Long-Term Results of Saphenous Vein Graft for Coronary Stenosis Caused by Kawasaki Disease

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Background Although saphenous vein grafts (SVG) have been used from 1975 to treat coronary stenosis caused by Kawasaki disease, long-term results after more than 20 years remain unknown.

Methods and Results From 1981 to 1997, 13 patients underwent coronary artery bypass grafting using SVG (n=20). The age at operation ranged from 2 to 20 years (median 11 years), the age at latest angiography from 15 to 36 years (median 30 years) and the postoperative follow-up period was from 10 to 26 years (median 22 years). The patency rate of the SVG was determined by postoperative angiography, graft wall morphology was graded and the late clinical course was reviewed. The patency rates at 1, 10, and 25 years after operation were 84.4%, 57.2%, and 51.5%, respectively. Irregularity of the SVG wall was slight in 3 of 7 patients with long-term patency. One patient with obesity and hyperlipidemia underwent stent implantation in the SVG because of graft stenosis.

Conclusion Although the patency rates for SVG are low, there are patients with long-term patency over 20 years. Obesity and hyperlipidemia in these patients should be vigorously pursued. (Circ J 2009; 73: 73–77)

Key Words: Coronary artery bypass grafting; Coronary artery disease; Kawasaki disease

In 1983 Kitamura reported the first use of an internal thoracic artery (ITA) graft for coronary artery bypass grafting (CABG) in a patient with coronary arterial lesions caused by Kawasaki disease (KD) and since then ITA grafts have been preferred and the results have been favorable. Previously, saphenous vein grafts (SVG) were used as the 1st choice for CABG in this population from 1975 to the early 1980s. The 2002 national survey of CABG for KD patients in Japan identified a total of 85 grafts in 65 patients. Because the long-term results of SVG in this population have not been reported, we reviewed our clinical results, including the patency rate of SVG assessed by coronary angiography (CAG).

Methods

We identified 13 patients (11 males, 2 females) who had undergone CABG using SVG from 1981 to 1997 (Table 1). Among them, 10 patients had both SVG and ITA grafts, and the total number of SVGs was 20. One patient had a sequential graft to the posterolateral artery (PL) and the posterior descending artery (PD). One patient also underwent mitral valve replacement with a 25-mm St Jude Medical valve. Their present ages range from 21 to 41 years (median 30 years); their age at operation was from 2 to 20 years (median 11 years), and the interval from the onset of KD to surgery was from 1.4 to 19 years (median 6 years). The postoperative follow-up period was from 10 to 26 years (median 22 years). All the patients underwent postoperative angiography at least twice. The age at the latest angiography ranged from 15 to 36 years (median 27 years), and the interval from the operation to the latest angiography ranged from 4 to 25 years (median 16 years). The number of grafted vessels was 1 in 1 patient (7%), 2 in 6 (46%), 3 in 5 (38%) and 5 vessels in 1 (7%). The coronary arteries grafted with saphenous vein were the left anterior descending artery (LAD: 3), the right coronary artery (RCA: 9), the left circumflex (LCX: 2), the obtuse marginal branch (1), PL (3) and the diagonal branch (2). Other grafts used were the ITA (8) and gastroepiploic artery (1).

Five patients were not recognized as having KD in the acute phase. Aspirin was administered to 4 patients, steroids to 2 patients, and intravenous immunoglobulin to 1 patient for treatment of acute KD. Previous myocardial infarction had occurred in 2 patients (15%). Preoperative symptoms occurred in 4 patients, consisting of syncope in 2 and chest pain in 2. One patient developed hemiplegia because of cerebral infarction 2 years after acute KD. After CABG, 11 patients received antiplatelet agents (aspirin, 8; flurbiprofen, 1; ticlopidine, 1; dipyridamole, 1). Coumadin and nitrates were given to 2 and 1 patients, respectively. Beta-blockers, enalapril, and valsartan were given to 2, 1 and 1 patients, respectively. One patient received no medications (patient 1) and in 3 patients compliance was poor (patients 4, 10, 12).

Patency of the SVG and ITA was determined by postoperative angiography. In this study, complete occlusion was defined as total obstruction of the grafts. The age at operation was compared between the SVG occluded group and the SVG patent group. Furthermore, we measured the ratio of the maximum to minimum diameter of the SVG in 8 patients as a marker of the irregularity of the graft wall on postoperative angiograms, and we measured the left ventricular ejection fraction (LVEF) on the left ventriculogram. We recorded coronary risk factors such as obesity,
Results

Of the 20 SVG grafts, 11 (55%) were patent; 6 (67%) of the 9 occluded grafts had occluded within the first postoperative year. The age at operation in the SVG patent group (n=11) was significantly higher than that in SVG occluded group (n=9) (14.2±5.2 vs 7.1±5.3, P<0.01). Patency rates for SVG grafts at 1, 10, and 25 years after operation were 84.4%, 57.2%, and 51.5%, respectively (n=20) (Fig1). The ratio of the maximum to minimum diameter of the SVG in the SVG patent group (n=7) on the latest angiography was significantly lower than that in the SVG occluded group (n=4) on angiography before complete occlusion (1.5±0.4 vs 3.1±0.9, P<0.05). Patency rates for ITA grafts at 1, 10, and 20 years after operation were 100%, 90.9%, and 81.8%, respectively (n=11). There was no significant difference between SVG and ITA grafts in the patency rate, because of the small sample numbers in this study.

The change in the ratio of the maximum to minimum diameter of the SVG in the late period.

Table 1 Gaft Patency and Medications

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex</th>
<th>Age (years)</th>
<th>SVG vessel (stenosis)</th>
<th>Graft patency</th>
<th>Other operation (patency)</th>
<th>Medication Cardiac event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>11</td>
<td>RCA (50%)</td>
<td>O</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>16</td>
<td>RCA (SS)</td>
<td>O</td>
<td></td>
<td>Aspirin, carvedilol</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>15</td>
<td>LAD (100%)</td>
<td>O</td>
<td></td>
<td>Aspirin, (coumadin)</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>6</td>
<td>RCA (75%)</td>
<td>P</td>
<td>LITA to LAD (P)</td>
<td>Stent implantation, re-CABG</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>12</td>
<td>RCA (100%)</td>
<td>P</td>
<td>LITA to LAD (P)</td>
<td>Carvedilol, valsartan, furosemide</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>2</td>
<td>RCA (SS)</td>
<td>O</td>
<td>LITA to LAD (P)</td>
<td>Dipivardilone, Aspirin</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>6</td>
<td>RCA (SS)</td>
<td>O</td>
<td>LITA to LAD (P)</td>
<td>Flurbiprofen</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>7</td>
<td>RCA (SS)</td>
<td>O</td>
<td>LITA to LAD (O)</td>
<td>Aspirin, metoprolol</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>20</td>
<td>OM (90%)</td>
<td>P</td>
<td>LITA to LAD (P)</td>
<td>Nitrites</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>5</td>
<td>RCA (SS)</td>
<td>O</td>
<td>LITA to LAD (P)</td>
<td>Aspirin, carvedilol, enalapril</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>5</td>
<td>RCA (4PD) (100%)</td>
<td>O</td>
<td>LITA to LAD (P)</td>
<td>Aspirin, carvedilol</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>19</td>
<td>RCA (4PD) (100%)</td>
<td>P</td>
<td>RITA to LAD (P)</td>
<td>Aspirin</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>11</td>
<td>D1 (100%)</td>
<td>P</td>
<td>LITA to LAD (O)</td>
<td>Aspirin</td>
</tr>
</tbody>
</table>

SVG, saphenous vein grafts; RCA, right coronary artery; O, occluded; LAD, left ascending artery; P, patent; CABG, coronary artery bypass grafting; LITA, left internal thoracic artery; MVR, mitral valve replacement; SS, segmental stenosis; D1, 1st diagonal branch; PL, posterolateral artery; OM, obtuse marginal artery; LCX, left circumflex; PD, posterodescending artery; VT, ventricular tachycardia; GEA, gastroepiploic artery.

Fig1.  Patency rates of saphenous vein grafts.

Fig2. Changes in the ratio of the maximum to minimum diameter in saphenous vein grafts in the late period.
with a SVG when he was 7 years old. Five years after the operation, CAG showed 90% stenosis of the SVG and the ratio of the maximum to minimum diameter of SVG was 3.5 (Fig 3). The 3rd patient had undergone stent implantation 15 years after his operation (Fig 4). When he attended hospital because of effort angina, CAG showed 90% stenosis of the SVG with a filling defect in its mid-portion. Intravascular ultrasound imaging showed a low echoic area occupying the graft, which was suspected to be a lipid plaque. Stent implantation after balloon inflation with 4-atmosphere pressure was successful. His body mass index was 30 at that time, and his total cholesterol 235 mg/dl. Coumadin and aspirin was administered after the procedure. The patient has reduced his weight since then. Five years after stent implantation, the ratio of maximum to minimum diameter was 2.4.
after stent implantation chest pain on effort reoccurred and although the SVG was patent, CAG revealed 99% stenosis of the left circumflex artery. He had repeat CABG using both ITAs at age 35. The right ITA was anastomosed to the LAD instead of the SVG, and the left ITA combined with the radial artery was anastomosed to the PL and PD. Because the irregularity of the SVG wall was worse than immediately after stent implantation, we thought that long-patency of the SVG could not be expected. On the other hand, the wall of the SVG in 3 patients (patients 1, 5, 7) was very smooth (Fig 5 Left). Kinking of the grafted coronary artery with somatic growth occurred in the 7th and 13th patients (Fig 5 Right). At present, there is no ischemia induced by kinking of the grafted coronary artery in this group of patients.

All the patients are alive at the time of this study, and all are New York Heart Association class 1. Two female patients have given birth by vaginal delivery. The LVEF values on the left ventriculograms in the late period after CABG were as follows: ≥50% in 10 patients, and 240% and <50% in 3 patients (patients 4, 9, 10). Two patients had ST-T depression on the Master-double step test (patients 2, 9), and hypoperfusion on radioisotope myocardial perfusion imaging at rest was detected in 4 patients (patients 2, 3, 9, 10).

Cardiac events occurred after CABG in 4 (31%) of the 13 patients: 3 patients (23%) had re-CABG, and 1 had ventricular tachycardia. In all 3 patients who underwent re-CABG the failed graft was to the LAD, in addition to multivessel disease. The second patient underwent re-CABG with the left ITA to the LAD 7 years after operation. The third patient underwent stent implantation 15 years after operation, and he had re-CABG with the right ITA 20 years after operation as mentioned previously. The 8th patient had re-CABG 20 years after operation, because he had occlusion of both previous grafts. The right ITA combined with the radial artery was anastomosed to the LAD and PD of the RCA. The 10th patient with a LVEF of 45% required an implantable cardiac defibrillator (ICD) because of ventricular tachycardia at the age of 26 years. He had had a low LVEF because of a previous inferior myocardial infarction before CABG.

Regarding coronary risk factors, the 3rd patient was obese and had hyperlipidemia, and the 5th patient was also obese. The 4th patient had smoked for 10 years. The remaining 10 patients did not have any risk factors.

**Discussion**

Although the patency rate for SVG in this study was low compared with that of ITA grafts in adults7; there was long-term patency of approximately 50% of the SVGs. Patency seems to be determined within the first year in most patients and a previous report stated that patency of SVG was often determined within the first 2 postoperative weeks in adults6. This early occlusion may also occur in children and adolescents. In adults, thrombosis and neointimal hyperplasia are considered to be the main causes of occlusion in the first postoperative year.8 In our study, operation at a younger age was more likely to result in an occluded graft. In children, the diameters of both the grafted arteries and the grafts are small, which may decrease the patency rates of SVGs9. In 9 occluded grafts, 6 of the grafted vessels were the RCA. The long-term predictors of SVG graft patency are considered to be grafting into the LAD, grafting into a vessel that is ≥2.0 mm in diameter, and older patients with good left ventricular function.6–7 Because the number of patients was small in our study, other factors regarding early graft occlusion, other than age at operation, could not be clarified.

SVG diameter and wall thickness also significantly influenced graft patency, similar to the results in adults10. Our findings suggest that a high ratio of the maximum to minimum diameter of the SVG indicates the likelihood of graft occlusion in the late period. On the other hand, it is considered that graft atherosclerosis begins to develop a few years later in adults. Further, vein graft atherosclerosis continues to be a major problem causing luminal defects of 81% at more than 15 years8–12. In our study, although SVG tissue was not obtained, a major luminal defect with suspected lipid plaque in the late period was found in only 1 patient with obesity and hyperlipidemia. The yellow plaque and thrombi were shown in the SVG early after CABG by intravascular angioscopy12. In contrast, the wall of the SVG...
was smooth in 3 patients with long-term patency, and as a marker of SVG wall irregularity their maximum/minimum ratios were less than 1.5. When patency of the SVG exceeds 1 year after operation, and there is no wall irregularity it may be possible to preserve long-term patency provided coronary risk factors are controlled. Because the mean age of the KD population differs from that of adults with atherosclerosis, the time of development of vein graft atherosclerosis may be different. Therefore, long-term patency of SVGs greater than the 20 years in our study may be possible in adolescents and young adults without severe atherosclerosis. Reduction of coronary risk factors, such as obesity, hyperlipidemia, hypertension and smoking, is as important as anticoagulant therapy. Although kinking of the grafted coronary artery developed with somatic growth in 2 patients, it has not been associated with any problems at present, but requires careful follow-up. Three patients with re-operation developed graft failure to the LAD or LCX. As a minimum, good coronary revascularization to the left coronary artery would represent a good result in this population. In coronary revascularization using a SVG, the graft has remained patent in some patients for more than 20 years, but when both the SVG and ITA are available, arterial grafts should be selected for pediatric CABG after KD.

Conclusions
Although the patency rates for SVG were less than those for ITA grafts, SVGs remained patent for more than 20 years in approximately 50% of the present patients. A few patients with wall irregularities developed atherosclerotic disease in adulthood, and 1 required repeat revascularization. Reduction of coronary risk factors in these patients with SVG should be kept in mind.

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References