Myocardial Metabolic, Hemodynamic, and Electrocardiographic Significance of Reversible Thallium-201 Abnormalities in Hypertrophic Cardiomyopathy

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Background. Exercise-induced abnormalities during thallium-201 scintigraphy that normalize at rest frequently occur in patients with hypertrophic cardiomyopathy. However, it is not known whether these abnormalities are indicative of myocardial ischemia.

Methods and Results. Fifty patients with hypertrophic cardiomyopathy underwent exercise 201Tl scintigraphy and, during the same week, measurement of myocardial lactate metabolism and hemodynamics during pacing stress. Thirty-seven patients (74%) had one or more 201Tl abnormalities that completely normalized after 3 hours of rest; 26 had regional myocardial 201Tl defects, and 26 had apparent left ventricular cavity dilatation with exercise, with 15 having coexistence of these abnormal findings. Of the 37 patients with reversible 201Tl abnormalities, 27 (73%) had metabolic evidence of myocardial ischemia during rapid atrial pacing (myocardial lactate extraction of 0 mmol/l or less) compared with four of 13 patients (31%) with normal 201Tl scans (p<0.01). Eleven patients had apparent cavity dilatation as their only 201Tl abnormality; their mean postpacing left ventricular end-diastolic pressure was significantly higher than that of the 13 patients with normal 201Tl studies (33±5 versus 21±10 mm Hg, p<0.001). There was no correlation between the angiographic presence of systolic septal or epicardial coronary arterial compression and the presence or distribution of 201Tl abnormalities. Patients with ischemic ST segment responses to exercise had an 80% prevalence rate of reversible 201Tl abnormalities and a 70% prevalence rate of pacing-induced ischemia. However, 69% of patients with nonischemic ST segment responses had reversible 201Tl abnormalities, and 55% had pacing-induced ischemia.

Conclusions. Reversible 201Tl abnormalities during exercise stress are markers of myocardial ischemia in hypertrophic cardiomyopathy and most likely identify relatively underperfused myocardium. In contrast, ST segment changes with exercise and systolic compression of coronary arteries on angiography are unreliable markers of inducible myocardial ischemia in hypertrophic cardiomyopathy. Apparent cavity dilatation during 201Tl scintigraphy may indicate ischemia-related changes in left ventricular filling, with elevation in diastolic pressures and endocardial compression. (Circulation 1991;83:1660–1667)

Myocardial defects during exercise thallium-201 scintigraphy frequently develop in patients with hypertrophic cardiomyopathy.1–5 Both fixed and reversible 201Tl abnormalities have been described using single-photon emission computed tomography in symptomatic and asymptomatic patients6 and are often improved or eliminated by treatment with verapamil.6 In the larger experience of 201Tl imaging in patients with coronary artery disease, reversible 201Tl abnormalities identify regions of relative myocardial hypoperfusion during stress as a consequence of obstructive atherosclerotic disease of epicardial coronary arteries,7–9 compatible with regional myocardial ischemia. However, the mechanism and significance of 201Tl abnormalities in patients with hypertrophic cardiomyopathy despite

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angiographically normal coronary arteries are unclear. Nonischemic pathophysiological features of hypertrophic cardiomyopathy, such as fibrosis, regional inhomogeneity of early diastolic relaxation, abnormal myocellular architecture, or altered cellular kinetics for thallium, could account for $^{201}$TI abnormalities. Furthermore, reversible $^{201}$TI abnormalities have been detected as frequently in asymptomatic as in symptomatic patients. Thus, the present study was conducted to investigate the relation of reversible $^{201}$TI abnormalities during exercise in patients with hypertrophic cardiomyopathy to invasive studies of coronary flow, hemodynamics, and myocardial metabolism.

**Methods**

We studied 50 patients with hypertrophic cardiomyopathy, defined as the echocardiographic demonstration of a hypertrophied, nondilated left ventricle in the absence of another cardiac or systemic disease that could produce left ventricular hypertrophy. There were 35 men and 15 women (age range, 18–64 years; average age, 43 years). Forty patients were significantly symptomatic with chest pain and dyspnea (New York Heart Association functional class III or IV) and catheterized for consideration of surgical relief of left ventricular outflow obstruction. Ten patients were entirely asymptomatic for chest pain and dyspnea and were catheterized for electrophysiological study because of a history of syncope or cardiac arrest. Catheterization and exercise $^{201}$TI studies were performed during the same hospitalization in all patients at least 2 days or five drug half-lives after discontinuation of cardiac medications. This represents a consecutive series of patients who underwent combined catheterization and $^{201}$TI studies performed free from cardiac medication. These studies were approved by the National Heart, Lung, and Blood Institute review board, and informed consent was obtained from all patients.

**Catheterization Study**

Full details of our catheterization study protocol, including on-line measurement of great cardiac vein flow and analysis of great cardiac vein and arterial blood samples for lactate content, have been reported previously. Forty-five patients underwent coronary angiography; all had normal epicardial coronary arteries. The presence of systolic septal and epicardial arterial compression was noted during coronary angiography. Five patients who underwent electrophysiological study, were asymptomatic for chest pain and dyspnea, and were less than 35 years old did not undergo coronary angiography. Left ventricular pressure was obtained by a 7F end-hole pigtail catheter referenced to the sidearm of an 8F vascular sheath apparatus in the right femoral artery, with care taken to avoid entrapment artifact. A thermomodulation flow catheter (Elecath, Rahway, N.J.) was positioned by fluoroscopic guidance in the great cardiac vein via the right internal jugular vein. The relative advantages and disadvantages of using thermomodulation measurement of great cardiac vein flow for estimating coronary flow in the anterior left ventricle and septum have been discussed by us previously. Approximately 20 minutes after angiography, duplicate measurements of great cardiac vein flow and blood pressure were recorded as well as cardiac output and pulmonary arterial wedge and left ventricular end-diastolic pressures. Blood samples were obtained from the femoral artery and great cardiac vein. Myocardial lactate extraction indicated the difference between arterial and great cardiac vein lactate contents. After completion of basal measurements, atrial pacing was performed via the thermomodulation catheter for 2–3-minute intervals at paced heart rates of 100, 130, and 150 beats/min, with 1–2 minutes between each interval. Great cardiac vein flows, systemic blood pressure, and postspacing left ventricular end-diastolic pressures were measured at each paced heart rate. Blood samples for lactate content were obtained at a paced heart rate of 150 beats/min. In 30 patients, repeat measurements were performed during isoproterenol infusion, titrated to achieve a heart rate of approximately 130 beats/min. The hemodynamic, metabolic, and coronary flow determinations in 19 patients in this series have been reported previously.

$^{201}$TI Emission Computed Tomography

Graded treadmill exercise was performed according to the National Institutes of Health combined protocol (19 patients) or standard Bruce protocol (31 patients). Heart rate, rhythm, and systemic blood pressure by arm cuff were monitored during exercise, including recording of the 12-lead electrocardiogram at 1-minute intervals throughout exercise. Ischemic ST segment responses were interpreted as more than 1 mm horizontal or downsloping depression if isoelectric at baseline or as more than 2 mm horizontal or downsloping depression from baseline if baseline ST segment depression was present. In all studies, exercise was symptom limited. At peak exercise, patients received 2.0–3.5 mCi i.v. $^{201}$TI. Exercise was continued for an additional 60 seconds to allow adequate circulation of the isotope. Imaging was begun within 10 minutes of the completion of exercise and repeated after a 3–4-hour delay. $^{201}$TI emission computed tomographic studies were performed with a wide field of view, rotating gamma camera equipped with a low-energy, medium-resolution, high-sensitivity, parallel-hole collimator (Apex 415, APC-3 Elscint, Boston, Mass.) centered on the 68-kev photopeak with a 20% window. The camera was rotated over 180° in an elliptical orbit around the patient’s anterior thorax from the right anterior oblique (−40°) to the left posterior oblique (+140°) position. Thirty images were obtained in a 64×64 matrix for 30 seconds, each at 6° intervals. Details of count acquisition and analyses have been described previously. The tomographic images were graded by at least two independent observers who were
unaware of the catheterization data using a semi-quantitative regional scoring system. Regional thallium uptake was graded on a scale of from 0 to 2.0, in 0.5 increments, with a score of 2 signifying normal activity and a score of 0 signifying absent activity. Scores for each segment were averaged; a score of 1.5 or less was considered to represent a perfusion defect, and a change of 0.5 or more from the exercise to the redistribution study was considered a significant change in perfusion. A counts-based quantitative analysis based on absolute thallium activity was not performed because the marked regional heterogeneity of wall thickness in hypertrophic cardiomyopathy would accentuate partial volume effects in a region-to-region comparison within one tomographic plane. Exercise-induced cavity dilatation and increased lung uptake were also assessed qualitatively and determined to be absent, mild, or marked by consensus among the observers. The 201Tl scintigraphic results of 19 patients in this series have been reported previously.5,6

Radionuclide Ventriculography

Radionuclide ventriculography was performed in 45 patients at rest in the supine position after in vivo labeling of red blood cells with 2 mCi technetium-99m. Eight patients underwent repeat study after symptom-limited treadmill exercise testing to determine changes in postexercise ventricular volume compared with baseline rest study. Scintigraphic data were acquired in the modified left anterior oblique position, which allowed optimal visual separation of the left and right ventricles. Peak left ventricular filling rates were determined by fitting third-order polynomial functions to the rapid diastolic filling portion of the high temporal resolution time-activity curve by a least-squares technique. Peak filling rate, time to peak filling rate, and ejection fraction were computed as previously described.17

Statistical Analysis

All data are reported as mean±1 SD. Continuous variables were compared by the two-tailed, unpaired t test. Group comparisons were performed by the χ² test, correcting for small sample sizes when necessary by Fisher’s exact test.

Results

201Tl Scintigraphy

Thirty-seven of the 50 patients (74%) with hypertrophic cardiomyopathy demonstrated myocardial 201Tl abnormalities during exercise that completely normalized after 3 hours of rest (Figure 1). Twenty-six patients had reversible regional myocardial 201Tl perfusion defects, most often in the anterior septum and the anterolateral and postero-inferior free walls of the left ventricle (Table 1); 22 patients had defects in more than one region. Twenty-six patients had apparent left ventricular cavity dilatation during exercise; 15 were associated with reversible regional myocardial 201Tl defects. Sixteen patients had increased lung uptake of 201Tl during exercise, all of whom had apparent left ventricular cavity dilatation (n=14) and/or regional myocardial 201Tl defects (n=13). Of the 15 patients with both regional myocardial 201Tl defects and apparent left ventricular cavity dilatation, 11 (73%) had increased lung uptake of 201Tl.

Comparison of 201Tl and Catheterization Results

The 37 patients with reversible 201Tl abnormalities (regional myocardial defects and/or apparent cavity dilatation) had similar peak left ventricular outflow gradients, peak great cardiac vein flows during pacing, and increases in great cardiac vein flow from baseline at catheterization compared with the 13 patients with normal 201Tl scans (Table 2). However, the 37 patients with reversible 201Tl abnormalities had a higher prevalence of myocardial lactate extraction of 0 mmol/l or less during rapid atrial pacing (27 patients, 73%), metabolic evidence of myocardial ischemia, compared with four of 13 patients (31%) with normal scans (p<0.01) (Figure 1). All cases of lactate extraction of 0 mmol/l or less during pacing represented a decline from net positive lactate extraction before pacing. The 37 patients with any reversible 201Tl abnormality had higher mean left ventricular end-diastolic filling pressure after pacing than those without reversible perfusion abnormalities (31±7 versus 21±10 mm Hg, p<0.001).

The 26 patients with reversible regional myocardial 201Tl defects, 15 of whom also had apparent cavity

| TABLE 1. Location of Reversible Myocardial Thallium-201 Defects |
|--------------------------------|---|
| Location                      | Defects (n) |
| Anterior septum               | 17          |
| Anterolateral free wall       | 11          |
| Postero-inferior free wall    | 12          |
| Apex                          | 5           |
| Posterior septum              | 4           |
TABLE 2. Exercise Thallium-201 and Pacing Study Results

<table>
<thead>
<tr>
<th>Any reversible T201 abnormality</th>
<th>Present (n=37)</th>
<th>Absent (n=13)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal left ventricular gradient (mm Hg)</td>
<td>49±46</td>
<td>32±41</td>
<td></td>
</tr>
<tr>
<td>Basal LVEDP (mm Hg)</td>
<td>19±7</td>
<td>17±7</td>
<td></td>
</tr>
<tr>
<td>Peak left ventricular gradient (mm Hg)</td>
<td>108±48</td>
<td>85±48</td>
<td></td>
</tr>
<tr>
<td>Pacing lactate extraction of 0 mmol/l or less</td>
<td>27/37 (73%)</td>
<td>4/13 (31%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pacing increase in GCV flow (ml/min)</td>
<td>50±27</td>
<td>62±39</td>
<td></td>
</tr>
<tr>
<td>Pacing peak GCV flow (ml/min)</td>
<td>139±38</td>
<td>141±45</td>
<td></td>
</tr>
<tr>
<td>Postpacing LVEDP (mm Hg)</td>
<td>31±7</td>
<td>21±10</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LVEDP, left ventricular end-diastolic pressure; GCV, great cardiac vein.

dilation, were similar in all hemodynamic and metabolic parameters to the 24 patients without such defects (Table 3). However, the 21 patients with anteroseptal and/or anterior free wall T201 defects had a smaller mean increase in great cardiac vein (drainage for anteroseptal regions) flow from baseline (43±31 ml/min) and a lower mean peak great cardiac vein flow (130±42 ml/min) during pacing than those without this reversible defect (59±29 and 146±36 ml/min, respectively), although these differences did not achieve statistical significance. Furthermore, 16 of these 21 patients (76%) had metabolic evidence of myocardial ischemia as measured in great cardiac vein blood draining from these regions. Eleven patients had reversible regional myocardial T201 defects without associated apparent left ventricular cavity dilatation. Six of eight patients (75%) with anteroseptal and/or anterior free wall regional T201 defects alone had metabolic evidence of myocardial ischemia measured in great cardiac vein blood during pacing. In contrast, none of three patients with posteroinferior free wall or posteroseptal defects had evidence of myocardial ischemia during pacing by assessment of great cardiac vein blood (Figure 2).

For the 26 patients with apparent left ventricular cavity dilatation during exercise, of whom 15 also had regional T201 defects, mean basal left ventricular outflow gradient (61±48 versus 27±35 mm Hg, p<0.001) and basal (20±7 versus 16±6 mm Hg, p<0.05) and postpacing left ventricular end-diastolic pressures (32±5 versus 24±10 mm Hg, p<0.001) were significantly higher than those of the 24 patients without this finding (Table 4). Furthermore, the prevalence of metabolic evidence of myocardial ischemia during pacing was greater in the 26 patients with apparent cavity dilatation (21 of 26 versus 10 of 24 patients, p<0.02). Eleven patients had apparent cavity dilatation during exercise without associated regional T201 defects (Table 2). Nine of these 11 patients (82%) had metabolic evidence of myocardial ischemia during pacing (Figure 2) compared with four of 13 (31%) with normal scans (p<0.04). Furthermore, their postpacing left ventricular end-diastolic pressures were significantly higher after pacing (33±5 versus 21±10 mm Hg, p<0.001).

Fifteen patients had both reversible regional myocardial T201 defects and apparent cavity dilatation. Of these 15, 12 (80%) had pacing-induced myocar-

TABLE 3. Exercise Thallium-201 and Pacing Study Results—Reversible Regional Myocardial Defects

<table>
<thead>
<tr>
<th>Regional myocardial T201 defects</th>
<th>Present (n=26)</th>
<th>Absent (n=24)</th>
<th>Regional myocardial T201 defects only</th>
<th>Present (n=11)</th>
<th>Absent (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal left ventricular outflow gradient</td>
<td>45±45</td>
<td>45±47</td>
<td>Basal T201 defects only</td>
<td>21±28</td>
<td>32±41</td>
</tr>
<tr>
<td>Basal LVEDP</td>
<td>19±7</td>
<td>17±6</td>
<td>16±7</td>
<td>17±7</td>
<td></td>
</tr>
<tr>
<td>Peak left ventricular outflow gradient</td>
<td>99±52</td>
<td>105±45</td>
<td>96±63</td>
<td>85±48</td>
<td></td>
</tr>
<tr>
<td>Pacing lactate extraction of 0 mmol/l or less</td>
<td>18/26 (69%)</td>
<td>13/24 (54%)</td>
<td>6/11 (55%)</td>
<td>4/13 (31%)</td>
<td></td>
</tr>
<tr>
<td>Pacing increase in GCV flow</td>
<td>49±31</td>
<td>57±30</td>
<td>57±29</td>
<td>62±39</td>
<td></td>
</tr>
<tr>
<td>Pacing peak GCV flow</td>
<td>137±40</td>
<td>142±37</td>
<td>138±47</td>
<td>141±45</td>
<td></td>
</tr>
<tr>
<td>Postpacing LVEDP</td>
<td>30±8</td>
<td>26±10</td>
<td>27±9</td>
<td>21±10</td>
<td></td>
</tr>
</tbody>
</table>

LVEDP, left ventricular end-diastolic pressure; GCV, great cardiac vein.

FIGURE 2. Flow diagram showing relative prevalence of pacing-induced ischemia as measured in great cardiac vein (GCV) blood related to specific reversible thallium-201 abnormalities noted after exercise.
dial ischemia (Figure 2). Furthermore, 11 of the 15 had increased lung uptake of $^{201}$TI with exercise compared with only two of 11 patients with regional $^{201}$TI defects alone ($p<0.02$), only three of 11 patients with apparent cavity dilatation alone ($p=0.054$), and no patients with a normal $^{201}$TI study ($p<0.001$).

**Symptom Status**

The majority of patients participating in the present study were significantly symptomatic (New York Heart Association functional class III or IV) with chest pain and dyspnea (40 patients, or 80%). However, seven of 10 asymptomatic patients had reversible $^{201}$TI defects, and four of these seven had evidence of myocardial ischemia during pacing stress. The three asymptomatic patients without exercise $^{201}$TI abnormalities during exercise had no transmural evidence of myocardial ischemia during pacing.

**Isoproterenol Infusion**

Among the 30 patients who were administered isoproterenol in the catheterization laboratory, titrated to achieve a heart rate response of approximately 130 beats/min, 23 (77%) had reversible $^{201}$TI abnormalities with exercise: nine had regional myocardial $^{201}$TI defects alone, seven had apparent left ventricular cavity dilatation alone, and seven had both. Of these 23 patients with reversible $^{201}$TI abnormalities, 15 (65%) had metabolic evidence of myocardial ischemia during isoproterenol infusion (Figure 3). Of the remaining seven patients with normal $^{201}$TI studies, four (57%) had evidence of ischemia during isoproterenol infusion. The left ventricular end-diastolic pressure during isoproterenol infusion was significantly higher in the 14 patients with apparent cavity dilatation during exercise $^{201}$TI study compared with the 16 patients without this perfusion abnormality ($23\pm10$ versus $14\pm12$ mm Hg, $p<0.05$).

**Radionuclide Ventriculography**

The 45 patients who underwent resting radionuclide angiographic study had a mean left ventricular ejection fraction of $72\pm13\%$, mean peak filling rate of $3.5\pm1.2$ end-diastolic vol/sec, and mean time to peak filling rate of $182\pm37$ msec. There were no group differences in these indexes of systolic and diastolic function between patients with and patients without reversible $^{201}$TI abnormalities during exercise, including all subgroups of $^{201}$TI abnormalities analyzed.

Eight patients underwent repeat study after treadmill exercise testing of the same duration as their $^{201}$TI study to determine changes in postexercise left ventricular end-diastolic volume compared with baseline study. The group mean ratio of end-diastolic postexercise count to preexercise count was $1.05\pm0.10$. The six patients with apparent left ventricular cavity dilatation noted on short-axis tomographic $^{201}$TI images had a count ratio (1.08±0.08) similar to that of seven patients (two from the present series, plus five previously reported by our group) without this abnormality (1.05±0.12). Thus, left ventricular end-diastolic volume changes compared with initial rest study were minimal and not responsible for the postexercise apparent cavity dilatation noted in the subgroup analyzed.

**Exercise Electrocardiographic Results**

All 50 patients had evidence of left ventricular hypertrophy on resting electrocardiograms. Only 20 patients (40%) developed ischemic-appearing ST segment depression at end exercise; 16 patients (80%) had associated reversible $^{201}$TI abnormalities, and 14 (70%) had metabolic evidence of myocardial ischemia during pacing. One patient who had both a

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**TABLE 4. Exercise Thallium-201 and Pacing Study Results—Apparent Cavity Dilatation**

<table>
<thead>
<tr>
<th></th>
<th>Apparent cavity dilatation</th>
<th>Apparent cavity dilatation only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Basal left ventricular outflow gradient</td>
<td>61 ± 48</td>
<td>27 ± 55</td>
</tr>
<tr>
<td>Basal LVEDP</td>
<td>20 ± 7</td>
<td>16 ± 6</td>
</tr>
<tr>
<td>Peak left ventricular outflow gradient</td>
<td>114 ± 35</td>
<td>89 ± 54</td>
</tr>
<tr>
<td>Pacing lactate extraction of 0 mmol/l or less</td>
<td>21/26 (81%)</td>
<td>10/24 (42%)</td>
</tr>
<tr>
<td>Pacing increase in GCV flow</td>
<td>46 ± 25</td>
<td>60 ± 34</td>
</tr>
<tr>
<td>Pacing peak GCV flow</td>
<td>139 ± 34</td>
<td>132 ± 52</td>
</tr>
<tr>
<td>Postpacing LVEDP</td>
<td>32 ± 5</td>
<td>24 ± 10</td>
</tr>
</tbody>
</table>

LVEDP, left ventricular end-diastolic pressure; GCV, great cardiac vein.
reversible 201TI abnormality (apparent cavity dilatation) and metabolic evidence of ischemia during pacing developed a right bundle branch block pattern during exercise. Although the remaining 29 patients did not manifest ischemic ST segment responses to exercise, 20 (69%) had reversible 201TI abnormalities during exercise, and 16 (55%) had metabolic evidence of myocardial ischemia during pacing.

Angiographic Data

Of the 45 patients in the present series who underwent coronary angiography, evidence of complete systolic compression of septal perforating arteries was noted in 26 patients, including 19 (73%) with reversible 201TI abnormalities and seven (54%) with normal 201TI scans. Fourteen of 19 patients (74%) without complete systolic septal artery compression also had reversible 201TI abnormalities. Of the 19 patients with complete systolic septal arterial compression and abnormal 201TI scans, reversible anteroseptal 201TI defects were noted in eight (42%). Reversible anteroseptal 201TI defects were also seen in five of 19 patients (26%) without systolic compression of septal arteries. Eighteen of the 26 patients (69%) with septal arterial compression had pacing-induced myocardial ischemia, as did 10 of 19 patients (53%) without septal arterial compression. Only four patients had complete systolic compression of epicardial coronary arteries (three mid–left anterior descending coronary and one obtuse marginal); two of these four patients had reversible anterolateral wall 201TI defects.

Discussion

Our previous studies have shown that patients with hypertrophic cardiomyopathy frequently have reversible abnormalities during exercise 201TI scintigraphy using tomographic techniques.2,6 Furthermore, regional myocardial 201TI defects were unrelated to the distribution or severity of left ventricular hypertrophy.5 However, the relation of these findings to metabolic evidence of inducible myocardial ischemia and to coronary angiographic findings as well as the hemodynamic significance of apparent left ventricular cavity dilatation were not investigated. The current comparison of 201TI data to catheterization-based studies of myocardial metabolism during stress indicates that exercise 201TI scintigraphy is useful in identifying patients with either pacing-induced (73% prevalence) or isoproterenol-induced (65% prevalence) myocardial ischemia. Three fourths of patients with reversible regional myocardial 201TI defects in areas drained by the great cardiac vein had evidence of myocardial ischemia during pacing stress compared with one fourth of the patients with posteroinferior defects alone or normal scans. More than 80% of patients with apparent cavity dilatation alone had myocardial ischemia during pacing stress. The apparent absence of inducible ischemia in some patients with reversible 201TI abnormalities may reflect the strict criteria for myocardial ischemia used in the present study (i.e., lactate extraction of 0 mmol/l or less).

Studies in patients with coronary artery disease have shown that a decrease in lactate extraction but with net positive extraction may also indicate ischemia, representing an admixture of venous blood from the ischemic subendocardium and the more normally metabolic outer walls of the heart during stress.20 In addition, great cardiac vein sampling might have missed venous drainage from other regionally ischemic areas. Conversely, approximately one third of patients without reversible 201TI defects had metabolic evidence of ischemia during pacing stress, and one half had evidence during isoproterenol stress.

A common reversible 201TI abnormality in our series was apparent cavity dilatation (26 of 50 patients) during exercise. This tomographic abnormality occurred in the absence of any significant change in left ventricular cavity size by radionuclide angiography in the subset in whom this determination was made, suggesting that this abnormality represents subendocardial hypoperfusion. In the present study, we found that patients with apparent cavity dilatation on 201TI scintigraphy had higher left ventricular end-diastolic pressures after pacing than those without this thallium defect. The significant finding of higher postpacing end-diastolic pressures in patients with apparent cavity dilatation may reflect elevations in left ventricular filling pressures as a consequence of ischemia and/or impaired myocardial relaxation and aggravation of pressure–volume relations during stress. Furthermore, compressive effects of elevated filling pressures could worsen subendocardial perfusion, contributing directly to myocardial ischemia. The association of elevated left ventricular filling pressures and apparent cavity dilatation is strengthened by the observation that 14 of 16 patients with increased lung uptake of thallium during exercise had this finding.

There were no significant differences in peak great cardiac vein flow for patients with regional myocardial defects and/or cavity dilatation on 201TI scanning and those without such abnormalities, indicating a large variation in peak great cardiac vein flow and an increase in great cardiac vein flow at which myocardial ischemia may occur. This is not surprising in view of numerous pathophysiological features of hypertrophic cardiomyopathy that might contribute to myocardial ischemia.11,13 There was a trend, however, toward less of an increase in coronary flow and lower peak flows during pacing in those with anteroseptal 201TI defects (regions drained by the great cardiac vein).

The prevalence rates of inducible ischemia during pacing stress were similar for patients with reversible 201TI abnormalities (73%) and patients with ischemic ST segment responses to treadmill exercise (70%). Patients with normal 201TI studies had somewhat lower prevalence rates of pacing-induced ischemia (31%) compared with patients with nonischemic ST segment responses to exercise (55%). The concordance of a reversible 201TI defect and an ischemic ST segment response to exercise
minimally increased the sensitivity of identifying patients with pacing-induced ischemia to 75% (12 of 16 patients). However, a concordance of negative studies was associated with only a 22% prevalence (two of nine patients, p < 0.02) of pacing-induced ischemia.

Reversible 201TI abnormalities were similarly prevalent in patients with (19 of 26, 73%) and patients without (14 of 19, 74%) complete systolic compression of septal perforating arteries. Furthermore, the prevalence rates of ischemia during pacing were similar in those with (18 of 26, 69%) and those without (10 of 19, 53%) septal arterial compression. Two of four patients with epicardial coronary arterial compression had reversible regional 201TI defects; the vast majority of patients with reversible regional 201TI defects had no epicardial arterial compression. These observations suggest that septal and epicardial coronary arterial compressions may not be important mechanisms of ischemia in hypertrophic cardiomyopathy, although the angiographic distribution and severity of systolic compression of these arteries during exercise stress are unknown.

In the present study and previous studies from our laboratory, the incidence of reversible 201TI abnormalities was higher than that in the smaller series of Rubin et al. — perhaps because the tomographic technique used in our study allowed for identification of smaller perfusion defects and of apparent left ventricular cavity dilatation in contrast to the planar thallium imaging used in other studies. Our prevalence rates of 201TI defects are more consistent with those from the study by Pitcher et al., particularly that of their symptomatic subgroup with chest pain, although metabolic, hemodynamic, and coronary flow studies were not performed in their study population. To our knowledge, the study of Hanrath et al. is the only other study that measured lactate metabolism via great cardiac vein sampling during atrial pacing during the same week as exercise 201TI scanning. In that smaller series of patients, 10 of 14 patients produced lactate; of these 10 patients, three had both fixed and reversible perfusion defects, and two had only fixed defects. The higher incidence of reversible 201TI defects in our study may relate to our tomographic imaging technique, as noted previously.

The analysis of regional thallium activity based on only a visual scoring of the tomographic images is a potential limitation of the present study. More quantitative methods to assess regional thallium activity as well as regional coronary blood flow and blood flow in general would be preferable. However, although such objective analyses have been applied to regional thallium activity in normal subjects and patients with coronary arterial disease, there are limitations to such quantitative analyses in patients with hypertrophic cardiomyopathy. Partial volume effects, related to physical imaging characteristics in the acquisition of tomographic images when the ventricular walls vary in thickness in the same patient, may result in reduced counts in thinner myocardial segments compared with more hypertrophied segments, even if absolute flow to both regions per gram of tissue was identical. Despite visual assessment of the thallium data, there was a significant concordance between the presence or absence of reversible defects and metabolic evidence of myocardial ischemia during pacing stress.

Many patients in our series with normal thallium studies had metabolic evidence of ischemia with pacing or isoproterenol. This suggests that either small regions of myocardial ischemia are not detected by thallium scintigraphy, despite tomographic methods, or exercise provokes different myocardial supply–demand imbalances than those provoked by pacing or isoproterenol. Nonetheless, the high concordance in the present study of reversible 201TI defects during exercise with the ability to induce ischemia by either pacing stress or isoproterenol stress indicates that exercise tomographic 201TI imaging exercise is a useful technique for the identification of inducible ischemia in symptomatic patients with hypertrophic cardiomyopathy. Because both reversible and fixed 201TI abnormalities may also develop in asymptomatic patients, it is apparent that not all ischemia in hypertrophic cardiomyopathy is symptomatically appreciated by the patient. In the present study, seven of 10 asymptomatic patients had reversible 201TI abnormalities during exercise, and four had metabolic evidence of myocardial ischemia during pacing stress. Thus, the association of exercise-induced 201TI abnormalities with metabolic evidence of stress-induced ischemia suggests that the common finding of reversible 201TI abnormalities in asymptomatic patients represents a true form of silent ischemia in hypertrophic cardiomyopathy.

References


Key Words • thallium scintigraphy • myocardial ischemia • hypertrophic cardiomyopathy
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