak exercise percent area reduction of all 25 normal subjects. The middle curve represents the segmental area reduction for the same normal subject depicted in figure 3. Note that, although the mean percent area reduction has increased with exercise, there is still a difference of 25 percentage units in area reduction between segment 1 (63%) and segment 13 (88%).

**FIGURE 3.** Segmental endocardial motion in a normal subject at rest. The upper and lower curves are the 95% confidence limits, derived from the percent area reduction of all 25 subjects for each segment at rest. The middle curve is the percent segmental area reduction for the normal individual. Note that the area reduction varies 27 percentage units, from 45% in segment 4 to 72% in segment 27.
TABLE 1
Percent segmental area reduction (PAR) at rest and peak exercise in 25 normal subjects

<table>
<thead>
<tr>
<th>Segment No.</th>
<th>Mean PAR</th>
<th>Standard deviation</th>
<th>Mean PAR</th>
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Regional segmental wall motion than could be accounted for by intraobserver variability. Theoretically, if the variation were equal to the intraobserver variation, a p value ≤ .05 would be expected for data from only 1.25 subjects at rest, and for those from 1.25 subjects at peak exercise.

Intraobserver variability in calculation of quantitative segmental wall motion was assessed by one observer tracing the same video image on 5 separate days, while blinded to the results of the other days. The standard deviation of percent area reduction for 32 segments of the five measurements averaged 5.9%, with a range for individual segments of from 2.3% to 14.9%.

Interobserver variation in measurement of percent area reduction was assessed by having four observers trace the same video image, without knowledge of the others’ results. The interobserver variance for each radial segment was compared with the intraobserver variance for that segment with the use of the F test of variance homogeneity, in which a p ≤ .05 would indicate significant interobserver variation. The p value averaged .35 for the 32 radial segments, and for only four of the 32 segments was p ≤ .05 (segments 11, 17, 18, and 19). Thus, the amount of variation demonstrated between different observers did not differ statistically from the intraobserver variance.

Discussion

In clinical practice, left ventricular endocardial motion has often been assumed to be symmetric and of uniform magnitude. Consequently, pathologic significance has been assigned to reduced endocardial segment motion, especially if it occurs with stress such as exercise. For example, the development of "hypokinesis" during exercise is widely used as a radionuclide angiographic marker of the presence of significant coronary artery disease. Similarly, "hypokinesis" on left ventricular cineangiograms is frequently used to assess the functional significance of coronary artery stenoses. However, a number of studies have shown that considerable variability in regional left ventricular endocardial motion occurs in normal individuals.

Although some of the variability in normal segmental wall motion may be related to technical limitations of the experimental or diagnostic methods used, there is a substantial body of evidence to indicate that at least some of the variability represents true biologic variation. With the use of implanted sonomicrometers in normal dogs, apical segments have been demonstrated to have longer resting fiber lengths and greater magnitudes of systolic shortening than basilar segments. Radionuclide angiographic studies of normal individuals also have demonstrated greater endocardial motion at the apex in comparison with the base at rest. In addition, variability in the magnitude of left ventricular endocardial motion of adjacent segments at rest has been documented by both contrast cineangiographic and echocardiographic techniques.

Variability in the time from the onset of contraction to the peak of maximal contraction has been found to be a source of some, but not all, of the variability in regional left ventricular wall motion. Indeed, the sequence of electrical activation of the heart would predict differing times to the peak of ventricular contraction. Falsetti et al have reported that heterogeneity of regional myocardial blood flow exists in normal dogs. Using microsphere techniques they demonstrat-
ed heterogeneity in blood flow to different segments at the same moment in time and also that the distribution of blood flow varied with time. Because these authors did not examine regional myocardial motion or thickening in relation to the alterations in regional blood flow, the functional significance of the variations in blood flow in relation to the variation in endocardial motion is unknown.

In this study we have demonstrated variability in left ventricular segmental endocardial motion in subjects at rest and at the peak of maximal upright bicycle exercise. The magnitude of the segmental area reduction increased with exercise as expected, but the differences between reduction in the area of the radial segment in the same individual was of a similar degree at rest and at peak exercise. The amount of variability identified at rest was similar to that reported by previous cineangiographic,8-11 radionuclide,10, 21 and two-dimensional echocardiographic12-19 reports. With the use of the F test as a rigorous test of the homogeneity of variance, the magnitude of the differences in percent area reduction between radial segments in the same individual exceeded what could be accounted for by intraobserver variability in 20 of the subjects at rest and 14 at peak exercise. In other words, the variability introduced by intraobserver variation would account for the observed intersegment differences in percent area reduction in only 20% of the normal subjects at rest and in only 36% of the subjects at peak exercise.

There are no studies that have directly addressed the issue of the variability in normal endocardial motion at peak exercise. However, two recent studies have demonstrated variability in normal left ventricular endocardial motion similar to that found in the present study. Using quantitative radionuclide angiography, Areeda et al.21 described variability in regional wall motion during exercise in normal humans. Kondo et al.31 found similar variability in segmental wall motion as assessed by two-dimensional echocardiography during atrial pacing in normal dogs.

There are three potential technical limitations to this study. The first involves the difficulty in obtaining consistent views of the left ventricle in resting and exercising subjects. Inconsistency in identifying the same portion of the left ventricle at rest and at exercise could yield considerable variability in endocardial motion. However, we have found that adherence to the echocardiographic protocol that we have described does provide highly reproducible images of the left ventricle at rest and at exercise. This conclusion is supported by the high correlation previously reported between echocardiographic and first-pass radionuclide angiographic ejection fractions at rest and at exercise (r = .91),23 as well as the correlation between qualitative regional wall motion assessments in subjects at rest and exercise by two-dimensional echocardiography and first-pass radionuclide angiography (chi-square values 37 to 52, p < .001).22

The second potential limitation is the frame acquisition rate of the echocardiographic equipment used. Images are acquired at a rate of 25 per second. Thus, at a heart rate of 180 beats/min there are eight to 10 echocardiographic frames during one cardiac cycle. Inappropriate selection of end-diastolic and end-systolic contours could result in underestimating end-diastolic volume or over-estimating end-systolic volume. We have found, however, that by careful analysis of the videotape to select the largest end-diastolic volume and the frame before mitral valve opening demonstrating the longest left ventricular cavity length for end-systole we have minimized the potential errors of the frame acquisition rate at peak exercise. We have previously conducted studies of the reproducibility of measurements of left ventricular end-diastolic and end-systolic volumes at peak exercise and have found the beat-to-beat variability to be on the order of 6% to 8%. This is similar to the degree of variability others have reported in subjects at rest.32-35 In addition, if the frame rate were a significant influence on the variability of endocardial motion, it would be expected that the variability would increase at peak exercise, when there are fewer frames per cardiac cycle. In fact, the degree of variability was similar at rest and exercise, suggesting that the frame rate did not significantly influence the results of this study. It should be emphasized that the difficulties with respect to suboptimal data acquisition rates during tachycardia are not unique to two-dimensional echocardiography but exist in similar measure for contrast cineangiography and radionuclide angiography.

Lastly, the method of realigning the end-diastolic and end-systolic contours may introduce some artifactual variation into segmental wall motion analysis. We have found that some method of realignment is necessary for segmental wall motion analysis, particularly during exercise, to account for different heart positions due to respiration and body motion. We have examined other reference systems and have noted similar degrees of wall motion variability in all alignment methods tested. This conclusion is consistent with the results of others12, 14, 16-19 who have studied segmental wall motion at rest and found different realignment methods to result in similar degrees of variability.

In conclusion, this study has confirmed findings of
previous cineangiographic, radionuclide, and two-dimensional echocardiographic studies that quantitative assessment of regional normal left ventricular endocardial motion demonstrates variability in segmental area reduction of the same segment in different normal subjects and between segments in the same subject. This study has extended these results to the peak of maximal upright dynamic exercise, when a similar magnitude of variability in segmental endocardial motion has been demonstrated. Although some of the variability may be related to technical limitations, there appears to be a sound physiologic basis for temporal as well as spatial variability in segmental endocardial motion. The wide range of the standard deviation in normal segmental wall motion and the degree of variability between segments in the same individual suggests that “hypokinesis,” as commonly assessed clinically, may be a normal event. It may thus be inappropriate, in the absence of other findings, to assign the pathologic significance previously associated with milder degrees of regional qualitatively determined hypokinesis unless the hypokinesis exceeds the limits of normal, carefully defined for the diagnostic modality used and the conditions of observation. On the other hand, segmental akinesis or dyskinesis occurs only rarely at rest and never during exercise so that akinesis or dyskinesis must be considered abnormal events. Furthermore, this study emphasizes the need for additional studies of regional left ventricular function in normal subjects at rest and exercise to define the limits of normal for the body position, type of stress, and diagnostic modality used.

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