Hemodynamics and Coronary Blood Flow During Exercise After Coronary Artery Bypass Grafting With Internal Mammary Arteries in Children With Kawasaki Disease

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Background. Saphenous vein grafts (SVG) and internal mammary artery (IMA) grafts have been used for coronary artery bypass grafting. In adult patients with bypass grafting for atherosclerotic coronary artery disease, IMA grafts have been reported to have long-term patency; however, results are conflicting on whether the graft is sufficient to meet increased myocardial oxygen demand during exercise. There have been no studies on hemodynamics and blood flow during exercise after bypass grafting with IMA in pediatric patients with Kawasaki disease.

Methods and Results. We studied 17 pediatric patients with Kawasaki disease (average age, 7.5±3.1 years), who underwent coronary artery bypass grafting with the IMA. The average number of coronary artery bypass grafts was 2.1±0.7/patient. For all patients, the left IMA was anastomosed to the left anterior descending coronary artery; for eight patients, the right IMA was also anastomosed to the right coronary artery. In addition, 11 SVGs were used. The postoperative patency rates after 1 month were 100% with the IMA graft and 91% with SVG. One year after the operation, the patency rates were 100% with IMA and 50% with SVG. Hemodynamics during exercise were measured with a bicycle ergometer, and coronary sinus blood flow was measured by the continuous thermodilution method in six patients. The relation between ΔLVEDP (the difference between left ventricular end-diastolic pressure at rest and during exercise) and ΔSVI (the difference between the stroke volume index at rest and during exercise) was analyzed. Four of six patients had reduced cardiac function before operation (ΔLVEDP, positive; ΔSVI, negative). However, after the operation, all patients demonstrated improvements in cardiac function during exercise (ΔLVEDP, positive; ΔSVI, positive). Coronary sinus flow per left ventricular mass increased after operation from 70±46 to 87±56 ml/min at rest (p<0.05) and from 139±118 to 183±150 ml/min during exercise (p<0.05).

Conclusions. In conclusion, this study reveals improvements in both hemodynamics and coronary blood flow during exercise after coronary artery bypass grafting with IMA grafts in pediatric patients with Kawasaki disease. (Circulation 1991;84:618–624)

Methods of surgical treatment for the cardiovascular lesions of febrile mucocutaneous lymph node syndrome (Kawasaki disease) are increasing. Recently, not only has the saphenous vein graft (SVG) been used for coronary artery bypass grafting (CABG), but the internal mammary artery (IMA) graft has been used as well. In adult patients with CABG for atherosclerotic coronary artery disease, there have been many studies reporting the long-term patency of IMA grafts. Despite these positive findings, it is uncertain whether the blood flow through the IMA graft is sufficient to satisfy the increased myocardial oxygen demand during exercise. There has been no report concerning the hemodynamics and coronary artery blood flow during exercise after the CABG with IMA graft in pediatric patients with Kawasaki disease. Therefore, in the present study, we examined the hemodynamics and coronary blood flow during exercise before and
after operation in CABG with IMA grafts in pediatric patients with Kawasaki disease.

**Methods**

We studied 17 patients (14 male, three female) who had had Kawasaki heart disease and who underwent CABG with IMA grafts and SVGs in combination (Table 1). At the time of operation, the average age was 7.5±3.1 (range, 3–13) years; average height was 125.1±20.5 (range, 98–166) cm; average weight was 27.1±12.3 (range, 16–59) kg; and average body surface area was 0.97±0.29 (range, 0.65–1.65) m². Nine patients had angina; six had myocardial ischemia according to radionuclide scans during exercise, and eight had myocardial ischemia according to exercise electrocardiograms. In all patients, multiple large aneurysms and occlusion or stenosis in the coronary artery were present. Angiographically, the major indications for CABG were as follows: significant stenosis of left main coronary artery, multiple coronary artery stenoses, or severe stenosis of the proximal left anterior descending artery (LAD). Aneurysms were present in the left main trunk artery in eight patients, in the LAD in 10, in the left circumflex artery (LCx) in six, and in the right coronary artery (RCA) in 16. Stenosis or obstruction was present in the LAD in all 17 patients, in the LCx in four, and in the RCA in 14. Evidence of prior myocardial infarctions was noted in seven patients, inferior wall myocardial infarction in four, anterior wall myocardial infarction in one, both anterior and inferior wall myocardial infarction in one, and inferoposterior myocardial infarction in one. During surgery, one CABG was performed in two patients, two CABGs in 12 patients, three CABGs in two patients, and four CABGs in one patient. The average number of bypass grafts was 2.1±0.7/patient. In one patient with mitral regurgitation, replacement of the mitral valve was performed with CABG. In all 17 patients, left IMAs were anastomosed to the LAD. In eight patients, right IMAs were anastomosed to the RCA. Bilateral IMA grafts were used in eight patients. In addition, SVGs were used, six to the RCA, four to the LCx, and one to the diagonal branch. Thus, a total of 25 IMAs and 11 SVGs were anastomosed.

Approximately 1 month after the operation, all 17 patients underwent cardiac catheterization. For nine patients, the procedure was repeated about after 1 year as a mid-term follow-up. The angiographic patency of the graft was evaluated. Hemodynamics and coronary blood flow dynamics both at rest and during exercise in the supine position were examined before angiocardiology in six older children (average age, 10.8±2.1 years; range, 8–13 years). Coronary blood flow was measured as coronary sinus blood flow (CSF) with the continuous thermodilution method after introducing a Webster catheter into the coronary sinus.5,6 The catheter position was confirmed by visualization after injection of contrast medium. Assuming that CSF reflects the coronary blood flow of the left ventricle,7 CSF per 100 g left ventricular mass was calculated on the basis of left ventricular mass determined from cine left ventriculograms. The left ventricular mass was calculated by the method of Rackley and colleagues,8 with the following formula:

\[ V_{c+w} = \frac{4}{3} \pi (L/2 + h)(D/2 + h)^2 \]

\[ LVM = 1.05(V_{c+w} - V_c) \]

where \( V_{c+w} \) is the volume of the left ventricular cavity and myocardium, \( L \) is the longitudinal axis, \( D \) is the short axis, \( h \) is the thickness of the left ventricular wall, 1.05 is the myocardial specific gravity, and \( LVM \) is the left ventricular mass. Cardiac output was measured by the thermodilution method through the Swan-Ganz catheter. Exercise was performed in the supine position with a bicycle ergometer with a constant load of 1 W/kg for 5 minutes.

**Statistical Analysis**

Statistical analysis of resting hemodynamics and CSF was carried out with a paired Student’s \( t \) test, and analysis of exercise hemodynamics was carried

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**Table 1. Patient Characteristics in 17 Patients With Kawasaki Disease With Internal Mammary Artery Grafts**

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>7.5±3.1 (3–13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>3F, 14M</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>125.1±20.5 (98–166)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>27.1±12.3 (16–59)</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>0.97±0.29 (0.65–1.65)</td>
</tr>
<tr>
<td>Coronary lesion (n)</td>
<td>7</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>LMT 8</td>
</tr>
<tr>
<td></td>
<td>LAD 10</td>
</tr>
<tr>
<td></td>
<td>LCx 6</td>
</tr>
<tr>
<td></td>
<td>RCA 16</td>
</tr>
<tr>
<td>Stenosis or obstruction</td>
<td>LMT 0</td>
</tr>
<tr>
<td></td>
<td>LAD 17</td>
</tr>
<tr>
<td></td>
<td>LCx 4</td>
</tr>
<tr>
<td></td>
<td>RCA 14</td>
</tr>
<tr>
<td>Myocardial infarction (n)</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Anterior 1</td>
</tr>
<tr>
<td></td>
<td>Anterior, inferior 1</td>
</tr>
<tr>
<td></td>
<td>Inferior 4</td>
</tr>
<tr>
<td></td>
<td>Inferior, posterior 1</td>
</tr>
<tr>
<td>Patent IMA grafts</td>
<td>1 mo after surgery 25/25 (100%)</td>
</tr>
<tr>
<td></td>
<td>1 yr after surgery 12/12 (100%)</td>
</tr>
<tr>
<td>Patent SVG grafts</td>
<td>1 mo after surgery 10/11 (91%)</td>
</tr>
<tr>
<td></td>
<td>1 yr after surgery 5/10 (50%)</td>
</tr>
</tbody>
</table>

Values are mean±SD.

LMT, left main trunk; LAD, left anterior descending coronary artery; LCx, left circumflex artery; RCA, right coronary artery; IMA, internal mammary artery; SV, saphenous vein.
Three patients had a temporary recurrence of angina attributable to closure of SVG. The angina has been controlled with medication. At present, all patients have nearly normal lives.

**Graft Patency Rates**

One month after surgery, all 25 IMA grafts were patent (100%), and 10 of 11 SVGs were also patent (91%) (Table 1). Twelve IMA grafts after 1 year were patent (100%), whereas five of 10 SVGs were occluded (50%).

**Hemodynamics at Rest Before and After Surgery**

The averages of the cardiac index (CI) before and after surgery were 4.87±0.81 and 4.86±0.94 l/min/m², respectively (Figure 1). Both values were in the normal range, and no significant differences were seen. Averages for the stroke volume index (SVI) before and after surgery were 53±7 and 46±7 ml/m², respectively (p=NS). Averages for left ventricular end-diastolic pressure (LVEDP) were 5.5±2.0 and 6.3±1.4 mm Hg before and after surgery, respectively (p=NS). Averages for ejection fraction before and after surgery were 0.59±0.05 and 0.61±0.08, respectively (p=NS). In summary, hemodynamics before and after surgery at rest showed no significant differences.

**Hemodynamics During Exercise Before and After Surgery**

Changes of heart rate, cardiac index, left ventricular end-diastolic pressure, and stroke volume index. The heart rate (HR) before the operation increased from 92±10 beats/min at rest to 122±12 beats/min during exercise (p<0.01) (Figure 2). HR after the operation increased from 106±11 at rest to 138±17 beats/min during exercise (p<0.01). The rates of increase were 33% and 30%, respectively. A comparison of HR before and after the operation showed no significant increase both at rest and during exercise. The LVEDP before the operation showed a slight increase from 5.5±2.0 at rest to 8.7±1.8 mm Hg during

**Results**

In all 17 patients, no death occurred during surgery or during 29.5±17.5 (range, 7–65) months of the mean follow-up period.
exercise. After the operation, the LVEDP increased slightly from 6.3±1.4 at rest to 8.8±2.4 mm Hg during exercise (Figure 2). Both increases were not significant and were within the normal range. Preoperative and postoperative comparisons revealed no significant differences either at rest or during exercise. Averages for CI were 4.87±0.81 at rest and 6.18±1.08 during exercise (Figure 3). No significant differences were seen; however, the CI after the operation increased significantly from 4.86±0.94 at rest to 6.90±1.45 l/min/m² during exercise. Comparisons of respective results before and after the operation revealed no significant difference either at rest or during exercise. The SVI before the operation was 53±7 at rest and 51±11 ml/m² during exercise (p=NS) (Figure 3). After the operation, SVI slightly increased from 46±7 at rest to 50±6 ml/m² during exercise (p=NS).

**Relation between ∆LVEDP and ∆SVI.** As shown in Figure 4, the horizontal axis shows the difference between LVEDP at rest and during exercise (∆LVEDP) and the vertical axis shows the difference between the SVI at rest and during exercise (∆SVI) so that their relation could be examined. Before the operation, in four of six patients, ∆LVEDP was positive, whereas ∆SVI was negative, which indicated a “depressed left ventricular function” as reported by Ross et al.9 After operation in all patients, both ∆LVEDP and ∆SVI were positive. This relation between ∆LVEDP and ∆SVI can be identified as a point in the upper right area of Figure 4, which is in the area of normal or abnormal left ventricular function. According to this graph, preoperative and postoperative functional responses of the left ventricle to exercise indicate a postoperative improvement in left ventricular function during exercise.

**Coronary Sinus Flow per Left Ventricular Mass (CSF/LV) and CSF/LV per Heart Rate at Rest and During Exercise Before and After Operation**

The CSF per left ventricular mass at rest increased significantly from 70±46 before to 87±56 ml/min after the operation (p<0.05). During exercise, CSF increased significantly from a preoperative value of 139±118 to a postoperative value of 183±150 ml/min (p<0.05) (Figure 5). The average CSF/LV/HR values at rest before and after surgery were 0.75±0.50 and 0.81±0.51 ml/beat, respectively (p=NS). The mean CSF/LV/HR values during exercise before and after surgery were 1.08±0.77 and 1.30±1.03 ml/beat, respectively (p=NS) (Figure 6).
Discussion

The postoperative patency rate of SVGs implanted as aortocoronary bypass grafts in adults was 86% and 78% at 1 and 4 years, respectively, whereas that of IMA grafts was 96% and 94% at 1 and 4 years, respectively. Grondin et al. reported that 10-year patency rates were 84.1% for the IMA grafts and 52.8% for SVGs. According to Tector et al., patency rates after 5–9 years were 94% with IMA grafts and 64% with SVGs. The patency rate of SVGs in pediatric patients with Kawasaki disease was lower than that in adult patients. We previously reported that the IMA graft in pediatric patients with Kawasaki disease can increase in length and diameter because the IMA is a living graft and, therefore, has a self-regulating function. It follows that the IMA is a graft of choice for CABG for pediatric diseases, such as Kawasaki disease.

According to a report by Suma et al., ejection fractions at rest before and after surgery were 0.45 and 0.49, respectively; LVEDPs were 13 and 15 mm Hg, respectively, showing no significant differences. The results obtained in our present study showed no significant differences in hemodynamic parameters at rest. Ross et al. showed that the relation between ΔLVEDP and ΔSVI was meaningful and useful in evaluating hemodynamics during exercise in adult patients. They indicated that the lower right area in their graph depicted a “depressed LV function.” The fact that the area in our graph (Figure 4) changed from the lower right before surgery to the upper right after surgery demonstrated the improvements in hemodynamics during exercise. Thadani et al. reported that the normal response during exercise is that the SVI increases while the LVEDP increases, and the increase limit of LVEDP was less than 16 mm Hg. The postoperative LVEDP during exercise in the present study was less than 15 mm Hg, which is considered to be almost within the normal range.

There has been no report on the CSF at rest and during exercise in pediatric patients who have under-
gone CABG with IMA grafts. Because of the narrower diameter of IMA graft compared with that of SVG, there may be the risk of insufficient blood flow with the IMA graft. Flemmia et al. reported that at CABG with SVG and IMA graft to the LAD, blood flow through the SVG was two to three times higher than that through the IMA graft. They reported that the SVG was superior to the IMA graft with regard to blood flow. Barner measured graft blood flow during surgery and found no difference between the blood flow through SVG and IMA grafts. Barner also measured reactive hyperemic flow, which increases after the temporary occlusion of a graft, and found that the reactive hyperemic flow of the IMA graft was less than that of SVG. However, upon reopening the thoracic cavity to perform a subsequently necessary procedure, Barner again measured blood flow of the IMA graft and found that blood flow had increased. He further demonstrated that blood flow through the IMA graft could increase hourly. Schmidt et al. administered isoproterenol to examine blood flow increases, and they reported no difference in blood flow between the IMA graft and SVG. Johnson et al. compared the blood flow of the IMA graft with that of the SVG by use of thallium-201 myocardial scintigraphy, and they found no differences even during exercise. We also compared the blood flow of the IMA graft with that of the SVG and found no difference in blood flow 1 month after surgery.

Until the present study, changes in blood flow after coronary bypass in pediatric patients with Kawasaki disease were unknown. In the present study, we found an increase in coronary blood flow even in the early postoperative period both at rest and during exercise. The reason for a postoperative increase of CSF may be based upon the absence of a significant increase in HR after surgery compared with the HR before surgery. About 1 or 2 months after surgery, nonspecific stress of surgery may result in sympathetic stimulation. The increase of HR after surgery may be increased by sympathetic stimulation. However, the increase in postoperative CSF at rest and during exercise is probably due to the effect of revascularization surgery. In conclusion, from this study, the revascularization procedure with the IMA graft for coronary artery obstructive lesions in Kawasaki disease is considered extremely satisfactory from the clinical and hemodynamic viewpoints.

References

KEY WORDS: Kawasaki disease • blood flow, coronary sinus • exercise • hemodynamics • coronary artery bypass grafting • internal mammary artery graft
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