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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

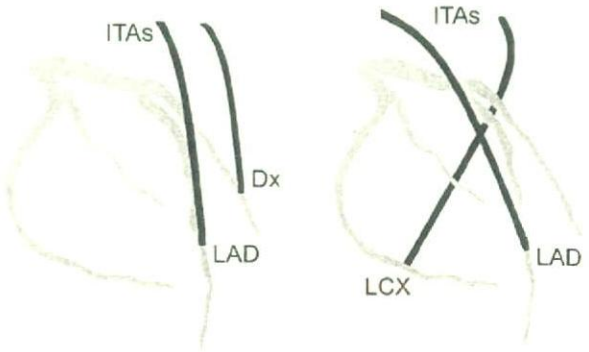

Fig. 1. In the BITA group, bilateral ITAs were individually anastomosed to LAD and the diagonal or circumflex artery. Solid lines indicate the in situ ITA. ITA: internal thoracic artery; LAD: left anterior descending; Dx: diagonal branch; LCX: left circumflex artery.

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

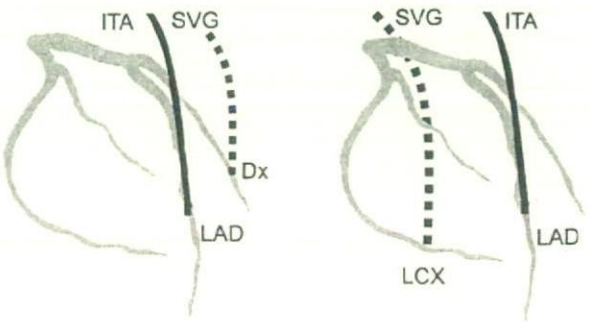

Fig. 2. In the ITA/SV group, an in situ ITA was anastomosed to LAD and the SV graft were anastomosed to Dx or LCX as an aorto-coronary bypass. Solid lines and dash lines indicate ITA and SV graft, respectively. ITA: internal thoracic artery; SV: saphenous vein; LAD: left anterior descending; Dx: diagonal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

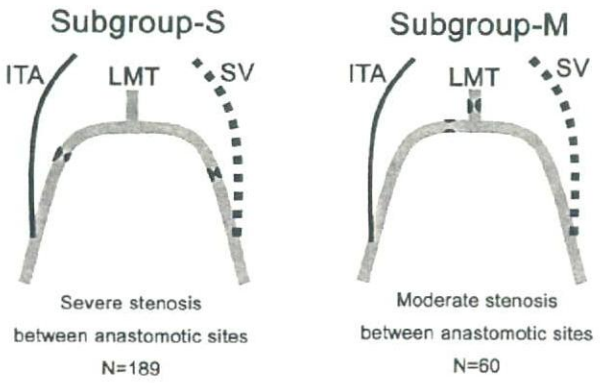

Fig. 3. Patients in the ITA/SV group were divided into two subgroups in regard to severity of the native coronary stenosis between two anastomotic sites (solid line: ITA; dash line: SV graft). ITA: internal thoracic artery; SV: saphenous vein; LMT: left main trunk.

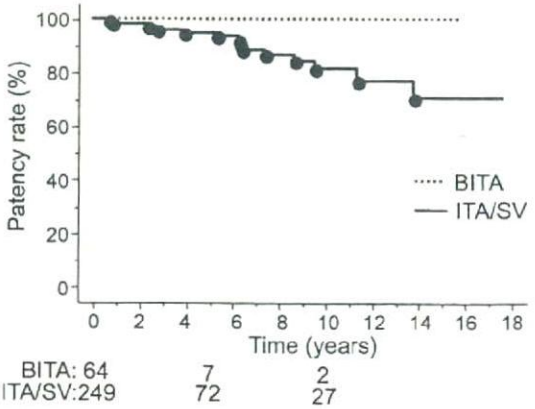

Fig. 4. The cumulative patency rate of the ITA to LAD bypass grafts. The cumulative patency rates at 10 years were 100% in the BITA group and 81.4% in the ITA/SV group. Number at risk is described below the x-axis.

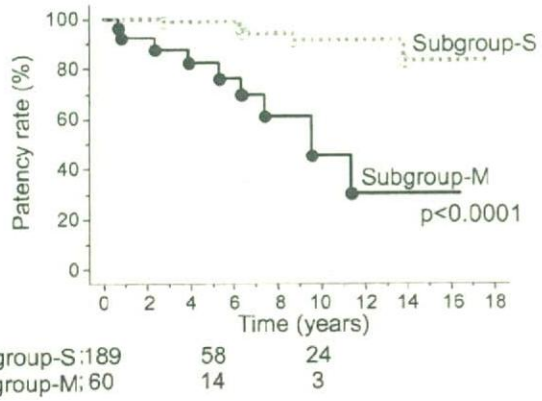

Fig. 5. The cumulative patency of the ITA to LAD bypass grafts. The cumulative patency rates at 10 years were 91.2% in the subgroup S and 45.6% in the subgroup M ($p < 0.0001$). Number at risk is described below the x-axis.

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.

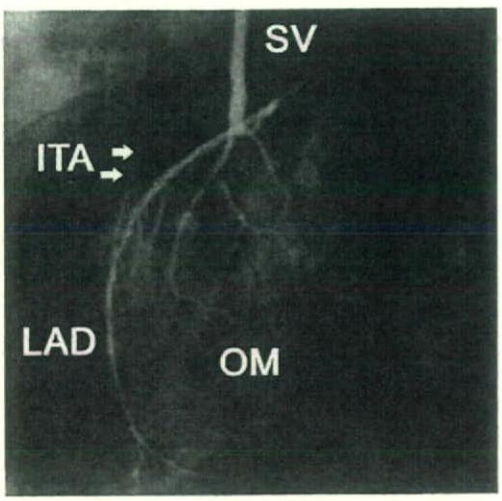

Fig. 6. The distal portion of the ITA graft was visualized by retrograde flow from the SV graft injection (arrows). ITA: internal thoracic artery; SV: saphenous vein; LAD: left anterior descending; OM: obtuse marginal branch.

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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Which Factors Predict the Recovery of Natural Heart Function After Insertion of a Left Ventricular Assist System?

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Which Factors Predict the Recovery of Natural Heart Function After Insertion of a Left Ventricular Assist System?

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Background: Recent reports have demonstrated that use of a left ventricular assist system (LVAS) can initiate recovery of cardiac function, and subsequent weaning from the LVAS has attracted considerable interest. In this study we investigated reliable predictors of LVAS weaning.

Methods: Eighty-two patients underwent LVAS implantation between April 1994 and July 2006 at our institution. Cardiac function was restored in 8 patients, who were weaned from LVAS after a mean of 5 months (Group R). Thirty-three patients remained on LVAS support for >1 year (Group N) because natural heart function did not show adequate improvement. We retrospectively evaluated the differences between these two groups. Group R was younger, and had a shorter duration of heart failure than Group N (23.4 vs 36.7 years and 13.3 vs 56.1 months, $p < 0.01$, respectively). Pathologic findings showed that the interstitial fibrosis score was lower in Group R ($p < 0.01$). Three months after LVAS insertion, B-type natriuretic peptide (BNP) and fractional shortening (FS) were more favorable (66.6 ± 46 vs 264.5 ± 170 pg/ml, $p < 0.01$, and 23 ± 17.1 vs 12 ± 9.1%, $p < 0.05$, respectively) in Group R. Furthermore, Group R received a higher dose of β-blocker (15.4 ± 8.4 vs 5.8 ± 3.9 mg, $p < 0.05$).

Conclusions: Younger age, shorter history of heart failure, and less interstitial fibrosis were effective predictors of weaning from LVAS. Restoration of natural heart function was more rapid and more persistent in candidates for LVAS explantation, and presence of β-blocker played a prominent role in improving cardiac function after LVAS implantation. J Heart Lung Transplant 2008;27:869-74. Copyright © 2008 by the International Society for Heart and Lung Transplantation.

The left ventricular assist system (LVAS) is a powerful tool for saving patients with end-stage heart failure. The primary objective of this device is to provide sufficient circulation, to help patients recover from secondary organ dysfunction, and to stabilize them until their own heart function recovers or suitable donor organs are found. However, relatively few patients receive the benefit of heart transplantation, especially in Japan, due to a shortage of donor organs. In a previous study, we have described the possibility of natural heart recovery after profound heart failure using long-term LVAS support.[1] Several recent reports have demonstrated the restoration of native cardiac function during LVAS support, and weaning from LVAS is recognized as a desirable option. Several factors are associated with improvement of natural heart function after LVAS implantation. Levin et al reported reverse remodeling with a decreased LV mass in LVAS-supported patients.[2] Reduced cellular edema,[3] improved myocardial metabolism,[4] reversal of neurohumoral stimulation[5] and decreased apoptosis[6] have also been suggested. Assessment of myocardial recovery during LVAS support is also an area of interest.[7] However, it remains unclear which patients are appropriate candidates for LVAS explantation. In this study we investigated the factors that could predict weaning from LVAS.

METHODS

Patient Population

Between April 1994 and July 2006, 82 patients except post-cardiotomy cases underwent LVAS implantation for end-stage heart failure at our institution. All patients had New York Heart Association Class IV status and were supported by intravenous inotropic agents and/or percutaneous mechanical support. Among these patients, natural heart function was restored and general condition was sufficiently stable in 8 patients (ages 17

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to 38 years, 7 males and 1 female; 7 with dilated cardiomyopathy [DCM], 1 with myocarditis) and they were weaned from LVAS after 89 to 310 days (recovery group: Group R). Thirty-three patients were supported by LVAS for >1 year. They remained generally stable, but they could not be weaned from LVAS because of poor native heart function (non-recovery group: Group N). This group comprised 22 males and 11 females, ages 16 to 55 years, and whose etiologies were as follows: 27 had DCM; 3 were in the dilated phase of hypertrophic cardiomyopathy (dHCM); and 3 had secondary cardiomyopathy (sarcoidosis, myopathy and drugs). Of these, 15 patients underwent heart transplantation, 13 died (6 cerebral hemorrhages, 1 cerebral infarction, 6 infections), and 5 remain on the waiting list. Another 3 patients were weaned from LVAS due to cerebral events despite insufficient natural heart recovery. LVAS support was discontinued within 1 year in the other 35 patients because of transplantation or death.

In Group R, 3 patients were given a Toyobo LA LVAS, 4 a Toyobo LV LVAS and 1 a Novacor device. In Group N, 30 patients were given a Toyobo LV LVAS and 3 a HeartMate VE device. We retrospectively evaluated the differences between Group R and Group N. To assess natural heart function, we followed-up echocardiographic parameters and the brain natriuretic peptide (BNP) levels at 1 and 3 months after LVAS implantation. Medical therapy regimens were also evaluated. The investigations complied with the principles outlined in the Declaration of Helsinki. The study was approved by the institutional review board of the National Cardiovascular Center, and all patients provided written informed consent.

Management After LVAS Implantation

After general stabilization, we re-administered a β-blocker (carvedilol), an angiotensin-converting enzyme inhibitor (ACE-I, enarapril) and an aldosterone antagonist (spironolactone).

The maximum titrated doses were 20, 5 and 25 mg, respectively. The criteria by which we introduced or increased these drugs were as follows: systolic blood pressure >80 mm Hg; heart rate >60 beats/min; and no sign of deterioration of heart failure. Adequate rehabilitation was also combined with medical treatments. Nutritional states were assessed and the patients received nutritional intervention if necessary. The pump rate was gradually reduced to 60/min when cardiac function showed no deterioration.

Weaning Protocol

Device explantation was considered if the patients met the following criteria: left ventricular diameter in diastole (LVDd) <55 mm; fractional shortening (FS) >20%; and BNP < 100 pg/ml under minimal LVAS support (60 pumps/min). Candidates for LVAS explantation then underwent dobutamine stress testing. Dobutamine was titrated from 5 to 40 μg/kg/min, and hemodynamic and echocardiographic data were evaluated at each dose level. The test outcome was classified as favorable if the patients showed an increase in cardiac output and FS with an increase in dobutamine, without an increase in pulmonary capillary wedge pressure (PCWP), LVDd and symptoms of heart failure. Those who responded appropriately to dobutamine stress testing were considered candidates for LVAS explantation.

Statistical Analysis

We used Student's unpaired *t*-test to compare continuous variables (all data expressed as mean ± SD) and the chi-square test to compare categoric variables. In time-course analysis (Figure 1), data were analyzed by 2-way analysis of variance (ANOVA) followed by Tukey's post hoc test. $p < 0.05$ was considered statistically significant. All analyses were performed using SPSS software (version 14-J).

RESULTS

Before LVAS Implantation

Table 1 summarizes the demographics and baseline characteristics of Groups R and N. Group R was significantly younger and had a shorter duration of heart failure than Group N ($p < 0.01$, respectively). Group R had less myocardial fibrosis than Group N ($p < 0.01$). Myocardial hypertrophy tended to be milder in Group R, but the difference did not reach statistical significance. The ratio (%) of patients with dilated cardiomyopathy was similar in both groups. Hemodynamic parameters, echocardiographic parameters, dose of intravenous inotropic agents, ratio (%) of patients supported by percutaneous mechanical assist devices, BNP levels, and degree of other organ dysfunction or anemia did not significantly differ between the two groups. The regimens of medical treatment did not significantly differ between the two groups (Table 2), but the percentage of patients who were given an ACE-I, a β-blocker, a spironolactone or an amiodarone tended to be higher in Group N.

One Month After LVAS Implantation

Echocardiographic parameters (Dd and FS) and BNP levels were more favorable in Group R, but the differences were not statistically significant (Table 3). The ratio (%) of patients who tolerated treatment with a β-blocker was significantly higher in Group R ($p < 0.05$) (Table 4).

Three Months After LVAS Implantation

FS was significantly higher, and BNP levels was significantly lower ($p < 0.05$ and $p < 0.01$, respectively) in Group R than in Group N (Table 5). Furthermore, the

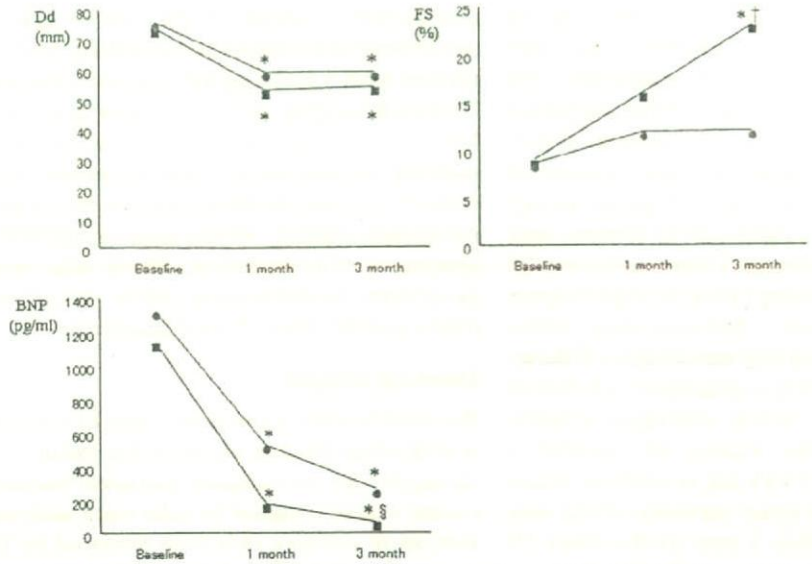

Figure 1. Changes in Dd, FS and BNP after LVAS implantation. Filled squares: Group R; filled circles: Group N. $^{*}p < 0.05$ vs baseline, $^{\dagger}p < 0.05$ vs Group N and $^{\S}p < 0.01$ vs Group N. LVDd, left ventricular end-diastolic dimension; FS, fractional shortening; BNP, brain natriuretic peptide.

increasing rate of FS and the decreasing rate of BNP (3 months after vs before LVAS implantation) were significantly higher in Group R ($p < 0.05$, respectively, data not shown). The dose of β-blocker was higher in Group R ($p < 0.05$) (Table 6). More patients tolerated treatment with an ACE-I or a β-blocker, and Dd tended to be smaller in Group R, but statistical significance was not demonstrated.

Time Course After LVAS Implantation

Figure 1 shows changes in Dd, FS and BNP after LVAS implantation. Improvement of Dd was almost complete

Table 1. Demographics and Baseline Characteristics of Study Population

	Group R ($n = 8$)	Group N ($n = 33$)	p-value
Age (years)	23.4 ± 7.1	36.7 ± 12.4	<0.01[a]
Gender (% female)	12.5	35.3	0.21
Etiology (% dilated cardiomyopathy)	87.5	79.4	0.6
Duration of heart failure (month)	13.3 ± 22	56.1 ± 52	<0.01[a]
Myocardial fibrosis (score)	1.4 ± 0.5	2.5 ± 0.6	<0.01[a]
Myocardial hypertrophy (score)	1.7 ± 0.5	2.2 ± 0.8	0.1
Dose of inotropic agents (DOA + DOB)	9.7 ± 5.6	10.2 ± 4.8	0.83
Use of mechanical support (% IABP and/or PCPS)	62.5	67.6	0.78
Systolic blood pressure (mm Hg)	93 ± 9.0	86 ± 12	0.16
Heart rate (bpm)	116 ± 13	103 ± 25	0.19
Cardiac output (liters/min)	3.21 ± 1.0	3.36 ± 1.0	0.77
Pulmonary capillary wedge pressure (mm Hg)	27.2 ± 4.3	27.2 ± 8.5	0.1
Right atrial pressure (mm Hg)	14.2 ± 5.8	10.2 ± 6.1	0.17
Left ventricular diastolic dimension (mm)	74.1 ± 8.9	75.9 ± 11	0.66
Fractional shortening (%)	9.0 ± 3.7	8.6 ± 4.6	0.84
Wall thickness (mm)	7.6 ± 0.4	7.4 ± 1.4	0.7
B-type natriuretic peptide (pg/ml)	1,140 ± 660	1,282 ± 1,074	0.76
Total bilirubin (mg/dl)	2.6 ± 1.0	1.8 ± 1.0	0.06
Creatine (mg/dl)	1.1 ± 0.5	1.4 ± 1.1	0.52
Hemoglobin (g/dl)	11.4 ± 2.5	10.5 ± 1.8	0.31

Myocardial fibrosis or hypertrophy was classified as mild, moderate or severe and scored as follows: 1 = mild; 2 = moderate; 3 = severe. Dose of inotropic agents is shown as the sum of dopamine (DOA) + dobutamine (DOB). Wall thickness is shown as the mean of the septum and posterior wall. IABP, intra-aortic balloon pump; PCPS, percutaneous cardiopulmonary support.

[a]Statistically significant.

Table 2. Medical Regimens Before LVAS Implantation

	Group R	Group N	*p*-value
ACE-I (%)	37.5	55.9	0.35
β-blocker (%)	12.5	47.1	0.07
Furosemide (%)	100	82.4	0.2
Spironolactone (%)	25	55.9	0.12
hANP (%)	37.5	23.5	0.42
Amiodarone (%)	12.5	50	0.05
Digitalis (%)	37.5	29.4	0.66

Ratio (%) represents drug induction rate. LVAS, left ventricular assist system; ACE-I, angiotensin-converting enzyme inhibitor.

within 1 month in both groups. Augmentation of FS continued during the follow-up period in Group R, but was complete at about 1 month in Group N. BNP levels decreased during the first month and continued to decrease thereafter in both groups.

Prognosis of Patients After LVAS Explantation

Table 7 shows prognosis of patients after LVAS explantation. Three of 8 patients have continued to maintain normal ventricular function during follow-up periods ranging from 8 months to 8 years. Four patients developed recurrent but mild heart failure, and were treated in the outpatient clinic for up to 10.5 years. All are being given an ACE-I (enarapril, mean dose 3.75 mg) and a β-blocker (carvedilol, mean dose 16 mg). The other patient did well up to 8 to 9 years after LVAS removal, but then had episodes of heart failure that required re-LVAS implantation 12 years after explantation. He is now on the waiting list.

DISCUSSION

This study has demonstrated that: (1) young patients with a short history of heart failure and less myocardial fibrosis are candidates for LVAS removal; (2) patients who can be weaned from LVAS show rapid and persistent improvement of natural heart function; and (3) a β-blocker is a potent agent that can induce LVAS removal.

Several mechanisms about restoration of the natural heart by LVAS have been reported. Wohlschlaeger et al showed that ventricular pressure and volume unloading by LVAS reduces harmful neurohumoral and cytokine stimulation (systemic and local), and decreases myocardial apoptosis.[8] Heerdt et al suggested that LVAS support increases the gene and protein levels of SERCA 2a, normalizes Ca^{2+} handling[9] and improves myocardial contraction. Brodde et al demonstrated an up-regulation of a β-receptor after LVAS support.[10] The regression of myocyte hypertrophy and interstitial fibrosis has been also suggested.[11,12] These effects, which occur as a result of maximal ventricular unloading, lead to functional recovery of the native heart.

Basal cardiac states, however, might influence the process of functional improvement. Histologic analysis has demonstrated that less myocardial fibrosis is one of the predictors of LVAS weaning.[13] This finding was also demonstrated in our study. Furthermore, in the present study, myocardial hypertrophy tends to be less common in patients who could be weaned from the device, but a significant difference was not detected. Our study found that younger patients with a shorter duration of heart failure before LVAS implantation were suitable candidates for LVAS explantation. These features indicate less pre-operative myocardial degeneration. The timing of LVAS implantation is very important. LVAS implantation in necessary before myocardial damage becomes irreversible for restoration of natural heart after LVAS implantation. Cardiac function and dysfunctional severity of other organs before LVAS implantation were not statistically different between Groups R and N.

The process of natural heart improvement might reach completion within 4 to 5 months after device implantation.[14] Continued ventricular unloading be-

Table 3. Echocardiographic Parameters and BNP Levels 1 Month After LVAS Implantation

	Group R	Group N	*p*-value
Left ventricular diastolic diameter (mm)	53.7 ± 12.4	59.5 ± 17.6	0.42
Fractional shortening (%)	16.1 ± 12.7	11.9 ± 7.7	0.43
BNP (pg/ml)	176.8 ± 151.6	526.2 ± 483.8	0.09

BNP, B-type natriuretic peptide; LVAS, left ventricular assist system.

Table 4. Medical Regimens at 1 Month After LVAS Implantation

	Group R	Group N	*p*-value
ACE-I (%)	71.4	41.2	0.14
β-blocker (%)	71.4	26.5	<0.05[a]
Furosemide (%)	85.7	88.2	0.85
Spironolactone (%)	57.1	70.6	0.49
Amiodarone (%)	0	20.6	0.19
Digitalis (%)	57.1	26.5	0.11

Ratio (%) represents drug induction rate. LVAS, left ventricular assist system.
[a]Statistically significant.

Table 5. Echocardiographic Parameters and BNP Levels 3 Months After LVAS Implantation

	Group R	Group N	*p*-value
Left ventricular diastolic diameter (mm)	54.7 ± 11.7	58.9 ± 15.4	0.49
Fractional shortening (%)	23.0 ± 17.1	12.0 ± 9.0	<0.05[a]
BNP (pg/ml)	66.6 ± 46.1	264.6 ± 170.1	<0.01[a]

BNP, B-type natriuretic peptide; LVAS, left ventricular assist system.
[a]Statistically significant.

Table 6. Medical Regimens at 3 Months After LVAS Implantation

	Group R	Group N	*p*-value
ACE-I (%)	85.7	55.9	0.14
β-blocker (%)	85.7	55.9	0.14
β-blocker (mg)	15.4 ± 8.4	5.8 ± 3.9	<0.05[a]
Furosemide (%)	57.1	85.3	0.09
Spironolactone (%)	57.1	70.6	0.49
Amiodarone (%)	57.1	32.4	0.22
Digitalis (%)	57.1	29.4	0.16

Ratio (%) represents drug induction rate. LVAS, left ventricular assist system; ACE-I, angiotensin converting enzyme inhibitor.
[a]Statistically significant.

yond this time frame may induce myocardial atrophy and fibrosis. Farrar et al reported that waiting 50 days would capture half of the patients who would ultimately recover ventricular function followed by successful device removal, and waiting up to 90 days could capture 80% of them.[5] We evaluated several parameters at 1 and 3 months after LVAS implantation. Natural heart function was restored more rapidly and the improvement persisted for longer in the weaned patients (Group R). They recovered completely, essentially within 3 months, and were weaned from LVAS after a mean of 5 months of support. BNP was the first representative indicator of native cardiac recovery, which was followed by echocardiographic improvement. None of the patients in whom restoration of the native heart was not indicated for these periods could be weaned from LVAS. This timing is compatible with the findings of Farrar et al.

Recently, the β-blocker has been recognized as being highly beneficial for patients with chronic heart failure, and is becoming the first-line drug treatment for heart failure.[15–17] However, the effect of a β-blocker in patients with LVAS is unclear. We found here that the ratio (%) of patients who tolerated treatment with a β-blocker at 1 month after LVAS insertion and the dose of a β-blocker at 3 months after device implantation were significantly higher in weaned than in non-weaned patients. This result indicates that a β-blocker is useful in patients with LVAS. Several mechanisms underlying the favorable effects of β-receptor blockage have been suggested. A β-blocker restores the function of the calcium-release channel and improves cardiac muscle performance.[18] It also improves myocardial energetics, attenuates myocardial apoptosis, and abrogates induction of the fetal gene program.[19] These effects ultimately help to prevent and reverse ventricular remodeling. Also, these mechanisms might strengthen restoration of the natural heart induced by LVAS. Our findings directly show the importance of β-blocker treatment in patients with first-time LVAS. The percentage of patients who tolerated treatment with an ACE-I after LVAS implantation was also higher in the weaned group, but the values did not reach statistical significance. Conversely, more patients were given a β-blocker, ACE-I, spironolactone and amiodarone before LVAS implantation in the non-weaned group. This may be dependent on the longer duration of heart failure in those patients.

Study Limitations

The present study has several limitations. First, the population size in this investigation was relatively small because the percentage of patients able to be weaned from LVAS is small. Second, the etiologies of patients are various due to the same reason (we could not focus specifically on DCM patients). Third, we demonstrated the effect of a β-blocker. However, we could not standardize the medical regimens after LVAS implantation. Further examinations on larger numbers of patients with uniform etiology and medical treatments are necessary.

In conclusion, weaning from LVAS might be feasible in selected patients. Adjunctive treatments as well as adequate unloading are important in those who

Table 7. Prognosis After Explanation of the Left Ventricular Assist System

Patient no.	Age (years)	Gender	Left ventricular diastolic dimension (mm)	Fractional shortening (%)	B-type natriuretic peptide (pg/ml)	New York Heart Association class	Current status	Duration after explantation
1	29	M	69	5	124	I	Re-LVAS implantation, in hospital, on waiting list	12 years
2	31	M	66	17	103	II	Well, at home	10 years 5 months
3	33	M	50	28	12	I	Well, at home	8 years
4	44	F	53	36	21	I	Well, at home	5 years 7 months
5	25	M	69	10	548	I	Well, at home	5 years 5 months
6	30	M	72	8	275	II	Well, at home	4 years 1 month
7	19	M	91	12	848	II	Well, at home	3 years
8	26	M	51	31	26	I	Well, at home	8 months

have the capability of natural heart restoration. Further studies on LVAS weaning are desirable.

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Replacement of the descending aorta: Recent outcomes of open surgery performed with partial cardiopulmonary bypass

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Objective: Surgical replacement is our standard treatment for descending aortic aneurysm, despite the advent of thoracic endoprostheses. We retrospectively analyzed outcomes of descending aortic replacement performed with partial cardiopulmonary bypass.

Methods: Since 1994, a total of 113 patients in our institution (mean age 68 ± 12 years, n = 75 male) have undergone graft replacement of the descending aorta for nondissecting aneurysm. There were 16 emergency cases (14.2%). All operations were performed through left thoracotomy with partial cardiopulmonary bypass with segmental clamping. Since 1998, preoperative magnetic resonance angiography has been performed to detect the Adamkiewicz artery in elective cases. Motor evoked potentials are now measured intraoperatively.

Results: Early mortalities were 5.3% overall (6/113), 1.0% (1/97) in elective cases, and 31.3% (5/16) in emergency cases. Rates of spinal cord dysfunction were 2.7% overall (3/113), 1.0% (1/97) in elective cases, and 12.5% (2/16) in emergency cases. Stroke rates were 7.1% overall (8/113), 4.1% (4/97) in elective cases, and 25.0% (4/16) in emergency cases. Rates of respiratory failure were 9.7% overall (11/113), 9.2% (9/97) in elective cases, and 12.5% (2/16) in emergency cases. No patient underwent reoperation for the same lesion as a result of repair problems in the follow-up period. Kaplan–Meier overall survival estimates were 92.2% at 3 years, 90.6% at 5 years, and 70.2% at 10 years.

Conclusion: Although it is more invasive than stent graft repair, descending aorta replacement performed with partial cardiopulmonary bypass involves a risk comparable to that associated with thoracic endoprosthesis placement.

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Surgical treatment for a descending thoracic aneurysm (DTA) is changing drastically in response to the advent of endovascular treatment. Endoprostheses have been used for DTA, with generally favorable results.[1,2] Stent graft repair for thoracic aortic diseases is a therapeutic option even for high-risk patients who are not candidates for open surgery. Open surgical replacement, however, is still our current standard treatment for DTA. There are several operative strategies for DTA, such as the single-clamp technique,[3] distal perfusion with left heart bypass,[4] hypothermic circulatory arrest,[5] and partial cardiopulmonary bypass (PCPB).[6] We have usually used PCPB for DTA, with hypothermic circulatory arrest when there is no space for crossclamping. We retrospectively analyzed the outcomes for DTA repair performed with PCPB and compared them with those reported in the literature for endoprostheses.

Materials and Methods

Patients

From 1994 to 2004, a total of 113 patients (75 men, mean age 68 ± 12 years) underwent graft replacement of the descending aorta for nondissecting aneurysm. The cases that required open

Abbreviations and Acronyms
AKA = Adamkiewicz artery
DTA = descending thoracic aneurysm
MEP = motor evoked potential
PCPB = partial cardiopulmonary bypass

proximal anastomosis under circulatory arrest were excluded, and the patients in this study had sufficient space for crossclamping next to the left subclavian artery and celiac artery. There were 16 cases of emergency surgery (14.2%), all because of rupture of the aneurysm. Fifteen patients had undergone previous abdominal aortic replacement, 3 had undergone previous thoracoabdominal aortic replacement, and 11 had undergone previous thoracic aortic replacement. Since 1998, preoperative magnetic resonance angiography has been performed to detect the Adamkiewicz artery (AKA) in elective cases.[7] The AKA was preoperatively imaged by contrast magnetic resonance angiography with gadolinium dimeglumine (0.3 mmol/kg body weight). Early- and late-phase images were used to differentiate arteries from veins. Imaging volumes covered the levels between T6 and L3. The AKA and the anterior spinal artery were identified by at least two radiologists in 0.6-mm contiguous sections processed by multiplanar reconstruction. Our institution approved this retrospective study and did not require patient consent on the condition that patients not be identified.

Operative Techniques

The patients were anesthetized and intubated with a double-lumen endotracheal tube. The patients were then positioned in the right lateral decubitus position with the hips flexed 60°. An incision was made from the vertebral border of the scapula to the costal cartilage along the intercostal space. From the 4th to the 7th intercostal space, access to the left thorax was selected according to the location of the aneurysm. The left or right femoral artery and vein were dissected and looped with umbilical tape. A cannula was inserted in the femoral artery for perfusion inflow, and another cannula was inserted in the femoral vein for perfusion outflow. The tip of the venous cannula was placed at the opening of the inferior vena cava in the right atrium, with placement confirmed by transesophageal echocardiography. PCPB was initiated, and normal proximal aortic pressure was maintained; the flow rate was usually around 1.5 to 2.0 mL/(min · m^2). The pump circuit had an extracorporeal membrane oxygenator, including a heat exchanger. The bladder temperature was cooled to between 33°C and 34°C during PCPB.[8] The DTA was exposed and clamped after establishment of PCPB. The clamps were placed sequentially when the aneurysm involved a long segment. The aorta was opened longitudinally, and intercostal arteries were ligated or oversewn for hemostasis when they were considered to be unimportant. Intercostal arteries that had to be reattached or preserved were temporarily closed with a bulldog clamp or small balloon-tip catheters. The anastomosis was always performed with complete transection of the descending aorta. An appropriately sized Dacron polyester fabric graft was chosen, and the proximal anastomosis was performed first with running 3-0 or 4-0 polypropylene suture with a polytetrafluoroethylene felt strip. Intercostal arteries were reattached with a short, small-caliber graft. The distal anastomosis was then performed with running 3-0 or 4-0 polypropylene suture with a polytetrafluoroethylene felt strip. The flow of PCPB was reduced, and the aortic clamps were then gently released. The patient was weaned from PCPB once the bladder temperature reached 36.5°C.

We have been measuring motor evoked potentials (MEPs) during surgery since 1998 to detect spinal ischemia and have previously described the details.[9] With sufficient anesthesia maintained with low doses of fentanyl (0.02–4 mg/kg), propofol (4—6 mg/[kg · h]), and vecuronium (0.04 mg/[kg · h]), the motor cortex was activated by 600 V transcranial electrical stimulation. The action potentials conducted through the anterior horn motor neurons were recorded from the skin over the upper extremity muscles (as a control), the lower extremity muscles, and the thenar muscles. The signals of the MEPs are affected by femoral arterial cannulation; the probe was therefore always placed on the contralateral side from femoral cannulation. Monitoring of MEPs is also influenced by anesthesia, including neuromuscular blockade, only a low dose of vecuronium was therefore used during the operation. During crossclamping, MEP levels were determined every 2 to 5 minutes. A fall in MEP amplitude below 25% of the baseline was taken to indicate ischemia of the spinal cord. When critical reduction of MEP amplitude was observed, rapid revascularization of the spinal cord blood supply was performed. Additionally, the blood pressures of upper and lower body were increased with use of catecholamines, transfusion, and perfusion flow.

Definitions

Early mortality was defined as death during the hospital stay. Postoperative stroke was defined as newly developing neurologic deficit confirmed by computed tomography. Neurologic diagnoses were made by neurologists. Respiratory failure was defined as the need for intubation and ventilatory support longer than 72 hours.

Statistical Analysis

Values are the mean ± SD. Data were analyzed with Fisher exact tests for categorical variables.

Results

The early mortalities were 5.3% overall (6/113), 1.0% (1/97) in elective cases, and 31.3% (5/16) in emergency cases. The rates of spinal cord dysfunction were 2.7% overall (3/113), 1.0% (1/97) in elective cases, and 12.5% (2/16) in emergency cases. Spinal cord dysfunction occurred more frequently in patients older than 75 years and was not prevented by preoperative AKA detection (Table 1). The stroke rates were 7.1% overall (8/113), 4.1% (4/97) in elective cases, and 25.0% (4/16) in emergency cases. Stroke occurred most frequently in emergency cases, but it was not related to crossclamping adjacent to the aortic arch (Table 2). The rates of respiratory failure were 9.7% overall (11/113), 9.2% (9/97) in elective cases, and 12.5% (2/16) in emergency cases.

Thirty-two patients were older than 75 years, and 9 of these underwent emergency operations. The older patients' mortality was 6.3% (2/32), and the 2 patients who died had both undergone emergency operations. The rates of spinal

TABLE 1. Spinal cord dysfunction and variables

	Total	Spinal cord dysfunction	*P* value
All	113	3 (2.7%)	
Male	76	3 (3.9%)	.55
Age			
>70 y	56	3 (5.4%)	.12
>75 y	32	3 (9.4%)	.02
Partial cardiopulmonary bypass duration			
>60 min	83	3 (3.6%)	.99
>90 min	39	1 (2.5%)	.99
>120 min	15	1 (6.7%)	.36
Emergency operation	16	2 (12.5%)	.05
Preoperative Adamkiewicz artery detection	50	2 (4.0%)	.59

cord dysfunction in this age group were 9.3% overall (3/32), 4.3% (1/23) in elective cases, and 22.2% (2/9) in emergency cases. The stroke rates were 9.4% overall (3/32), 0% (0/23) in elective cases, and 33.3% (3/9) in emergency cases. The rates of respiratory failure were 12.5% overall (4/32), 13.0% (3/23) in elective cases, and 11.1% (1/9) in emergency cases.

Overall, the mean operative time was 291 ± 93 minutes, the mean PCPB time was 84.8 ± 32.1 minutes, the mean bleeding volume was 1187 ± 1432 mL, and the mean transfusion volume was 1335 ± 2642 mL, with 45.1% of the patients not requiring transfusion. In elective cases, the mean operative time was 280 ± 78 minutes, the mean PCPB time was 80.7 ± 27.7 minutes, the mean bleeding volume was 921 ± 845 mL, and the mean transfusion volume was 851 ± 1870 mL, with 51.5 % of the patients not requiring transfusion.

Magnetic resonance angiography was performed in 65 cases, and the AKA was detected in 50 patients (76.9%). Among these patients, 2 had paraplegia; the AKA had been detected in both. Three patients had paraplegia or paraparesis; 1 had undergone surgery without MEP monitoring, another showed MEP change, and the third patient showed no change in MEPs. MEPs were altered in 2 patients; 1 had paraplegia and the other had a postoperative stroke.

None of the patients underwent reoperation for the same lesion to repair problems in the follow-up period. Kaplan–Meier overall survival estimates were 92.2% at 3 years, 90.6% at 5 years, and 70.2% at 10 years (Figure 1).

Discussion

DTA repair is usually discussed in combination with thoracoabdominal aortic aneurysms. Reports focusing solely on surgical repair for DTA are relatively uncommon. Many DTAs will probably be repaired with endoprostheses, because a DTA has no visceral branches. The advent of endovascular treatment is believed to be a great innovation in treatment for aortic aneurysm. Endoprostheses have been used for abdominal aortic aneurysms, and some surgeons are now using them for DTA repair. Makaroun and colleagues[2] used the GORE TAG thoracic endoprosthesis in 139 patients with DTA. They reported that the procedure time was 150 minutes on average, blood loss was 506 mL on average, and that mortality, stroke, and spinal ischemia rates were 1.5%, 4% and 3%, respectively. Fattori and colleagues[10] used the Talent thoracic stent graft for DTA in 457 patients. They reported mortalities of 7.9% in acute cases and 4% in elective cases, a stroke rate of 3.7%, and a spinal ischemia rate of 1.7%.

The articles on endoprostheses refer to open repair of DTA, and they often point out that the mortality associated with open repair is greater than 10% and that the risk of spinal ischemia is 4% to 5%. On the other hand, the results of open repair are improving. Coselli and colleagues[11] reported a mortality of 4.4% and a paraplegia rate of 2.6% after open repair of DTA. Estrera and associates[12] reported a mortality of 8.8%

TABLE 2. Stroke and variables

	Total	Stroke	*P* value
All	113	8 (7.1%)	
Male	76	5 (6.6%)	.72
Age			
>70 y	56	4 (7.1%)	.99
>75 y	32	3 (9.4%)	.69
Partial cardiopulmonary bypass duration			
>60 min	83	8 (9.6%)	.20
>90 min	39	5 (12.8%)	.13
>120 min	15	3 (20.0%)	.08
Emergency operation	16	4 (25.0%)	.01
Crossclamp near arch	37	4 (10.8%)	.43

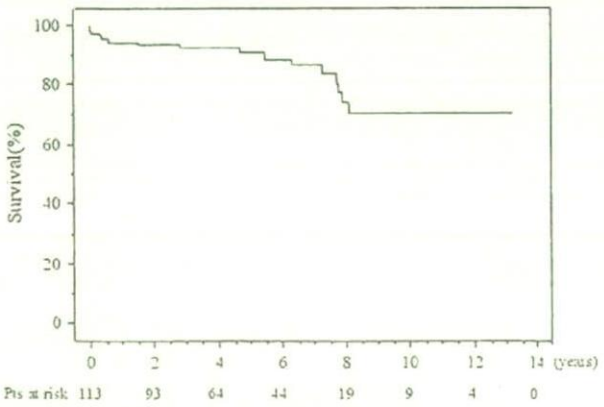

Figure 1. Kaplan–Meier cumulative actuarial survival curve.

and a paraplegia rate of 2.7% after open repair of DTA with cerebrospinal fluid drainage and distal perfusion. Even with hypothermic circulatory arrest, Patel and coworkers[13] reported a mortality of 6.0%, a stroke rate of 6.8%, and a spinal ischemia rate of 4.5%. Our results were comparable with or even better than those reported for open repair and for endoprostheses. Open repair of DTA has several merits relative to repair with an endoprosthesis, especially long-term durability. Moreover, there are no anatomic limitations such as interfere with the applicability of an endoprosthesis, including short or wide proximal or distal landing zones, severe neck angulations, and tortuous or stenotic access arteries.[14]

Stroke is a devastating complication after aortic surgery. The incidence and etiology of stroke related to DTA repair have not been frequently described. Attention is generally paid to spinal ischemia as a primary neurologic complication of DTA repair. Actually, DTA repair with PCPB involves a certain risk of stroke, as indicated in this study. Goldstein and colleagues[15] reported a stroke rate of 8.1 % in DTA repair and also noted that stroke was a significant predictor of postoperative death. Patel and coworkers[13] reported a stroke rate of 6.8% in DTA repair with hypothermic circulatory arrest. The retrograde flow of PCPB from femoral cannulation when normal proximal aortic pressure is not maintained could be a reason for the stroke risk. Moreover, crossclamping adjacent to the aortic arch has also been mentioned as a cause of stroke.[16] In our study, however, some patients without crossclamping adjacent to the aortic arch still had stroke occur under normal proximal aortic pressure. Crossclamping adjacent to the aortic arch was not a statistically significant risk factor of stroke in our study.

The preoperative detection of AKA by magnetic resonance angiography is, we believe, useful in preventing spinal cord injury during DTA repair. The utility of the detection of AKA has already been described elsewhere, and the effects were reflected in the lower rate of spinal ischemia. Although the spinal blood supply is not completely understood, we consider that reimplantation or preservation of the intercostal arteries, which connect the AKA, contributes to improved results. In this study, however, 2 patients showed spinal ischemia despite detection of the AKA. This implies that preservation of the AKA per se is not enough to prevent spinal ischemia. MEPs have been reported to be a rapid indicator of spinal cord injury during thoracoabdominal aortic repair.[17] We also believe that MEP monitoring contributes to prevention of spinal cord injury, even during DTA repair, but such an effect was not clear in this study.

Advanced age is supposed to be among the risks for DTA repair. Huynh and colleagues[18] reported a stroke rate of 9% in their series of descending and thoracoabdominal aortic replacements in patients of advanced age. In this study, the frequencies of stroke in patients older than 70 years and in those older than 75 years old were comparable. No deaths and no postoperative strokes were seen among elective cases. The rate of respiratory failure, however, was high even in elective cases, as expected.

In conclusion, outcomes of traditional open DTA repair are improving. The long-term result of this technique is in clear contrast to that of endoprosthesis. Even in patients older than 75 years, open DTA repair can be performed with acceptable risk. Although open DTA repair is by definition more invasive and should be further improved, the risks involved in replacement of the descending aorta under PCPB were comparable to those associated with thoracic endoprosthesis placement at this time.

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Abstract | Figures/Tables

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Activation of cardiac progenitor cells through paracrine effects of mesenchymal stem cells

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Abstract

Mesenchymal stem cells (MSC) transplantation has been proved to be promising strategy to treat the failing heart. The effect of MSC transplantation is thought to be mediated mainly in a paracrine manner. Recent reports have suggested that cardiac progenitor cells (CPC) reside in the heart. In this study, we investigated whether MSC had paracrine effects on CPC in vitro. CPC were isolated from the neonatal rat heart using an explant method. MSC were isolated from the adult rat bone marrow. MSC-derived conditioned medium promoted proliferation of CPC and inhibited apoptosis of CPC induced by hypoxia and serum starvation. Chemotaxis chamber assay demonstrated that MSC-derived conditioned medium enhanced migration of CPC. Furthermore, MSC-derived conditioned medium upregulated expression of cardiomyocyte-related genes in CPC such as β-myosin heavy chain (β-MHC) and atrial natriuretic peptide (ANP). In conclusion, MSC-derived conditioned medium had protective effects on CPC and enhanced their migration and differentiation.

Keywords: Cardiac progenitor cell; Mesenchymal stem cell; Paracrine effect; Proliferation; Migration; Differentiation

Article Outline