Rapid Resolution of Hyperkinesis After Exercise

Two-Dimensional Echocardiographic Studies in Normal Subjects

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Abnormal wall motion detected with exercise echocardiography identifies ischemic myocardium, while normal myocardium exhibits hyperkinetic motion. The normal, hyperkinetic response to exercise is transient and is predictive of an excellent prognosis. However, there are few data on the duration of the hyperkinesis after peak exercise. Our purpose was to determine the time course of wall thickening after exercise in eight normal subjects with two-dimensional echocardiography. Percentage of wall thickening increased from 53 ± 24 percent at baseline to 82 ± 24 percent at 0 to 2 min postexercise (p < 0.001 vs baseline) and then decreased to 64 ± 27 percent at 2 to 4 min, and 54 ± 20 percent at 5 to 7 min (both NS vs baseline). We conclude that (1) systolic wall thickening is maximal within the initial 2 min following peak exercise, and (2) accurate identification of hyperkinetic, normal myocardium with exercise echocardiography requires immediate postexercise imaging.

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METHODS

Subjects

Eight normal male subjects (age, 29 ± 4 years; range, 25 to 33 years) were studied. All subjects gave informed consent. The institutional committee on human research approved the study protocol. All had a normal history, physical examination, and 12-lead electrocardiogram. In addition, they were screened to assure adequate acoustic windows prior to exercise and echocardiographic imaging. The chest wall was marked with a marker in order to approximate imaging of similar acoustic windows at baseline and after exercise.

Exercise Echocardiography Protocol

Two-dimensional echocardiographic images were obtained with an echocardiographic machine (Hewlett-Packard Sonos 1000), using 2.5- or 3.5-MHz transducers. Parasternal long-axis and short-axis, as well as apical four- and two-chamber views, were obtained prior to exercise. Subjects were exercised on a treadmill according to the maximal Bruce protocol to at least 85 percent of their predicted maximal heart rate for age and to completion of stage 5 of the protocol. Electrocardiograms were recorded during each of the five stages of exercise, then at immediate recovery, and at 1, 3, and 5 min postexercise.

Immediately after completion of exercise, the subjects were placed in a left lateral decubitus position. Within 2 min of exercise, the echocardiographic examination was repeated. Acoustic windows for parasternal views were chosen to obtain similar views as baseline. At 2 to 4 and 5 to 7 min after exercise, additional imaging was performed. At each of the echocardiographic examinations, gain settings were optimized to identify endocardial borders without "blooming" of the surfaces.

Image Processing and Measurements

Only the parasternal long- and short-axis views were used for wall thickening measurements; endocardial surfaces were not consistently visualized from the apical views at peak exercise. End-diastolic and end-systolic frames were digitized from videotape using a frame grabber (Nova Microsonics Color-Vue II) (512 × 240 × 6 bit matrix). End-diastole was defined as the frame just prior to, or during, mitral valve closure. End-systole was defined as the frame prior to mitral valve opening in long-axis views or as the smallest cavity area in short-axis views. Parasternal long- and short-axis views were divided into four and six regions, respectively (Fig 1). Regional end-diastolic and end-systolic wall thickness was measured by averaging ten lengths evenly distributed within each region, using the leading edge-to-leading edge method.

Wall thickening was measured after review of videotapes in order to identify endocardial and epicardial surfaces. Care was taken to exclude the chords and epicardium from the posterior wall endocardial surface; right-sided chords were excluded from the right ventricular side of the septum. When these structures appeared to overlie the surfaces, the myocardial thickness was not measured.

Wall thickness change was the difference between end-systolic and end-diastolic thickness. Fractional systolic wall thickening was calculated using the following formula:
Table 1—Results of Heart Rate, Systolic BP, and Rate Pressure Product (RPP)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Immediately</th>
<th>0-2 min</th>
<th>2-4 min</th>
<th>5-7 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, %</td>
<td>78 ± 19</td>
<td>179 ± 20*</td>
<td>129 ± 18*</td>
<td>104 ± 22*</td>
<td>98 ± 17*</td>
</tr>
<tr>
<td>% maximum predicted</td>
<td>(94 ± 9%)</td>
<td>(69 ± 9%)</td>
<td>(55 ± 12%)</td>
<td>(52 ± 9%)</td>
<td></td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>119 ± 11</td>
<td>164 ± 18†</td>
<td>159 ± 27†</td>
<td>146 ± 31†</td>
<td>119 ± 18</td>
</tr>
<tr>
<td>Rate pressure product</td>
<td>9,216 ± 2,361</td>
<td>29,422 ± 5,075‡</td>
<td>20,353 ± 3,613‡</td>
<td>15,299 ± 4,683‡</td>
<td>11,639 ± 2,924</td>
</tr>
</tbody>
</table>

*p<0.01 vs baseline.
†p<0.005 vs baseline.
‡p<0.001 vs baseline.

Percentage wall thickening =

End-systolic thickness – End-diastolic thickness × 100

End-diastolic thickness

Measurements were made by an investigator blinded to the subject and time interval studied. Measurements were repeated in order to determine intraobserver variability. A second investigator performed measurements to determine interobserver variability.

Statistical Analysis

Data are expressed as mean ± standard deviation. A two-factor repeated measures analysis of variance model (with factors subject and time) was fitted to the heart rate, systolic BP and rate pressure product data. A three-factor repeated measures analysis of variance model (with factors subject, time, and region) was fitted to the systolic wall thickness change and the percentage of systolic wall thickening data. Time by region interaction effects were also included in the three-factor model. Post hoc multiple pairwise comparisons were conducted following the overall analyses using the Bonferroni procedure to control the overall experimentwise error rate at 0.05. Variability was calculated as the mean percent error (difference between two measurements divided by the mean of two measurements × 100).

Results

There were significant (p<0.0001) changes over the time course of the study for heart rate, systolic BP, and rate pressure product (Table 1). Each postexercise heart rate mean was significantly increased over baseline (p<0.01). There was a significant elevation (p<0.005) of systolic BP until 5 to 7 min postexercise when there was a return to baseline. The pattern of elevation and recovery of the rate pressure product was the same as for systolic BP with a significant elevation (p<0.001) until 5 to 7 minutes postexercise when there was a return to baseline.

Wall thickness change could be measured in six of the eight subjects at 0 to 2 minutes postexercise. In the parasternal long-axis view, wall thickness change could be measured from the basal anterior septum (n = 6) and basal posterior region (n = 5), but not from the mid anterior or mid inferior lateral regions. In the parasternal short-axis view, wall thickness could be measured from the mid-inferior lateral (n = 5), mid-anterior septal (n = 3), mid-inferior (n = 2), and mid-septal (n = 1) regions, but not from the mid-anterior and lateral regions. Wall thickening is reported for the regions with the highest yields for measurement: in the parasternal long-axis view, the basal anterior septal and basal posterior regions, and in the parasternal short-axis views, the mid-anterior septal and mid-inferior lateral regions. These four regions were included in the analysis of variance model.

Means and standard deviations for the wall thickening variables are shown in Table 2 by time and region. There were significant time (p<0.0005) and region (p<0.0001) differences for both systolic wall thickness change and percentage of systolic wall thickening from the analysis of variance. There was no

Table 2—Regional Differences in Wall Thickening Over Time After Peak Exercise

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>0-2 min*</th>
<th>2-4 min</th>
<th>5-7 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal anterior septum (long axis)†</td>
<td>(n = 8)</td>
<td>(n = 6)</td>
<td>(n = 4)</td>
<td>(n = 8)</td>
</tr>
<tr>
<td>Thickness change</td>
<td>0.4 ± 0.1</td>
<td>0.7 ± 0.2</td>
<td>0.5 ± 0.1</td>
<td>0.4 ± 0.1</td>
</tr>
<tr>
<td>Percentage of thickness change</td>
<td>42 ± 15</td>
<td>72 ± 20</td>
<td>52 ± 8</td>
<td>42 ± 16</td>
</tr>
<tr>
<td>Basal posterior (long axis)</td>
<td>(n = 8)</td>
<td>(n = 5)</td>
<td>(n = 5)</td>
<td>(n = 7)</td>
</tr>
<tr>
<td>Thickness change</td>
<td>0.6 ± 0.2</td>
<td>0.9 ± 0.1</td>
<td>0.8 ± 0.2</td>
<td>0.7 ± 0.1</td>
</tr>
<tr>
<td>Percentage of thickness change</td>
<td>75 ± 24</td>
<td>92 ± 22</td>
<td>88 ± 19</td>
<td>69 ± 16</td>
</tr>
<tr>
<td>Mid anterior septum (short axis)†</td>
<td>(n = 8)</td>
<td>(n = 3)</td>
<td>(n = 4)</td>
<td>(n = 6)</td>
</tr>
<tr>
<td>Thickness change</td>
<td>0.4 ± 0.1</td>
<td>0.6 ± 0.1</td>
<td>0.3 ± 0.1</td>
<td>0.4 ± 0.1</td>
</tr>
<tr>
<td>Percentage of thickness change</td>
<td>30 ± 31</td>
<td>72 ± 5</td>
<td>34 ± 10</td>
<td>46 ± 10</td>
</tr>
<tr>
<td>Mid inferior lateral (short axis)</td>
<td>(n = 8)</td>
<td>(n = 5)</td>
<td>(n = 5)</td>
<td>(n = 7)</td>
</tr>
<tr>
<td>Thickness change</td>
<td>0.5 ± 0.2</td>
<td>0.8 ± 0.3</td>
<td>0.7 ± 0.2</td>
<td>0.6 ± 0.2</td>
</tr>
<tr>
<td>Percentage of thickness change</td>
<td>57 ± 17</td>
<td>91 ± 33</td>
<td>76 ± 25</td>
<td>61 ± 23</td>
</tr>
</tbody>
</table>

*p<0.001 vs baseline combined over regions.
†p<0.001 vs basal posterior (long axis) and mid inferior lateral (short axis) for thickness change over time; and p<0.001 vs basal posterior (long axis) and p<0.01 vs mid inferior lateral (short axis) for percentage of thickness change combined over time.
indication that the time course was different from one region to the next for either variable since the interaction effects were not significant ($p > 0.80$). Because the interaction effects were not significant, time comparisons were made by combining the data over all four regions. Overall systolic wall thickness change (Fig 2) and percentage of systolic wall thickening (Fig 3) increased from baseline to 0 to 2 min postexercise, but returned to baseline at 2 to 4 min. Percentage of wall thickening increased from $53 \pm 24$ percent at baseline to $82 \pm 24$ percent at 0 to 2 min postexercise ($p < 0.001$ vs baseline) then decreased to $64 \pm 27$ percent at 2 to 4 min and $54 \pm 20$ percent at 5 to 7 min postexercise (both NS vs baseline). Wall thickness change increased from $0.47 \pm 0.20$ cm at baseline to $0.77 \pm 0.23$ cm at 0 to 2 min postexercise ($p < 0.001$ vs baseline) then decreased to $0.60 \pm 0.25$ cm at 2 to 4 min and $0.49 \pm 0.18$ cm at 5 to 7 min postexercise (both NS vs baseline).

Regional comparisons were made by combining the data over all four times, again, because of the nonsignificant interaction effects. Systolic wall thickness change was significantly lower in the basal anterior septum (long axis) and in the mid anterior septum (short axis) compared with the basal posterior (long axis) or the mid inferior lateral (short axis) regions ($p < 0.001$). The percentage of systolic wall thickening was also significantly lower in the basal anterior septum (long axis) and in the mid anterior septum (short axis) compared with the basal posterior (long axis) ($p < 0.001$) or the mid inferior lateral (short axis) regions ($p < 0.01$).

Interobserver variability in wall thickness measurement was 8 percent and intraobserver variability was 9 percent.

**Discussion**

The major finding of this study was that maximal systolic wall thickening occurred within 2 min after exercise, then returned to baseline, corresponding to changes in hemodynamics.

**Temporal Variability in Thickening**

Exercise two-dimensional echocardiography is used to identify wall motion abnormalities that develop during ischemia in patients with coronary artery

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**Figure 1.** End-systolic parasternal long-axis (upper panel) and short-axis (lower panel) views of the left ventricle at baseline, 0 to 2, 2 to 4, and 5 to 7 min after peak exercise. The regions used for measurements are identified at baseline. In the parasternal long-axis view, wall thickness was measured in the basal anterior septal and mid infero septal regions and also in the basal posterior and mid-inferior lateral regions. In the parasternal short-axis view, wall thickness was measured in (starting at 12 o'clock position, then clockwise) mid-anterior septal, mid-anterior, mid-lateral, mid-inferior lateral, mid-inferior, and mid-septal regions.
disease. When myocardial perfusion is inadequate during the increased oxygen consumption associated with exercise, wall motion is reduced.\(^1\,\!{}^3\,\!{}^11\,\!{}^17\) In contrast, normal myocardium, after exercise, is hyperkinetic, with increased wall thickening, decreased systolic cavity size, and essentially normal diastolic dimensions.\(^5\) However, there are few studies on the time course of normal systolic function after exercise.

In an M-mode echocardiographic study of normal subjects, Berberich et al\(^18\) demonstrated a trend toward baseline function by 3 min after exercise; by 4 to 5 minutes, function had returned to baseline. In their study, cavity dimensions, not wall thicknesses, were measured.

In our study, the return of systolic wall thickening to baseline occurred with the return of hemodynamics toward normal. This reflects the influence of circulating catecholamines on both contractility (specifically, wall thickening) and heart rate.\(^19\) Since systolic wall thickening returned to baseline at 2 to 4 min after exercise, our study provides objective data in support of the recommendations of other authors that imaging should be completed within 2 min of peak exercise\(^13\,\!{}^16\,\!{}^20\) in order to assess maximal wall thickening.

**Regional Heterogeneity of Wall Thickening**

Our findings of regional variability in wall thickening at baseline are similar to previous studies using M-mode echocardiography. Corya et al\(^19\) demonstrated that the normal septum thickened by 36±12 percent (range, 14 to 57 percent) compared with 47±16 percent (range, 21 to 92 percent) in the normal posterior wall. A similar difference was also suggested in a study by Mason et al\(^21\) of normal subjects at rest and after exercise. Septal thickening increased from 56±3 (SEM) percent to 77±7 percent and posterior wall thickening increased from 89±9 percent to 115±8 percent with exercise. While these studies suggested a trend toward increased thickening in the posterior wall compared with the septum at rest, as well as with exercise, the statistical significance of the differences was not tested.

Similar to the M-mode study by Corya et al,\(^19\) we calculated wall thickness change in addition to percentage wall thickening. Thickness change is useful since it may be readily applied to computer-based analysis systems of two-dimensional echocardiograms that have calibrated reference bars for the measurement of relative changes in endocardial motion.\(^5\) In the study by Corya et al, wall thickness change was 3±1.2 mm (range, 1 to 5 mm) in the septum and 5±1.88 mm (range, 3 to 11 mm) in the posterior wall. These measurements, obtained at rest, are similar to our results.

The mechanism for the regional heterogeneity in systolic function between the septum and posterior wall is uncertain. Possible explanations include regional variation in the response to loading conditions\(^22\) or increased longitudinal shortening of the left ventricular free wall compared with the ventricular sep-
These differences in regional loading conditions and longitudinal shortening probably explain the regional variation in recovery of normal function after exercise.

Quantitative Two-Dimensional Echocardiography

While there are few data on intraobserver variability in wall thickness measurements, the 8 percent interobserver variability was similar to the 6 to 8 percent reported by others.22,24 These previous studies, however, used area-based methods for wall thickness measurements, tracing the endocardial and epicardial borders, and measuring myocardial area at end-diastole and end-systole.22,24 We used a linear method, since acoustic shadowing from ribs and lung at peak exercise prevented the visualization of the entire endocardial circumference. While an area method may be more robust than a linear method because of spatial averaging, we averaged multiple linear dimensions. Such clinically useful linear measurements of wall thickness obtained from two-dimensional echocardiograms are similar to those obtained with M-mode echocardiography.25

Limitations

In our study, we were not able to quantitatively analyze wall motion because of the inability to visualize and trace the entire endocardium. The medial and lateral segments of the endocardium were not visible 0 to 2 min postexercise; thus, the center of the short-axis cavity area could not be determined for wall motion analysis. The relationship of wall thickening to wall motion in recovery may be feasible with pharmacologic stress when respiratory artifact is minimized and the entire endocardium is demonstrated.

There may be age-related differences in the time course of wall thickening after exercise; thus, our results may not apply to an older population. In our study, we selected young patients because of their lower prevalence of coronary artery disease.29 Since only normal subjects were exercised, we were not able to compare the time course of normal vs abnormal myocardial wall thickening. Such a study would be worthwhile in order to assess the influence of recovery time on return of wall thickening to normal in patients with coronary artery disease.

Conclusion

Maximum wall thickening occurs within 2 min of peak exercise, then returns to baseline. Accurate identification of hyperkINETIC, normal myocardium with exercise echocardiography requires immediate, postexercise imaging.

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