Coronary artery bypass grafting in patients with systemic lupus erythematosus

Masashi Ura¹, Ryuzo Sakata²*, Yoshihiro Nakayama⁴, Yohichirou Ohtsuka⁵, Taro Saito⁶

¹Department of Cardiovascular Surgery, Kumamoto Central Hospital, 96 Tainoshima, Tamukae-machi, Kumamoto City 862-0965, Japan
²Department of Pathology, Kumamoto Central Hospital, 96 Tainoshima, Tamukae-machi, Kumamoto City 862-0965, Japan
³Department of Cardiology, Kumamoto Central Hospital, 96 Tainoshima, Tamukae-machi, Kumamoto City 862-0965, Japan

Received 1 December 1998; received in revised form 26 January 1999; accepted 2 February 1999

Abstract

Objective: Few reports exist on the results of coronary artery bypass grafting (CABG) in patients with systemic lupus erythematosus (SLE).

Methods: We retrospectively reviewed eight CABG in seven SLE patients. In early and late postoperative angiography, all grafts were evaluated for occlusion, development of string sign, or presence of significant stenosis. The early and late results were compared. The pathological studies were performed on the segments of the internal thoracic artery (ITA) and saphenous vein collected from each patient. Atherosclerosis of the ITA was analyzed using the subjective evaluation proposed by Kay et al. (Kay HR, Korns ME, Flemma RJ, Tector AJ, Lepley D. Atherosclerosis of the internal mammary artery. Ann Thorac Surg 21:1976:504–507) scale 0–4 (0 = normal, 1 = minimal disease, 2 = less than 25% luminal narrowing, 3 = 25–50% narrowing, and 4 = greater than 50% narrowing).

Results: The patients consisted of three men and four women with a mean age of 59.8 years. Co-morbid diseases were frequent and there were three patients (37.5%) with renal failure (two dialysis patients, one with renal dysfunction) and two patients with severe atherosclerosis of the aorta. The ITA was used in four patients. Saphenous vein graft was used in seven patients. Concomitant procedures included aortic valve replacement and mitral annuloplasty, mitral valvuloplasty and tricuspid annuloplasty, mitral valve replacement and tricuspid annuloplasty (TAP). There was one hospital death (12.5%). Early patency rates were 87.5% (21/24). No other atherosclerotic changes or stenosis suggesting vasculitis were noted. In pathological studies, there was no significant atherosclerosis in the six ITA specimens from four patients, although three patients had degree two atherosclerosis. No vasculitis was found in ITA or saphenous vein grafts. During the mean follow-up period of 35.3 months (range, 5–91 months), there was one non-cardiac late death. Late restudy (in three patients, 12, 57 and 64 months later respectively) revealed no deterioration in either ITA or vein grafts. Overall prognosis after the operation in SLE patients appears to be good. No other cardiac events were observed, and patients demonstrated marked clinical improvement.

Conclusions: CABG in SLE patients can be performed with acceptable morbidity and mortality. Our data so far reveals no evidence to preclude the use of ITA and vein grafts in SLE patients. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Coronary artery bypass grafting; Systemic lupus erythematosus

1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disorder resulting in multisystemic inflammatory damage. Cardiovascular disease has been recognized as a major cause of mortality in SLE patients [1–6]. Multiple factors appear to be related to the etiology of coronary artery disease in SLE patients, including coronary arteritis and steroid-induced accelerated atherosclerosis [1,4–6]. Although there have been several case reports of coronary artery bypass grafting (CABG) on SLE patients, it is still an open question as to whether CABG can provide satisfactory results similar to those established in non-SLE patients [1,7,8]. Reviewing the experience in our institution might provide additional support to the rather meager published experience in patients considered to be at greater than usual risk.

2. Patients and methods

We retrospectively reviewed eight CABG in seven patients with SLE at our institution. The patients consisted
of three men and four women with a mean age of 59.8 years (range, 37–78). Patient characteristics are summarized in Table 1. The duration of SLE was 10.4 ± 8.0 years. In all patients SLE was in remission at the time of surgery. There were three patients (37.5%) with renal failure, including two dialysis patients and one patient with renal dysfunction (creatinine > 2.0 mg/dl). All patients were taking prednisolone at the time of the operation. Presenting symptoms included angina in five and dyspnea in three. Two patients had been referred after unsuccessful percutaneous transluminal coronary angioplasty (PTCA).

Early postoperative angiography was performed in all patients 2–3 weeks after surgery. All grafts were evaluated for occlusion, development of string signs, or presence of significant stenosis (flow limiting or stenosis of more than 50% of the vessel diameter at any point along the body of the graft or at any anastomoses). Only grafts of good caliper, with no occlusion, string signs, or significant stenosis, were considered patent. Repeat angiography was performed in three patients in the follow-up period of 12, 57 and 64 months, respectively.

2.1. Operative procedures

All the operations were performed using standard CPB with moderate hypothermia (30–32°C). With the exception of one patient, all anastomoses, including the proximals, were performed during a single period of aortic cross-clamping (Fogarty soft-jaw clamp, 86 mm, Baxter, CA). In one patient with severe atherosclerosis of the ascending aorta, bilateral internal thoracic artery (ITA) grafting was performed during hypothermic ventricular fibrillation. Operative procedures are summarized in Table 2. In regard to the selection of conduit, the use of at least one ITA graft was attempted for revascularization in patients under 70-years-old. Thus, the ITA was used in four patients and, in two of these, the bilateral ITA was used. The ITA was not used in one patient less than 70-years-old with dissecting aneurysm (IIIb) because of the risk of injury to the ITA graft in any future thoracic operation. Saphenous vein graft was used in seven patients. Mean number of distal anastomoses was 2.3 ± 0.9. Concomitant procedures included aortic valve replacement (AVR) and mitral annuloplasty in one, mitral valvuloplasty and tricuspid annuloplasty (TAP) in one, and mitral valve replacement and TAP in one. Intravenous prednisolone was used as a supplement until oral prednisolone was restarted on the first or second postoperative day. The postoperative dose of oral prednisolone was usually same as that used preoperatively.

2.2. Pathological studies

The segments of ITA and saphenous vein collected from each patients were fixed in formalin, embedded in paraffin blocks, and sectioned. Sections were stained with hematoxylin and eosin and Elastica von Gieson. Atherosclerosis of the ITA was analyzed using the subjective evaluation proposed by Kay et al. [9]: scale 0–4 (0 = normal, 1 = minimal disease, 2 = less than 25% luminal narrowing, 3 = 25–50% luminal narrowing, and 4 = greater than 50% luminal narrowing). A greater than 25% luminal narrowing was considered as significant atherosclerosis. The ITA and saphenous vein were also evaluated for the existence of vasculitis.

2.3. Late follow-up

Late follow-up information was collected from the patients’ most recent clinical visits, supported by telephone interviews with home physicians or patients.

3. Results

3.1. Operative results

One hospital death (12.5%) occurred. A 71-year-old woman (Case 3) who had mediastinitis and prosthetic valve endocarditis after AVR, MAP and CABG died 2 years after the operation of sepsis after being transferred to a satellite hospital. There were no other postoperative complications.

3.2. Early examinations

Early postoperative angiography was performed in all patients 2–3 weeks after surgery. String-like artery and significant stenosis were present in each single patient for a patency rate of all grafts of 88.9% (16/18). The two incompetent grafts were both arterial grafts. In situ RITA via the transverse sinus anastomosed to the circumflex artery became string-like due to significant stenosis at the anastomotic site (Case 6). There was significant stenosis at the anastomotic site of LITA to the circumflex artery in Case 1. This patient underwent PTCA 3 months later with successful dilatation. The most probable causes of stenosis and
string-like artery appear to be intraoperative technical failures. No other atherosclerotic changes or stenosis suggesting vasculitis were noted along the ITA body or vein grafts (Table 3).

3.3. Pathological studies

There was no significant atherosclerosis in the six ITA specimens from four patients, although three patients had degree two atherosclerosis. No vasculitis was found in ITA or saphenous vein grafts (Table 3).

3.4. Late follow-up

All seven survivors were traced.

There were one late death among the operative survivors during the mean follow-up of 35.3 ± 28.7 months (range, 5–91 months). Case 2 died in an accident 24 months after the operation. Three patients underwent repeat angiography during the follow-up period; in two because of follow-up reasons after PTCA and stent implantation (Cases 1 and 6), in one because of preoperative evaluation (Case 4). Case 1, who underwent PTCA after the operation as mentioned above, underwent follow-up angiography 64 months after the operation. Repeat angiography revealed no re-stenosis of LITA after coronary angioplasty and patent sequential vein graft.

Case 6, with string-like RITA, had recurrent angina 8 months after discharge. Repeat angiography showed pro-

---

### Table 2
Operative procedures

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Number of coronary artery disease</th>
<th>CABG</th>
<th>Concomitant procedures</th>
<th>Duration of SLE (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>69</td>
<td>M</td>
<td>2</td>
<td>LITA-CX, Ao-CX-RCA</td>
<td>none</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td>F</td>
<td>2</td>
<td>LITA-D, Ao-D-LAD</td>
<td>none</td>
<td>22</td>
</tr>
<tr>
<td>3</td>
<td>71</td>
<td>F</td>
<td>1</td>
<td>Ao-LAD</td>
<td>AVR, MAP</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>74</td>
<td>M</td>
<td>1</td>
<td>Ao-CX</td>
<td>MAP, MVP, TAP</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>49</td>
<td>F</td>
<td>3</td>
<td>Ao-LAD, Ao-CX, Ao-RCA</td>
<td>none</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>37</td>
<td>F</td>
<td>LMT + 2</td>
<td>LITA-LAD, RITA-CX, Ao-D</td>
<td>none</td>
<td>18</td>
</tr>
<tr>
<td>7</td>
<td>43</td>
<td>M</td>
<td>LMT + 2</td>
<td>LITA-LAD, RITA-CX</td>
<td>none</td>
<td>15</td>
</tr>
<tr>
<td>8</td>
<td>78</td>
<td>M</td>
<td>3</td>
<td>Ao-LAD, Ao-RCA</td>
<td>MVR, TAP</td>
<td>3</td>
</tr>
</tbody>
</table>

Aorta cross-clamp time(min)

SLE, systemic lupus erythematos; AVR, aortic valve replacement; MVR, mitral valve replacement; MAP, mitral annuloplasty; MVP, mitral valvuloplasty; TAP, tricuspid annuloplasty; CABG, coronary artery bypass grafting; Ao, aorta; LAD, left anterior descending artery; CX, circumflex artery; RCA, right coronary artery; D, diagonal artery; ITA, internal thoracic artery (R, right; L, left); LMT, left main trunk disease. Cases 5 and 7 were dialysis patients. Case 4 and Case 8 were the same patient.

---

### Table 3
Results of angiographic study and pathological studies

<table>
<thead>
<tr>
<th>Case</th>
<th>Pathological study</th>
<th>Early angiography (number of patent grafts/number of grafts)</th>
<th>Late angiography (number of patent grafts/number of grafts)</th>
<th>Interval between operation and late angiography (months)</th>
<th>Follow-up period (Outcome)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(2) No vasculitis</td>
<td>No vasculitis</td>
<td>0/1**</td>
<td>1/1**</td>
<td>2/2</td>
</tr>
<tr>
<td>2</td>
<td>(2) No vasculitis</td>
<td>No vasculitis</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>3</td>
<td>–</td>
<td>No vasculitis</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>4</td>
<td>–</td>
<td>No vasculitis</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>5</td>
<td>–</td>
<td>No vasculitis</td>
<td>3/3</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>6</td>
<td>(0) No vasculitis</td>
<td>No vasculitis</td>
<td>1/2***</td>
<td>1/2**</td>
<td>1/1</td>
</tr>
<tr>
<td>7</td>
<td>(2) No vasculitis, calcium deposition</td>
<td>–</td>
<td>2/2</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>8</td>
<td>–</td>
<td>–</td>
<td>2/2</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

ITA, internal thoracic artery; SVG, saphenous vein graft. *Atherosclerotic scale proposed by Kay et al. [9] (from 0 to 4) is expressed in parentheses. **Late angiography showed successful dilatation of stenosed ITA. ***Right ITA anastomosed to circumflex artery was string-like.
progression of left main trunk disease (from 50 to 99%). Although the previously string-like RITA had dilated and the LITA anastomosed to LAD was patent, because of recurrent angina, a Palmaz–Schatz stent was placed in the left main trunk without any sequelae. Repeat angiography 6 months later revealed string-like RITA as in the first angiography with no stenosis in the LMT. The LITA anastomosed to the LAD and the vein grafts to the diagonal branch were patent throughout the repeat studies. The LITA changed its caliber to meet the demand in accordance with the severity of LMT lesions.

Another patient (Case 4) who underwent combined operation had dyspnea 4.5 years after the initial operation due to the recurrence of mitral and tricuspid regurgitation. Although preoperative angiography showed patent vein graft to circumflex artery without angina, because of the progression of disease in the native coronary arteries, CABG was also performed in a second operation.

No atherosclerotic changes were noted along the ITA body or vein grafts in either of the late restudies.

There was no other cardiac event or myocardial infarction during the follow-up period.

3.5. Clinical improvement

All the survivors demonstrated excellent clinical improvement according to the NYHA functional classification. Four were in Class IV, three in Class III, and one in Class II preoperatively, whereas five were in Class I, and three in Class II postoperatively. Every patient demonstrated improved NYHA functional status.

4. Discussion

Cardiovascular disease has emerged as a major cause of mortality in SLE patients even though the overall prognosis has improved. Although there have been a number of reports on coronary angioplasty and CABG in patients with SLE, little is known about CABG in SLE patients [1,4,7,8].

CABG in SLE patients is a surgical challenge because the patients have unique characteristics of multiple organ involvement and long-term use of steroids. In a report describing 36 surgical procedures on 29 patients with SLE, Papa et al. [10] concluded that surgical complications are frequent in SLE patients. He identified four factors predictive of increased morbidity: higher mean doses of steroid preoperatively, more organ involvement by SLE, emergent operation and renal involvement [10]. In addition, SLE affects the heart in numerous ways: pericarditis, myocarditis, endocarditis, valvular abnormalities and coronary arterial lesions (arteritis or atherosclerotic changes), which sometimes present complex lesions [5,6]. Harrison et al. [11] reported a case of rapidly progressive carditis with associated aneurysm of the left ventricle free wall and prosthetic valve ring following mitral valve replacement in a patient with SLE. In our series of eight patients, there were three combined procedures involving CABG and valvular operation. Extracardiac lesions were also frequent and there were three patients (37.5%) with renal failure (two dialysis patients, one with renal dysfunction) and two patients with severe atherosclerosis of the aorta (dissecting aneurysm in one, atherosclerosis of the ascending aorta precluding aortic clamp in one). SLE patients are at greater risk of postoperative morbidity and mortality. Doherty [6] reported that the combined surgical mortality of valvular disease was as high as 25%. In our series, there was one hospital death (12.5%). This patient had been operated on an emergent basis because of acute heart failure with ejection fraction of 26%. After complex operation for ischemic and valvular heart operation, she had mediastinitis and prosthetic valve endocarditis and died of sepsis 2 years after the operation after being transferred to a satellite hospital.

Use of steroids poses surgery with various difficult problems. These include poor wound healing and perioperative steroid withdrawal syndrome. In our unit, the oral prednisolone regimen was continued until the day before the operation and oral prednisolone was restarted on the first or second postoperative day. Intravenous prednisolone was sometimes used as a supplement depending on the postoperative course of each patient. The postoperative dose of oral prednisolone was usually the same as that used preoperatively. Although our perioperative management of the prednisolone was simple, no recurrence of SLE or steroid withdrawal syndrome was observed. There was one case of mediastinitis in a patient who underwent an emergency operation, but there were no wound problems or infections in the other patients, including patients with ITA grafting.

It is a widely held notion that patients with SLE often have vasculitis. In a report by Drenkard et al. [12] vasculitis occurred in 36% of SLE patients and had a cumulative incidence of 41% at 10 years. However, numerous studies have demonstrated the exceptional resistance of the ITA to the atherosclerotic process [9]. In our pathological study, although minor atherosclerotic changes were observed in four ITAs out of six ITA specimens from four patients, there was no arteritis or significant atherosclerosis. Petri et al. [13] reported that changes in prednisolone dosage led to definable changes in risk factors for coronary artery disease, even after adjustment for other variables known to affect these risk factors. In spite of the fact that all of our patients were on a long-term steroid regimen, the ITA appeared to be resistant to atherosclerotic changes. In addition, ITA flow seemed to be adequate intraoperatively, even though graft flows were not measured. Although only the distal parts of the ITA were studied pathologically, the excellent angiographic appearance of the ITA, without stenosis, suggests disease-free ITAs in our series.

There has been no definite answer about which conduit should be used for coronary revascularization in SLE patients. Due to coexisting disease such as diabetes mellitus,
hyperlipidemia and nephropathy in SLE patients, saphenous vein grafts appear to deteriorate early. Although the long-term patency of ITA grafts has been demonstrated in various studies, there is concern about the possibility of arteritis and accelerated atherosclerosis in ITA grafts in SLE patients. In our study, repeat angiography in two patients with ITA grafting showed no signs of newly developed atherosclerosis or arteritis. In spite of significant stenosis, one of the ITA grafts anastomosed to the circumflex artery via the transverse sinus dilated as the disease in the native coronary progressed, as was reported in previous studies [14,15]. This may suggest the physiological adaptability of the RITA and intact vascular smooth muscle [15]. Although the number and the follow-up period are small in our series, the mid-term results seem to be encouraging for ITA use in SLE patients.

Late follow-up studies in three patients at 12, 57 and 64 months, respectively, revealed no newly developed atherosclerosis in the grafts, and no restenosis; of the native coronary artery or ITA after coronary angioplasty. With a combination of CABG and coronary angioplasty, overall prognosis after the operation in SLE patients is good, requiring no repeat CABG. There was no myocardial infarction or other cardiac events: patients showed significant clinical improvement.

5. Conclusions

CABG in SLE patients can be performed with acceptable morbidity and mortality in spite of coexisting complex diseases.

Early studies showed that patency rate of all grafts was 88.9% (16/18) with two stenosed or string-like grafts due to intraoperative technical failures. Follow-up angiography in three patients showed no signs of newly developed atherosclerosis or vasculitis in the grafts, or restenosis of the native coronary artery or the ITA after coronary angioplasty. Although our sample was small, our data so far reveals no evidence to preclude the use of ITA grafts and SVG in SLE patients.

References