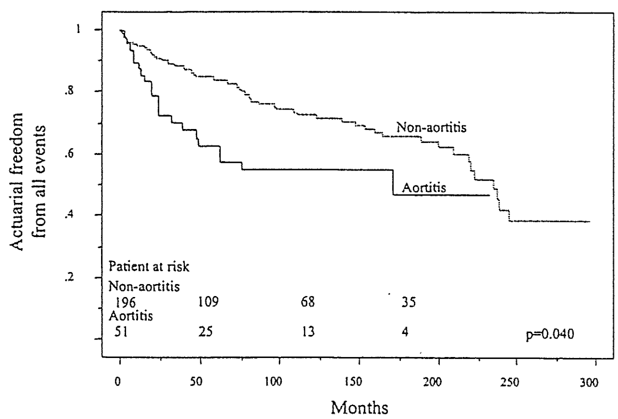

Fig 3. Actuarial freedom from all events including late deaths in aortitis and nonaortitis patients.

60.7% at 5, 10, and 15 years, respectively. The incidence of prosthesis-related complication was significantly high in aortitis patients (Fig 3).

Comment

Several large studies have demonstrated excellent outcomes associated with a CGR with low 30-day mortality rates ranging from 4.3 to 9.0% [2, 3, 7]. The current study documented a comparable result of 9.5% of the in-hospital mortality, even including that of the emergency surgeries. The mortality of elective surgery was 4.3%. Since 1995, no in-hospital death has occurred in 95 elective patients. The increased experience, as well as other factors, such as the development of a refined pump oxygenator system and the myocardial protection technique, the availability of "zero porosity" vascular grafts, and improved perioperative management, has contributed to the improvement of the outcome.

The actuarial survival rate was also comparable with the range of 62% to 93% at 10 years, which were previously published [7–9]. The present results suggest that one of the significant independent risk factors of late death is aortitis, which is predominant in Asian countries. The prevalence of aortitis leading to surgery is high in the current series. Takayasu arteritis was dominant among the 56 patients with the pathology of aortitis. The main pathologic findings associated with Takayasu arteritis are severe destruction of the medial elastic fibers and thickening of intima, media, and adventitia. The pathologic fragility causes frequent detachment of the prosthesis after an aortic valve replacement or CGR [10, 11]. Indeed, in the current study, late graft detachment was observed in 5 of 56 aortitis patients (8.9%). Although the appropriate approach to the aortic valve diseases associated with aortitis is unclear, we prefer a CGR, especially in the active stage, because the graft detachment was less frequent when treated with a CGR than with an isolated aortic valve replacement [10]. Ishikawa and colleagues [12] reported the long-term mortality of the patients having Takayasu arteritis with major complications who require surgical treatment was considerably poor, with only 43% at 15 years [12]. In the present study, the 10-year and 15-year survival rates of aortitis patients were 69% and 58%, respectively. In addition, the incidence of prosthesis-related complications was significantly high in aortitis patients; 5 graft infections (8.9%), 4 cerebral infarctions (7.1%), and 2 coronary arterial obstructions (3.4%). Not only the poor natural history of this subset, but also the frequent need for a reoperation for graft detachment, the life-long steroid therapy, and the high incidence of graft infection can thus influence the poor long-term survival.

Although controversy remains in regard to whether Marfan syndrome decreases the late survival rate [2, 7, 13, 14], the current results suggested that Marfan syndrome was one of the significant predictors of late deaths. The high incidence of an aortic dissection and an aneurysm of the residual aorta, or subsequent operations can potentially increase the late mortality in Marfan patients. In fact, in the current series, the incidence of a reoperation on the residual aorta was significantly higher in Marfan patients (27 patients; 29%) than in non-Marfan patients (5%). In addition, 16 of 27 Marfan patients who required an operation on the residual aorta required a third or fourth operation. The incidence of graft detachment and coronary ostial true aneurysm were significantly high in Marfan patients. To reduce these complications, a direct button technique can be the most favorable technique, especially in Marfan patients. The size of the side hole made in the graft must be reduced to fit the diameter of the coronary artery, and a suture should be placed inside the origin of the coronary artery so that a residual aortic wall can be eliminated [15].

A composite valve graft root is one of the best treatment strategies for an acute type A aortic dissection and aortic regurgitation [16, 17]. In the current study only 25 patients had acute type A aortic dissection. The low prevalence of acute aortic dissection in this study can be explained by the fact that most of patients with acute type A aortic dissection and aortic regurgitation were effectively treated by an aortic valve resuspension and ascending aortic replacement, unless aortic root was pathologically dilated or destroyed by the dissection process. In addition, recently, an aortic valve-sparing operation has been used as an alternative strategy for this condition.

Although recent studies report an excellent early survival rate for a proximal reoperation after a CGR, ranging between 70% and 86% [15, 18, 19], a redo CGR remains a challenging procedure with a high morbidity and mortality, especially in the setting of graft infection. Graft detachment is one of the predominant indications for late reoperation [3, 8, 15, 20–23]. In the present study, graft detachment occurred in 11 patients with Marfan syndrome or aortitis. Extreme caution is necessary for the anastomosis in these patient subsets. The direct button technique is widely utilized and has reduced the rate of reoperation on the ascending aorta or aortic valve after a CGR (0% to 19% at 3 to 10 years) [2, 3, 8, 9, 14, 20]. Since 1985, we have utilized the direct button technique for coronary artery reconstruction and that technique has contributed to reducing the incidence of graft detachment and coronary complications. At present, the direct button technique is our first-line technique. However, if there is anatomic difficulty or dense adhesion precluding the direct button anastomosis, especially in a redo root surgery, the alternative is a short-length graft interposition technique [4]. The current data support the efficacy of the graft interposition technique with nearly the same long-term reliability as the direct button technique. With regard to the proximal anastomosis, the skirted technique has been the current preference. The concept of translocating the prosthetic valve, initially described by Cabrol and colleagues in 1981 [5], was adopted in 1989 to secure the anastomosis without bleeding and to reduce the risk of late graft detachment. In the skirted technique, the prosthetic valve does not apply direct stress on the aortic annulus by separating the suture-line of the prosthetic valve from that of the aortic annulus [24]. Although the current study was not designed to compare the two proximal anastomosis techniques and it was not assumed that the skirted technique would completely surpass the standard technique, the current results demonstrate some advantages of the skirted technique by improving the frequency of late proximal graft detachment and the long-term survival. The results encourage the continued utilization of the skirted technique, especially in patients with a fragile aortic annulus, such as those with aortitis and Marfan syndrome. However, 2 patients experienced proximal graft detachment after a CGR using the skirted technique. One patient had giant cell aortitis and another had Behçet disease. The former underwent a second skirted CGR and repeated graft detachment of the right coronary ostium and was eventually treated with an aortic homograft root replacement. The latter underwent 3 CGR procedures for repeated graft detachment. In patients with a fragile inflammatory aortic pathology, further refinement of the anastomotic technique, such as buttress sutures from the lateral side of the aortic wall for reinforcement of the prosthesis at the aortic annulus, placement of thick belt-like Teflon felt on the lateral side of the aortic wall, is required to reduce late graft detachment [24].

The use of a bioprosthesis is an independent risk factor for a late reoperation. It is obvious that the prosthetic valve dysfunction is an inherent late complication of a bioprosthesis. However, all of the valve failures occurred in use of the Ionescu-Shiley (Shiley Laboratory) bioprosthesis implanted early in the study period. Since 1987, the Carpentier-Edwards bovine pericardial prosthesis has been used and there have been no valve failures. The durability of the manufactured bioprosthesis, especially the pericardial valve, is well-documented [25]. Galla and colleagues [26] also reported excellent long-term performance of bioprosthetic CGR with no instances of valve failure during a 5-year follow-up. A CGR using a bioprosthesis is a useful option for some subsets such as elderly patients, or those who are contraindicated for anticoagulation therapy. Currently, a "Valsalva graft" has been used with a bioprosthetic aortic valve for the long-term valve durability.

The current study has inherent biases. The series of patients examined were derived from a retrospective review covering a long time interval and the patients included in this study had various different surgical indications and were treated by different surgeons.

This report presented the 27-year experience in performing a CGR and concluded that a CGR is a safe and reliable procedure for various aortic root diseases, thus resulting in sufficient early and long-term results. Aortitis is the significant predictor of late death after CGR, with a high incidence of late graft detachment and other complications. The skirted proximal anastomotic technique can help surgeons to avoid late proximal graft detachment and the need to perform a reoperation.

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Patency rate of the internal thoracic artery to the left anterior descending artery bypass is reduced by competitive flow from the concomitant saphenous vein graft in the left coronary artery

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Abstract

Objective: In coronary artery bypass grafting (CABG), insufficient bypass flow can be a cause of occlusion or string sign of the internal thoracic artery (ITA) graft. A patent saphenous vein (SV) graft from the ascending aorta can reduce the blood flow through the ITA graft, and may affect its long-term patency. In the present study, we examined the impact of the patent SV graft to the left coronary artery on the long-term patency of the ITA to left anterior descending (LAD) artery bypass. **Methods:** We reviewed the coronary angiograms of 313 patients who had two bypasses to the left coronary artery including 1 in situ ITA to LAD graft between March 1986 and December 2006. Patients who had occlusion of either bypass grafts to the left coronary artery in the early angiography, were excluded. In 64 patients (20.4%), bilateral ITAs were individually anastomosed to the LAD and the second target branch in the left coronary artery (BITA group), while 249 patients (79.6%) had the ITA to LAD bypass and the SV graft to the second target branch in the left coronary artery (ITA/SV group). The mean follow-up period was 6.8 ± 4.9 years. **Results:** The cumulative patency rate of ITA-LAD bypasses at 10 years was 100% in the BITA group and 81.4% in the ITA/SV group. The ITA to LAD bypass was occluded in 14 (5.6%) patients of the ITA/SV group. In the ITA/SV group, the cumulative graft patency rate of the ITA to LAD bypass in patients who had severe (≥76%) native coronary stenosis between the two anastomotic sites was 98.6% at 5 years, and was significantly higher than that of 82.3% in patients without severe stenosis ($p < 0.0001$). **Conclusions:** Long-term patency of the ITA-LAD bypass was affected by the presence of the patent SV graft to the left coronary artery, particularly when the native coronary stenosis between the two anastomotic sites was not severe. Competitive flow from SV graft could play an important role in occlusion of the in-situ arterial graft.

Keywords: Coronary artery bypass grafting; Internal thoracic artery; Saphenous vein graft; Competitive flow; Graft arrangement

1. Introduction

The utilization of an internal thoracic artery (ITA) in coronary artery bypass grafting (CABG) has decreased the operative mortality without increasing the operative complications [1,2]. The ITA to the left anterior descending artery (LAD) in coronary revascularization has been proven to have a superior long-term patency rate [3], and it improves the long-term mortality and morbidity in patients with coronary artery disease [4–8] as compared to use of vein grafts to the LAD.

On the other hand, a current issue regarding the ITA graft is that competitive flow in the ITA graft causes graft occlusion or 'string sign', which represents the narrowing of the artery along its whole length [9]. In previous reports, competitive flow usually arose when native coronary stenosis was not severe, and the patency rate of the ITA graft inversely correlated with severity of native stenosis [10–12].

Recently, various grafts such as ITA, radial artery, gastroepiploic artery, and saphenous vein (SV) graft are applied and designed in various configurations. There are several reports investigating the hemodynamic features of bypass grafts. Kawasuji and colleagues compared the flow capacities of arterial grafts and SV graft and demonstrated that the flow capacity of the in situ ITA graft which represented diastolic blood pressure, was less than that of SV graft, whose proximal anastomosis was placed on the ascending aorta [13]. When the in situ ITA and the SV graft were connected to the same coronary artery system, the patent SV graft may affect the in situ ITA graft. Such

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interactions between the SV graft and arterial bypass grafts have not yet been delineated.

The purposes of this study are to examine the effects of the graft material, for the circumflex or diagonal branch on the long-term patency of the ITA to LAD graft, and to delineate the interactive effect between the bypass grafts aiming at establishing appropriate usage of the SV graft and strategy for optimal graft arrangement in CABG.

2. Materials and methods

We reviewed the coronary angiograms of 313 patients who underwent CABG with two bypasses to the left coronary artery including one in situ ITA to LAD graft and early postoperative angiography between March 1986 and December 2006. Of these, 263 were male and 50 female with a mean age of 60.9 ± 8.9 years and a mean follow-up period of 6.8 ± 4.9 years. In our institution, early postoperative coronary and graft angiography was routinely performed about 2 weeks after surgery, except for patients with renal insufficiency, severe atherosclerosis in the aorta or aged more than 80 years. Late coronary angiography was done when patients suffered from chest pain or recurrence of angina pectoris was suspected by electrocardiogram or other clinical symptoms. Late coronary angiograms were carried out on 133 patients in this series (42.5%; 133/313). All coronary angiograms were independently evaluated by cardiologists for coronary artery stenosis and graft patency. Stenoses were grouped as 51–75% and 76–100% by a precise measurement of the minimal luminal diameter and labeled as 'moderate' and 'severe', respectively in the present study.

The in situ ITA graft or the SV graft as an aorto-coronary bypass was exclusively used in an individual fashion for these patients. The patients who did not undergo early postoperative angiography, who had graft occlusion in either of two bypass grafts to the left coronary artery in the early angiography, and who had a gastroepiploic artery, radial artery, sequential or composite graft, were excluded from this study. Patients whose bypass graft to the right coronary artery was occluded, but both bypass grafts to the left coronary artery were patent in early angiography, were included. Ninety-three patients had two bypass grafts in the left coronary artery, and 220 patients had two bypass grafts in the left coronary artery and 1 in the right coronary artery. The second target site in the left coronary artery was the left circumflex artery (LCX) in 270 patients and the diagonal branch (Dx) in 43 patients.

Patients were divided into two groups based on the graft selection for the second target site in the left coronary artery. The BITA group comprised 64 patients in whom the bilateral in situ ITAs were individually anastomosed to the LAD and the second target site (Fig. 1). In the ITA/SV group, 249 patients had a single in situ ITA to LAD and the SV graft to the second target site in the left coronary artery (Fig. 2). Characteristics of both groups are shown in Table 1. In addition, the ITA/SV group was divided into two subgroups based on the severity of native left coronary stenosis between two distal anastomotic sites, which was referred from preoperative coronary angiography (Fig. 3). The subgroup S comprised 189 patients who had

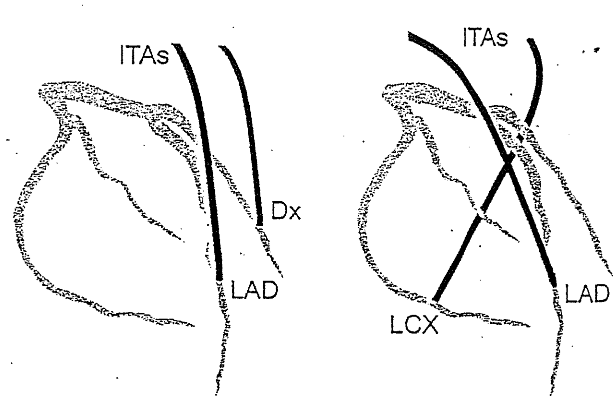

Fig. 1. In the BITA group, bilateral ITAs were individually anastomosed to LAD and the diagonal or circumflex artery. Solid lines indicate the in situ ITA. ITA: internal thoracic artery; LAD: left anterior descending; Dx: diagonal branch; LCX: left circumflex artery.

severe (76–100%) stenosis between two anastomotic sites, while the subgroup M consisted of 60 patients who had moderate (51–75%) or less stenosis between two anastomotic sites. For example, the subgroup S included patients who had severe stenosis at the origin of LAD or circumflex, and the subgroup M included patients with the stenotic lesion localized in the left main trunk.

3. Operative technique

Our current operative technique has been described previously [14]. In brief, our standard technique since 2000 was off-pump CABG without aortic manipulation. Additionally, we preferably use the bilateral in situ ITAs when we place two bypass grafts to relatively large branches in the left coronary artery region in patients without considerable operative risk, such as chronic obstructive pulmonary disease or an advanced age of more than 75 years. A suction-type stabilizer and an apical heart positioner were used for off-pump CABG. The surgical field was maintained by a CO_2 blower and an intracoronary shunt.

Before introduction of an off-pump operation, conventional CABG was performed with ascending aortic and bicaval cannulations. The core temperature was maintained between

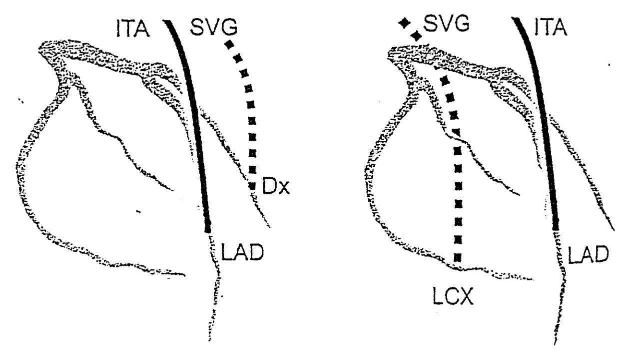

Fig. 2. In the ITA/SV group, an in situ ITA was anastomosed to LAD and the SV graft were anastomosed to Dx or LCX as an aorto-coronary bypass. Solid lines and dash lines indicate ITA and SV graft, respectively. ITA: internal thoracic artery; SV: saphenous vein; LAD: left anterior descending; Dx: diagonal branch; LCX: left circumflex artery.

Table 1
Baseline characteristics in both groups

Characteristics	BITA	ITA/SV	*p* value
Number of patients	64	249	
Age	59.8 ± 8.7	61.2 ± 8.9	0.30
Follow-up period (years)	4.6 ± 4.4	7.3 ± 4.9	<0.0001
Male/female	59 (92%)/5 (8%)	204 (82%)/45 (18%)	0.046
Hypertension	40 (63%)	117 (47%)	0.03
Hyperlipidemia	38 (59%)	126 (52%)	0.34
Diabetes mellitus	30 (47%)	109 (44%)	0.66
LVEF (%)	50.4 ± 12.2	52.8 ± 13.5	0.26
Operative procedure			
On-pump/off-pump	29 (45%)/35 (55%)	248 (99.6%)/1 (0.4%)	<0.0001
Second target branch in the left coronary artery			
Dx/LCX	6 (9%)/58 (91%)	37 (15%)/212 (85%)	0.26
+ Bypass graft to RCA	19 (30%)	201 (81%)	<0.0001

Mean ± standard deviation. LVEF: left ventricular ejection fraction; CABG: coronary artery bypass grafting; LAD: left anterior descending artery; Dx: diagonal branch; LCX: left circumflex artery; ITA: internal thoracic artery; RCA: right coronary artery; SV: saphenous vein.

32 °C and 34 °C. Intermittent tepid blood cardioplegia was infused antegradely and retrogradely.

The ITA was harvested in either conventional (combined with vein and fascia), semiskeletonized (partially combined with vein) or skeletonized fashion [14]. All distal portions of ITA grafts were greater than 1.5 mm in diameter assessed by insertion of a 1.5-mm flexible probe.

4. Long-term patency rate of the ITA to LAD bypass

We analyzed the long-term patency of the ITA to LAD bypass and examined the effects of graft materials anastomosed to the second target site in the left coronary artery and severity of the native coronary stenosis between two distal anastomotic sites.

5. Statistical analysis

The continuous variables are expressed as mean values ± standard deviations and compared between the two groups by using Wilcoxon rank-sum test. The data of two independent groups were compared using Fisher's exact probability test. The Kaplan—Meier method was used to determine the cumulative graft patency rate and log-rank test was used to compare two groups. The differences in the outcomes were considered statistically significant at a probability value of <0.05.

6. Results

The baseline rate of off-pump CABG in the BITA group was significantly higher than that in the ITA/SV group. Male and hypertensive patients were included in the BITA group with a significantly higher rate as compared to the ITA/SV group. On the other hand, the population of CABG with three distal anastomoses was significantly higher in the ITA/SV group than in the BITA group.

In the ITA/SV group, 14 bypass grafts were occluded during the follow-up period (5.6%; 14/249), whereas, all the ITA-LAD bypasses remained patent in the BITA group. The cumulative patency rate of the ITA-LAD bypass in the ITA/SV group was 94.9% at 5 years and 81.4% at 10 years (Fig. 4).

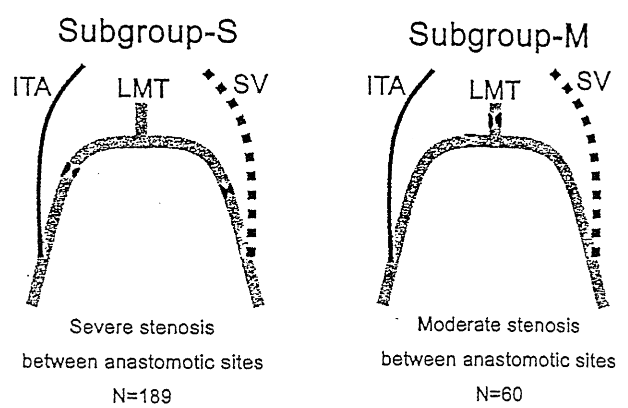

Fig. 3. Patients in the ITA/SV group were divided into two subgroups in regard to severity of the native coronary stenosis between two anastomotic sites (solid line: ITA; dash line: SV graft). ITA: internal thoracic artery; SV: saphenous vein; LMT: left main trunk.

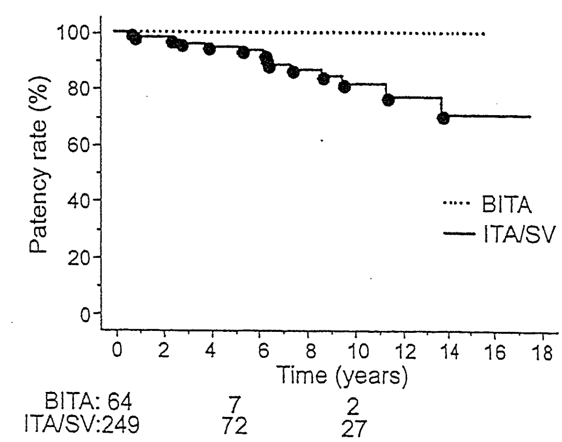

Fig. 4. The cumulative patency rate of the ITA to LAD bypass grafts. The cumulative patency rates at 10 years were 100% in the BITA group and 81.4% in the ITA/SV group. Number at risk is described below the *x*-axis.

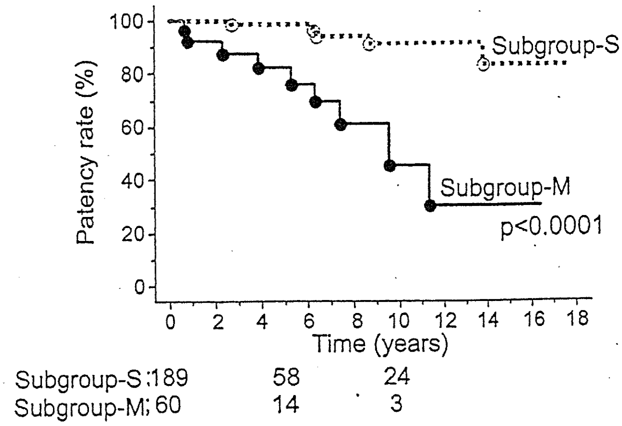

Fig. 5. The cumulative patency of the ITA to LAD bypass grafts. The cumulative patency rates at 10 years were 91.2% in the subgroup S and 45.6% in the subgroup M ($p < 0.0001$). Number at risk is described below the *x*-axis.

In a comparison of two subgroups of the ITA/SV group, the ITA to LAD bypass graft was occluded in five patients of the subgroup S (2.6%; 5/189) and in nine patients of the subgroup M (15%; 9/60). The cumulative patency rate of the ITA to LAD bypass in the subgroup S were 98.6% at 5 years and 91.2% at 10 years, whereas those in the subgroup M were 82.3% at 5 years and 45.6% at 10 years ($p < 0.0001$) (Fig. 5).

The early and late coronary angiograms of 14 patients with occlusions of the ITA to LAD bypass were carefully reviewed. In 4 out of 14 patients, there were no stenoses of the ITA-LAD bypasses in the early angiograms. However, through SV graft injection of the late angiograms, strong bypass flow from SV graft opacified not only the left circumflex artery but also LAD. In addition, the ITA grafts were visualized by retrograde flow and exhibited 'string sign' (Fig. 6).

7. Discussion

Significant differences in hemodynamic characteristics between the ITA graft and the SV graft have been reported.

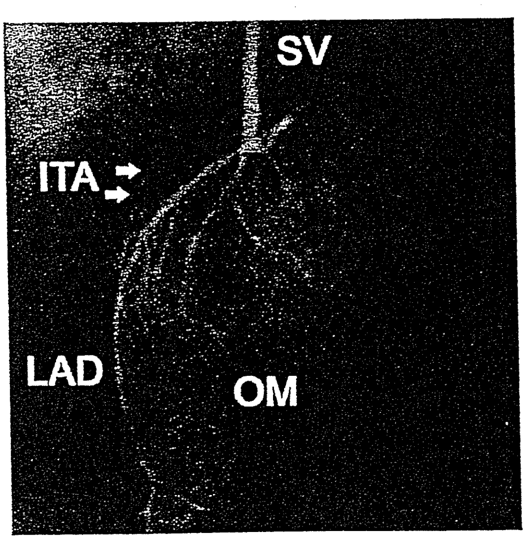

Fig. 6. The distal portion of the ITA graft was visualized by retrograde flow from the SV graft injection (arrows). ITA: internal thoracic artery; SV: saphenous vein; LAD: left anterior descending; OM: obtuse marginal branch.

The SV graft as the aorto-coronary bypass has higher flow capacity than the in situ ITA graft [13] owing to higher blood pressure directly from the ascending aorta and its greater diameter of the SV graft, as compared with those of the in situ ITA graft. Therefore, we presumed that if the patent SV graft to the left coronary artery was present, it might decrease the blood flow in the in situ ITA graft, and diminish its advantage as arterial materials.

In the present study, we attempted to prove the interactive effect between the individual bypass grafts with the different blood source, investigating from a viewpoint of blood flow and patency of arterial grafts. To minimize a bias associated with the bypass grafts and coronary arteries, only patients who had a simple graft arrangement and coronary artery lesions were included. In particular, to eliminate procedural differences, such as on-pump versus off-pump and technical failure, which would be one of the most fundamental biases, patients who had early occlusion of the bypass graft to the left coronary artery were entirely excluded. We focused on the patency of the ITA to LAD bypass, because it is clinically important for survival after CABG.

The results of this study demonstrated that the presence of the patent SV graft anastomosed to the second target site in the left coronary artery reduced the patency rate of the ITA to LAD graft, particularly when the native coronary stenosis between the two distal anastomoses in the left coronary artery was not severe. It was suspected that a mechanism of occlusion of the ITA-LAD bypass was associated with competitive flow from the SV graft by our careful observation of the late coronary angiogram about string of the ITA-LAD bypass.

We previously investigated competitive and reversal flow in sequential and composite arterial grafts, and identified that some specific situations, which were related to two or more coronary branches and arrangement of bypass grafts, significantly increased the incidence of competitive and reversal flow [15]. Moreover, we reported that the graft arrangement with maximized antegrade bypass flow in the arterial grafts played an important role in achieving the advantages of arterial materials and minimizing the incidence of cardiac events after CABG [16]. Since arterial graft occlusion due to insufficient bypass flow mostly occurs within 1 or 2 years [10,16], the long-term prognosis could be jeopardized. We believe that this interactive effect from the SV graft should be avoided as far as possible to achieve the advantage of the arterial graft.

Schmidt and colleagues recommended the use of arterial graft to the second target branch in the left coronary artery because of the superior survival rate [17]. Importance of the circumflex artery over the right coronary artery and inferior patency of the venous graft [18] are considered as primary reasons for the superiority. Results of our study may suggest that interactions of the SV graft on the in situ ITA may be another possible explanation for the superiority of arterial grafting to the second target site in the left coronary artery. We suppose that the use of the SV graft in the right coronary artery region hardly affects the bypass flow in the ITA to LAD graft.

Implications of this study are as follows: patency rate of the ITA to LAD bypass had been believed similar, irrespective of graft arrangement for the second target branch in the left coronary artery. However, the results of this study strongly suggested that the in situ ITA to LAD bypass only, bilateral ITA grafting, sequential grafting and the composite Y graft to the LAD and the second target branch will provide the higher patency rate of the ITA to LAD bypass than the use of the SV graft to the circumflex or diagonal branch, when the stenosis between the two anastomotic sites in the native left coronary artery is moderate or less. Even in patients unsuitable for bilateral ITA harvest, the avoidance of the SV graft from ascending aorta should be considered.

We suggest that, on the contrary, the in situ ITA to LAD bypass concomitant with the aorto-coronary bypass is suitable when the left coronary and circumflex artery is remarkably large or a large mount of bypass flow is required. The isolated ITA to LAD can be a reasonable option of choice in patients with a localized lesion in the left main trunk. For the concomitant diagonal branch, Dion and colleagues reported excellent long-term patency of sequential grafting with the in situ ITA [19]. According to our previous study, when the circumflex artery is almost occluded and the stenosis in LAD is moderate, the composite Y graft is not recommended, because of the high incidence of competitive flow in the ITA to LAD bypass graft [15]. The severity and location of stenoses in the native coronary artery, the size of the target branch, the distance between and positional relationship of the two target sites, quality of the ITA graft, anticipated flow demand and atherosclerosis of the aorta, etc., should be taken into account for decision of strategy for the second target branch in the left coronary artery.

Limitations of the present study are as follows: first, because this study was retrospective and non-randomized, some differences regarding the characteristics of the BITA and ITA/SV groups were noted. Furthermore, the sample size was considered relatively small. However, the influence of these differences on the late angiographic results could be minimized, because early angiography confirmed that all 313 patients had patent grafts to the left coronary artery, and 133 (42.5%) patients underwent late angiography. Since more than 85% of patients after CABG underwent early angiography in our institution between 1986 and 2006, we considered that the selection bias for angiography was not so significant. Second, although the follow-up period was not enough for development of vein graft disease and ischemia in the left coronary artery region, it would be sufficient for examining correlations between the insufficient flow and arterial graft occlusion, as compared with previous studies [10,16]. In addition, progression of native coronary artery disease during the follow-up period, the length and the location of the stenotic lesion, the size of the circumflex coronary artery could not be taken into account. Moreover, peripheral vascular resistance in the myocardial tissue, and flow demands could also have important roles in the coronary perfusion. However, these factors could not be quantified by reliable methods. The effects of diabetes, hypertension, hyperlipidemia, aspirin and statin medical therapy may be the next concern in the future.

It may be controversial in management of 'string sign', which differs from graft occlusion. Several previous reports documented that the ITA graft with string sign could recover its own lumen when the native coronary artery disease became severe [20,21]. In the statistical analyses of this study, graft occlusion probably associated with string sign was not separated from the other graft occlusion. The reasons for this were as following: (1) contrast medium from the ITA injection did not reach LAD, (2) reversibility is not guaranteed for all ITA grafts presenting string sign, (3) the purpose of this study is to delineate the effect of the abundant blood flow from the SV graft, and (4) it is generally accepted that both graft occlusion and string sign are commonly associated with the abundant native coronary flow.

When we use the combination of the in situ arterial and in situ aorta-coronary venous grafts, it would be necessary to pay attention not to place influence on the patency of the important bypass especially created with the in situ ITA graft. This study is not conclusive in nature and is hypothesis generating only. Further investigations for interactive effects and considerations for the appropriate usage of the SV graft are necessary to establish the strategy for graft arrangement.

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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.[1,2] 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.[3] 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 angiograms 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,

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Table 1 Gaft Patency and Medications

Patient no.	Sex	Age (years)	SVG vessel (stenosis)	Graft patency	Other operation (patency)	Medication	Cardiac event
1	F	11	RCA (50%)	O		None	
			LAD (100%)	P			
2	M	16	RCA (SS)	O		Aspirin, carvedilol	Re-CABG
			LAD (SS)	O			
3	M	15	LAD (100%)	P		Aspirin, (coumadin)	Stent implantation, re-CABG
4	M	6	RCA (75%)	P	LITA to LAD (P)	Coumadin, ticlopidine	
					MVR	Carvedilol, valsartan, furosemide	
5	M	12	RCA (100%)	P	LITA to LAD (P)	Dipyridamole	
6	M	2	RCA (SS)	O	LITA to LAD (P)	Aspirin	
			D1 (Seg 5, 75%)	O			
7	M	6	RCA (SS)	O	LITA to LAD (P)	Flurubrofen	
			PL (Seg 11, 50%)	P			
8	M	7	RCA (SS)	O	LITA to LAD (O)	Aspirin, metoprolol	Re-CABG
9	F	20	OM (90%)	P	LITA to LAD (P)	Nitrates	
10	M	5	RCA (SS)	O	LITA to LAD (P)	Aspirin, carvedilol, enalapril	VT
			LCX (SS)	O			
11	M	5	RCA (4PD) (100%)	O	LITA to LAD (P)	Aspirin	
12	M	19	RCA (4PD) (100%)	P	RITA to LAD (P)	Aspirin	
			PL1 (100%)	P	LITA to D1 (P)		
			PL2 (100%)	P			
13	M	11	D1 (100%)	P	LITA to LAD (O)	Aspirin	
					GEA to 4PD (P)		

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.

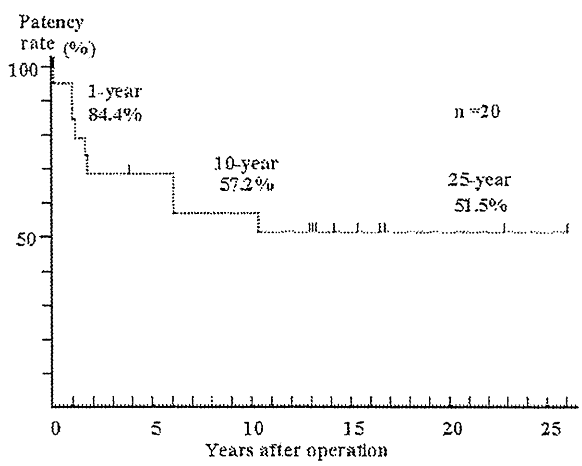

Fig 1. Patency rates of saphenous vein grafts.

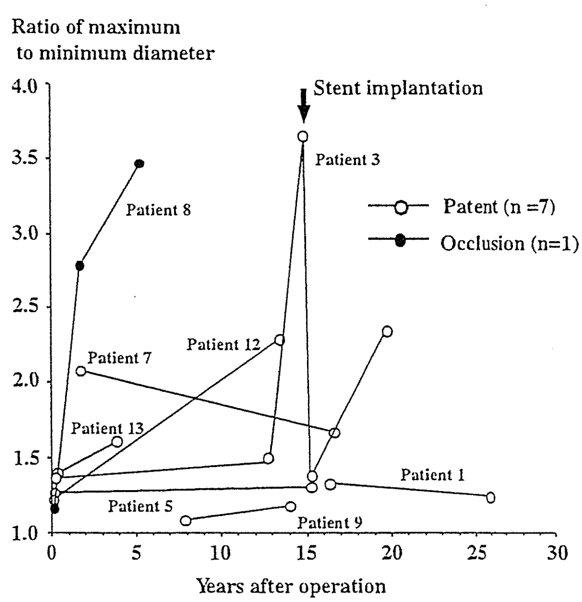

Fig 2. Changes in the ratio of the maximum to minimum diameter in saphenous vein grafts in the late period.

smoking, hyperlipidemia, diabetes, and hypertension. Graft patency rates were analyzed by the Kaplan-Meier method, and differences were assessed by the Cox-Mantel test. The mean values are shown as mean ± SD, and the unpaired t-test was used to compare the differences between groups.

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) (**Fig 1**). 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 on serial postoperative angiograms is shown in **Fig 2**. The 8th patient had an occluded graft 10 years after operation. He had undergone CABG to the RCA

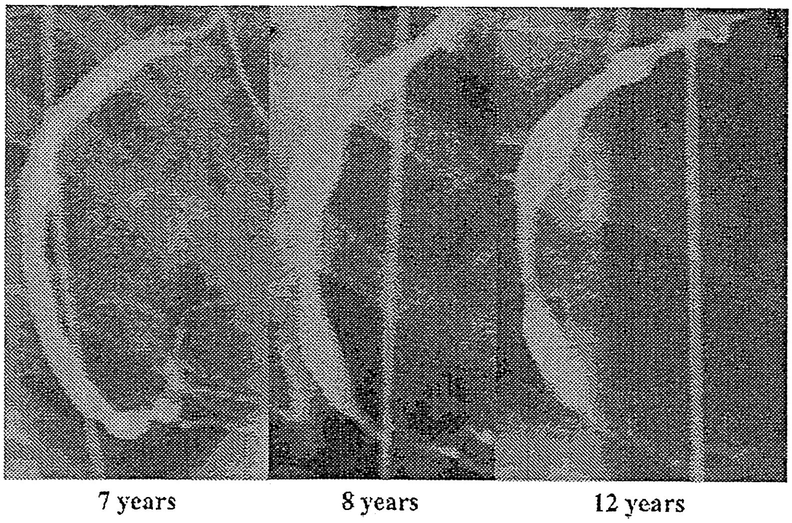

Fig 3. Serial angiograms of saphenous vein graft in the 8th patient. **(Left)** 7 years. **(Middle)** 8 years. **(Right)** 12 years. The ratio at 1 month, 1 year, and 5 years after operation was 1.2, 2.8, and 3.5, respectively.

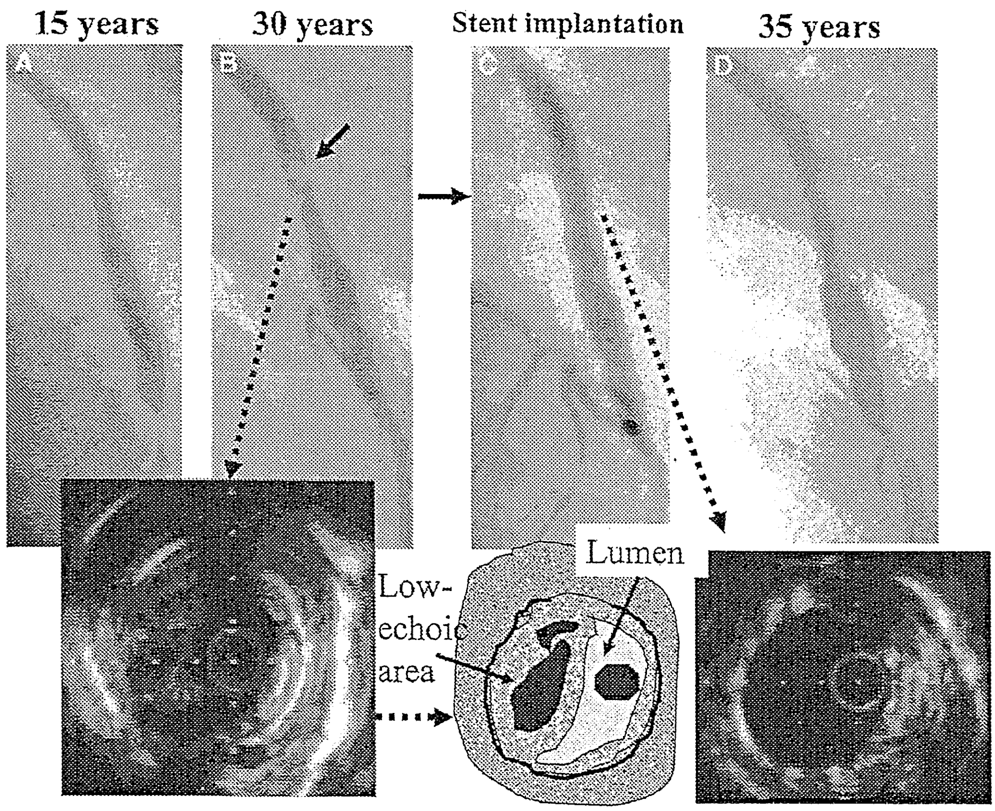

Fig 4. Serial angiograms of saphenous vein graft (SVG) in the 3rd patient. (A) One month after operation. The ratio of the maximum to minimum diameter of the SVG was 1.5. (B) Fifteen years after operation. Angiogram shows SVG stenosis with filling defect. On intravascular ultrasound imaging, the low echoic area is suspected to be a lipid plaque, seen as a filling defect on angiography. The ratio of the maximum to minimum diameter of the SVG was 3.6. (C) After stent implantation. The ratio of the maximum to minimum diameter was 1.4. (D) Five years after stent implantation, the ratio of maximum to minimum diameter was 2.4.

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**).[4] 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

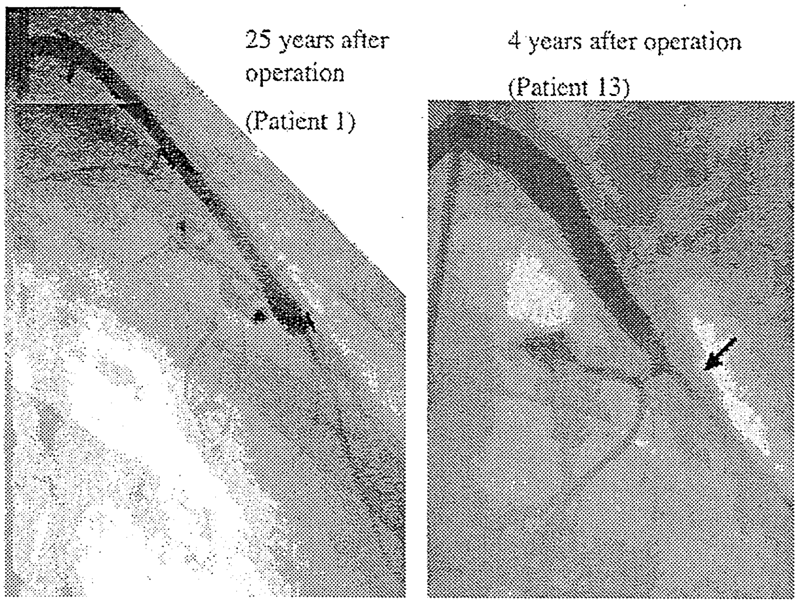

Fig 5. Angiograms of saphenous vein grafts. (Left) The 1st patient. The wall of the graft in this 36-year-old woman is smooth at 25 years after operation. (Right) The 13th patient. Angiogram at 4 years after operation in this 15 year-old boy with a saphenous vein graft shows distortion of the coronary artery secondary to growth.

after stent implantation chest pain on effort reoccurred and although the SVG was patent, CAG revealed 99% stenosis of the left circumflex rtery. 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 ≥40% 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 wa 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 adults,[5] 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 adults.[6] 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.[7,8] In our study, operation at a younger age were 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 SVGs.[9] 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.[5–7] 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 adults.[10] 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 years.[9–12] 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 angioscopy.[12] 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.[9–12] 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.[4,13] 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.[14]

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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Evolving Selective Cerebral Perfusion for Aortic Arch Replacement: High Flow Rate With Moderate Hypothermic Circulatory Arrest

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Background. Although hypothermic circulatory arrest (HCA) combined with selective cerebral perfusion (SCP) is a safe strategy for aortic arch surgery, neither the optimal temperature of hypothermia nor the optimal SCP flow rate has been clearly determined. We have since 2002 gradually elevated the temperature of HCA from 20°C to 28°C for aortic arch surgery. This study explored the impact of different temperatures during HCA with SCP on neurologic complications.

Methods. Since January 2002, 229 patients have undergone aortic arch replacement (mean age, 70.8 ± 9.7 years; 156 male) with HCA and SCP through median sternotomy in our institution. Eighty-one patients were cooled to 20°C (group A), 81 were cooled to 25°C (group B), and 67 were cooled to 28°C (group C). The brachiocephalic and left common carotid arteries were perfused separately during SCP in all cases. The left subclavian artery was additionally perfused in group C. Twenty-two operations in group A, 17 in group B, and 6 in group C were performed emergently ($p = 0.58$). The SCP flow rate was maintained at approximately 10 $mL \cdot kg^{-1} \cdot min^{-1}$ in groups A and B and approximately 15 $mL \cdot kg^{-1} \cdot min^{-1}$ in group C to keep blood pressure in the temporal artery at approximately 60 mm Hg.

Results. The early mortality rate was 3.7% (3 of 81) in group A, 0% in group B, and 1.5% (1 of 67) in group C ($p = 0.19$). Postoperative stroke occurred in 2 patients (2.5%) in group A, in 3 (3.7%) in group B, and in 4 (6.0%) in group C ($p = 0.55$). Postoperative transient neurologic dysfunction occurred in 7 patients (8.6%) in group A, in 9 patients (11.1%) in group B, and in 4 patients (6.0%) in group C ($p = 0.54$). No patients in any group had postoperative paraplegia. The mean durations of circulatory arrest were 64 ± 21 minutes in group A, 49 ± 14 minutes in group B, and 46 ± 13 minutes in group C ($p < 0.0001$). The mean durations of SCP were 145 ± 67 minutes in group A, 116 ± 48 minutes in group B, and 111 ± 61 minutes in group C ($p = 0.0007$). Mean SCP flow rates were 8.8 ± 1.9 $mL \cdot kg^{-1} \cdot min^{-1}$ in group A, 10.5 ± 3.1 $mL \cdot kg^{-1} \cdot min^{-1}$ in group B, and 19.0 ± 4.2 $mL \cdot kg^{-1} \cdot min^{-1}$ in group C ($p < 0.0001$).

Conclusions. The rate of postoperative neurologic events did not increase with use of higher temperature. The temperature during HCA could be safely increased to 28°C with high SCP flow rate. Use of moderate HCA with SCP during aortic arch replacement permits radical reconstruction of the aortic arch and can avoid the need for deep hypothermia.

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Neurologic events are among the most devastating complications of aortic surgery. Although use of adjunctive techniques such as antegrade selective cerebral perfusion (SCP) or retrograde cerebral perfusion (RCP) have yielded better results in many studies [1], the basic method of neurologic protection during aortic surgery is still hypothermic circulatory arrest (HCA). Deep hypothermia is required when prolonged periods of possible brain ischemia are anticipated [2], and in such cases, body temperature has been lowered to near 20°C. However, because deep hypothermia is associated with an increased risk of bleeding and increased rate of blood transfusion, many institutions have recently attempted to elevate body temperature [3–7].

Although HCA combined with SCP is a safe strategy for aortic arch surgery, neither the optimal temperature of hypothermia nor the optimal SCP flow rate has been clearly determined. We have since 2002 gradually elevated the temperature of HCA from 20°C to 28°C for aortic arch surgery. This study explored the impact of different temperatures during HCA with SCP on neurologic complications.

Patients and Methods

Patients

From January 2002 to February 2005, 229 patients underwent aortic arch replacement (mean age, 70.8 ± 9.7 years;

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Table 1. Patient Demographics

	Group A (n = 81)	Group B (n = 81)	Group C (n = 67)	*p* Value
Emergency	22 (27.2%)	17 (21.0%)	12 (17.9%)	0.20
Dissection	19 (23.5%)	24 (29.6%)	13 (19.4%)	0.34
Total arch replacement	73 (90.1%)	66 (81.5%)	46 (68.7%)	0.04

156 male) with HCA and SCP through median sternotomy in our institution. One hundred seventy-eight patients with chronic lesions underwent elective surgery, and 51 underwent emergent surgery. The reason for emergency surgery was acute aortic dissection in 39 patients and rupture of chronic aneurysm in 12 patients. One hundred eighty-five patients underwent total arch replacement, and 44 underwent hemiarch replacement. Eighty-one patients were cooled to 20°C (group A), 81 patients to 25°C (group B), and 67 patients to 28°C (group C). Mean age was 70.8 ± 9.7 years in group A, 71.1 ± 8.4 years in group B, and 70.4 ± 11.3 years in group C. Table 1 shows demographic data of the population, and Table 2 shows preoperative morbidity of the population. Our institution approved this retrospective study and waived patient consent on the condition that patients are not identified.

Operative Techniques

The skin incision extended from the suprasternal notch to a point equidistant from the xiphoid process and umbilicus. A left hemicollar incision was added to improve exposure of the branches of the aortic arch. All operative maneuvers were performed through a median sternotomy.

The femoral artery or ascending aorta was used as a site of cannulation for arterial return. Ascending cannulation is preferable when atherosclerotic change in the ascending aorta is minimal on epiaortic echography, although femoral arterial cannulation is opted for when the ascending aorta has severe atherosclerotic changes or there is acute aortic dissection. Additional cannulation into the right axillary artery was performed in most cases (97.8%) [8, 9]. The patients were cooled using the α-stat method of pH control until nasopharyngeal temperature reached 20°C (group A), 25°C (group B), or 28°C (group C). Reperfusion and rewarming were always performed in antegrade fashion through the side branch of the graft. A collagen woven or gelatin-impregnated knitted Dacron (C.R. Bard, Haverhill, Pennsylvania) graft was used for graft replacement. One branched graft was used for hemiarch replacement, and a quadrifurcated graft was used for total arch replacement. When total arch replacement was performed, arch vessels were independently reconstructed using a quadrifurcated graft without the en-bloc repair technique.

Open distal anastomosis was performed in all cases. The anastomosis was always performed with complete transection of the descending aorta distal to the left subclavian artery for total arch replacement, and with complete transection of the aortic arch for hemiarch replacement. Stepwise technique was employed for distal anastomosis in most cases of total arch replacement [10]. A short graft was introduced into the lumen of the descending aorta from the stump, and then sewn to the aortic wall with running 3-0 or 4-0 polypropylene suture. The short graft was then pulled out of the descending aorta. At the suture line, the graft was inverted circumferentially and fixed to the aortic wall in appropriate fashion. This suture line may in rare cases bleed, although if bleeding occurs, it is easily stopped with an additional stitch. Finally, the quadrifurcated graft was anastomosed to the short graft with running 3-0 polypropylene suture. That was followed by anastomosis of the left subclavian artery, proximal anastomosis to the ascending aorta, reconstruction of the left internal carotid artery, and final anastomosis of the brachiocephalic artery. Rewarming was commenced after the reconstruction of the left subclavian artery.

Selective cerebral perfusion was performed with an ordinary arterial cannula in the right axillary artery or with a balloon-tip cannula inserted directly into the brachiocephalic artery from inside the aortic arch and into the left common carotid artery. The left subclavian artery was clamped in groups A and B, and was perfused with a balloon-tip cannula in group C. Selective cerebral perfusion was continued until all branches of arch were reconstructed. Cerebral perfusion was regulated to maintain the mean pressure in the superficial temporal arteries at 60 mm Hg. Monitoring of the perfusion pressure in the bilateral superficial temporal arteries was performed using standard methods in most cases. However, perfusion pressure measured at the top of the perfusion balloon was used when the temporal arteries were not available.

For reinforcement of the stump of the aorta in cases of acute aortic dissection, gelatin-resorcin-formaldehyde (GRF) glue or Bioglue Surgical Adhesive (CryoLife, Kennesaw, Georgia) was applied to obliterate the false lumen

Table 2. Preoperative Morbidity

Preoperative History	Group A (n = 81)	Group B (n = 81)	Group C (n = 67)	*p* Value
Cerebrovascular disease (%)	19.2	12.5	14.9	0.50
Coronary artery disease (%)	26.9	23.8	22.4	0.81
COPD (%)	10.3	5.0	4.5	0.29
Hypertension (%)	92.4	87.7	83.6	0.26
Diabetes mellitus (%)	5.1	10.0	10.4	0.43
Gout (%)	1.3	6.3	9.0	0.11
Smoking (%)	47.4	45.0	40.3	0.68
Hyperlipidemia (%)	10.3	16.3	22.4	0.13

COPD = chronic obstructive pulmonary disease.

Table 3. Preoperative Morbidity of Elective Total Arch Replacement Without Concomitant Procedures

Preoperative History	Group A	Group B	Group C	*p* Value
Cerebrovascular disease (%)	24.3	15.9	15.2	0.53
Coronary artery disease (%)	10.8	15.9	24.2	0.32
COPD (%)	16.2	6.8	9.1	0.37
Hypertension (%)	91.9	90.9	90.9	0.99
Diabetes mellitus (%)	5.4	15.9	9.1	0.29
Gout (%)	0	9.1	12.1	0.11
Smoking (%)	43.2	47.7	60.6	0.32
Hyperlipidemia (%)	8.1	22.7	30.3	0.06

COPD = chronic obstructive pulmonary disease.

in most cases. In addition to usage of chemical glue, all stumps were reinforced with Teflon (Impra, subsidiary of L.R. Bard, Tempe, Arizona) felt strips. For total arch replacement, Teflon felt strips were placed on the outer side of aortic stump, and a graft 5 to 7 cm in length and 18 to 22 mm in diameter was inserted into the true lumen of the descending aorta as an elephant trunk. They were sutured and fixed with running 5-0 polypropylene suture, obliterating the false lumen in sandwichlike fashion. The quadrifurcated graft was anastomosed to the stump of the descending aorta, where sandwichlike reinforcement was applied. For hemiarch replacement, Teflon felt strips were placed on the outer and inner sides of the aortic stump. The stump was thus reinforced and the false lumen obliterated in sandwichlike fashion with running 5-0 polypropylene suture.

Concomitant Procedures

Concomitant procedures included aortic valve resuspension in 16 patients, aortic valve replacement in 13, aortic root replacement in 8, mitral valve operations in 5, and coronary artery grafting in 33 patients.

Definitions

Early mortality was defined as death within the hospital. Postoperative stroke was defined as newly developing neurologic deficit, with confirmation by computed tomography. Transient neurologic dysfunction was defined as postoperative confusion, agitation, delirium, or prolonged obtundation with a negative brain computed tomography scan and complete resolution before discharge. The neurologic diagnosis was made by neurologists.

Statistical Analysis

Values are the mean ± SD. Data were analyzed using the χ^2 test for categorical variables, and continuous variables were examined with analysis of variance (ANOVA).

Results

The early mortality rate was 3.7% (3 of 81) in group A, 0% in group B, and 1.5% (1 of 67) in group C ($p = 0.19$). All 3 patients in group A who had early death had undergone emergent surgery for acute aortic dissection. The patient in group C had mega-aortic syndrome and underwent two-stage operation. He successfully underwent the first aortic arch operation, but died of multiorgan failure after the second operation for thoracoabdominal aortic aneurysm performed a few weeks after the first operation. Postoperative stroke occurred in 2 patients (2.5%) in group A, 3 patients (3.7%) in group B, and 4 patients (6.0%) in group C ($p = 0.55$). Of the 9 patients who had a postoperative stroke, 6 underwent emergent surgery. Seven patients (8.6%) had postoperative transient neurologic dysfunction in group A, 9 (11.1%) in group B, and 4 (6.0%) in group C ($p = 0.54$). No patients had postoperative paraplegia in any group. Postoperative recurrent laryngeal nerve palsy occurred in 8 patients (9.9%) in group A, 4 (4.9%) in group B, and 2 (3.0%) in group C ($p = 0.19$). No patient had chylothorax in group A and B, but 3 did in group C ($p = 0.03$).

The mean durations of cardiopulmonary bypass were 234 ± 116 minutes in group A, 202 ± 64 minutes in group

Table 4. Operative Variables

Variables	Group A	Group B	Group C	*p* Value
Cardiopulmonary bypass (min)	195 ± 41	197 ± 54	194 ± 50	0.97
Circulatory arrest (min)	67 ± 16	55 ± 12	51 ± 9	<0.0001
SCP (min)	133 ± 41	126 ± 28	131 ± 30	0.69
SCP flow ($mL \cdot kg^{-1} \cdot min^{-1}$)	9.1 ± 1.8	10.9 ± 3.3	19.0 ± 4.2	<0.001
Cooling (min)	27 ± 7	31 ± 10	36 ± 2	<0.001
Rewarming (min)	162 ± 38	147 ± 50	108 ± 42	<0.0001
Lowest blood temperature (°C)	16.0 ± 3.2	21.6 ± 2.7	25.9 ± 1.3	<0.0001
Transfusion (mL)	2430 ± 2270	3200 ± 2600	3160 ± 3300	0.39
Platelet transfusion (%)	45.9	63.6	33.3	0.028
Blood temperature at ICU admission (°C)	35.6 ± 0.8	36.1 ± 0.7	36.3 ± 0.7	0.0006
Lactate at ICU admission (mmol/L)	3.4 ± 1.7	2.7 ± 1.0	2.7 ± 1.1	0.026

ICU = intensive care unit; SCP = selective cerebral perfusion.

B, and 206 ± 61 minutes in group C ($p < 0.03$). The mean durations of circulatory arrest were 64 ± 21 minutes in group A, 49 ± 14 minutes in group B, and 46 ± 13 minutes in group C ($p < 0.0001$). The mean durations of SCP were 145 ± 67 minutes in group A, 116 ± 48 minutes in group B, and 111 ± 61 minutes in group C ($p = 0.0007$). Mean SCP flow rate was 8.8 ± 1.9 $mL \cdot kg^{-1} \cdot min^{-1}$ in group A, 10.5 ± 3.1 $mL \cdot kg^{-1} \cdot min^{-1}$ in group B, and 19.0 ± 4.2 $mL \cdot kg^{-1} \cdot min^{-1}$ in group C ($p < 0.0001$). Transfusion volume was 3,689 ± 4,200 mL in group A, 4,050 ± 3,322 mL in group B, and 3,643 ± 3,159 mL in group C ($p = 0.74$). The rates of requirement of platelet transfusion were 63.0% in group A, 67.9% in group B, and 46.3% in group C ($p = 0.0066$). Lactate levels at admission to the intensive care unit after surgery were 3.9 ± 2.3 mmol/L in group A, 3.1 ± 1.5 mmol/L in group B, and 3.0 ± 1.5 mmol/L in group C ($p = 0.007$).

To clearly determine the impact of SCP with HCA, the subset of patients who underwent elective total arch replacement for chronic aortic pathology without concomitant surgery was examined. This population consisted of 37 patients in group A, 44 in group B, and 33 in group C. Table 3 shows preoperative morbidity in this subset. No significant differences among groups were found in this subset for any of the factors examined. The early mortality rate was 0% in group A (0 of 37 patients), 0% in group B (0 of 44), and 3.0% (1 of 33) in group C ($p = 0.29$). The patient in group C was the one with mega-aortic syndrome described above. One patient (2.7%) had a postoperative stroke in group A, 0 in group B, and 1 (3.0%) in group C ($p = 0.52$). Postoperative transient neurologic dysfunction occurred in 5 patients (13.5%) in group A, 4 (9.1%) in group B, and 0 in group C ($p = 0.10$). Table 4 shows the other results.

Comment

Regulation of flow to the brain during SCP should be performed to keep the perfusion pressure within the range allowing cerebral autoregulation to preclude cerebral ischemia or hyperperfusion [11]. Kazui and colleagues [12] reported their methods with SCP in 1992 that included cooling of rectal temperature to 20° to 22°C with a selective cerebral flow rate of 10 $mL \cdot kg^{-1} \cdot min^{-1}$. Cerebral perfusion pressure was adjusted by monitoring the right radial artery pressure, which was maintained at 60 to 80 mm Hg. Selective cerebral perfusion flow rates used clinically have been based on the results of their experimental study [13], and perfusion pressure is thought to be more important than flow rate for brain protection. Autoregulation of the cerebral circulation maintains relatively constant cerebral blood flow within a range of perfusion pressures. The constancy of cerebral blood flow is achieved by dilatation or constriction of cerebral resistance vessels in response to changes in perfusion pressure.

Henriksen and colleagues [14] reported that perfusion pressure less than 55 mm Hg was significantly correlated with a decrease in cerebral blood flow, indicating that cerebral autoregulation was lost below this level. This conclusion is widely accepted in the performance of aortic arch surgery. Although the flow was around 10 $mL \cdot kg^{-1} \cdot min^{-1}$ in groups A and B, the selective cerebral flow rate was increased to 19.0 $mL \cdot kg^{-1} \cdot min^{-1}$ in group C to keep the perfusion pressure near 60 mm Hg in the present study. This flow rate was almost twice that in groups A and B. The rate of postoperative neurologic complications was not affected by this high rate of SCP flow.

Our findings suggest that use of SCP has a sound physiologic basis at predetermined target perfusion pressures rather than fixed flow rates. There may be two principal reasons for the need for this high rate of flow. One is the increase in metabolic demand on the brain with warmer temperature. It is possible that vascular resistance changes to meet metabolic demands of the brain, with higher flow rate required to meet this demand. Another possible reason is increase in collateral circulation from the axillary and subclavian arteries, which connect to the systemic circulation. The vascular tone of the branches of the arteries may be decreased at higher temperature, leading to higher blood flow. Although several groups also using moderate hypothermia with SCP reported SCP flow rates different from our own, they perfuse the brain directly using only arch vessels. Touati and colleagues [15] reported totally normothermic aortic arch replacement without circulatory arrest. Their cerebral pump flow rates to maintain the right radial artery pressure at 70 mm Hg or more varied from 680 mL/min to 1,100 mL/min, which are flow rates not as high as ours. Jacobs and colleagues [6] used a higher SCP flow rate of 15 $mL \cdot kg^{-1} \cdot min^{-1}$ when performing elective aortic arch operations under moderate hypothermic circulatory arrest.

Another concern is spinal ischemia when circulatory arrest with moderate hypothermia is employed. Despite the accumulation of findings on circulation in the vertebral spine, no method yet exists to completely prevent spinal ischemia. Although we started the third cannulation at the left subclavian artery for SCP, expecting an increase in blood perfusion in spinal cord when we raised the temperature, we in fact observed spurting of blood from numerous intercostal arteries inside the descending aorta when a high SCP flow rate was applied in group C. Although the origin of this backflow from the intercostal arteries is unknown, it may be the bilateral internal mammary arteries. The internal mammary arteries are connected to the subclavian arteries, which are perfused with high flow. The vertebral artery, which connects to the subclavian artery, is another important source of flow to the anterior cerebral artery. The safe duration of circulatory arrest at 28 °C for prevention of spinal ischemia has yet to be determined. However, the high flow rate of SCP might contribute to sufficient perfusion of the spinal cord and prevent spinal ischemia during circulatory arrest at this temperature. In group C, several patients were restarted at lower body perfusion using femoral artery cannulation, because of concerns related to spinal ischemia. We believe that this maneuver significantly shortened HCA in group C.

In conclusion, use of SCP appears to have a sound physiologic basis at predetermined target perfusion pressures rather than fixed flow rates under autoregulation of cerebral blood flow. The temperature during HCA could be raised to 28°C safely with high SCP flow rate. The rate of postoperative neurologic events was not increased with higher temperature under HCA with SCP. No spinal ischemia was observed. Use of moderate HCA with SCP during aortic arch replacement permits radical reconstruction of the aortic arch and can avoid the need for deep hypothermia.

Study Limitations

This study was performed using a retrospective nonrandomized design in the clinical setting of aortic arch surgery. The conclusions obtained from the observations performed on the three nonrandomized groups may, therefore, represent a source of bias in the comparisons. To overcome the limitations, a prospective randomized study should be performed.

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Efficacy and Safety of Sotalol for Refractory Tachyarrhythmias in Congenital Heart Disease

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