Table 3. Completeness of Revascularization

No. of bypass grafts minus no. of coronary involvements including aneurysms	Patients, n
+2	1
+1	8
0	53
−1	45
−2	7

Fifty-four percent of patients had complete (0 to +2) and 46% had incomplete (−1 to −2) revascularization.

posterior descending arteries, and 21 left circumflex arteries (LCX). Target vessels for each graft are shown in Tables 2 and 3. In this series, PCI was not attempted before the operation because we believe that surgery is safer for complicated coronary lesions in children.

Statistical Analysis

Quantitative values are expressed as mean±SD or median with range. The time-related survival, event-free, and graft patency rates were calculated by the Kaplan-Meier method with 95% confidence interval (CI). Differences of graft patency rates were assessed by log-rank test, and differences were considered statistically significant at $P<0.05$. Different grafts within the same patient were treated as separate entities because graft patency has been proven to depend on graft materials and target vessels within a single patient.[12] We used the Cox proportional hazards model to assess the association between variables and the incidence of cardiac events. Variables included gender, age at KD onset, age at operation, presence or absence of previous MI, completeness of revascularization (the number of grafts minus the number of lesions; −2 to +2, as shown in Table 3), left main trunk involvement, presence of SVG, graft patency, and left ventricular EF ≥0.5 or <0.5. Statistical analyses were performed with SAS statistical software, version 9.1 (SAS Institute, Inc, Cary, NC).

Results

Long-Term Survival Rates

There were no operative or hospital deaths, but 5 late deaths occurred (4%), 4 males and 1 female, from 3 months to 12 years after the operation. Demographic data of the 5 deaths are shown in Table 4. Death was sudden in 3 patients, and 1 death was due to cardiac allograft vasculopathy after heart transplantation for severe left ventricular failure unresponsive to bypass surgery. All 5 had a history of previous MI resulting in a reduced left ventricular EF of ≤0.5 in addition to frequent ventricular arrhythmias. ITAs were used in all 5 late death patients, and patency of the graft had been confirmed before death. Among survivors, no one needed a heart transplant. The 10-, 20-, and 25-year survival rates were 98% (95% CI, 93 to 100), 95%, and 95% (95% CI, 88 to 98), respectively (Figure 1).

Cardiac Event–Free Rate

Cardiac events occurred 36 times in 33 patients (29%), including the aforementioned deaths, nonfatal acute MI in 1 patient, angina pectoris in 1, syncope in 1, ventricular tachyarrhythmias in 2, and indications for postoperative PCI or redo bypass operation in 26 patients (23%). Two patients with ventricular tachyarrhythmias received an implantable cardiac defibrillator. PCI was performed in 17 patients (15%) and reoperation in 9 (8%). Three patients experienced >1 event. The 5-, 10-, 20-, and 25-year cardiac event–free rates were 87%, 81%, 67% (95% CI, 55 to 76), and 60% (95% CI, 46 to 72), respectively (Figure 2).

Indications for Postoperative Reinterventions (PCI or Reoperation)

Indication for further intervention was the most frequent cardiac event. When significant stenosis ≥75% or obstruction

Table 4. Demographic Characteristics of 5 Deaths After the Operation

	Case No.				
	1	2	3	4	5
Age at operation, y	11	1–8/12	16	13	13
No. of bypass grafts	1	1	1	3	2
Type of graft	ITA-LAD	ITA-LAD	ITA-LAD	ITA-LAD, ITA-LCX, GEA-RCA	ITA-LAD, ITA-LCX
Age at KD onset, y	4	1–4/12	1	2	4/12
Age of death, y	22	1–11/12	26	25	17
Interval from operation to death, y	11	3/12	10	12	4
Gender	Male	Male	Female	Male	Male
History of MI	Yes	Yes	Yes	Yes	Yes
Location of MI	Anterior+Inferior	Inferior	Inferior+lateral	Inferior	Inferior
Left ventricular EF	0.24	0.50	0.39	0.47	0.49
Coronary lesions	2	2	LMTD+2	LMTD+2	3
Obstruction and aneurysm	LAD, RCA	LAD, RCA	LAD, RCA	LAD, RCA	LAD, LCX, RCA
Ventricular arrhythmias	PVC short run	No	PVC short run	PVC	PVC
Other	(Later) heart transplanted	...	...	Severe obesity (BMI 33), fatty liver	Syncope; could not be ruled out
Cause of death	Cardiac graft failure	Sudden	Sudden	Sudden	Traffic accident

LMTD indicates left main trunk disease; PVC, premature ventricular contraction; and BMI, body mass index.

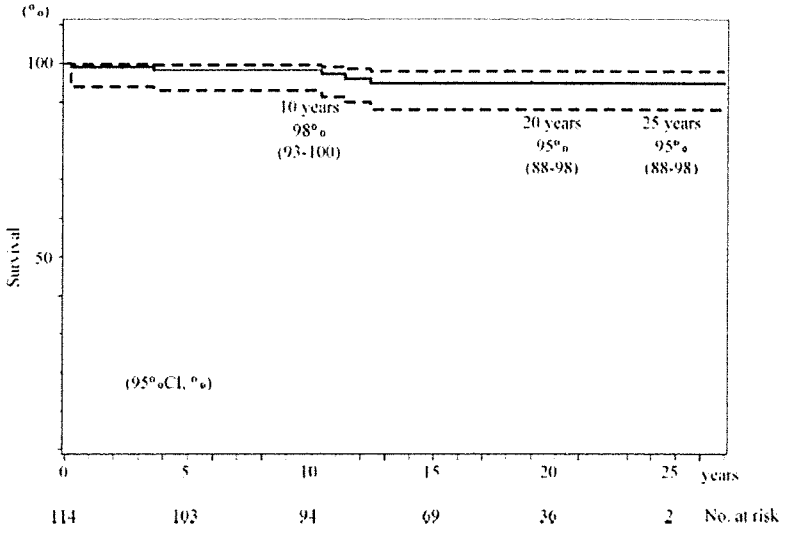

Figure 1. The long-term survival rate of 114 patients is shown. There were 5 deaths during follow-up. All deaths seemed to be cardiac in origin. Survival at both 20 and 25 years was 95% (95% CI, 88 to 98).

of the graft and/or the native coronary artery was angiographically identified, exercise ECG, echocardiography, and myocardial scintigraphy were repeated as needed. Even in the absence of subjective symptoms, PCI or redo operation was undertaken to correct anatomic lesions when studies confirmed the presence of stenosis ≥75%, ischemia, or regional contraction abnormality of the left ventricle related to obstructive coronary lesions.

Of the 26 patients who underwent reinterventions, 17 underwent PCI 9±6 years after the operation (aged 17±9 years). Six patients had a percutaneous transluminal coronary rotational ablation: 3 for original coronary lesions because of graft failure and 3 for new obstructive coronary lesions that had been considered insignificant at the first operation and were left untreated. Ten patients had percutaneous transluminal balloon angioplasty for ITA–coronary artery anastomotic stenosis, and 1 patient in adulthood had a stent inserted for SVG midportion stenosis with atherosclerosis. Nine patients had a coronary reoperation at 22±8 years of age, 13±8 years after the first operation. The indications for reintervention, postoperative term at reintervention, and their success rates are shown in Table 5. When the cardiac event–free rate from reintervention (PCI and reoperation) was analyzed separately from other cardiac events, the reintervention-free rate at 20 years was 75% (95% CI, 64 to 84), and that at 25 years was 68% (95% CI, 52 to 79) (Figure 3). The early postoperative indication for reintervention was mainly percutaneous transluminal balloon angioplasty for ITA–coronary artery anastomotic stenosis that occurred 1.8±3.6 years after the operation. Newly developed coronary lesions (13.0±6.5 years) and SVG atherosclerosis (15 years) were late indications for PCI, stenting, and reoperation. In the midterm, graft obstruction due to graft shrinkage, intimal hyperplasia, and thrombosis was the most common reason for reinterventions. The success rate for reinterventions was acceptable. The right or left ITAs together with the GEA or radial artery were used for all reoperations to ensure total arterial grafting. None of the patients who needed additional treatment by either PCI or reoperation died. Analysis of the risk factor variables for cardiac events or postoperative reinterventions by the Cox proportional hazards model showed no significant associations.

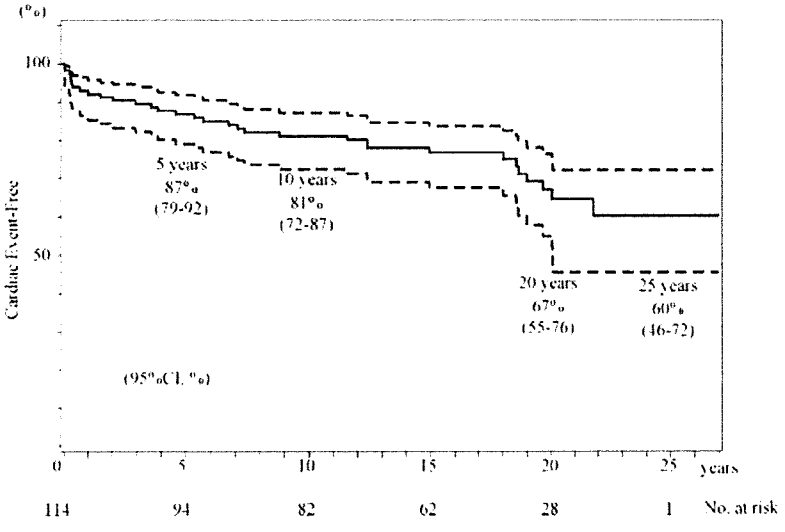

Figure 2. The cardiac event-free rate of 114 patients is shown. Cardiac events occurred 35 times in 32 patients during the follow-up term. The 20- and 25-year cardiac event-free rates were 67% (95% CI, 55 to 76) and 60% (95% CI, 46 to 72), respectively. Importantly, there was a trend for the cardiac event-free curve to decline slowly but progressively. Postoperative PCI and reoperation were the most common cardiac events during follow-up.

Table 5. Postoperative Requirements for Reinterventions (PCI and Reoperation) in 26 Patients

	Reasons for Reinterventions	No. of Patients	Postoperative Term, y	Procedures	Success, n/N (%)
Early events	ITA graft anastomotic stenosis	10	1.8±3.6	PTBA	10/10 (100)
Midterm events	Graft closure	3*		PTCRA	
		10	11.0±8.0		
		7†		Reoperation	
Late events	SVG graft atherosclerosis	1	15.0	Stenting	1/1 (100)
	New coronary lesions	3*		PTCRA	4/6* (67)
		5	13.0±6.5		
		2†		Reoperation	7/9† (80)

PTBA indicates percutaneous transluminal balloon angioplasty; PTCRA, percutaneous transluminal coronary rotational ablation. Success rate of percutaneous transluminal coronary angioplasty and reoperation was calculated by combining both midterm and late events.

*PTCRA (n=6) was performed for native coronary arteries in all patients.

†Reoperation (n=9) was performed for ITA graft closure in 4, SVG closure in 3, and new lesions in 2 patients.

Postoperative Left Ventricular Function

Postoperative left ventricular EF was measured in 72 patients (63%). The mean postoperative EF was 0.55±0.08. A depressed EF depended on a history of preoperative MI, and the EF at rest was essentially unchanged after surgery. All 5 subjects who died had an EF of ≤0.5 due to previous MI.

Medications After Surgery

Only 26 patients (23%) were medication free at their last follow-up. The remaining 88 patients (77%), including the patients who died, were receiving various combinations of 1 to 6 medications including warfarin, aspirin, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium antagonists, diuretics, nitrates, statins, and β-blockers. All 88 patients were on aspirin, as recommended by the guidelines.[6,13] Those with a giant left main trunk aneurysm not supported by 2 patent grafts for the LAD and LCX (n=21) were kept on both warfarin and aspirin, maintaining an international normalized ratio ≈2.0.[6] Aspirin was given at 5 mg/kg daily, and the maximum dose was 100 mg per day.

Generally, medication-free patients were those with good left ventricular function and single-vessel disease with a patent ITA graft 3 to 5 years after the operation. Other patients with additional nonstenotic coronary aneurysms, SVG, or mild to moderately depressed left ventricular function with or without ventricular arrhythmias were placed on medications selected from those listed.

Postoperative Activity Restrictions

Although the cardiac event–free rate at 20 years after the operation was 67% and that at 25 years was only 60% (95% CI, 46 to 72), all 109 surviving patients were symptom free at their last assessment. In accord with the level of exercise advised by their cardiologist, 45 (41%) of the survivors were presently permitted all physical activities, including long-distance swimming and/or running, although all of them had been strictly prohibited from exercise or sport activities before the operation. Forty-two patients (39%) were allowed unlimited daily activities but were prohibited from long-distance swimming and/or running. Ten patients (9%) were prohibited from strenuous exercise, and 12 (11%) were recommended not to participate in athletic events. Six female patients had uneventful delivery of babies during their follow-up.

Long-Term Graft Patency

As demonstrated in Figure 4, the 20-year graft patency for 154 ITAs as a whole was 87% (95% CI, 78 to 93), and that

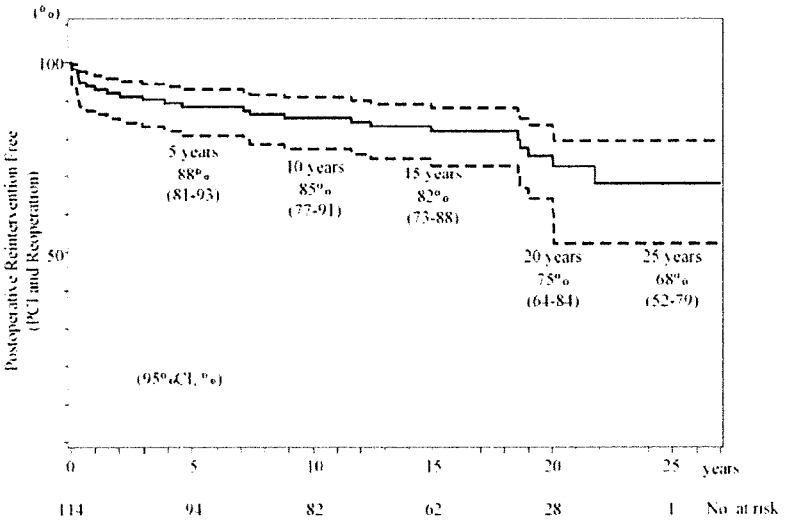

Figure 3. The reintervention (postoperative PCI and reoperation)-free rate at 25 years after the operation was 68% (95% CI, 52 to 79). The early decline during the first 5 years was attributed to the need for balloon dilatation for ITA–coronary artery anastomosis stenosis, and the late decline between 15 and 20 years after the operation depended mainly on reinterventions for new obstructive lesions and SVG atherosclerosis. The midterm decline was mostly due to graft failure.

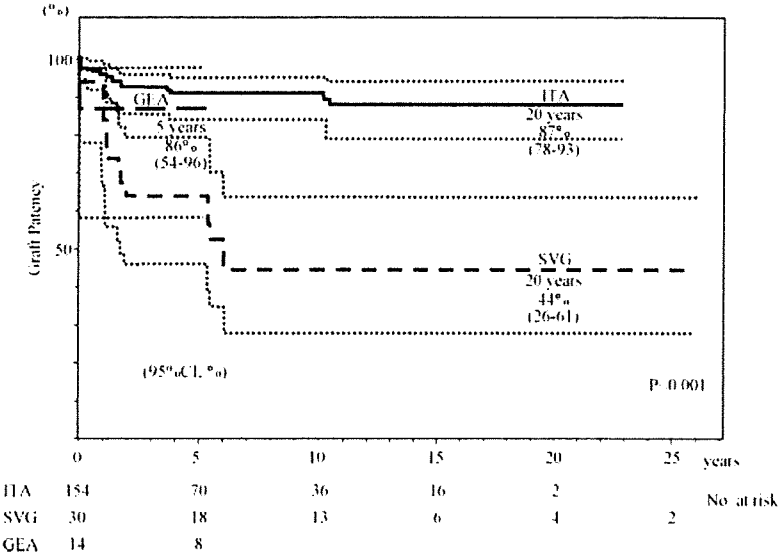

Figure 4. The long-term patency of the ITA, SVG, and GEA is shown. The 20-year patency rates for the ITA and SVG were 87% (95% CI, 78 to 93) (n=154) and 44% (95% CI, 26 to 61) (n=30), respectively. The difference of patency between the ITA and SVG was significant at $P<0.001$. The 5-year patency rate for the GEA was 86% (95% CI, 54 to 96) (n=14), not different from that for the ITA at 5-year follow-up.

for 30 SVGs was 44% (95% CI, 26 to 61). This difference was highly significant at $P<0.001$. The 5-year patency for the GEA was 86% (n=14), similar to the ITA, although the observation period was short for this graft.

Twenty-year patency of the ITA was 91% for the LAD (n=109), 100% for the LCX (n=10), and 84% for the RCA (n=31). In contrast, 20-year patency of the SVG was 67% for the LAD (n=3), 69% for the LCX (n=11), and 25% for the RCA (n=12). Because the ITA was used primarily for the LAD, and the SVG was used mainly for the RCA and LCX, graft patency rates for the non-LAD vessels are also compared in Figure 5. When we analyzed the patency of the ITA plus GEA and SVG for the non-LAD vessels, a significant patency difference between the arterial graft and SVG was again apparent ($P=0.002$). The arterial graft patency rate for the non-LAD vessels was 87% (95% CI, 73 to 94) (n=59) at 20 years after operation. In contrast, the SVG patency for the same target vessels was only 42% (95% CI, 23 to 60) (n=27). The ITA patency rate was similar for both the LAD and the non-LAD vessels. In Figure 6, differences in graft patency according to the age at operation (≥10 or <10 years) are shown. The long-term patency for the ITA was not significantly different regardless of the patient's age (≥10 or <10 years) (93% [95% CI, 83 to 97] versus 86% [95% CI, 74 to 93]; $P=0.163$). In contrast, SVG patency was significantly lower for the patients aged <10 years (58% [95% CI, 32 to 78] versus 25% [95% CI, 6 to 51]; $P=0.004$).

Characteristics of the Graft

The 20-year patency of the SVG was as low as 44%, but 14 SVGs have remained patent with the aid of medications, PCI, and/or stenting at the time of last angiographic evaluation. However, most of the patent SVGs showed various degrees of degenerative changes (n=10; 71%),[14] such as irregularity of the graft wall and caliber with a maximum/minimum diameter ratio >1.5 (n=6), shortening or growth failure of the SVG resulting in traction or kinking of the target coronary artery that jeopardized distal runoff flow (n=3),[15] and apparent development of SVG atherosclerosis (n=1) before 40 years of age. On the other hand, the wall characteristics of the ITA were very smooth and appropriately size matched with the adjacent coronary artery and its flow situation. ITA graft

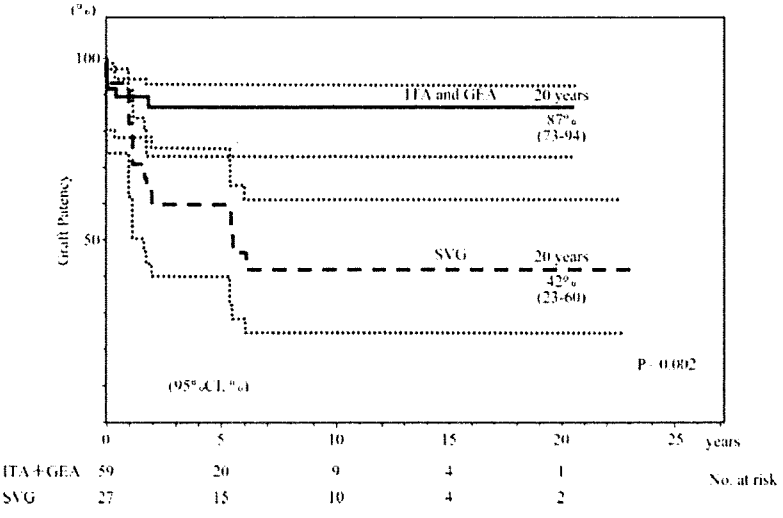

Figure 5. The difference of graft patency rates for the non-LAD target vessels is shown because the ITA was used exclusively for the LAD, and the SVG was used mainly for the non-LAD vessels. The 20-year patency for the arterial grafts for the non-LAD arteries was 87% (95% CI, 73 to 94) (n=59), and that for the SVG was 42% (95% CI, 23 to 60) (n=27). The difference was significant at $P=0.002$. The patency rates of the ITA and SVG differed similarly even for the non-LAD arteries.

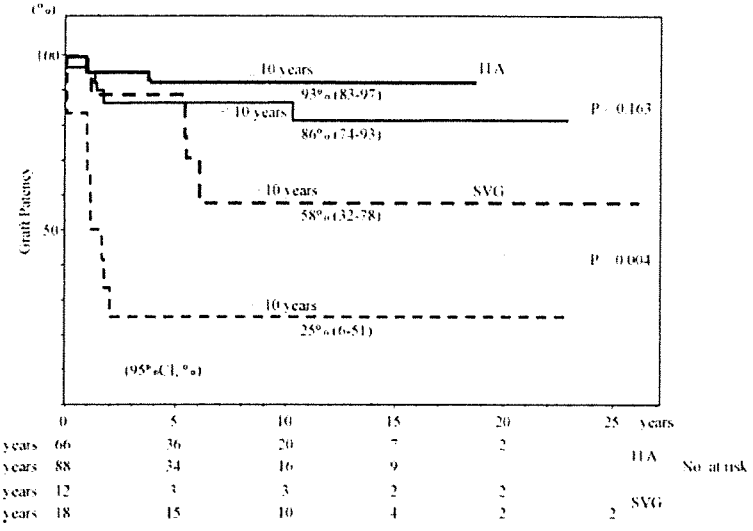

Figure 6. The difference in graft patency rates according to the age of patients at operation (≥10 or <10 years) is shown. The long-term patency for the ITA was not significantly different between the patients aged ≥10 years (93%; 95% CI, 83 to 97) and <10 years (86%; 95% CI, 74 to 93) (P=0.163); however, that of the SVG was significantly lower for the younger patients aged <10 years (25%; 95% CI, 6 to 51) than for the older patients ≥10 years (58%; 95% CI, 32 to 78) (P=0.004).

failure due to flow competition (string phenomenon) reversed and the graft became patent in 4 patients when their native coronary lesions progressed over nearly 10 years.[16] This reverse remodeling of the ITA graft increased the ITA patency rate by ≈3%. This phenomenon did not occur with SVGs. Growth of the ITA graft was also apparent in these patients.[17,18]

Discussion

Survival for >20 years of children and adolescents after a bypass operation for severe coronary artery involvement secondary to KD is encouraging. In many patients, the coronary circulation was maintained by the graft, and in some, both coronary orifices were totally obstructed and coronary blood supply was completely dependent on enlarged ITA grafts.[8,11] Less satisfactorily, the cardiac event–free curve slowly but progressively declined, being 67% after 20 years and only 60% (95% CI, 46 to 72) at 25 years (Figure 2). Among the cardiac events, the need for reintervention was the most common. The early decline of the reintervention-free curve (Figure 3) reflects ITA–coronary artery anastomotic stenosis necessitating percutaneous transluminal balloon angioplasty with excellent patency thereafter. The late decline at ≈15 to 20 years depended primarily on the development of new lesions, and SVG atherosclerosis and midterm reinterventions were attributed mainly to graft closure, as shown in Table 5. Analysis of variables by the Cox proportional hazards model, however, failed to demonstrate significant contributing factors among the variables we evaluated to the occurrence of cardiac events or to the need for reinterventions, probably because of the small sample size and the unpredictable fate of the remaining coronary lesions after surgery.

The number of coronary arteries involved, including both obstructive and aneurysmal lesions, was 2.1±0.6 lesions per patient, ranging from 1 to 3. In addition, left main trunk disease involved aneurysm formation in the majority of patients. The number of bypass grafts was 1.7±0.8 per patient. The difference in the number of diseased vessels and number of grafts was attributed to the presence of aneurysms without obstructive lesions that did not require a bypass graft at the first operation. However, additional interventions will be needed in the future because the remaining coronary aneurysmal lesions may evolve into new obstructive lesions with time. For now, all patients with patent aneurysms with no distal support by bypass grafts are kept on a combination of warfarin and aspirin to decrease the possibility of MI or sudden death.[19]

The ITA is the most important vessel for coronary revascularization in growing children and adolescents who will be entering the age of atherosclerosis in 20 to 30 years. Its importance is emphasized by evidence that it is apparently spared from atherosclerosis,[20] and adult patients revascularized with this graft survive longer than those revascularized with a SVG.[12] The importance of the ITA graft should be even greater in children[7,8,21,22] because of its ability to grow in accordance with the somatic growth of the patient.[17,18] In addition, ITA involvement in KD is extremely rare, quite different from the coronary artery. The effect of ITA grafts on survival may depend not only on graft longevity but also on the function of the ITA endothelium. Endothelial function of the coronary artery affected by KD is probably impaired and depressed[3–5]; thus, the supplemental endothelial function from the less affected ITA, such as production of nitric oxide and other bioactive products, may enhance and possibly reverse the depressed endothelial function of the diseased coronary artery.[19,23–25]

In contrast, SVG implants in childhood showed a high incidence of closure and degenerative changes. The first pediatric patient who underwent a bypass operation in 1975 with 2 autologous SVGs had patent vein grafts at 1 month[1]; unfortunately, both SVGs were totally occluded within a couple of years with life-saving collateral developments. Evaluation of the angiographic graft morphology in this study suggests that vein grafts may progressively fail in the future. Among 14 patent SVGs, 10 (71%) showed degenerative changes. Thus, whenever feasible, we believe that total arterial bypass grafting provides a greater likelihood of an event-free future for children with KD, and, in fact, all of our reoperations for KD employed arterial grafts such as the

remaining ITA, GEA, and/or the radial artery, anticipating longer patency and better quality of graft status.

In 1994[26] and 2004,[27] we reported the Japanese national survey of operations for KD, in which detailed analysis of cardiac events was difficult because data collection by mailed questionnaire was limited. However, the survey showed that ITA graft patency was less favorable in patients aged <9 to 12 years, most probably because of technical difficulties in small children. In our present study, as shown in Figure 6, the difference in ITA graft patency according to the patient's age at operation (<10 or ≥10 years) no longer exists ($P=0.163$); however, SVG graft patency was significantly worse ($P=0.004$) in children aged <10 years compared with older children. The ITA graft tended to close within a couple of years after surgery because of technical factors or flow competition in the coronary artery with a less stenotic lesion. However, ITA graft failure due to string phenomena may reverse, and the graft may function well when native coronary lesions progress after many years.[16,25] Since 1994, with more aggressive correction of anastomotic stenosis by simple balloon dilation, ITA graft patency has significantly improved, up to 94% in our institute.[28] We recommend this strategy for children with an ITA bypass graft. Once good flow of the ITA graft is confirmed, closure of the ITA graft seldom occurred during the next 20 years.

The presence of giant coronary aneurysms with no apparent obstructive element creates difficulties when surgery is considered. In our present series, none of such patients underwent either resection of the aneurysm or coronary ligation with distal grafting, partly because coronary aneurysms due to KD never rupture except in the acute phase of the disease and partly because surgery on the aneurysm creates difficulties in reconstructing branch vessels and raises some ethical issues about intentional progression of the grade of coronary stenosis by ligation, which may enhance the risk of MI when an ITA bypass graft fails to function well or is too narrow to carry sufficient blood flow for myocardial recovery after anoxic arrest during operation.[8] Recently, partial resection of the noncalcific anterior aneurysmal wall for size reduction of the aneurysm was reported in 9 patients.[29] Vortex blood flow was reduced, but long-term clinical benefits remain uncertain, with high occlusion and ineffective rates (56%) after the procedure.[29]

Although postoperative data on left ventricular function were available in only 72 patients (63%), the left ventricular EF appeared to be an important determinant of outcome in these patients. The postoperative EF averaged 0.55, and that for the 5 deaths was ≤0.5. Poor left ventricular function tended to be associated with sudden death and ventricular arrhythmias, which occurred in 4 of the deaths in this series. Although the EF did not improve after surgery, left ventricular function during exercise improved after successful bypass operations.[30] In fact, it was found that 80% of survivors were enjoying unlimited daily activities, including sports.

All of the patients in this series are now adults with increased risk of atherosclerotic changes that may significantly modify future cardiac status.[4,5] Prolonged observation is mandatory for these patients because of the progressive decline in the cardiac event–free curve demonstrated in this study. By employing early additional therapeutic procedures such as PCI and redo operations, the patients' survival and quality of life were favorably influenced during 25 postoperative years. All of the patients who underwent additional procedures are asymptomatic at present.

Study Limitations and Conclusions

This is an observational study with the usual drawback of possible bias in the selection of patients for surgery, but surgical indications have not changed significantly since the first operation for KD coronary sequelae. During the 25-year follow-up, there has been a decreasing trend for small children to undergo operation because of progress in medical care, including early γ-globulin administration,[6,13] and improved PCI is now more frequently attempted before surgical treatments.[31] Although less frequent than before, patients with severe complicated disease still occur. Eight thousand new KD patients and 20 to 30 operations per year are currently reported in Japan.[13] The indications for and long-term effects of PCI and coronary stenting in growing children remain uncertain, and comprehensive reports on PCI for KD are lacking. Despite its limitations, this study shows that patient survival with surgery is excellent and that the increase in cardiac events with time can be successfully managed with reinterventions. In addition, a continued benefit of the ITA graft on clinical outcome up to 25 years was demonstrated. Pediatric coronary bypass surgery with the use of the ITA should be an established treatment for severe coronary disease due to KD.

Disclosures

None.

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CLINICAL PERSPECTIVE

Nearly 25 years have passed since the first operation for severe inflammatory coronary artery pathology due to Kawasaki disease. We present a comprehensive long-term follow-up study of 114 such patients. There were no operative or hospital deaths, but 5 late deaths, mostly sudden, occurred during the follow-up. Nonsurvivors were characterized by previous myocardial infarction, frequent ventricular arrhythmias, and a left ventricular ejection fraction of ≤0.5. Survival after coronary bypass operation in childhood and adolescence was excellent, with a 20- to 25-year rate of 95% (95% confidence interval, 88 to 98). However, the cardiac event–free rate declined to 67% at 20 years and 60% (95% confidence interval, 46 to 72) at 25 years. Postoperative interventions (percutaneous coronary intervention or reoperation) were most common as a result of graft anastomotic stenosis (early event), graft closure (midterm), new obstructive lesions, and vein graft atherosclerosis (late events). The increase in cardiac events with time can be successfully managed with reinterventions. Internal thoracic artery grafts had significantly better 20-year patency (87%; 95% confidence interval, 78 to 93) than vein grafts (44%; 95% confidence interval, 26 to 61) ($P<0.001$) regardless of the patient's age at operation or target coronary vessels. All 109 survivors are symptom free, and 80% of them are performing unlimited daily activities, although 77% are still receiving 1 to 6 medications, including aspirin in all and warfarin in 21 patients with a patent aneurysm not supported by distal grafts. Pediatric coronary bypass surgery with the use of the internal thoracic artery graft is an established effective treatment for children and adolescents with complicated coronary lesions due to Kawasaki disease.

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Hemodynamic and Echocardiographic Evaluation of Orthotopic Heart Transplantation With the Modified Bicaval Anastomosis Technique

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Background: The purpose of this study was to evaluate the hemodynamic and echocardiographic function of hearts transplanted with the modified bicaval anastomosis technique (mBCAT).

Methods and Results: Twenty consecutive patients (14 males, 6 females, age range 14–61 [41.3±11.5 years]) were evaluated 3.4±2.2 years after heart transplantation using the mBCAT. All patients were in status I on the waiting list, and 18 (90%) had had a left ventricular assist device. The donor age was 39±12 years. Triple immunosuppressive regimen and cardiac biopsy were routinely performed. There was no hospital mortality. One death occurred 4.2 years after the operation because of bone marrow dysplasia and infection. The 8-year survival was 89% (95% confidence interval: 0.43–0.98). All the hemodynamic variables returned to the normal range. Low right atrial pressure (3.2±1.5 mmHg) and low pulmonary wedge pressure (6.7±2.1 mmHg) were associated with an excellent cardiac index (3.9±0.7 $L \cdot min^{-1} \cdot m^{-2}$). Echocardiography revealed an excellent late peak velocity (52±19 cm/s) and an E/A ratio (1.4±0.6) of tricuspid flow. The grade (0–4) of tricuspid regurgitation averaged 1.5±0.8.

Conclusions: Hemodynamic and echocardiographic results for mBCAT were excellent. The 8-year survival was 89% with all surviving patients in New York Heart Association class I. The mBCAT is easy to perform and further facilitates cardiac transplantation. (*Circ J* 2009; **73**: 1235–1239)

Key Words: Cardiac function; Cardiomyopathy; Hemodynamics; Transplantation

The new Japanese legislation for organ transplantation from brain death donors was established in October 1996, and 49 heart transplants have been performed in Japan to the end of 2007[1,2] At the National Cardiovascular Center, 22 patients received heart transplants during the same period. Of the first 2 patients, 1 had the standard biatrial anastomosis technique (BAAT) and the other underwent the original bicaval anastomosis technique (BCAT)[2] The following 20 consecutive patients underwent transplantation using a modified BCAT (mBCAT) developed at our center[3] At present, nearly 70% of heart transplant operations in Japan use this technique, probably because of its easy applicability and some advantages[4] We report the results of a mid-term hemodynamic and echocardiographic evaluation of 20 consecutive patients who have undergone heart transplantation using the mBCAT. We also compare our results with previously published functional results of different transplant techniques.

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Methods

The 20 consecutive patients comprised 14 males and 6 females, ranging in age from 14 to 61 years, with a mean of 41±11 years; the body surface area (BSA) varied from 1.35 to 1.83 m^2 (mean 1.60±0.16 m^2). The diagnosis confirmed by pathological examination of the recipients' original heart was idiopathic dilated cardiomyopathy (DCM) in 17 patients, dilated phase of hypertrophic cardiomyopathy in 1 and cardiac sarcoidosis in 2. Preoperatively, 5 patients had a pacemaker and 2 had an implantable cardiac defibrillator (ICD); 18 (90%) patients had had a left ventricular assist device (LVAD) before transplantation and the remaining 2 patients had been on multiple inotropic agents, requiring intensive care. Consequently, all 20 patients were in the status 1 category. Most LVAD implantations were preceded by insertion of an intraaortic balloon pump, and the LVAD was a Toyobo type for 16 patients and a HeartMate VX device for 2. The average waiting time for transplantation from the time of registration with the Japan Organ Transplant Network and that of heart transplantation varied from 59 to 2,748 days, with a mean of 947±697 days, and the period on LVAD was 702±366 days, varying from 99 to 1,444 days.

Pre- and postoperative cardiac dimensions were assessed by ultrasound cardiography, and hemodynamics were evaluated by cardiac catheterization using a Swan-Ganz catheter.

Table 1. Demographics of 20 Patients Who Underwent Heart Transplantation With the mBCAT

Male/female	14/6
Age (years)	41.3±11.5 (14–61)
Height (cm)	166±10 (146–175)
Weight (kg)	54.2±9.8 (41.5–77.6)
BSA (m^2)	1.60±0.16 (1.35–1.83)
BMI	19.3±2.7 (14.8–23.8)
Blood type	A 7, B 1, O 9, AB 3
Diagnosis	DCM 17, dHCM 1, cardiac sarcoidosis 2
LVAD	18 (90%)
LVAD supported time (days)	702±366 (99–1,444)
Waiting status I	20 (100%)
Waiting time (days)	947±697 (59–2,748)
Donor age (years)	39±12 (18–54)
Total ischemic time (min)	207±26 (137–255)
Rejection episode > grade 2 (times/patient)	1.1±1.4

Values are mean±SD (range).
mBCAT, modified bicaval anastomosis technique; BSA, body surface area; BMI, body mass index; DCM, dilated cardiomyopathy; dHCM, dilated phase of hypertrophic cardiomyopathy; LVAD, left ventricular assist device.

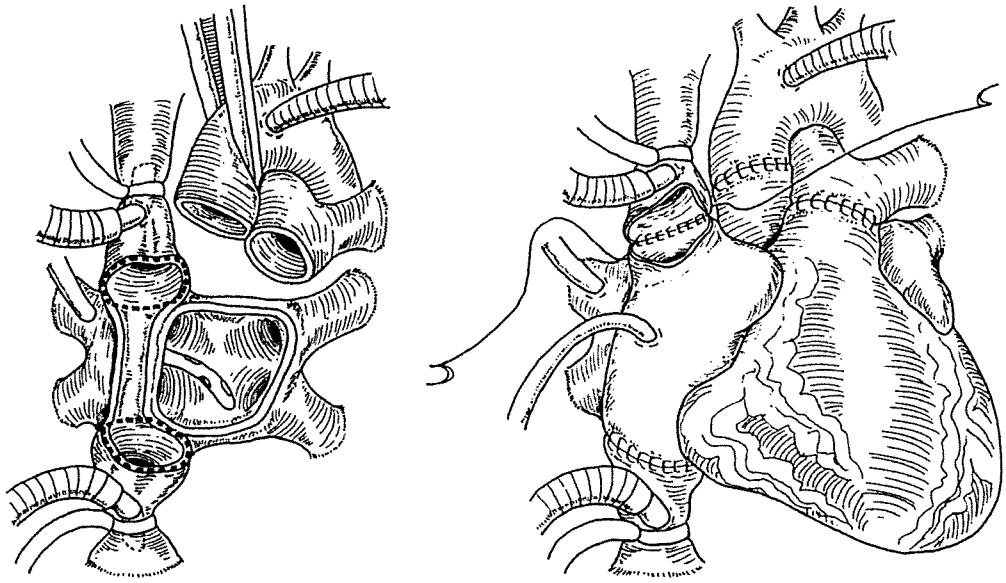

Figure 1. **(Left)** The modified bicaval anastomosis technique. The posterior right atrial wall is left undivided as a cuff bridging the superior and inferior venae cavae to maintain the anatomical orientation without traction, kinking or distortion of the superior and inferior venae cavae. **(Right)** By expanding the suture line into the preserved posterior wall of the right atrium, anastomosis with a large donor heart can be easily accomplished. Also, adjustment of the distance between the superior and inferior venae cavae can be done with ease when the donor heart is small.

Assessment of the pre-transplant hemodynamics and plasma brain natriuretic peptide (BNP) level was performed prior to LVAD installment. Post-transplant studies were done 3.4±2.2 years after operation. The demographics of the 20 patients are listed in **Table 1**.

Operation

Donor Heart Procurement The age of the donors averaged 39±12 years, ranging from 18 to 54 years. The donor hearts were recovered at various locations in Japan and usually transported by jet charter flight unless they were retrieved at a near-by hospital in which case road transport was used. For the most of recent patients (80%), Celsior solution[5] was used for both cardioplegic arrest during extraction and storage during transportation, whereas for the initial 4 patients in this series, St Thomas solution was used[2] The total ischemic time from cardiac extraction to aortic declamping at the final stage of the transplant procedures varied from 137 to 255 min with a mean of 207±26 min.

Transplant Procedure The transplantation procedure used in the present series was the mBCAT, reported by us in 2000[3] Briefly, the posterior right atrial (RA) wall is left undivided as a cuff connecting the superior (SVC) and inferior venae cavae (IVC), as illustrated in **Figure 1**. Without complete division and separation of the SVC and IVC their anatomical orientation is well maintained and the distance required for the graft tissue to fit exactly between them is easily judged, thereby avoiding traction, kinking or distortion of either of the vessels. This modification is particularly useful when there is a size mismatch between the donor and recipient hearts.

Postoperative Management and Episodes of Rejection Triple immunosuppressive regimen was routinely used. All patients, except 4 (80%), started with Neoral (cyclosporine

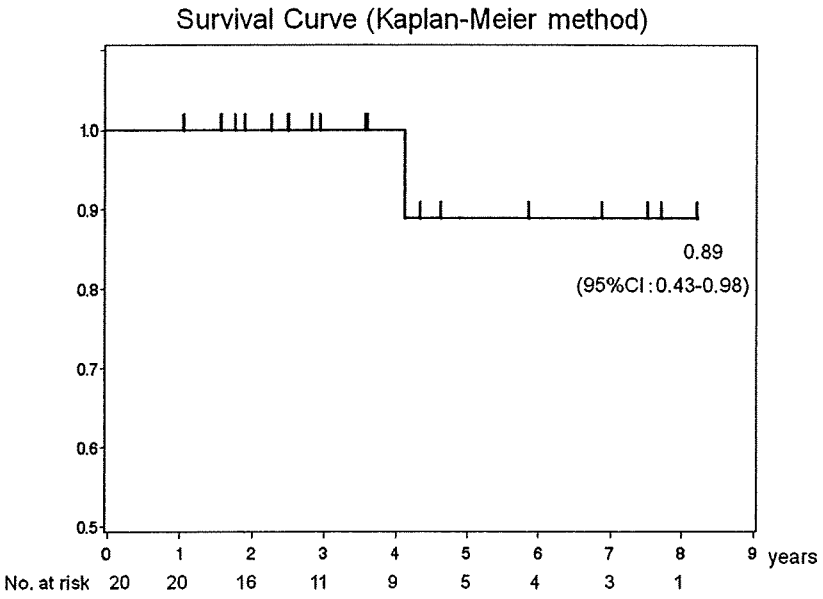

Figure 2. The 8 years survival of 20 consecutive patients with a heart transplanted using the modified bicaval anastomosis technique was 89% with a 95% confidence interval (CI) of 0.43 to 0.98. All surviving patients are in New York Heart Association class I at present.

Table 2. Pre- and Post-Transplant Hemodynamic Variables

	Pre-OP (n=20), mean±SD	Post-HTx (n=20), mean±SD	P valve
Echocardiography			
LVDd (mm)	72.0±8.5	40.7±4.9	<0.001
LVDs (mm)	65.2±9.0	24.9±4.1	<0.001
EF	0.20±0.08	0.6±0.07	<0.001
FS (%)	10±4	40±6	<0.001
IVS thickness (mm)	7.3±2.0	9.0±1.3	<0.001
PW thickness (mm)	7.3±1.9	8.9±1.3	<0.001
Catheterization			
HR (beats/min)	88±9	92±7	0.089
CO (L/min)	3.1±0.7	6.1±1.2	<0.001
CI ($L \cdot min^{-1} \cdot m^{-2}$)	1.9±0.4	3.9±0.7	<0.001
PAWP (mmHg)	25.8±0.6	6.7±2.1	<0.001
PAs (mmHg)	45.8±15.7	20.8±3.8	<0.001
PAd (mmHg)	20.6±9.0	7.8±2.2	<0.001
PAm (mmHg)	31.0±11.0	13.0±2.6	<0.001
RVs (mmHg)	45.5±16.0	23.0±4.0	<0.001
RVEDP (mmHg)	11.3±5.5	4.4±1.8	<0.001
RA (mmHg)	11.7±5.5	3.2±1.5	<0.001
TPG (mmHg)	5.3±7.0	6.3±2.7	0.56
PVR (WU)	1.7±2.3	1.1±0.6	0.25
Plasma BNP (pg/ml)	725±291	55±49	<0.001

OP, operation; HTx, heart transplant; LVDd, left ventricular diameter (diastolic); LVDs, left ventricular diameter (systolic); EF, ejection fraction; FS, fractional shortening; IVS, interventricular septum; PW, posterior wall; HR, heart rate; CO, cardiac output; CI, cardiac index; PAWP, pulmonary artery wedge pressure; PAs, pulmonary artery pressure systolic; PAd, pulmonary artery pressure diastolic; PAm, pulmonary artery pressure mean; RVs, right ventricular systolic pressure; RVEDP, right ventricular end-diastolic pressure; RA, right atrial pressure; TPG, trans-pulmonary pressure gradient; PVR (WU), pulmonary vascular resistance (Wood units); BNP, brain natriuretic peptide.

A), Cellcept (mycophenolate mofetil), and prednisone[6] Prograf (tacrolimus) was selected as the first calcineurin inhibitor in 4 patients, mainly to enhance our clinical experience with this drug. Serum concentrations of cyclosporine A, tacrolimus and mycophenolate mofetil were routinely monitored to facilitate dose adjustment[7]

Endomyocardial biopsy was performed according to schedule in the usual manner. Rejection was judged microscopically, based on the criteria of the 1990 report of the International Society of Heart and Lung Transplantation[8] with reference to the 2004 revision[9] Rejection episodes greater than grade 2 occurred 1.1±1.4 times per patient during the follow-up. Rejection of more than 3A was identified in 2.7% of 340 biopsy specimens from the 20 patients, and was successfully controlled by steroid pulse therapy, switching cyclosporine A to tacrolimus or a combination.

Statistical Analysis

Values are mean±standard deviation. Pre- and post transplant cardiac dimensions and function in each patient were compared by paired t-test. Survival was calculated by the Kaplan-Meier method. Differences were judged statistically significant at $P<0.05$.

Table 3. Post-Transplant Trans-Atrioventricular Valve Flow and Regurgitation by Echocardiography

	Tricuspid valve (n=20)	Mitral valve (n=20)
Regurgitation (grade 0–4)	1.5±0.8 (0–3*)	0.6±0.6 (0–2)
Late peak velocity of flow (cm/s)	52±19	40±11
E/A ratio	1.4±0.6	2.2±0.7

*Grade 3 tricuspid regurgitation resulted from chordal damage at endomyocardial biopsy (1 patient).

Results

Survival

There were no operative or hospital deaths and all patients were successfully discharged from hospital. A 59-year-old male patient died 4 years and 2 months after transplantation. His postoperative course was complicated by dysplasia of the bone marrow and cytomegalovirus gastric ulcer requiring an emergency gastrectomy. The final cause of death was pneumonia. The remaining 19 patients were all doing well in New York Heart Association class I, and the Kaplan-Meier survival rate up to 8 years was 89% (95% confidence interval 43–98) (**Figure 2**). No one required a pacemaker or ICD implantation after transplantation.

Hemodynamic and Echocardiographic Assessments

The hemodynamic and echocardiographic assessments of the heart before and after transplantation are shown in **Tables 2,3**. After transplantation, all cardiac function parameters and dimensions completely returned to normal. Preoperative and post-transplant differences in the hemodynamic and echocardiographic variables were all markedly significant at $P<0.001$, except for heart rate ($P=0.089$) and pulmonary vascular resistance ($P=0.25$). All patients were in normal sinus rhythm. The mean RA pressure in the mBCAT patients was 3.2±1.5 mmHg. There were no measurable pressure gradients between the SVC or IVC and the RA. The late peak velocity of tricuspid flow was 52±19 cm/s and the E/A ratios of tricuspid and mitral flow were 1.4±0.6 and 2.2±0.7, respectively. The incidence of moderate to severe tricuspid valve regurgitation (TVR) was 5%, with a mean grade of 1.5±0.8 (range 0–3). In 1 patient in this series, chordal injury of the tricuspid valve accidentally occurred at the time of endomyocardial biopsy, which resulted in grade 3 TVR. The pre-transplant plasma level of BNP was 725±291 pg/ml (range 342–1,099) and it was significantly reduced to 55±49 pg/ml (range 5–172), postoperatively ($P<0.0001$).

Discussion

Orthotropic heart transplantation is a well-established treatment for end-stage heart failure and the post-transplant recovery of patients is dramatic. Although life-long care for the control of rejection and infection is necessary, this has significantly improved in recent years. As shown in this study, the grade of hemodynamic improvement with heart transplantation was really excellent, with a resultant 8-year survival of 89%, in contrast to that for left ventricular restoration surgery for congestive heart failure because of DCM.[10]

On the other hand, operative techniques for heart transplantation have not changed significantly from the original BAAT developed in the experimental era by Shumway, Lower, and Stofer.[11] The only option to the standard BAAT is the BCAT developed by Dreyfus et al.[12] Multiple comparisons of these surgical techniques have been conducted to date,[13–17] most of which favor the BCAT because the well-maintained RA architecture and function (contraction) reduces the incidence of TVR.

The hemodynamic and echocardiographic data for our patients undergoing the mBCAT resembled those previously reported for the original BCAT.[13–17] The values for RA, right ventricular, pulmonary arterial and pulmonary capillary wedge pressures in our series agreed with those obtained after BCAT and reported by El-Gamel et al,[13] Aziz et al,[14] Traversi et al,[15] and Sun et al.[16] The RA pressure was always lower with the BCAT than with the BAAT. The increased late diastolic tricuspid flow (52±19 cm/s) in the present patients after the mBCAT was similar to that with the BCAT (48±18 cm/s) reported by Sun et al[16] and clearly indicated more vigorous RA contraction followed by better RA and right ventricular relaxation with the BCAT or mBCAT. Also, the E/A ratio of tricuspid flow in our patients (1.4±0.6) was close to that with BCAT in Traversi et al's series (1.2±0.5).[15] The incidence of moderate to severe TVR was as low as 5%, with a mean grade of 1.5±0.8 (range 0–3), and that of mitral regurgitation was essentially none, and there has been no requirement for pacemaker implantation in any of the patients from this series. Accidental chordal damage of the tricuspid valve at the time of endomyocardial biopsy is an important causative factor for significant TVR, and occurred in 1 patient in this series, causing acute onset of grade 3 TVR (5%). The biopsy specimen contained a piece of the chordal tissue. Otherwise, the grade of TVR has been mild and stable to date in this series.

The adverse impact of significant TVR on mortality or the need for re-transplantation has also been stressed in pediatric heart transplantation,[18] and prophylactic donor tricuspid annuloplasty by the DeVega method in order to prevent post transplant TVR was recently reported to be effective in decreasing cardiac-related mortality.[19] In addition, some previous articles[15,16,19] strongly suggested benefits of the BCAT that contribute to a reduction in long-term cardiac-related mortality. However, 2 recent papers dealing with the same subject either by conducting a systemic review and meta-analysis[20] or by analyzing the UNOS database[21] reached a similar conclusion, namely, that both the BCAT and BAAT lead to equivalent survival, and that the long-term beneficial effects, such as exercise capacity and health-related quality of life, remain to be evaluated. Nevertheless, both reports again admit the clinically relevant beneficial effects of the BCAT in comparison with the standard BAAT.

Although this was an observational study and it is difficult to demonstrate the superiority of the mBCAT compared with the original BCAT, which was performed in only 1 patient[2] not included in this series, clinical outcomes, including the survival rate up to 8 years, were excellent with similar hemodynamic and echocardiographic results to those previously reported for the BCAT.[13–17] With this modified technique, there have been no adverse effects attributable to

leaving a strip of the posterior wall of the right atrium. The mBCAT has been accepted as an easy alternative in nearly 70% of orthotopic heart transplantation in Japan[4] The mBCAT can prevent some technical disadvantages encountered with the original BCAT, such as shrinkage, retraction and distortion of the SVC and IVC, with no additional operating time required. Moreover, we often found that the anastomosis could be carried out with ease in cases of mismatched donor–recipient hearts because we could create a large anastomotic orifice by expanding the suture line into the preserved posterior wall of the right atrium when the donor heart was large or we could easily adjust the distance between the SVC and IVC when the donor heart was small. There have been no episodes of caval anastomotic stenosis[22] in our series. In conclusion, this modification further facilitates techniques for transplantation with the same hemodynamic and echocardiographic benefits as with the original BCAT.

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Is Diabetic Nephropathy a Predicted Risk Factor?
—— Kaplan-Meier and Multivariate Analysis of Confounding Risk Factors in Off-Pump Coronary Artery Bypass Grafting for Chronic Dialysis Patients ——

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Is Diabetic Nephropathy a Predicted Risk Factor?
—— Kaplan-Meier and Multivariate Analysis of Confounding Risk Factors in Off-Pump Coronary Artery Bypass Grafting for Chronic Dialysis Patients ——

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Background: The purpose of this study was to investigate the preoperative risk factors of performing off-pump coronary artery bypass grafting (OPCAB) in patients on chronic dialysis.
Methods and Results: The 41 consecutive patients on chronic dialysis who underwent OPCAB from February 2000 to April 2006 at the National Cardiovascular Center were studied retrospectively. Of them, 29 had diabetic nephropathy (DN group) and the remaining 12 did not (NDN group). There were significant differences in the duration of dialysis before surgery (9.1±7.5 years in NDN vs 4.2±5.5 years in DN, P=0.028) and low cardiac function (left ventricular ejection fraction <30%), which was recognized only in the DN group (7/29, P=0.048). The early mortality rate was 6.9% (2/29) in the DN group and 16.7% (2/12) in the NDN group (P=0.349). The actuarial survival rates in the DN group were 85% at 1 year, 45% at 3 years, and 30% at 5 years, whereas in the NDN group they were 71%, 49%, and 49%, respectively (P=0.789). Arteriosclerosis obliterans (ASO) and age (>65 years) were independent risk factors of late death.
Conclusions: For patients on chronic dialysis ASO and aging were predicted risk factors for OPCAB, whereas diabetic nephropathy was not. (*Circ J* 2009; **73**: 2056–2060)

Key Words: Diabetic nephropathy; Dialysis; Off-pump coronary artery bypass grafting

It is still controversial whether off-pump coronary artery bypass grafting (OPCAB) is more effective than conventional on-pump coronary artery bypass grafting (CABG) in the population of poor prognosis patients. OPCAB is the most common strategy of CABG for low-risk patients in Japan,[1] but often there are patients with severe complications who require CABG and for whom either on-pump or off-pump surgery might be reasonable. A recent prospective study showed that chronic renal disease is independently associated with adverse long-term outcomes in a broad cohort of Japanese patients,[2] making chronic dialysis one of the most high-risk preoperative comorbidities in Japan. These days, the number of patients on chronic dialysis is increasing in parallel with the increase in diabetes, which is known as the leading cause of chronic renal failure requiring dialysis. In general, natural prognoses for patients on chronic dialysis are worse for those with diabetic nephropathy than for non-diabetic nephropathy patients. According to The United Kingdom Prospective Diabetes Study (2003), the largest-scale prospective study of diabetic nephropathy, when serum creatinine levels increase over 2.0 mg/dl, renal failure becomes end-stage, which requires dialysis within approximately 2.5 years and at which point the patient is likely to die within 3 years,[3] with the major cause of death being cardiovascular disease.[4,5]

We mainly perform OPCAB in chronic dialysis patients and their intraoperative management has been established with an acceptable clinical outcome. In the present study, we investigated the preoperative and intraoperative confounding factors for chronic dialysis patients who underwent OPCAB and we assessed the impact of diabetic nephropathy and other possible risk factors on midterm survival after OPCAB in this population.

Methods

Patients

Among 1,050 consecutive patients undergoing OPCAB at the Department of Cardiovascular Surgery, National Cardiovascular Center, between February 2000 and April 2006, there were 41 patients on chronic dialysis (3.9%).

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Table 1. Patient Demographics

	DN (n=29)	NDN (n=12)	P value
Duration of dialysis (years)	4.2±5.5	9.1±7.5	0.02
Age (years)	65.7±8.8	67.9±7.6	NS
M/F	23/6	11/1	NS
Hyperlipidemia	7 (24%)	3 (25%)	NS
Hypertension	12 (41%)	6 (50%)	NS
Arteriosclerosis obliterans	9 (36%)	2 (17%)	NS
History of AAA	0	4 (33.3%)	0.04
Calcified ascending aorta	5 (17%)	3 (25%)	NS
COPD	0	0	NS
History of cerebrovascular disease	5 (20.8%)	3 (23.1%)	NS
Extent of disease			
1VD	0	0	
2VD	6 (20.6%)	0	0.05
3VD	15 (51.7%)	12 (100%)	0.05
Left main trunk disease	3 (10.3%)	1 (8.3%)	NS
Mean no. of diseased vessels	2.8±0.4	2.7±0.6	NS
LVEF <30%	7 (24.1%)	0	0.04
Valvular disease			
Mitral (>Grade 3)	1 (3.4%)	0	NS
Aortic (>Grade 3)	0	0	NS
History of PCI	4 (13.7%)	2 (16.7%)	NS
Previous MI	11 (37.9%)	4 (33.3%)	NS
Unstable angina pectoris	7 (24.1%)	4 (33.3%)	NS
Acute MI	2 (7.0%)	1 (8.3%)	NS
Preoperative IABP	3 (10.3%)	1 (8.3%)	NS

DN, diabetic nephropathy; NDN, non-diabetic nephropathy; AAA, abdominal aortic aneurysm; COPD, chronic obstructive pulmonary disease; VD, vessel disease; LVEF, left ventricular ejection fraction; PCI, percutaneous catheter intervention; MI, myocardial infarction; IABP, intra-aortic balloon pumping.

These patients' preoperative characteristics are shown in **Table 1**: 29 (70.7%) had diabetic nephropathy (DN group) and 12 (29.3%) did not (NDN group). The causes of renal failure in the NDN group were chronic glomerulonephritis (n=4), nephrosclerosis (n=6) and unknown (n=2). There were no significant preoperative differences between the DN and NDN groups except for duration of dialysis and cardiac function. At the time of operation, the duration of dialysis was longer in the NDN group (9.1±7.5 years) than in the DN group (4.2±5.5 years) (P=0.028). Poor cardiac function (left ventricular ejection fraction (LVEF) <30%) was recognized only in the DN group (P=0.048).

Urgent operation was performed for 7 patients because of unstable angina or acute myocardial infarction with unstable hemodynamic conditions, and the remaining 34 patients underwent elective surgery in a stable condition.

Institutional approval for this study was obtained, and each patient gave informed consent to serve as a subject.

Surgical Technique

At the National Cardiovascular Center, OPCAB with extensive use of an arterial conduit has been performed since 2000. In our recent series, total arterial revascularization by OPCAB achieved excellent patency in the early postoperative period and showed good clinical results, and for this reason we prefer to perform it. Our standard technique is composite grafting of the radial artery (RA) in combination with 1 or both internal thoracic arteries (ITA).[6] In dialysis patients, however, the RA either needs to be reserved for shunt formation for dialysis or has already been used, so bilateral ITA composite grafting is often used for complete revascularization. The advantage of this method is that it avoids neurologic complications, because we use the aorta no-touch technique (ie, no side clamping of the diseased aorta). In high-risk patients, such as elderly patients, obese female patients and patients with chronic obstructive pulmonary disease (COPD), we occasionally use a single ITA plus either the saphenous vein (SV) or gastroepiploic artery (GEA) if they are in acceptable condition (**Table 2**).

Table 2. Surgical Results

	DN (n=29)	NDN (n=12)	P value
Mean no. of bypass grafts	3.0±0.8	3.4±1.1	NS
Urgent	5 (17.2%)	2 (16.7%)	NS
All arterial grafts	22 (75.8%)	6 (50.0%)	0.146
Bilateral ITA use	22 (75.8%)	3 (25.0%)	<0.0001
Composite grafting	19 (65.5%)	2 (16.6%)	0.006
All in-situ	7 (24.1%)	3 (25.0%)	NS
GEA use	1 (3.4%)	0	NS
Single ITA+GEA	0	2 (16.6%)	0.08
Single ITA+RA	2 (6.8%)	0	NS
Operation time (h)	309±81	307±35	NS
Graft patency	100% (88/88)	94% (30/32)	NS
Hospitalization (days)	37±47	36±48	NS

GEA, gastroepiploic artery; RA, radial artery. Other abbreviations see in Table 1.

Definitions

Early mortality was defined as any death occurring within 30 days after the operation or during the initial hospital stay, and late mortality was any death occurring after that. Development of congestive heart failure (CHF), fatal or non-fatal myocardial infarction, requirement for a cardiac intervention (redo-CABG, percutaneous transluminal coronary angiography etc) or sudden, unexplained death were all considered as cardiac events.

Patient Follow-up

Follow-up information was obtained from each patient's hospital record, interviews at the time of outpatient visits, telephone calls and from referring physicians.

Statistical Analysis

Comparison between groups was performed using the unpaired Student's t-test and the χ^2 test for categorical variables. Actuarial survival and cardiac event-free survival was calculated by the Kaplan-Meier method. Cox proportional hazard models were used to determine the influence of patients' characteristics and operative data on late survival. Hazard ratios, 95% confidence intervals, and levels of statistical significance (P value) were calculated. All results were expressed as mean±standard deviation and P<0.05 was considered statistically significant.

Results

Perioperative Data

Intraoperative data are shown in **Table 2**. There were no cases of conversion from OPCAB to CABG in either group. Complete revascularization was accomplished in all cases. Revascularization using only arterial grafts was more frequently performed in the DN group than in the NDN group (P=0.146). Bilateral ITAs were more often used in the DN group (P<0.001), as were composite grafts using only the left ITA (P=0.006).

Table 3. Postoperative Morbidity

	DN (n=29)	NDN (n=12)	P value
Postoperative morbidity	18 (62.0%)	7 (58.3%)	NS
GI complication	2 (6.9%)	2 (16.7%)	NS
Infection	7 (29.2%)	3 (23.1%)	NS
Superficial wound	4 (13.8%)	1 (8.3%)	NS
Deep sternum	1 (3.4%)	0	NS
Respiratory	2 (6.9%)	0	NS
Stroke	2 (6.9%)	1 (8.3%)	NS

GI, gastrointestinal. Other abbreviations see in Table 1.

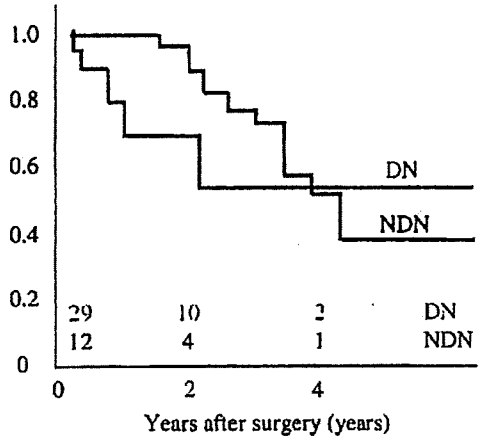

Figure 1. Freedom from any cardiac events after surgery between diabetic nephropathy (DN) and non-diabetic nephropathy (NDN) patients on dialysis.

Table 4. Postoperative Mortality

	DN (n=29)	NDN (n=12)	P value
Hospital death	2 (6.9%)	2 (16.6%)	NS
Mediastinitis	2 (100%)	0	
GI complication	0	2 (100%)	
Late death	11 (37.9%)	3 (10.3%)	NS
Heart failure	4 (36.3%)	1 (33.3%)	
MI	1 (9.0%)	1 (33.3%)	
Respiratory complication	1 (9.0%)	0	
GI complication	1 (9.0%)	0	
SIRS	1 (9.0%)	0	
Unknown	3 (27.2%)	1 (33.3%)	

SIRS, systemic inflammatory response syndrome. Other abbreviations see in Tables 1,3.

Postoperative coronary angiography was performed within 1 month after surgery in 33 patients (80.5%: 23 patients in the DN group, 10 patients in the NDN group). All grafts (88/88) were patent in the DN group compared with 94% (30/32) in the NDN group. Graft occlusion occurred in 2 patients in the NDN group: GEA–PL and RITA–D1. Neither patient had experienced any cardiac events after graft occlusion.

Morbidities and Mortalities

Operative morbidities are shown in **Table 3**. No differences were found in the incidence of postoperative morbidities, including mediastinitis and superficial wound problems.

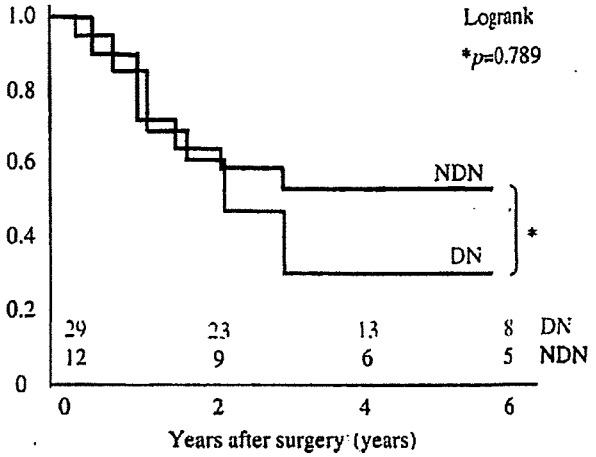

Figure 2. Survival after surgery between diabetic nephropathy (DN) and non-diabetic nephropathy (NDN) patients on dialysis.

Table 5. Preoperative and Intraoperative Confounding Factors for Cox Hazard Model

Preoperative confounding factors	Intraoperative confounding factors
Duration of dialysis (years)	Bilateral ITA
Age	Functional complete revascularization
M/F	
Diabetes	
Hyperlipidemia	
Hypertension	
ASO	
History of AAA	
Calcified ascending aorta	
COPD	
History of cerebrovascular disease	
3VD	
Left main trunk disease	
LVEF <30%	
History of PCI	
Previous MI	
Unstable angina pectoris	
Acute myocardial infarction	
Preoperative IABP	

ASO, arteriosclerosis obliterans; ITA, internal thoracic artery. Other abbreviations see in Table 1.

Table 6. Cox Proportional Hazard Model for Death at Midterm Follow-up

	HR	95%CI	P value
Age	0.534	0.306–0.890	0.016
ASO	0.367	0.194–0.681	0.002
History of AAA	0.475	0.238–1.053	0.064
No. of diseased vessels	0.364	0.112–1.215	0.098

HR, hazard ratio; CI, confidence interval. Other abbreviations see in Tables 1, 5.

Mediastinitis occurred only in patients from the DN group who had had both ITAs harvested.

Freedom from cardiac event is shown in **Figure 1**. The actuarial freedom from postoperative cardiac events among the DN group was 92% at 1 year, 60% at 3 years and 28% at 5 years, whereas in the NDN group it was 60%, 45% and 43%, respectively. There were no statistical differences

between the 2 groups. The linearized rate of postoperative cardiac events was 18.03 events per 100 patient-years in the DN group and 18.23 events per 100 patient-years in the NDN group, which showed no significant difference between the 2 groups (P>0.999).

Early and late mortalities are shown in **Table 4**. Early death occurred in 2 patients in the DN group (6.9%; mediastinitis caused by methicillin-resistant *Staphylococcus aureus*) and in 2 patients in the NDN group (16.7%; gastrointestinal complications) (P=0.349).

There were 11 (37.9%) late deaths in the DN group and 3 (25.0%) in the NDN group (P=0.439). The most frequent cause of death in the DN group was heart failure associated with dialysis cardiomyopathy, which was caused by long-term dialysis.

The actuarial survival after operation in the DN group was 85% at 1 year, 45% at 3 years, and 30% at 5 years, compared with 71%, 49%, and 49%, respectively, in the NDN group (**Figure 2**).There was no significant difference between the 2 groups (P=0.789). Cox proportional hazard models were used to assess the effect of preoperative and intraoperative confounding factors (**Table 5**) on late death. As shown in **Table 6**, the significant predictors of late death were arteriosclerosis obliterans (ASO) (P=002) and age (>65 years) (P=0.016).

Discussion

In the current era, diabetes is the most common reason for dialysis. According to a recent overview of dialysis treatment in Japan, diabetic nephropathy constitutes the highest proportion (42.9%) of primary renal diseases in patients who began dialysis, which is approximately twice as much compared with 20 years ago.[7] Cardiovascular disease is the major cause of death, accounting for more than 50% of cases.[8–11] In addition to significantly developed cardiovascular disease prior to the initiation of dialysis, the tissue deposition of advanced glycosylation end-products may also have an influence on cardiovascular mortality once dialysis has begun.[12–14] Based on these facts, adequate treatment for cardiovascular disease is the key to better prognosis for these patients.

Several recent reports on survival of patients with chronic dialysis after CABG[4,15–26] have demonstrates the operation can be performed with an acceptable mortality and morbidity for dialysis patients.[16,17,19,23,24,26] Herzog et al reported that dialysis patients have better long-term survival after CABG surgery than after percutaneous coronary intervention, especially diabetic patients.[23]

In Japan, OPCAB is currently the most common strategy for patients with coronary artery disease. According to the registry of the Japanese Association for Thoracic Surgery in 2006, 64% of patients on chronic dialysis had undergone OPCAB and mortality for patients on dialysis was 8.5%, whereas hospital mortality was 6.4%.[1] In the present study, hospital mortality was 6.9% in the DN group and 16.7% in the NDN group, both of which were higher than the hospital mortality of patients without dialysis, which was 1.9%.

With regard to the preoperative characteristics, there were several differences between the DN and NDN groups. The period from initiation of dialysis to surgery in the DN group was significantly shorter than that of the NDN group (P=0.02). Preoperative left ventricular function in the DN group was significantly lower than in the NDN group (P=0.04).

The surgical strategy, including graft selection, may be an important predictor for outcome of these patients. We use an arterial composite graft to achieve complete revascularization and avoid side-clamping of the diseased ascending aorta (ie, the aorta no-touch technique). In general, the use of a total arterial graft with bilateral ITAs has an advantage for long-term graft patency.[27–31] Recent reviews demonstrate that using the bilateral ITAs is effective for both diabetic and dialysis patients;[29,30] however, their use in diabetic patients, especially those on chronic dialysis, has the potential risk of mediastinitis. We had only 1 case of deep sternal infection (2.4%), which was in the DN group (bilateral ITAs were used for this patient). A skeletonized technique is preferable for reducing the risk of mediastinitis or other sternal wound problems in patients with poor risks, such as diabetes and renal failure.[29–31] Regarding graft selection in diabetic patients on dialysis, the RA is not available because of its use as a primary arteriovenous fistula for vascular access. The SV and GEA are also less available because of severe arteriosclerosis of the abdominal aorta or/and ASO. For these reasons we generally use the bilateral ITAs even in diabetic patients on dialysis.

Cox proportional hazard models were performed to assess the predicted factors for late death because there were several critical biases in both the preoperative and intraoperative conditions. As analyzed by the Kaplan-Meier method, diabetes was not a predicted risk factor in this population. Use of bilateral ITAs and complete revascularization were expected to be important factors for the survival, but, unexpectedly, the Cox model did not show any influence on midterm survival in this population. On the other hand, ASO and aging were the predicted risk factors in this population, which is a reasonable result because the presence of ASO suggests general progressive arteriosclerosis, not to mention aging.[32]

We also analyzed the actuarial survival of the diabetic and non-diabetic patients when patients with low cardiac function (LVEF <30%) are excluded. The result was that there was no significant difference between these patients (P=0.935).

Study Limitations

This was a retrospective study and had a relatively small number of patients. Longer follow-up and a larger number of patients will be necessary in order to obtain stronger evidence.

In conclusion, the midterm survival of both diabetic and non-diabetic nephropathy patients on chronic dialysis after OPCAB was acceptable. Multivariate analysis suggests that diabetes is not a predicted risk factor for OPCAB in chronic dialysis patients, whereas peripheral arterial disease and aging are.

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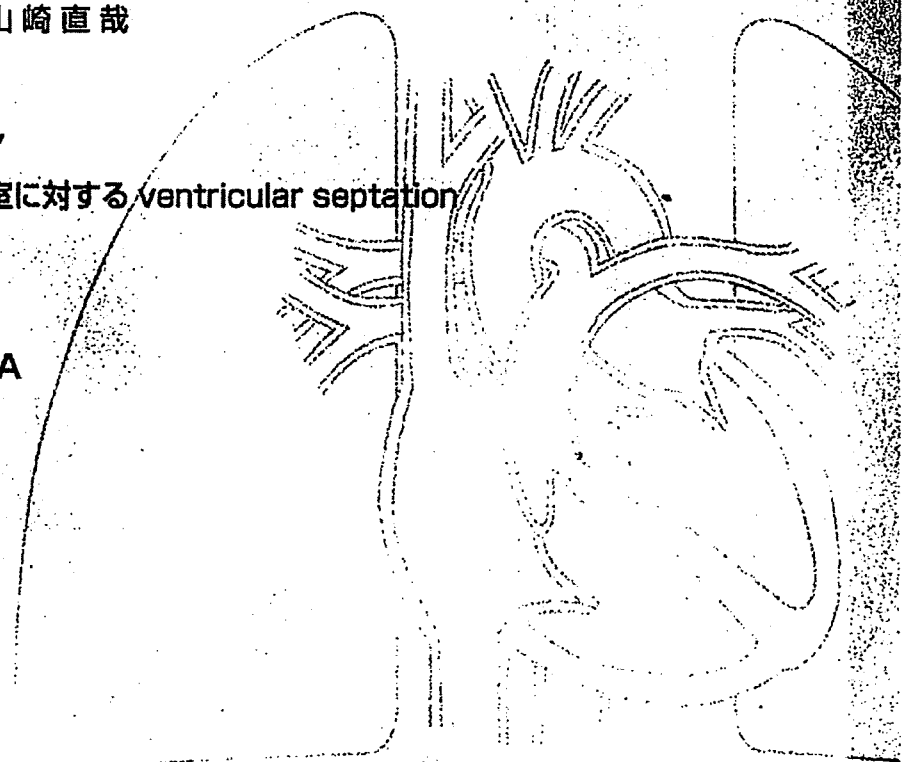

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