Effect of Surgical Reduction of Left Ventricular Outflow Obstruction on Hemodynamics, Coronary Flow, and Myocardial Metabolism in Hypertrophic Cardiomyopathy

Richard O. Cannon, III, MD, Charles L. McIntosh, MD, William H. Schenke, BA, Barry J. Maron, MD, Robert O. Bonow, MD, and Stephen E. Epstein, MD

To assess the impact of operative reduction of left ventricular outflow obstruction in hypertrophic cardiomyopathy, measurements of great cardiac vein flow, oxygen and lactate content, left ventricular pressures, and cardiac index were measured at rest and during pacing stress in 20 consecutive patients (13, myotomy-myectomy; six, mitral valve replacement; one, both myotomy-myectomy and mitral valve replacement) who underwent both preoperative and postoperative studies. All had angiographically normal epicardial coronary arteries. Operation resulted in reduction in outflow gradient (64±38 to 4±7 mm Hg, p<0.001) and in left ventricular systolic pressure (186±32 to 128±22 mm Hg, p<0.001) and was associated with reduction in great cardiac vein flow (101±26 to 78±16 ml/min, p<0.001) and oxygen consumption in the anterior left ventricle and septum (11.9±4.1 to 8.4±1.9 ml O₂/min, p<0.001) in the basal state. During rapid atrial pacing, 13 of 20 patients experienced chest pain postoperatively, whereas all 20 developed chest pain during preoperative pacing, with an improvement in pacing anginal threshold (or heart rate 150 if no chest pain was experienced) of 16±18 beats/min (p<0.001). The peak great cardiac vein flow (161±41 to 131±45 ml/min, p<0.025) and myocardial oxygen consumption (19.4±6.1 to 14.3±5.5 ml O₂/min, p<0.005) during pacing, which correlated directly with the severity of the basal left ventricular gradient (p=0.011 and p=0.002, respectively), were also reduced by surgery. Lactate metabolism during pacing changed from net production before surgery to net consumption after operation (−17±47.6 to 4.4±29.8 μmol/min, p<0.01), with six of 20 patients producing lactate after surgery compared with 13 of 20 before surgery (p=0.06). The six patients with the highest peak great cardiac vein flow (>175 ml/min) during preoperative pacing had greater symptom and metabolic benefit during pacing after surgery compared with the 14 patients with lower peak coronary flow. Postpacing left ventricular end-diastolic pressure (30±7 to 23±7 mm Hg, p<0.001) and pulmonary artery wedge pressure (24±6 to 20±5, p<0.001) were reduced after surgery. Thus, operative relief of left ventricular outflow obstruction and reduction in left ventricular systolic pressure favorably affects myocardial oxygen consumption and metabolism, due to more advantageous matching of myocardial oxygen delivery to oxygen demands during stress. The particularly marked benefit in those patients with the highest peak flow capacity before surgery may be due to less intrinsic abnormality in coronary flow delivery, perhaps due to less small vessel coronary disease, thereby favoring restoration of a more normal coronary flow reserve after surgery. (Circulation 1989;79:766–775)

S

ince 1960, various operations have been performed in an attempt to relieve left ventricular outflow obstruction in patients with hypertrophic cardiomyopathy, primarily by either removing muscle from the cephalad portion of the septum or replacing the mitral valve leaflets with prosthetic valve.1–5 Several studies have documented relief of outflow gradient by surgical intervention and improvement in symptom status and effort tolerance after surgery.1–14 However, questions have been raised about the pathophysiologic significance of outflow gradients in hypertrophic
cardiomyopathy, thereby challenging the surgical approach to such gradients, even in patients refractory to medical management. The purpose of our study was to determine the effects of operative relief of outflow obstruction on hemodynamics, coronary blood flow, and myocardial metabolism in patients with this disease.

Methods

This study was performed in conjunction with our standard hemodynamic assessment of the effects of left ventricular septal myotomy-myectomy or mitral valve replacement in patients with hypertrophic cardiomyopathy. This report includes data from 20 consecutive patients severely limited by symptoms (New York Heart Association functional classes III and IV) despite attempts at medical therapy with β-blockers and calcium channel blockers, who had large left ventricular outflow gradients (>50 mm Hg under basal conditions or during isoproterenol infusion) such that they were considered suitable for myotomy-myectomy or mitral valve replacement (depending on septal anatomy as defined below) and underwent identical preoperative and postoperative studies. There were 15 men and five women ranging in age from 28 to 62 years (average age, 44) who were admitted to the Clinical Center of the National Institutes of Health for preoperative and postoperative studies (approximately 6 months after surgery) following complete physical examination, routine blood work, chest radiograph, and electrocardiograms. All cardiac medications were discontinued for at least five drug half-lives before performance of noninvasive and invasive studies. The study protocol described below was approved by the Institute Review Board of the National Heart, Lung, and Blood Institute, and informed consent was obtained from all patients.

Echocardiography

Two-dimensional and M-mode echocardiograms were performed with a mechanical sector scanner (Advanced Technology Laboratories Mark 500) with a 3-MHz transducer. In all patients, the diagnosis of hypertrophic cardiomyopathy was based on echocardiographic demonstration of a nondilated, hypertrophied left ventricle without associated systemic or cardiac disorders. Assessment of the magnitude of left ventricular hypertrophy was obtained primarily from the parasternal short-axis planes; however, the parasternal long-axis and apical views were also used to integrate the observations, as previously described. Myocardial hypertrophy was assessed after the left ventricle was divided into four segments (anterior and posterior ventricular septum and lateral and posterior ventricular free wall) in the parasternal short-axis plane. Previously described parameters of left ventricular hypertrophy were measured, including maximal septal thickness obtained from M-mode echocardiograms, maximal left ventricular wall thickness (usually the septum), magnitude of hypertrophy (mild, moderate, or severe), and left ventricular hypertrophy index (sum of all ventricular segment thicknesses) from two-dimensional echocardiograms.

Radionuclide Angiography

Radionuclide angiograms were performed at rest in the supine position with red blood cells labeled in vivo with 15–20 mCi 99mTc before and after surgery proximate to the time of the catheterization study. High temporal resolution left ventricular time-activity curves, representing relative changes in ventricular volume during the average cardiac cycle, were generated, and left ventricular ejection fraction calculated using techniques previously described. Peak left ventricular filling rate was then computed as previously described by fitting a third-degree polynomial function to the systolic ejection and rapid diastolic filling portions of the time-activity curve, using a least-squares technique. The time to peak filling rate was measured from end systole to the time of peak left ventricular filling rate.

Catheterization Study

After an overnight fast and diazepam 10 mg orally 1 hour before study, patients were taken to the catheterization laboratory, usually at 8:00 AM. A short 20-gauge Teflon catheter was placed in the left brachial artery. Introducers were placed in the right femoral vein and artery and right internal jugular vein for catheter access, followed by 5,000 units heparin i.v. A balloon-tipped thermodiode catheter was positioned in the pulmonary artery for measurement of pulmonary artery and pulmonary artery wedge pressure and cardiac output (average of at least three measurements). Systemic vascular resistance index was calculated as the mean systemic blood pressure divided by the cardiac output normalized for body surface area (cardiac index). A precalibrated end-hole pigtail catheter (Millar Instruments) was positioned with the distal sensor in the body of the left ventricle, and proximal sensor in the ascending aorta in 18 patients. Fluid-filled end-hole pigtail catheters were used in two patients. In all cases, catheters were positioned with attention to avoiding catheter entrapment. Left ventricular and left brachial arterial pressures were measured simultaneously in the basal state in all patients, and during Valsalva maneuver, amyl nitrite inhalation, and isoproterenol infusion in eight patients. The left ventricular gradient was localized to the left ventricular outflow tract during pull-back of the catheter from left ventricular apex to aorta in all cases. All patients subsequently underwent left ventriculography, using an angiographic pigtail catheter. During the preoperative study only, all patients underwent selective coronary arteriography, using multiple angled views. All patients had completely normal epicardial coronary arteries as assessed by at least one cardiologist during formal review of the cineangiograms, and the consensus of staff cardiologists at
a weekly conference. Systolic compression of septal perforating vessels was noted in 15 patients. No epicardial artery compression was noted. Left ventricular cineangiography was performed in both preoperative and postoperative studies in 17 patients with end-diastolic volumes calculated by the single-plane method of Sandler and Dodge.22 End-systolic volumes were not computed because of the marked deformity of the ventricle in systole, characteristic of hypertrophic cardiomyopathy.

A thermodilution catheter (EleCath Corp) was introduced into the coronary sinus via the right internal jugular vein and advanced into the great cardiac vein in all cases. Position of the catheter in the great cardiac vein was initially verified by small injections of contrast material and kept constant throughout the study by frequent inspection of the relation of the pacing electrodes to bony landmarks via fluoroscopy. The thermodilution technique for determining great cardiac vein flow using this catheter,23 and the relative merits and liabilities of this technique have been discussed by us previously.24,25 Measurement of great cardiac vein flow allows estimation of coronary flow and metabolism in that portion of the ventricle most hypertrophied in the majority of patients with hypertrophic cardiomyopathy (i.e., the anterior septum and free wall). Arterial and left ventricular pressures, and electrocardiographic leads I, aVr, and V5 were recorded with each great cardiac vein flow measurement. Coronary resistance was calculated as the mean systemic blood pressure divided by great cardiac vein flow. Lactate samples were obtained from the great cardiac vein, immediately transferred to tubes containing sodium fluoride and potassium oxalate for inhibition of glycolysis, and centrifuged at 4°C at 5,000 rpm for 5 minutes. The decanted serum was then processed for lactate content on a Dupont Automatic Clinical Analyzer by a modification of the technique of Marbach and Weil.26 Lactate consumption was calculated as great cardiac vein flow multiplied by the difference between the arterial and great cardiac vein lactate concentration. Oxygen content was measured with a Lex-O2-Con Oxygen Analyzer (Lexington Instruments). Myocardial oxygen consumption was calculated as great cardiac vein flow multiplied by the difference between arterial and great cardiac vein oxygen content.

Pacing Coronary Flow Study

At least 20 minutes after use of contrast dye, great cardiac vein flow, arterial and left ventricular end-diastolic and pulmonary artery wedge pressures were recorded, and blood samples obtained for lactate and oxygen content. Pacing via the thermodilution catheter in the great cardiac vein was then initiated at a heart rate of 100 beats/min and increased by increments of 10 beats/min at 1–2-minute intervals up to a heart rate of 150 beats/min. This pacing sequence was possible in 17 patients preoperatively but was terminated at lower heart rates in three patients because of severe chest pain. Preoperatively, five patients received atropine 0.5–1.0 mg intravenously to permit rapid atrial pacing without atrioventricular block. Measurements of great cardiac vein flow, arterial and left ventricular pressures, and blood for lactate and oxygen were made at each heart rate interval, up to 150 beats/min (or the highest achieved heart rate in three patients during the preoperative study: 120, 130, or 140 beats/min). Pacing was terminated after approximately 3 minutes at the highest paced heart rate, with measurement of postpacing left ventricular end-diastolic and pulmonary artery wedge pressures averaged over 10 seconds in 19 patients.

Eight patients with basal gradients less than or equal to 50 mm Hg (range, 0–50 mm Hg) underwent measurement of these same parameters during isoproterenol administration (range, 2–5 μg/min) to a heart rate of approximately 130 beats/min. The basal left ventricular outflow gradients in the remaining 12 patients were sufficiently high to preclude administration of isoproterenol.

All patients underwent identical study approximately 6 months after surgery, with six patients requiring atropine to permit rapid atrial pacing to heart rate 150, including four patients who received atropine during the preoperative study. The preoperative pacing data have previously been reported as part of a larger series of patients with hypertrophic cardiomyopathy in which comparison was made between patients with and patients without left ventricular outflow obstruction in the basal state.25

Operative Treatment

All patients were eligible for surgical relief of outflow obstruction because of left ventricular gradients more than 50 mm Hg in the basal state (12 patients) or during isoproterenol infusion (eight patients). Thirteen patients underwent septal myotomy and myectomy, six patients underwent mitral valve replacement because the anterior basal septum was not considered to be of sufficient thickness (>18 mm) to perform myotomy-myectomy, and one patient underwent mitral valve replacement 5 months after myotomy-myectomy because of both incomplete relief of outflow obstruction during provocation and persistent symptoms after the initial operation.

Statistics

All group data are reported as mean ± SD. Continuous variables were analyzed by the two-tailed Student's t test for paired or unpaired data, when appropriate. Regression analyses were performed when appropriate. Discrete variables were analyzed by the χ2 or Fisher's exact test. A p value less than 0.05 was considered significant.

Results

Change in Basal Hemodynamics and Coronary Flow

There were no group changes in heart rate (all patients remained in sinus rhythm), ejection frac-
TABLE 1. Basal Hemodynamics Before and After Surgical Relief of Left Ventricular Outflow Obstruction

<table>
<thead>
<tr>
<th></th>
<th>Before surgery</th>
<th>After surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>76±10</td>
<td>76±11</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>76±14</td>
<td>72±12</td>
</tr>
<tr>
<td>Peak LV filling rate (EDV/sec)</td>
<td>3.6±1.4</td>
<td>3.2±1.2</td>
</tr>
<tr>
<td>Time to peak filling rate (msec)</td>
<td>183±37</td>
<td>209±49</td>
</tr>
<tr>
<td>Mean blood pressure (mm Hg)</td>
<td>91±16</td>
<td>92±15</td>
</tr>
<tr>
<td>LV systolic pressure (mm Hg)</td>
<td>186±32</td>
<td>128±22*</td>
</tr>
<tr>
<td>LV outflow gradient (mm Hg)</td>
<td>64±38</td>
<td>4±7*</td>
</tr>
<tr>
<td>Cardiac index (l/min/m2)</td>
<td>3.0±0.4</td>
<td>3.0±0.6</td>
</tr>
<tr>
<td>Systemic vascular resistance index (mm Hg/min/m2/l)</td>
<td>31.4±26</td>
<td>31.9±7.0</td>
</tr>
<tr>
<td>GCV flow (ml/min)</td>
<td>101±26</td>
<td>78±16*</td>
</tr>
<tr>
<td>Coronary resistance (mm Hg .min/ml)</td>
<td>0.98±0.34</td>
<td>1.23±0.31*</td>
</tr>
<tr>
<td>(Arterial−GCV) O2 (ml O2/100 ml)</td>
<td>11.7±1.8</td>
<td>10.9±1.4</td>
</tr>
<tr>
<td>MVo2 (ml O2/min)</td>
<td>11.9±4.1</td>
<td>8.4±1.9*</td>
</tr>
<tr>
<td>Lactate consumption (μmol/min)</td>
<td>31.0±25.5</td>
<td>22.7±12.7</td>
</tr>
<tr>
<td>LV end-diastolic volume (ml)</td>
<td>93±38</td>
<td>83±22</td>
</tr>
<tr>
<td>LV end-diastolic pressure (mm Hg)</td>
<td>18±6</td>
<td>15±5</td>
</tr>
<tr>
<td>Pulmonary artery wedge pressure (mm Hg)</td>
<td>13±4</td>
<td>13±5</td>
</tr>
</tbody>
</table>

Values are mean±SD.
See “Methods” section for derivation of parameters.
LV, left ventricle; EDV, end-diastolic volume; GCV, great cardiac vein; MVo2, myocardial oxygen consumption in the GCV distribution.
* p<0.001; †p<0.005.

tion, peak left ventricular filling rate, time to peak filling rate, mean blood pressure, or cardiac index in the basal state as a result of surgery (Table 1). There was substantial reduction in the left ventricular outflow gradient in the majority of patients (64±38 to 4±7 mm Hg, p<0.001) associated with significant reduction in left ventricular systolic pressure (186±32 to 128±22 mm Hg, p<0.001). The left ventricular end-diastolic pressure was marginally reduced after surgery (18±6 to 15±5 mm Hg, p=0.08). The pulmonary artery wedge pressure was unchanged, in part due to mitral prosthetic valve gradients (9±4 mm Hg), in the seven patients who underwent mitral valve replacement.

Great cardiac vein flow (101±26 to 78±16 ml/min, p<0.001) and myocardial oxygen consumption (11.9±4.1 to 8.4±1.9 ml O2/min, p<0.001) were significantly lower and coronary resistance higher (0.98±0.34 to 1.23±0.31 mm Hg .min/ml, p<0.005) after operation. The magnitude of change after operation in great cardiac vein flow and myocardial oxygen consumption in the anterior left ventricle and septum correlated significantly with the magnitude of reduction in left ventricular outflow gradient (Figure 1). Myocardial oxygen extraction was marginally reduced after operation (11.7±1.8 to 10.9±1.4 ml O2/100 ml, p=0.08). Basal lactate consumption was not significantly altered by surgery.

Change in Pacing Hemodynamics

During rapid atrial pacing, 13 of 20 patients experienced chest pain postoperatively, compared to all 20 patients experiencing chest pain during pacing before surgery. The change in pacing-induced anginal threshold (or if no pain was experienced during the postoperative study, the change from preoperative pacing anginal threshold to heart rate 150) was 16±18 beats/min (p<0.001) with 13 of

![Figure 1. Plots of correlation of reduction of left ventricular outflow gradient by septal myotomy or mitral valve replacement with (upper panel) reduction in basal myocardial oxygen consumption (MVo2) in the anterior left ventricle and septum and (lower panel) reduction in basal great cardiac vein (GCV) flow.](http://circ.ahajournals.org/)
20 experiencing a 20-beat or greater improvement in pacing anginal threshold.

The peak great cardiac vein flow and myocardial oxygen consumption in the anterior left ventricle correlated with the severity of basal left ventricular outflow gradients (p = 0.011 and 0.002, respectively; Figure 2). Surgery resulted in a significant reduction in the peak great cardiac vein flow (161 ± 41 to 131 ± 45 ml/min, p < 0.025) and myocardial oxygen consumption (19.4 ± 6.1 to 14.3 ± 5.5 ml O₂/min, p < 0.005), which was measured at a significantly higher heart rate (128 ± 16 to 140 ± 13 beats/min, p < 0.01) and lower left ventricular systolic pressure (165 ± 26 to 123 ± 19 mm Hg, p < 0.001) compared with the preoperative study (Figure 3).

At the highest paced heart rate after operation (150 in all patients), the left ventricular outflow gradient (25 ± 26 to 2 ± 4 mm Hg, p < 0.001), mean systemic blood pressure (107 ± 16 to 97 ± 19 mm Hg, p < 0.025), great cardiac vein flow (140 ± 39 to 125 ± 47 ml/min, p < 0.001), and myocardial oxygen consumption in the anterior left ventricle and septum (16.6 ± 5.5 to 14.0 ± 5.8 ml O₂/min, p < 0.001) were significantly reduced compared to the preoperative study (Table 2). Myocardial oxygen extraction was marginally less during pacing after surgery compared with the preoperative study (12.0 ± 1.4 to 11.1 ± 1.3 ml O₂/100 ml, p = 0.08). Lactate consumption was significantly higher during the postoperative study with net lactate consumption (4.4 ± 29.8 μmol/min) compared with net lactate production prior to surgery (-17.1 ± 47.6 μmol/min, p < 0.01; Figure 4), with six of 20 patients producing myocardial lactate during pacing after surgery compared with 13 patients producing lactate before surgery (p = 0.06). Postspacing left ventricular end-diastolic pressure (30 ± 7 to 23 ± 7 mm Hg, p < 0.001) and pulmonary artery wedge pressure (24 ± 6 to 20 ± 5 mm Hg, p < 0.001) were also reduced postoperatively compared with preoperative measurements (Figure 5).

**Coronary Hemodynamics Predictive of Operative Benefit**

To assess whether preoperative flow responses to pacing might predict hemodynamic, metabolic, and symptom benefit, patients were divided into a group with high peak great cardiac vein flow responses during pacing (peak flow more than 175 ml/min) and a group with lower peak great cardiac vein flow responses to pacing stress (less than 175 ml/min). As indicated in Table 3, the six patients with the highest great cardiac vein flow during pacing stress also had greater basal left ventricular outflow gradients (95 ± 30 compared with 50 ± 32 mm Hg,}

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** Plots of correlation of basal left ventricular gradient and (upper panel) peak myocardial oxygen consumption (MV₂) in the anterior left ventricle and septum and (lower panel) peak great cardiac vein flow during pacing stress.

![Figure 3](http://circ.ahajournals.org/)

**Figure 3.** Plots of (left) left ventricular systolic pressure, (center) myocardial oxygen consumption in the anterior left ventricle, and (right) great cardiac vein (GCV) flow at that paced heart rate (128 ± 16 beats/min, preoperative study; 140 ± 13 beats/min, postoperative study) where GCV flow was maximal.
TABLE 2. Hemodynamics at Highest Paced Heart Rate Before and After Surgical Relief of Left Ventricular Outflow Obstruction

<table>
<thead>
<tr>
<th></th>
<th>Before surgery</th>
<th>After surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>147±8</td>
<td>150±0</td>
</tr>
<tr>
<td>Mean blood pressure (mm Hg)</td>
<td>107±16</td>
<td>97±19‡</td>
</tr>
<tr>
<td>LV outflow gradient (mm Hg)</td>
<td>25±26</td>
<td>2±4‡</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.7±0.5</td>
<td>2.5±0.7</td>
</tr>
<tr>
<td>Systemic vascular resistance index (mm Hg/min/m²/l)</td>
<td>41.8±9.2</td>
<td>39.7±12.2</td>
</tr>
<tr>
<td>GCV flow (ml/min)</td>
<td>140±39</td>
<td>125±47†</td>
</tr>
<tr>
<td>(Arterial–GCV) O₂ (ml O₂/100 ml)</td>
<td>12.0±1.4</td>
<td>11.1±1.3</td>
</tr>
<tr>
<td>MVO₂ (ml O₂/min)</td>
<td>16.6±5.5</td>
<td>14.0±5.8†</td>
</tr>
<tr>
<td>Lactate consumption (μmol/min)</td>
<td>-17.2±47.6</td>
<td>4.4±29.8‡</td>
</tr>
<tr>
<td>LV end-diastolic pressure (mm Hg)</td>
<td>30±7</td>
<td>23±7†</td>
</tr>
<tr>
<td>Pulmonary artery wedge pressure (mm Hg)</td>
<td>24±6</td>
<td>20±5†</td>
</tr>
</tbody>
</table>

LV, left ventricle; EDV, end-diastolic volume; GCV, great cardiac vein; MVO₂, myocardial oxygen consumption.

*p<0.01 and higher basal great cardiac vein flow (121±16 compared with 92±24 ml/min, p<0.02). During the stress of rapid atrial pacing (150 beats/min in most patients), the increase from basal to peak flow was greater in the six patients with a peak flow greater than 175 ml/min compared with the remaining 14 patients (95±25 compared with 46±28 ml/min, p<0.005). Despite a greater increase in flow from baseline and greater peak absolute flow, those six patients demonstrated a trend to more severe ischemia (−32.8±30.5 compared with −10.4±52.8 μmol/min, NS) with lactate production by five of six patients and no net lactate extraction (lactate consumption, 0 μmol/min) by the sixth patient. Eight of 14 patients with the lower peak flows during pacing demonstrated lactate production.

Operative reduction in outflow obstruction was evident in both groups, with a trend toward greater reduction in basal great cardiac vein flow in the six patients with the highest preoperative peak flow (34±17 compared with 18±17 ml/min change from preoperative to postoperative basal state, p=0.07), probably due to the greater reduction in outflow gradient in this group. During pacing in the postoperative study, these six patients had a greater reduction in peak flow compared with their preoperative pacing flows, in comparison to the remaining 14 patients (65±41 compared with 15±45 ml/min, p<0.05). Three of these six were free of chest pain during pacing after surgery (compared with none preoperatively) with at least a 10 beats/min improvement in pacing anginal threshold in all six patients.

Further, all six patients demonstrated marked improvement in metabolic evidence for ischemia, with conversion from lactate production to consumption in four, from marked lactate production to no net extraction in one, and from no net extraction to lactate consumption in one. In the other 14 patients, 10 continued to experience chest pain during pacing, and five of 14 showed no improvement in pacing anginal threshold compared with the preoperative pacing study. Further, the marked improvement in lactate metabolism noted in the six patients with the highest preoperative flow during pacing (−32.8±30.5 to 28.6±23.9 μmol/min, p<0.001) was not seen in the remaining 14 patients (−10.4±52.8 to −6.0±26.2 μmol/min, NS). In those 14 patients with lower peak flows, there was no relation between magnitude of gradient, absolute flow during pacing, or reduction in gradient by operation and change in pacing anginal threshold and lactate consumption.

Operative Results in Patients With Mitral Valve Replacement Versus Myotomy-Myectomy

Basal and pacing stress hemodynamic parameters of the six patients who underwent mitral valve replacement were compared with those of the 13 patients who underwent septal myotomy-myectomy. Data from the one patient who underwent mitral valve replacement after a previous myotomy-

FIGURE 4. Plot of lactate metabolism at highest paced heart rate before and after operative relief of outflow obstruction. Above dashed line indicates lactate consumption, below dashed line indicates lactate production.
myectomy was eliminated from this comparison. There was no significant difference between prosthetic mitral valve recipients and patients who underwent myotomy-myectomy with regard to the preoperative to postoperative change in basal gradient, systemic blood pressure, cardiac index, great cardiac vein flow, myocardial oxygen extraction and consumption, lactate consumption, and pulmonary wedge and left ventricular end-diastolic pressures.

Similarly, the preoperative to postoperative change in these parameters during pacing stress also did not differ between the two groups, with the exception that postspacing left ventricular end-diastolic pressure decreased more (16±8 compared with 5±6 mm Hg, p<0.01) in patients who underwent mitral valve replacement, and lactate metabolism tended to improve more in patients with myotomy-myectomy (increase in consumption by 35.2±25.3 compared with −2.7±56.2 μmol/min, p=0.06).

Preoperative Left Ventricular Morphology and Operative Results

The 20 patients had maximum septal and left ventricular free wall thickness ranging from 14 to 32 mm and maximum left ventricular index scores ranging from 44 to 100 mm. There was no correlation between echocardiographic assessment of left ventricular morphology and mass and basal or peak great cardiac vein flow and myocardial oxygen consumption or lactate during pacing in the preoperative study or change in these parameters after surgery.

Effect of Operation on Isoproterenol-Induced Hemodynamics

Eight (five patients with myotomy-myectomy, three patients with mitral valve replacement) of 20 patients received isoproterenol during the preoperative study (3.4±1.0 μg/min) and again after surgery (4.0±1.2 μg/min) to achieve a heart rate of 120–130 beats/min. The preoperative heart rate response to isoproterenol was 122±10 beats/min, with a mean blood pressure of 95±14 mm Hg and a left ventricular outflow gradient of 111±33 mm Hg. After surgery, isoproterenol infusion resulted in a heart rate of 125±11 but a lower mean blood pressure (80±18 mm Hg, p<0.05) and lower left ventricular outflow gradient (27±31 mm Hg, p<0.001) compared with the preoperative study. The cardiac index response to isoproterenol was unchanged by surgery (4.3±0.6 compared with 4.4±0.7 l/min/m² preoperatively). Before surgery, isoproterenol infusion precipitated chest pain in all eight patients; only four patients experienced chest pain during isoproterenol infusion postoperatively, a significant reduction in chest pain provocation (p=0.04). After surgery, great cardiac vein flow (155±44 to 145±37 ml/min) and myocardial oxygen extraction (11.2±1.2 to 10.5±1.5 ml O₂/min) were all minimally and not significantly reduced compared with preoperative measurements. Lactate production tended to be less severe (−12.3±55.4 to −1.3±45.1 μmol/min, NS), with two of eight patients producing lactate postoperatively compared with five of eight patients preoperatively. The left ventricular end-diastolic pressure during isoproterenol was significantly reduced after surgery (19±8 to 12±6 mm Hg, p<0.001). The reduction in pulmonary artery wedge pressure after surgery (26±9 to 16±9 mm Hg, p=0.10) did not reach statistical significance because of mitral valve gradients that developed during isoproterenol infusion in the three mitral valve prosthetic recipients (14±7 mm Hg).

Discussion

We have previously reported that symptomatic patients with basal left ventricular outflow gradients have higher great cardiac vein flow at rest and during pacing stress than symptomatic patients without obstruction. This observation suggested that patients with obstruction rapidly exhausted coronary flow reserve due to high basal and stress-induced flow requirements as a consequence of elevated left ventricular systolic pressures and myocardial oxygen requirements. In contrast, symptomatic patients without obstruction demonstrated myocardial ischemia at lower peak flows, suggesting greater impairment in coronary flow delivery.

The present study demonstrates that coronary flow and myocardial oxygen consumption under basal conditions and during pacing correlate directly with the severity of left ventricular outflow obstruction and that both decrease after surgical relief of outflow obstruction by myotomy-myectomy or mitral valve replacement. The magnitude of reduction in
Table 3. Comparison of Hemodynamic, Metabolic and Symptom Parameters Between Patients With High Preoperative Coronary Flows and Patients With Lower Flows During Pacing Stress

<table>
<thead>
<tr>
<th>Basal LV gradient</th>
<th>Basal GCV flow</th>
<th>Peak GCV flow</th>
<th>Pacing lactate</th>
<th>Chest pain</th>
<th>ΔAT pacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop</td>
<td>Postop</td>
<td>Preop</td>
<td>Postop</td>
<td>Preop</td>
<td>Postop</td>
</tr>
<tr>
<td>Peak flow &gt; 175 ml/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. 140 0 131 90 246 110 -23.3 44.4 Yes No 20
2. * 70 0 89 71 220 168 -14.2 67.2 Yes No 40
3. 75 0 121 96 215 129 -37.2 12.9 Yes Yes 20
4. 65 10 121 95 215 237 -33.6 23.7 Yes Yes 10
5. 100 0 135 70 203 133 -88.5 0 Yes Yes 20
6. 120 0 126 98 194 126 0 23.6 Yes No 20

95 ± 30 2 ± 4 121 ± 16 87 ± 13 216 ± 18 151 ± 46 -32.8 ± 30.5 28.6 ± 23.9

Peak flow < 175 ml/min

7. 0 0 83 84 167 178 49.2 34.2 Yes Yes 0
8. 85 0 75 44 163 61 -81.5 -17.4 Yes Yes 0
9. 100 10 120 98 160 214 0 19.4 Yes Yes 20
10. * 5 0 96 88 149 109 -12.8 0 Yes No 20
11. 30 20 72 70 145 144 -40.8 -14.4 Yes Yes 20
12. * 90 10 93 58 145 81 -48.5 -60.0 Yes Yes 0
13. * 30 0 112 82 143 129 14.3 12.4 Yes No 30
14. * 50 0 67 56 143 67 114.4 20.1 Yes No 20
15. † 75 10 149 87 128 97 -7.6 -18.6 Yes Yes -10
16. 55 17 88 76 125 130 -100.0 -39.0 Yes Yes 0
17. 85 0 95 83 124 131 0 13.1 Yes Yes 10
18. * 35 0 107 84 122 106 -31.5 -34.3 Yes Yes 20
19. 40 10 74 69 112 168 -11.2 0 Yes No 40
20. 20 0 57 55 104 100 9.8 0 Yes Yes 40

50 ± 32 6 ± 7 92 ± 24 74 ± 16 138 ± 19 123 ± 43 -10.4 ± 52.8 -6.0 ± 26.2

p < 0.01 NS < 0.02 NS < 0.001 NS NS < 0.02
(by selection)

*Mitral valve replacement, †septal myotomy-myectomy and mitral valve replacement.
LV, left ventricular; GCV, great cardiac vein; ΔAT = change in pacing anginal threshold.

basal coronary flow and oxygen consumption correlated directly with the magnitude of postoperative reduction in gradient, and after surgery the patients with the highest preoperative basal gradients manifested the greatest reduction in basal left ventricular oxygen consumption and coronary flow. These salutary changes were paralleled by improved symptomatic and metabolic consequences of myocardial ischemia. Thus, patients who had a higher pacing anginal threshold postoperatively and were less likely to develop pacing-induced angina: seven patients, all of whom had pacing-induced angina before surgery, were paced to the maximal heart rate of 150 beats/min after surgery without experiencing angina. Furthermore, surgery reduced the postpacing left ventricular end-diastolic and pulmonary arterial wedge pressures. Whether this reflects improved diastolic filling relating to alterations in loading conditions or reduced or absent ischemia-induced impairment of left ventricular filling and distensibility cannot be ascertained from this study. Results in patients who underwent myotomy-myectomy were similar to those of patients who underwent mitral valve replacement, although mitral valve recipients had lower postpacing left ventricular end-diastolic pressure compared with preoperative studies.

The largest reduction in basal great cardiac vein flow and greatest relief of ischemia occurred in the six patients with the highest peak coronary flows during preoperative pacing stress; basal great cardiac vein flow decreased 28%, lactate production during pacing converted to lactate consumption, and all six patients had at least a 10-beat improvement in pacing anginal threshold after surgery (Table 3). In contrast, in the remaining 14 patients who had a lower peak flow response to pacing preoperatively, operation reduced basal great cardiac vein flow by only 20%, failed to improve lactate metabolism, and only inconsistently increased anginal pacing threshold, with five of the 14 patients demonstrating no change from preoperative study. Thus, patients with high peak flow responses to pacing preoperatively uniformly benefited from operation, whereas those with a limited flow response did not consistently benefit.

Because the level of myocardial oxygen demands in patients with hypertrophic cardiomyopathy correlates directly with the magnitude of the gradient,
the data suggest that ischemia occurs at lower levels of myocardial oxygen demand in the patients with the low peak coronary flow responses to pacing. This in turn suggests that impaired coronary flow delivery, not just increased myocardial oxygen demands, contributes to the ischemia experienced by these patients. This is further suggested by the fact that in the 14 patients with the lowest coronary flow responses to pacing, the lack of consistent benefit could not be ascribed to differences in the preoperative basal gradient, as the magnitude of preoperative gradient, and its relief by operation, did not correlate with the patients' metabolic and symptomatic response to postoperative pacing.

Several mechanisms might contribute to the impaired flow response. Abnormal early diastolic relaxation and systolic compression of septal arteries could impair flow delivery. In the basal state, there was no difference in indexes of early diastolic filling (peak filling rate, time to peak filling rate) or incidence of septal artery compression between the group with high peak flow and the group with lower peak flow responses to pacing, although these parameters were not reassessed during pacing. The lower peak flow capacity may be due, in at least some of these patients, to other defects in flow delivery, including small vessel disease, myocardial scarring, or reduced capillary to myocyte ratios.

These observations are compatible with the concept that there is a spectrum of coronary flow abnormalities in patients with hypertrophic cardiomyopathy and obstruction to left ventricular outflow. Some patients appear to have a normal or near normal peak flow capacity (i.e., similar to the flow of presumably normal individuals after administration of the potent coronary vasodilator dipyridamole). In general, these patients have large basal gradients and probably develop ischemia during stress because of high basal and stress-induced myocardial oxygen requirements and, thereby, high coronary flow requirements. By removal of the metabolic burden of outflow obstruction and reduction of basal and stress-induced coronary flow, coronary flow reserve is increased, thus preventing or lessening a mismatch between oxygen need and appropriate oxygen delivery during stress. The patients who have lower preoperative peak flow capacity, however, as a group have lower basal gradients. We hypothesize that some of these patients have, in addition to the mild to moderate increase in myocardial oxygen demands imposed by the left ventricular outflow tract obstruction, an intrinsic impairment in myocardial flow delivery. In these patients, peak coronary flow capacity should not change greatly after surgery, and such individuals would be expected to have a less consistent or more limited benefit from surgery.

Limitations of Study

The relative advantages and disadvantages of the thermodilution method for measuring coronary venous volume flow have been discussed by us previously. Because it was anticipated that surgery might influence basal coronary flow, methodology capable of measuring absolute volume flow was necessary in this study. Techniques measuring ratios of basal to peak flow velocity responses after administration of a coronary vasodilator, such as Doppler flow velocity or digital subtraction techniques, would have made it impossible to draw conclusions regarding the mechanism of improved flow reserve after surgery. Further, we used pacing as the primary stimulus to increase flow because we believed a metabolic stress to the heart is physiologic. The flow data derived from the use of papaverine or dipyridamole to stimulate flow may not be representative of nutritive flow available to the myocardium during stress. In our study, the same methodology was used before and after surgery, including attention to position the catheter in an identical position within the great cardiac vein, where fewer draining veins exit compared with the coronary sinus. Thus, by using each patient as his or her own control, errors in methodology would be expected to remain constant and thus allow valid observation of the impact of operation on coronary flow.

Conclusion

Operative relief of left ventricular outflow obstruction by myotomy-myectomy or by mitral valve replacement reduces left ventricular systolic pressures and thereby decreases myocardial oxygen consumption and coronary flow in the basal state and during pacing stress. Benefit, as evidenced by conversion from lactate production to lactate consumption and improvement in pacing anginal threshold, is least evident in those patients with the highest basal outflow gradients and the highest great cardiac vein flow capacity during preoperative pacing stress. This may indicate that patients with the capacity to increase peak coronary flow to high levels preoperatively will have greater coronary flow reserve after relief of obstruction, with resulting reduction in basal and stress-induced coronary flow requirements. Conversely, the lower peak coronary flows in patients with lower gradients implies an intrinsic abnormality of coronary resistance. Whether these observations will be predictive of future symptom status, effort tolerance, or survival awaits further investigation.

Acknowledgments

The authors thank Catherine S. Magruder for her secretarial assistance and Cecelia Bergamo, Ann Danforth, Donna Jo Fleagle, Greg Johnson, Rita Minemoyer, Terry Rumble, Annette Stine, Tim Stockdale, and Judy Winkler for their invaluable contribution to these studies.

References


KEY WORD • hypertrophic cardiomyopathy
Effect of surgical reduction of left ventricular outflow obstruction on hemodynamics, coronary flow, and myocardial metabolism in hypertrophic cardiomyopathy.
R O Cannon, 3rd, C L McIntosh, W H Schenke, B J Maron, R O Bonow and S E Epstein

Circulation. 1989;79:766-775
doi: 10.1161/01.CIR.79.4.766

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/79/4/766

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/