TABLE 3. Operative and postoperative data of patients with right internal thoracic artery as in situ or free graft

	All (n = 705)	In situ (n = 547)	Free (n = 158)	*P* value
Anastomoses per patient (mean ± SD)	4.2 ± 1.2	4.2 ± 1.2	4.2 ± 1.1	.9290
Anastomoses of right internal thoracic artery per patient (mean ± SD)	1.1 ± 0.5	1.0 ± 0.3	1.7 ± 0.7	<.0001
Grafts per patient (mean ± SD)		3.3 ± 0.6	3.1 ± 0.5	<.0001
Long segment reconstruction of left anterior descending artery (no.)	288 (40.9%)	218 (39.9%)	70 (44.3%)	.3625
Operative time (min, mean ± SD)	282.3 ± 59.1	278.3 ± 57.9	296.3 ± 61.2	.0007
Transfusion (no.)	257 (36.5%)	192 (35.1%)	65 (41.1%)	.1952
Intubation (h, mean ± SD)	10.1 ± 16.2	10.4 ± 17.3	9.0 ± 11.1	.3359
Intensive care unit stay (d, mean ± SD)	2.0 ± 8.2	2.1 ± 9.2	1.7 ± 1.6	.5414
Operative death (within 30 d, no.)	7 (1.0%)	5 (0.9%)	2 (1.3%)	.6569
Reexploration for bleeding (no.)	6 (0.9%)	4 (0.7%)	2 (1.3%)	.6208
Low output syndrome (no.)	12 (1.7%)	10 (1.8%)	2 (1.3%)	>.9999
Perioperative myocardial infarction (no.)	12 (1.7%)	9 (1.6%)	3 (1.9%)	.7366
Severe ventricular arrhythmia (no.)	5 (0.7%)	2 (0.4%)	3 (1.9%)	.0774
Atrial fibrillation (no.)	186 (26.4%)	147 (26.9%)	39 (24.7%)	.6542
Hemodialysis required (no.)	14 (2.0%)	10 (1.8%)	4 (2.5%)	.5282
Stroke (no.)	8 (1.1%)	6 (1.1%)	2 (1.3%)	>.9999
Mediastinitis (no.)	12 (1.7%)	7 (1.3%)	5 (3.2%)	.1534

We also analyzed the subgroup of 312 patients (44.3%) who underwent both early and 1-year angiographic studies. In this subgroup of patients, there were no significant differences in the patency rate at early ($P > .9999$) and 1-year ($P = .0711$) angiography between in situ and free right ITA groups. Among patients with in situ right ITA grafts (n = 257), 4 patients had nonpatent right ITA in the early study and 10 patients had nonpatent right ITA in the 1-year study. Six patients had newly developed nonpatency of right ITA graft at the 1-year study. Four of these 6 patients had a low stenosis rate (50%–75%) in the target coronary artery.

On the other hand, among patients with a free right ITA (n = 55), there was 1 patient whose right ITA was not patent in the early study and 6 patients whose right ITAs were not patent in the 1-year study. Five patients had newly developed nonpatent free right ITA grafts at the 1-year study. These 5 patients had a low stenosis rate (50%–75%) of the target coronary artery.

DISCUSSION

The right ITA is frequently used as a second or third arterial graft, as well as the radial artery or gastroepiploic artery.[9]

TABLE 4. Cumulative angiographic patency rates of in situ and free right internal thoracic artery grafts

	Early (n = 579)	1 y (n = 336)
Total	98.8% (572/579)	94.3% (317/336)
In situ	98.6% (438/444)	95.3% (264/277)
Anterior	99.4 % (307/309)	98.5% (197/200)
Lateral	98.1% (105/107)	89.3% (50/56)
Inflow	92.9% (26/28)	81.0% (17/21)
Free	99.3% (134/135)	89.8% (53/59)
Composite graft	99.1% (105/106)	89.8% (44/49)
Aorta	100% (29/29)	90% (9/10)

All figures represent percentages of patent grafts, with numbers of patent grafts and total grafts given in parentheses.

Because the right ITA is anatomically the same as the left ITA, a longer patency duration would be expected than with other arterial grafts. Because the length of the right ITA when it is used as an in situ graft is sometimes not sufficient for revascularization for lateral vessels, however, several configurations have been proposed,[10] such as an in situ graft to the LAD and a free graft with proximal anastomoses to the aorta or an in situ left ITA. Although there have been many reports describing the feasibility and efficacy of each technique, little has been reported about angiographic patency rates comparing several configurations simultaneously. This study demonstrated that clinical and angiographic outcomes were not significantly different between in situ and free right ITA grafts at early and 1-year follow-up. Additionally, in situ right ITA grafting to the LAD system had a superior patency rate to other types of right ITA grafting at early and 1-year angiography.

When the right ITA is used as an in situ graft, it can be useful for revascularization of anterior or lateral vessel for single anastomosis. When the in situ right ITA is anastomosed to the LAD or diagonal branch, it is directed anterior to the aorta.[11] In such cases, the right ITA should be wrapped in thymic tissue and covered with mediastinal fat to prevent injury at reopening.[12] We used an in situ right ITA for revascularization of the anterior territory in 70.7% of patients. An in situ right ITA has sufficient length to reach anterior vessels in almost all patients. It is useful for unstable left main and bifurcation disease when combined with the use of an in situ left ITA for lateral vessels. When the right ITA is anastomosed to the circumflex artery territory, it is passed through the transverse sinus.[13] In such cases, care should be taken not to twist the graft. We used an in situ right ITA for lateral territory in 23.2% of patients. It is useful for revascularization of single major lateral vessel when it is long enough. In this study, the patency rate at 1-year

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TABLE 5. Occluded right internal thoracic artery grafts

Inflow	Target vessel	Degree of native coronary stenosis	Occluded grafts
In situ			
Right ITA	Left anterior descending artery	50%	1
	Diagonal branch	50%	1
		90%	2
	Circumflex artery	50%	2
		75%	3
		90%	2
	Inflow of other grafts	75%	4
Free			
Left ITA	Diagonal branch	90%	1
	Circumflex artery	75%	2
Radial artery	Diagonal branch	75%	1
	Circumflex artery	50%	1
Aorta	Circumflex artery	50%	1

ITA, Internal thoracic artery.

angiography was superior when an in situ right ITA was used for anterior territory relative to when it was used for lateral territory.

A free right ITA graft is useful for revascularization of lateral or posterior vessels for single or multiple sequential anastomoses. It can reach the posterior descending artery with composite grafting when its proximal anastomosis is carried out on the left ITA.[14] Multiple sequential grafting to lateral vessels with the free right ITA can reduce the total number of grafts. In this study, the mean number of grafts was significantly less in the free right ITA group than in the situ right ITA group ($P < .0001$). Furthermore, the mean number of distal anastomoses of the free right ITA was significantly higher than that of the in situ right ITA ($P < .0001$). The proximal anastomosis site of the free right ITA (other grafts or aorta) did not affect the patency rate at both of early and 1-year angiographic studies. Calafiore and colleagues[15] reported that the patency rate of the free right ITA proximally anastomosed to the aorta was inferior to that anastomosed to the left ITA. They suggested that the reason for this poor graft patency rate was because of a mismatch between the aorta and the conduit wall and a difference in the flow pattern. We did not observe an inferior patency rate of the free right ITA anastomosed to the aorta relative to that anastomosed to other grafts. We speculate that the routine use of intraoperative epiaortic echocardiography to detect a disease-free area of the aorta for proximal anastomosis may minimize the mismatch of the wall discrepancy.

There have been a few reports comparing the patency rates between the in situ right ITA and the free right ITA.[16,17] Recently, Glineur and associates[18] demonstrated that patency rates were not different between an in situ group and a Y-grafting group at 6-month postoperative angiography in a prospective randomized trial. Our 1-year follow-up study supports their findings. In this study, both early and 1-year angiographic studies were performed in 312 patients. Among those patients, 11 patients were newly found to have nonpatent right ITA grafts at 1-year angiography. The target coronary arteries had a low stenosis rate in 9 of these 11 patients. Competitive or reverse flow related to a low stenosis rate could be the potential cause of 1-year new nonpatency. It has been suggested that arterial grafts tend to fail when they are used for revascularization of target vessels with low-grade stenosis.[8] This tendency was observed in both the in situ and free right ITA grafts in our study.

A skeletonized ITA provides a longer length and better flexibility than a pedicled ITA. Skeletonization ensures that the right ITA reaches the posterolateral vessels through the transverse sinus as an in situ graft. Furthermore, multiple sequential grafting can be easily performed with a skeletonized free right ITA. The blood flow of a skeletonized ITA is reported to be greater than that of a pedicled ITA.[19] With the skeletonization technique, the use of bilateral ITAs might no longer be a risk factor for mediastinitis, because the collateral blood supply to the sternum can be preserved.[20,21]

In situ ITA grafts are sometimes at risk for injury in reoperations. Recently, Roselli and colleagues[22] reported an occurrence of ITA injury of 3% at reoperative cardiac surgery. They commented that the best way to prevent injury to a patent ITA graft is to position it properly at the original operation. Preventive strategies are not always effective, however, and intraoperative adverse events are difficult to eliminate. On the other hand, Endo and coworkers[12] reported that the right ITA was surrounded by loose connective tissue at reoperation and the patent ITA did not increase the risk of reoperation in their study. Our own study showed that the best patency of the right ITA could be obtained with in situ grafting to the LAD. Other configurations, however, such as in situ grafting to the lateral wall through the transverse sinus and free grafting to the lateral vessel with Y-composite graft, had only slightly inferior patency. These configurations may be much safer at reoperation than in situ right ITA graft to the LAD. The actual graft strategy should be made after considering the risk of injury at potential reoperations as well as graft patency outcomes.

This clinical study has the several limitations. It was a retrospective observational study and was not randomized. Also, we could not follow up all patients with right ITA grafts. Our findings may not be applicable in such groups as elderly patients and patients with renal insufficiency, who did not have undergo follow-up angiography.

In conclusion, patency rates of in situ and free right ITAs were identical at early and 1-year angiographic studies. In situ grafting to the LAD had the best patency among various configurations of right ITA graft; however, other configurations had also excellent patency. Grafting strategy of right ITA should be determined on the basis of conduit availability, target location, and other clinical factors.

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Off-pump bilateral internal thoracic artery grafting in patients with left main disease

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Objective: This study assessed the safety and efficacy of off-pump bilateral internal thoracic artery grafting in patients with left main disease.

Methods: We reviewed the records of 768 patients who underwent off-pump bilateral internal thoracic artery grafting between September 2004 and June 2009. Bilateral internal thoracic artery grafts were used for the left coronary system in all patients, of whom 268 had left main disease and 500 did not. We compared operative and postoperative variables and early and 1-year angiographic patency rates of the bilateral internal thoracic artery between the 2 groups.

Results: The perioperative mortality and incidence of postoperative complications were not significantly different between groups. In patients without left main disease, the left and right internal thoracic arteries were used for the left anterior descending artery in 87.4% and 12.2% of patients, respectively. In patients with left main disease, the left and right internal thoracic arteries were used for the left anterior descending artery in 70.5% and 29.1% of patients, respectively. In patients with left main disease, the patency rates for the left and right internal thoracic arteries at 1-year postoperative follow-up were 97.0% and 93.2%, respectively. In patients without left main disease, the patency rates for the left and right internal thoracic arteries at 1-year follow-up were 97.6% and 91.6%, respectively. The patency rates of the left and right internal thoracic arteries did not differ significantly in patients with or without left main disease ($P = .9803$ and $P = .7205$ in left and right internal thoracic arteries, respectively).

Conclusions: Off-pump bilateral internal thoracic artery grafting was safe and effective in patients with left main disease. The patency rates of both grafts were comparable to those of patients without left main disease. (J Thorac Cardiovasc Surg 2010;140:1040-5)

ACD

Coronary artery disease (CAD) with left main disease (LMD) has historically been considered to carry a higher operative risk in coronary artery bypass grafting (CABG) than CAD without LMD.[1,2] Recent advancement in operative techniques and perioperative management has enabled surgeons to perform CABG safely in patients with LMD. Generally, off-pump CABG is not preferred in patients with LMD because the displacement of the heart could cause torsion of LMD and acute hemodynamic deterioration.[3] Some investigators have reported the safety of off-pump CABG in patients with LMD in studies with a relatively small sample size.[4-7]

Bilateral internal thoracic artery (ITA) grafting for revascularization has better survival benefits than single ITA grafting,[8] and patency rates and survival benefits are satisfactory when bilateral ITA grafts are used for the left coronary system.[9] The combination of off-pump CABG with bilateral ITA grafting also yields favorable outcomes.[10] However, the rate of bilateral ITA use is still low.[11]

The aims of the present study are to assess the safety and efficacy of off-pump bilateral ITA grafting in patients with LMD and to assess early and 1-year angiographic results of bilateral ITA grafts in these patients.

PATIENTS AND METHODS

Patient Population

Between September 2004 and June 2009, 930 patients underwent isolated CABG at Sakakibara Heart Institute. Of those, 884 patients (95.1% of all isolated CABG cases) underwent isolated off-pump CABG and 768 patients (86.9% of all isolated off-pump CABG cases) underwent off-pump bilateral ITA grafting (Table 1). Table 2 shows the preoperative characteristics of these 768 patients, of whom 268 had LMD (LMD group) and 500 did not have LMD (non-LMD group). LMD was defined as the presence of 50% or greater stenosis in any angiographic view according to the Society of Thoracic Surgeons database.

Operation

General anesthesia was induced with midazolam (0.2 mg/kg) and fentanyl (4 μg/kg). Neuromuscular block was achieved with vecuronium

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CAD = coronary artery disease
ITA = internal thoracic artery
LAD = left anterior descending
LMD = left main disease

(0.1 mg/kg). After intubating the trachea, the lung was ventilated with 2% to 2.5% of sevoflurane with an air–oxygen mixture. Nicorandil and landiolol, a short-acting beta-one selective antagonist, were administered throughout the operation. Anticoagulation was achieved with heparin at 300 U/kg after all grafts were harvested for coronary revascularization. Phenylephrine was continuously administered during distal coronary anastomosis to maintain the mean blood pressure at more than 60 mm Hg without accelerating the heart rate. Beta-agonists were administered after the proximal anastomosis if necessary. There was no difference in anesthetic methods in patients with and without LMD.

Bilateral ITA grafts were routinely used in patients who required revascularization of both the left anterior descending (LAD) artery and left circumflex artery territories. Bilateral ITAs were used as in situ grafts in preference to free grafts. In general, the left ITA was used for revascularizing the LAD and the right ITA was used for revascularizing the circumflex artery territory or diagonal branch. However, in patients with unstable hemodynamics caused by critical LMD, the LAD was revascularized with the right ITA first and then the circumflex artery territory with the left ITA. When multiple grafting was necessary in the circumflex artery territory, multiple sequential grafting was applied with the free right ITA. The left ITA was used as an in situ graft in 760 patients (99.0%) and as a free graft in 8 patients (1.0%). The right ITA was used as an in situ graft in 582 patients (75.8%) and as a free graft in 186 patients (24.2%). When the free right ITA was anastomosed to the ascending aorta, an intraoperative epiaortic ultrasound was routinely used to detect a disease-free area of the aorta. When the free right ITA was anastomosed proximally to another graft (left ITA, radial artery, or saphenous vein graft), a Y-composite graft was created.

The operative technique of off-pump CABG has been described.[12] All arterial grafts were harvested in a skeletonized fashion using an ultrasonic scalpel (Harmonic Scalpel, Ethicon Endosurgery, Cincinnati, OH). We grafted all significantly diseased coronary vessels (at least a 50% diameter reduction) larger than 1 mm in diameter. Long segmental reconstruction was performed when the LAD was diffusely diseased or the septal and diagonal arteries were affected by severe atheromatous plaques. An arteriotomy was extended proximally and distally to the intact segment of the LAD. Endarterectomy was performed if the atheromatous plaque was circumferential or too hard to pass a needle through. The left ITA was anastomosed to the LAD with a long onlay patch technique using 7-0 and 8-0 polypropylene running sutures. The detailed technique and outcomes of long segmental reconstruction of the LAD have been described.[13]

Angiography

Early postoperative angiography was performed in 615 patients (80.1%) after obtaining written informed consents. The median time to an early postoperative angiography was 10 days after surgery (range 1–20 days). If patients became symptomatic during a follow-up period, a diagnostic angiography was performed at that time. Unless patients became symptomatic within 1 year after surgery, a follow-up angiography was performed at 1 year after surgery. Follow-up postoperative angiography was performed in 381 patients (49.6%), and the median time was 12.2 months after surgery (range 2–21 months). Of these patients, 352 (45.8%) underwent both early and 1-year angiographic studies.

TABLE 1. Distribution of patients undergoing isolated coronary artery bypass grafting

	Single ITA	Bilateral ITA	Total
On-pump CABG	22	24	46
Off-pump CABG	116	768	884
Total	138	792	930

CABG, Coronary artery bypass grafting; *ITA*, internal thoracic artery.

Preoperative, intraoperative, postoperative, and angiographic variables were compared in patients with LMD and without LMD. The institutional review board approved this retrospective study and waived the need for written consents.

Nonelective operations included both emergency and urgent cases according to the definition of the Society of Thoracic Surgeons database. Operative death was defined as death occurring within 30 days after surgery. Low-output syndrome was defined as the postoperative need for any dose of adrenaline or more than 5 $\mu g/kg^{-1}/min^{-1}$ of dopamine or dobutamine. Perioperative myocardial infarction was defined as a positive result for new Q waves in an electrocardiogram or a peak creatine kinase MB level of greater than 10% of total creatine kinase. Respiratory failure was defined as requiring prolonged ventilation (>48 hours) or having pneumonia. A postoperative cerebrovascular accident was defined as having a new stroke or intracranial bleeding confirmed by computed tomography. In patients with preoperative stroke, postoperative stroke was defined as a worsening of the neurologic deficit with new radiologic findings.

Patent graft was defined as a graft without occlusion, significant stenosis (>90%), or string sign. String sign was defined as luminal narrowing throughout the entire conduit, including stenosis of 90% or greater.

Early and 1-year patency rates were calculated by dividing the number of patent grafts by the total number of grafts. If patients with early nonpatent grafts underwent a 1-year angiogram, those nonpatent grafts were also counted as 1-year nonpatent grafts.

Statistical Analysis

All statistical analyses were performed using StatView 5.0 software (SAS Institute Inc, Cary, NC). Continuous variables are reported as the mean ± standard deviation if they are normally distributed. Otherwise, they are reported as a median. Continuous variables were compared by the Student *t* test, and discrete variables were compared by the chi-square test or Fisher's exact test. Actuarial event-free survival curves were estimated by the Kaplan–Meier method. The log-rank test was used to assess whether there was a difference in survival between subject groups.

RESULTS

Clinical Outcomes

Preoperative characteristics of both groups are shown in Table 2. Patients with LMD were older than those without LMD ($P = .0226$). The rate of unstable angina ($P = .0010$) and the mean Canadian Cardiovascular Society class ($P = .0079$) were higher in patients with LMD than in those without LMD. The mean number of diseased vessels was larger in patients without LMD than in those with LMD ($P = .0117$). Preoperative ejection fraction ($P = .0492$) and creatinine levels ($P = .0318$) were significantly better in patients with LMD than in those without LMD. More patients without LMD had a history of congestive heart failure ($P = .0359$), prior myocardial infarction ($P = .0002$), previous stroke ($P = .0326$), and diabetes mellitus ($P = .0281$) than those with LMD. More patients with

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TABLE 2. Preoperative variables

	All	LMD group	Non-LMD group	*P* value
No.	768	268	500	
Age, y	68.0 ± 9.5	69.1 ± 9.7	67.4 ± 9.3	.0226
Gender, female	141 (18.4%)	56 (20.9%)	85 (17.0%)	.2182
Body surface area (m^2)	1.7 ± 0.2	1.7 ± 0.2	1.7 ± 0.2	.6108
Unstable angina	239 (31.1%)	104 (38.8%)	135 (27.0%)	.0010
CCS	2.3 ± 0.9	2.4 ± 0.9	2.2 ± 0.9	.0079
Ejection fraction (%)	56.1 ±11.8	57.3 ± 11.3	55.5 ± 12.0	.0492
Diseased vessels	2.8 ± 0.4	2.8 ± 0.4	2.8 ± 0.4	.0117
Previous PCI	222 (28.9%)	74 (27.6%)	148 (29.6%)	.6165
Congestive heart failure	103 (13.4%)	26 (9.7%)	77 (15.4%)	.0359
Prior myocardial infarction	363 (47.3%)	102 (38.1%)	261 (52.2%)	.0002
Hypertension	513 (66.8%)	174 (64.9%)	339 (67.8%)	.4679
Diabetes mellitus	361 (47.0%)	111 (41.4%)	250 (50.0%)	.0281
Insulin	79 (10.3%)	13 (4.9%)	66 (13.2%)	.0005
Hyperlipidemia	470 (61.2%)	172 (64.2%)	298 (59.6%)	.2446
Smoking	461 (60.0%)	156 (58.2%)	305 (61.0%)	.4995
Previous stroke	95 (12.4%)	24 (9.0%)	71 (14.2%)	.0326
Peripheral vascular disease	68 (8.9%)	21 (7.8%)	47 (9.4%)	.5525
Creatinine (mg/dL)	1.2 ± 1.3	1.0 ± 0.8	1.2 ± 1.6	.0318
COPD	31 (4.0%)	9 (3.4%)	22 (4.4%)	.6122
Nonelective	93 (12.1%)	54 (20.1%)	39 (7.8%)	<.0001
Preoperative IABP use	46 (6.0%)	29 (10.8%)	17 (3.4%)	<.0001
Redo	6 (0.8%)	2 (0.7%)	4 (0.8%)	>.9999

CCS, Canadian Cardiovascular Society; *COPD*, chronic obstructive pulmonary disease; *IABP*, intraaortic balloon pump; *LMD*, left main disease; *PCI*, percutaneous coronary intervention.

LMD had emergency or urgent operations ($P < .0001$) and preoperative use of intraaortic balloon pump ($P < .0001$) than those without LMD.

Target coronary artery vessels of left and right ITA grafts are shown in Table 3. In patients with LMD, the right ITA was used as an in situ graft in 207 patients (77.2%) and as a free graft in 61 patients (22.8%). In patients without LMD, the right ITA was used as an in situ graft in 375 patients (75.0%) and as a free graft in 125 patients (25.0%). There was no statistical difference between the 2 groups in the in situ rate of right ITA ($P = .5472$).

In patients with LMD, left and right ITA grafts were used for the LAD in 189 patients (70.5%) and 78 patients (29.1%), respectively. In patients without LMD, left and right ITAs were used for the LAD in 437 patients (87.4%) and 61 patients (12.2%), respectively. The right ITA was used for the LAD more frequently in patients with LMD than in those without LMD ($P < .0001$). This tendency was also found when the target of the right ITA was compared between patients with unstable angina and patients with stable angina. The right ITA was more frequently used for the LAD in patients with unstable angina than in patients with stable angina (36.5% vs 24.4%, $P = .046$).

Operative and postoperative variables are listed in Table 4. Patients without LMD had a higher mean number of distal anastomoses per patient than those with LMD ($P = .0012$). The rate of long segmental reconstruction of the LAD was higher in patients without LMD than in those with LMD ($P < .0001$). Patients without LMD had significantly longer operation times than those with LMD ($P < .0001$). The transfusion rate was significantly higher in patients with LMD than in those without LMD ($P = .0393$). The operative mortality and incidence of postoperative complications were not significantly different between the 2 groups.

During the follow-up period, 1 patient died of heart failure, 2 patients had recurrent angina, 4 patients had congestive heart failure, and 1 patient had a stroke in the group with LMD. Freedom from death and other cardiac or cerebrovascular events was 96.5% ± 1.2% at 3 years. One patient died of heart failure, 3 patients had recurrent angina, and 9 patients had congestive heart failure in the group without LMD. Freedom from death and other cardiac or cerebrovascular events was 96.3% ± 0.9% at 3 years. There was no significant difference between the groups regarding event-free rate ($P = .8603$).

Angiographic Outcomes

Early and 1-year postoperative angiograms were performed in 615 patients (80.1%) and 381 patients (49.6%), respectively. Table 5 lists the patency rates of the left and right ITAs at both early and 1-year angiographic studies.

In patients with LMD, the patency rates of the ITA grafts were 98.6% (left ITA) and 98.6% (right ITA) at early

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TABLE 3. Targets of left and right internal thoracic artery grafts

	Left internal thoracic artery	Right internal thoracic artery	No.
LMD group (n = 268)	LAD	Diagonal branch	89 (33.2%)
	LAD	Circumflex artery	95 (35.4%)
	LAD	Inflow of other graft	5 (1.9%)
	Diagonal branch	LAD	8 (3.0%)
	Diagonal branch	Circumflex artery	1 (0.3%)
	Circumflex artery	LAD	66 (24.6%)
	Inflow of other graft	LAD	4 (1.4%)
Non-LMD group (n = 500)	LAD	Diagonal branch	202 (40.4%)
	LAD	Circumflex artery	211 (42.2%)
	LAD	Inflow of other graft	24 (4.8%)
	Diagonal branch	LAD	5 (1%)
	Diagonal branch	Circumflex artery	1 (0.2%)
	Circumflex artery	LAD	49 (9.8%)
	Circumflex artery	Diagonal branch	1 (0.2%)
	Inflow of other graft	LAD	7 (1.4%)

LAD, Left anterior descending artery; *LMD*, left main disease.

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angiography and 97.0% (left ITA) and 93.2% (right ITA) at 1-year angiography. There were no significant differences in early ($P > .9999$) and 1-year ($P = .2547$) patency rates between the left and the right ITAs.

In patients without LMD, the patency rates of the ITA grafts were 99.0% (left ITA) and 99.3% (right ITA) at early angiography and 97.6% (left ITA) and 91.6% (right ITA) at 1-year angiography. Although there was no significant difference in the early patency rate ($P > .9999$) between the left and the right ITAs, there was a significant difference in the 1-year patency rate ($P = .0056$).

When patency rates of the left ITA were compared in patients with and without LMD, there were no significant differences in early ($P = .6999$) or 1-year ($P = .9803$) patency rates between the 2 groups. When the patency rates of the right ITA were compared in patients with and without LMD, there were no significant differences in early ($P = .4264$) or 1-year ($P = .7205$) patency rates between the 2 groups.

DISCUSSION

The present study demonstrates the safety and efficacy of off-pump bilateral ITA grafting in patients with LMD. Furthermore, this study showed good early and 1-year patency rates of bilateral ITA grafts in this patient group.

The current gold standard of care for LMD is CABG. The American College of Cardiology/American Heart Association guidelines recognize only CABG as having a class IA indication for treatment of LMD.[14,15] The evolution of surgical techniques and perioperative management has improved surgical outcomes. Percutaneous coronary intervention procedures recently have been performed for LMD and reported to have comparable results with

TABLE 4. Operative and postoperative data

	All	LMD group	Non-LMD group	*P* value
Anastomoses/patient	4.2 ± 1.2	4.0 ± 1.2	4.3 ± 1.1	.0012
Long segment reconstruction of LAD	309 (40.2%)	77 (28.7%)	232 (46.4%)	<.0001
Operation time (min)	279.5 ± 56.9	268.2 ± 56.8	285.5 ± 56.1	<.0001
Transfusion	268 (34.9%)	107 (39.9%)	161 (32.2%)	.0393
Intubation (h)	9.6 ± 14.8	10.0 ± 10.2	9.5 ± 16.8	.6485
Intensive care unit stay (d)	1.9 ± 7.8	2.6 ± 13.0	1.5 ± 1.8	.0598
Operative death (within 30 d)	7 (0.9%)	2 (0.7%)	5 (1.0%)	>.9999
Reexploration because of bleeding	6 (0.8%)	1 (0.4%)	5 (1.0%)	.6706
Low output syndrome	10 (1.3%)	6 (2.2%)	4 (0.8%)	.1055
Perioperative myocardial infarction	11 (1.4%)	4 (1.5%)	7 (1.4%)	>.9999
Severe ventricular arrhythmia	6 (0.8%)	0	6 (1.2%)	.0969
Atrial fibrillation	191 (24.9%)	66 (24.6%)	125 (25.0%)	.9789
Required hemodialysis	13 (1.7%)	7 (2.6%)	6 (1.2%)	.2492
Stroke	10 (1.3%)	3 (1.1%)	7 (1.4%)	>.9999
Mediastinitis	10 (1.3%)	3 (1.1%)	7 (1.4%)	>.9999

ITA, Internal thoracic artery; *LAD*, left anterior descending artery; *LMD*, left main disease.

TABLE 5. Cumulative angiographic patency rates of left and right internal thoracic artery grafts

	Early (n = 615)	1 y (n = 381)
Total	98.9% (1217/1230)	94.8% (722/762)
LMD group	98.6% (424/430)	95.1% (251/264)
Left internal thoracic artery	98.6% (212/215)	97.0% (128/132)
Right internal thoracic artery	98.6% (212/215)	93.2% (123/132)
Non-LMD group	99.1% (793/800)	94.6% (471/498)
Left internal thoracic artery	99.0% (396/400)	97.6% (243/249)
Right internal thoracic artery	99.3% (397/400)	91.6% (228/249)

LMD, Left main disease.

CABG;[16] however, long-term results have not been reported. A meta-analysis of LMD also supports the superiority of CABG over percutaneous coronary intervention in revascularization of LMD; the study showed that repeated revascularization was less frequent after CABG than after percutaneous coronary intervention.[17] Generally, off-pump CABG is not preferred in patients with LMD because displacement of the heart could induce hemodynamic deterioration.[3] On the other hand, several studies have shown the safety and feasibility of off-pump CABG in patients with LMD.[4-7] Dewey and colleagues[6] reported that the use of cardiopulmonary bypass is an independent risk factor for death in patients with LMD, with an odds ratio of 7.3 (95% confidence interval, 1.3–138.4). Thomas and colleagues[7] reported that off-pump CABG was safely performed in patients with and without LMD. They speculated that the favorable outcomes after off-pump CABG were achieved because of the improved myocardial preservation, reduced reperfusion injury, and absence of the hypothermic insult. Even in those series, bilateral ITA grafting was infrequently performed.

Several institutions have reported that bilateral ITA grafting results in better survival and greater freedom from reintervention than single ITA grafting.[18,19] However, the American College of Cardiology/American Heart Association guidelines still do not recommend the use of bilateral ITA grafting because there are insufficient data for detailed analysis.[14] Bilateral ITA grafting has not become a routine strategy, even in elective patients, for multiple reasons, including increased operative difficulty, increased operating times, and risk of wound complications.[14] There are only a few reports regarding myocardial revascularization with bilateral ITA grafting in patients with LMD.[20] We have routinely used bilateral ITA grafts for CABG when feasible even in high-risk patients with LMD. There are various grafting strategies with bilateral ITA grafts. Although our first choice is the left ITA for the LAD, we use the right ITA for the LAD more frequently in those with LMD than in those without LMD. Patients with unstable hemodynamics cannot tolerate torsion of the left main trunk because of the circumflex position without LAD grafting. In those patients, we graft the LAD with the right ITA and then graft the circumflex territory with the left ITA. The left ITA to the LAD would suffer from increased physical tension when the heart is pulled toward the right during the anastomosis of the circumflex territory. However, in patients with stable hemodynamics, revascularization of the LAD was performed with the left ITA as usual.

The present study used intraaortic balloon counterpulsation in a higher proportion of patients with LMD than in patients without LMD. Suzuki and colleagues[21] demonstrated that using an intraaortic balloon pump during off-pump CABG was effective in high-risk patients. They comment that the effects of intraaortic balloon pump support, such as the reduction of ventricular afterload, improvement of diastolic coronary perfusion, and enhancement of subendocardial perfusion, are beneficial to the displaced heart in maintaining hemodynamic stability during off-pump CABG. These benefits may have influenced the favorable results after off-pump CABG in our study. In the present study, all intraaortic balloon pumps were placed preoperatively. We believe that insertion of an intraaortic balloon pump should not be delayed in hemodynamically unstable patients with LMD.

We have demonstrated that clinical and angiographic outcomes are not significantly different in patients with and without LMD at early and 1-year follow-ups. The 1-year patency rate of the right ITA graft was relatively low in patients without LMD. However, there was no significant difference in the patency rates of the right ITA grafts in patients with or without LMD.

We used the ITA as a skeletonized graft. A skeletonized ITA provides a longer length and better flexibility than a pedicled ITA. Skeletonization ensures that the right ITA reaches the posterolateral vessels through the transverse sinus as an in situ graft. Furthermore, multiple sequential grafting can be performed easily with a skeletonized free right ITA. With the skeletonization technique, using bilateral ITAs may no longer be a risk factor for mediastinitis because the collateral blood supply to the sternum is preserved.[22] In the present study, the overall mediastinitis rate of 1.3% is not particularly high; however, the best practice in the literature is approximately 0.3%.[23] At Sakakibara Heart Insitute, the mediastinitis rate in patients undergoing non-bilateral ITA grafting was 0% (0/116). However, there was no difference regarding the mediastinitis rate between patients with bilateral ITA and patients with non-bilateral ITA (P = .3756).

Study Limitations

Our study has the following limitations. It is a retrospective observational study, not a randomized controlled trial. We did not compare off-pump CABG with bilateral ITAs with other types of CABG (single ITA grafting or conventional on-pump CABG) in patients with LMD; however, at least we showed that our routine off-pump CABG with bilateral ITAs is safe and effective in patients with LMD. In addition, we did not follow up all patients with bilateral ITA

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grafts. Our findings may not be applicable to patient groups who did not have a follow-up angiogram, namely, the elderly and patients with renal insufficiency.

CONCLUSIONS

Off-pump bilateral ITA grafting in patients with LMD can be performed safely with acceptable early and 1-year patency rates.

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Arterial graft deterioration one year after coronary artery bypass grafting

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Objective: Some arterial grafts have progressive narrowing or occlusion during the first postoperative year despite angiographic patency in the immediate postoperative period. This study analyzed the incidence and predictors of arterial graft deterioration.

Methods: We reviewed 778 distal anastomoses of arterial grafts in 243 patients who underwent off-pump coronary artery bypass grafting. All patients underwent both early and 1-year follow-up coronary angiography, with all arterial grafts patent on the early angiograms. Arterial graft deterioration was defined as diffuse graft stenosis or occlusion newly found at 1-year follow-up angiography.

Results: Graft deterioration was present in 13.8% (string sign, 6.9%; occlusion, 6.8%) of distal anastomoses. The incidence of graft deterioration was higher among cases of non–internal thoracic arterial graft (27.7% vs 6.0%, $P < .001$), non–left anterior descending coronary arterial anastomosis (19.1% vs 2.0%, $P < .001$), mild ($\leq$75%) stenosis of the target coronary artery (26.0% vs 7.6%, $P < .001$), composite grafting (19.9% vs 7.8%, $P < .001$), and multiple anastomoses from a single inflow source (19.5% vs 5.1%, $P < .001$). The incidence was particularly high when composite or multiple grafting from a single inflow source was performed to a target coronary artery with mild stenosis. Non–internal thoracic arterial graft, mild target stenosis, and multiple grafting from a single inflow source were independent predictors of graft deterioration.

Conclusions: Arterial graft deterioration was closely related to particular graft materials and designs. (J Thorac Cardiovasc Surg 2010;140:1306-11)

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The survival benefit of using a single internal thoracic artery (ITA) in coronary artery bypass grafting (CABG) was demonstrated in the mid 1980s,[1] and further beneficial effects of additional arterial graft use have been subsequently reported in several studies.[2-4] The clinical benefits provided by an arterial graft are usually considered to be related to superior patency.[5,6] The early failure of an arterial graft is rare and is related to several mechanisms, including anastomotic problems and poor quality of the graft material or the native coronary artery. Some arterial grafts, however, fail during the first year. Several studies have reported that some arterial grafts occlude in this time period, and this may result from competition with native coronary flow.[7,8] Other arterial grafts are reduced in caliber and show diffuse narrowing, the string sign. The incidence of string sign has not been negligible in some previous studies.[9,10] These findings suggest that some arterial grafts may lose the ability to function as a bypass conduit as a result of graft deterioration. In this study we therefore analyzed the incidence, predictors, and clinical consequences of arterial graft deterioration 1 year after CABG.

MATERIALS AND METHODS

Study Design

In this retrospective cohort study, we first examined a series of follow-up angiograms performed before discharge and 1 year after surgery and then investigated the predictors of arterial graft deterioration. In addition, we investigated the association between arterial graft deterioration and clinical outcomes. The Ethics Committee of Sakakibara Heart Institute approved this study, waived the need for patient consent, and provided approval before publication of the data.

Study Subjects and Data Collection

Between September 2004 and July 2007, a total of 536 patients underwent isolated CABG at our institution. All patients were scheduled for off-pump CABG. Twenty-five emergency cases were included. Six patients who had conversion to on-pump CABG were excluded from the study. We routinely performed coronary angiography before discharge and 1 year after surgery for patients who underwent off-pump CABG, regardless of the patient's symptoms. Patients who died, refused angiographic evaluation, were older than 75 years, or had renal dysfunction (serum creatinine >1.2 mg/dL) were excluded from the angiographic follow-up. Of the 536 patients, 432 underwent early angiography and 273 underwent 1-year follow-up angiography. For early angiography before discharge, 67 patients were excluded for old age, 15 were excluded for renal dysfunction, and 22 were excluded for patient refusal. For follow-up angiography at 1 year after surgery, 113 patients were excluded for old age, 24 were excluded

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Abbreviations and Acronyms
CABG = coronary artery bypass grafting
ITA = internal thoracic artery
LAD = left anterior descending artery

for renal dysfunction, and 126 were excluded for patient refusal. A total of 256 patients (47.8%) underwent both early and 1-year follow-up angiography. The angiographic results of these patients are shown in Table 1. Thirteen patients with multiple arterial grafting who had at least 1 occluded anastomosis were excluded from the study. Findings of the remaining 243 patients were retrospectively reviewed.

Perioperative clinical data were collected from patient medical records. All patients were followed up for at least 1 year, and mean follow-up was 21.8 months. A major adverse cardiac event was defined as the occurrence of a nonfatal myocardial infarction, the need for repeat revascularization, or cardiac death. Cardiac death was defined as death occurring in relation to myocardial infarction, cardiac arrhythmia, out-of-hospital sudden cardiac death, or deteriorating congestive heart failure. Undetermined causes of death were assumed to be cardiac.

One cardiologist initially reviewed all the coronary angiograms, and a consensus was reached among the surgical team after review. For native coronary arteries, mild stenosis was defined as a stenotic lesion of 75% or less. Distal anastomoses were assessed and classified as patent, focally stenosed, string sign, or occluded. A focally stenosed lesion was defined as one with a focal stenosis of 90% or greater anywhere within the conduit or at the anastomosis. String sign was defined as luminal narrowing throughout the entire conduit, including stenosis of 90% or greater. Each distal anastomosis represented a separate data point in the analysis. The patency rate was calculated as the number of distal anastomoses without occlusion per total distal anastomoses. Patent graft anastomosis included grafts with focal stenosis or string sign. Arterial graft deterioration was defined as a graft that had been patent on the early angiogram but appeared occluded or showed evidence of string sign on the 1-year angiogram. The incidence of arterial graft deterioration was calculated as the rate of distal anastomoses with arterial graft deterioration per total distal anastomoses.

Operative Strategy

Our surgical procedures and principles of off-pump CABG have been previously described.[11] The left-sided coronary arteries were revascularized with arterial grafts in most cases. The left anterior descending artery (LAD) was revascularized exclusively with the ITA, and the left ITA was used preferentially. The right ITA was revascularized to the LAD only when the left ITA was required to bypass a remote anastomotic site of the left circumflex artery. The most frequently used arrangement for diagonal artery and left circumflex artery was composite grafting with right ITA and radial artery. In this arrangement, the right ITA was used as an in situ graft for the diagonal, and the radial artery was anastomosed proximally to the right ITA and distally to the left circumflex artery. The right coronary artery was grafted with saphenous vein or gastroepiploic artery in most cases. Use of the gastroepiploic artery was usually limited to patients with severe stenosis of the right coronary artery. Grafts used in 242 study patients are shown in Table 2.

Aspirin (81 mg) was given to all patients before and after surgery. In 66 cases, ticlopidine hydrochloride (INN ticlopidine) was given for 1 month. Heparin (3.0 mg/kg) was administered intravenously after sternotomy, and it was neutralized at the end of the procedure with protamine sulfate (3.0 mg/kg). All radial arteries and saphenous veins were harvested open. The radial artery was soaked in a solution (20 mg olprinone plus 180 mL normal saline solution). After hemostasis was confirmed, all patients received a continuous heparin infusion until the second postoperative day. Patients with a radial artery graft received continuous administration of intravenous diltiazem during the first 24 hours after surgery.

Statistical Analysis

Continuous variables are reported as mean ± SD and categorical variables as percentages. Fisher's Exact test was used to compare categorical variables. The Mann–Whitney test was used to compare continuous variables. Actuarial and event-free survival curves were obtained with the Kaplan–Meier method. Statistical significance was calculated with the log-rank test. Multivariate analysis was performed to identify independent risk factors for arterial graft deterioration. A generalized estimating equation method was used to account for within-patient correlation. Predictors were discarded at a P value greater than .10. Covariates included in the generalized estimating equation models were graft material (ITA vs non-ITA), stenosis rate of target coronary artery (mild vs more than mild), and number of distal anastomoses from a single inflow source (single vs multiple). Target coronary artery (LAD vs non-LAD) and graft configuration (individual vs composite graft) were discarded, because LAD was grafted with ITA exclusively and composite grafting was involved in multiple grafting. Odds ratios were calculated with 95% confidence intervals. All statistical analyses were performed with SPSS statistical software (SPSS version 17.0; SPSS Japan, Tokyo, Japan).

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RESULTS

Characteristics of Study Patients

The preoperative characteristics of study patients were compared with those of the patients excluded from the study (Table 3). There were significant differences between the

TABLE 1. Angiographic results for early and 1-year patencies

		Early					1 y				
			Stenosis (no.)					Stenosis (no.)			
	Distal anastomoses	Patency (%)	PP	FS	SS	CO	Patency (%)	PP	FS	SS	CO
All arteries	830	97.5%	796	13	0	21	90.8%	689	8	57	76
Internal thoracic artery											
Any	527	99.1%	512	10	0	5	96.8%	486	5	19	17
Left	292	98.6%	279	9	0	4	97.3%	279	4	1	8
Right	235	99.6%	233	1	0	1	96.2%	207	1	18	9
Radial artery	260	93.9%	242	2	0	16	78.9%	170	2	33	55
Gastroepiploic artery	43	100%	42	1	0	0	90.7%	33	1	5	4
Saphenous vein	220	96.8%	212	1	0	7	81.8%	169	10	1	40

PP, Perfectly patent; *FS*, focally stenosed; *SS*, string sign; *CO*, completely occluded.

TABLE 2. Number of distal anastomoses for each graft type according to target coronary artery

	Target coronary artery			
Conduit	Left anterior descending	Diagonal	Left circumflex	Right
Left internal thoracic artery				
All	198	20	60	0
Individual	167	15	39	0
Composite	31	5	21	0
Right internal thoracic artery				
All	46	104	72	0
Individual	43	23	32	0
Composite	3	81	40	0
Radial artery				
All	0	37	183	19
Individual	0	10	30	6
Composite	0	27	153	13
Gastroepiploic artery				
All	0	3	6	30
Individual	0	1	1	29
Composite	0	2	5	1
Saphenous vein				
All	0	1	17	196
Individual	0	1	11	187
Composite	0	0	6	9

groups in age, sex, and the prevalence of hypertension. Midterm clinical results were also compared between these groups (Table 3). The 2-year survival of study patients was significantly higher than that of excluded patients.

TABLE 3. Comparison of patient characteristics and midterm clinical results between study patients and excluded patients

	Study (n = 243)	Excluded (n = 280)	*P* value
Preoperative			
Age (y, mean ± SD)	66.6 ± 7.7	71.0 ± 9.3	<.001
Male (no.)	243 (86.0%)	216 (77.1%)	.01
Coronary risk factor (no.)			
Hypertension	172 (70.8%)	220 (78.6%)	.043
Diabetes	99 (40.7%)	111 (39.6%)	.858
Hyperlipidemia	153 (63.0%)	156 (55.7%)	.108
Smoking	137 (56.4%)	152 (54.3%)	.660
Old cerebral infarct (no.)	18 (7.4%)	32 (11.4%)	.137
Peripheral vascular disease (no.)	13 (5.4%)	28 (10.0%)	.052
Long-term hemodialysis (no.)	9 (3.7%)	10 (3.6%)	1.00
Midterm clinical results			
Follow-up rate (%)	100.0%	94.6%	
Follow-up period (d, mean ± SD)	654 ± 321	521 ± 408.9	<.001
Survival (%)			<.001
1 y	100.0%	95.4%	
2 y	100.0%	93.2%	
Major adverse cardiac event–free survival (%)			.897
1 y	96.3%	95.5%	
2 y	91.4%	92.9%	

Angiographic Outcomes

Arterial graft deterioration was seen in 74 patients. Patient characteristics were compared between patients with and without deterioration of grafts (Table 4). There were no differences in preoperative patient characteristics and postoperative medications between these groups.

The incidence of arterial graft deterioration was 13.8% (107/778 distal anastomoses). In univariate analysis, the incidences of graft deterioration were significantly higher for non-ITA grafts (27.7% vs 6.0%, $P < .001$), non-LAD anastomoses (19.1% vs 2.0%, $P < .001$), mild (≤75%) stenosis of target coronary arteries (26.0% vs 7.6%, $P < .001$), composite grafting (19.9% vs 7.8%, $P < .001$), and multiple anastomoses from a single inflow source (19.5% vs 5.1%, $P < .001$; Table 5). The results of multivariate analysis are shown in Table 6. Non-ITA graft, mild target stenosis, and multiple grafting from a single inflow source were the independent predictors of graft deterioration. Figure 1 shows the effects of graft configuration and number of distal anastomoses from a single inflow source on the incidence of arterial graft deterioration according to the severity of target coronary artery stenosis. The differences in the incidence of graft deterioration according to graft configurations or numbers of distal anastomoses were much greater for target arteries with mild stenosis than for those with severe stenosis. For targets with mild stenosis, composite and multiple grafting from a single inflow source resulted in a high incidence of arterial graft deterioration.

Clinical Outcomes

The recurrence of angina symptoms was significantly greater among patients with graft deterioration than among

TABLE 4. Patient characteristics and postoperative medications

	Deterioration		
	No (n = 169)	Yes (n = 74)	*P* value
Preoperative			
Age (y, mean ± SD)	66.7 ± 7.5	66.3 ± 8.2	.909
Male (no.)	142 (84.0%)	67 (90.5%)	.229
Coronary risk factor (no.)			
Hypertension	118 (69.8%)	54 (73.0%)	.649
Diabetes	74 (43.8%)	25 (33.8%)	.158
Hyperlipidemia	106 (62.7%)	47 (63.5%)	>.999
Smoking	91 (53.9%)	46 (62.2%)	.262
Old cerebral infarct (no.)	14 (8.3%)	4 (5.4%)	.596
Peripheral vascular disease (no.)	7 (4.1%)	6 (8.1%)	.224
Long-term hemodialysis (no.)	9 (5.3%)	0 (0%)	
Postoperative medication (no.)			
β-Blocker	72 (42.6%)	39 (52.7%)	.163
Statin	57 (33.7%)	23 (31.1%)	.767
Angiotensin-converting enzyme inhibitor	11 (6.5%)	5 (6.8%)	>.999
Angiotensin receptor blocker	35 (20.7%)	15 (20.3%)	>.999
Calcium blockade	31 (18.3%)	8 (10.8%)	.184
Warfarin	111 (65.7%)	49 (66.2%)	>.999

TABLE 5. Prevalences of arterial graft deterioration

Predictor	Total	Deteriorated	Occluded	String	*P* value
Conduit					<.001
Internal thoracic artery	500	30 (6.0%)	12 (2.4%)	18 (3.6%)	
Left	278	5 (1.8%)	4 (1.4%)	1 (0.4%)	
Right	222	25 (11.3%)	8 (3.6%)	17 (7.7%)	
Non–internal thoracic artery	278	77 (27.7%)	41 (14.8%)	36 (13.0%)	
Radial artery	239	69 (28.9%)	38 (15.9%)	31 (13.0%)	
Gastroepiploic artery	39	82 (0.5%)	3 (7.7%)	5 (12.8%)	
Target coronary artery					<.001
Left anterior descending	244	5 (2.0%)	3 (1.2%)	2 (0.8%)	
Non–left anterior descending	534	102 (19.1%)	50 (9.4%)	52 (9.7%)	
Diagonal	164	19 (11.6%)	9 (5.5%)	10 (6.1%)	
Left circumflex	321	74 (23.1%)	36 (11.2%)	38 (11.8%)	
Right	49	9 (18.4%)	5 (10.2%)	4 (8.2%)	
Stenosis of target coronary artery					<.001
More than mild (>75%)	516	39 (7.6%)	19 (3.7%)	20 (3.9%)	
Mild ≥75%	262	68 (26.0%)	34 (13.0%)	34 (13.0%)	
Graft configuration					<.001
Individual	396	31 (7.8%)	15 (3.8%)	16 (4.0%)	
Composite	382	76 (19.9%)	38 (9.9%)	38 (9.9%)	
No. of distal anastomoses from single inflow source					<.001
1	16	312 (5.1%)	6 (1.9%)	10 (3.2%)	
≥2	466	91 (19.5%)	47 (10.1%)	44 (9.4%)	
2	173	31 (17.9%)	18 (10.4%)	13 (7.5%)	
3	206	39 (18.9%)	14 (6.8%)	25 (12.1%)	
4 or 5	87	21 (24.1%)	15 (17.2%)	6 (6.9%)	

All data represent numbers of grafts.

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those without graft deterioration (9.5% vs 3.0%, $P = .049$). The incidence of major adverse cardiac events tended to be higher among patients with graft deterioration, but the difference was not statistically significant (13.5% vs 6.5%, $P = .104$).

DISCUSSION

Arterial Graft Deterioration

In this study, we focused on arterial grafts that had been patent immediately after surgery and became occluded or diffusely narrowed during the first postoperative year. Most previous studies have used patency rate as an index of the graft function, and the patency rates in our study were comparable with those in previous studies.[12,13] We also treated string sign as graft dysfunction, and the incidence of string sign was nearly identical to that of graft occlusion. There is still some debate whether graft occlusion and string sign have to be viewed in a similar manner. It was sometimes difficult to discriminate clearly between grafts showing string sign and those showing occlusion, however, because some grafts appeared to be intermediate between these states. Graft occlusion and string sign were sometimes intermingled in the same graft, and some grafts were halfway patent, showing string sign and occlusion in the latter half. Moreover, the prevalence and predictors were nearly identical for graft occlusion and string sign. In this study, string sign and graft occlusion were therefore similarly viewed as evidence of a deteriorated graft.

TABLE 6. Results of multivariate analysis

Predictor	Odds ratio	95% Confidence interval	*P* value
Non–internal thoracic artery graft	5.05	2.79–9.13	<.001
Mild target stenosis	4.52	2.77–7.37	<.001
Multiple grafting from single inflow source	2.68	1.37–5.25	.004

Predictors of Graft Deterioration

Our study revealed several predictors of arterial graft deterioration 1 year after CABG. Mild stenosis of the target coronary artery was an independent predictor of graft deterioration. Other studies have also shown mild stenosis to be an independent predictor of graft occlusion[8] or string sign.[14,15] Graft material was also an independent predictor. Radial artery and gastroepiploic artery were more susceptible to graft deterioration. The susceptibilities of various graft materials to graft occlusion or string sign have not yet been fully determined, but in our study ITA grafts were apparently resistant to graft deterioration. Multiple grafts originating from a single inflow source were susceptible to graft deterioration. In this study, complex design, such as

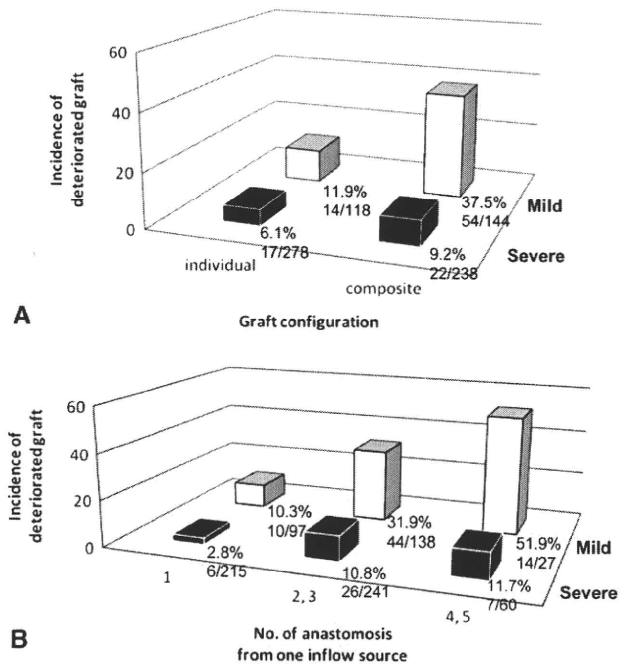

FIGURE 1. Effects of graft configuration (A) and number of distal anastomoses from single inflow source (B) on incidence of arterial graft deterioration according to severity of target coronary artery stenosis.

composite grafting and sequential multiple grafting, appeared to have certain pitfalls, although several studies have reported excellent patency rates for such grafts.[16,17] When planning these types of grafts, selection of the target coronary artery is considered extremely important. For the target with mild stenosis, these types of grafts would result in a high failure rate, and individual grafts should be selected instead. This finding is in agreement with a previous study[18] that demonstrated reduced blood flow in a composite graft used for a less stenosed target. On the other hand, patient characteristics and postoperative medications were not related to graft deterioration. These results enhance the importance of graft design in the prevention of graft deterioration in multiple arterial revascularization procedure.

Clinical Significance of Graft Deterioration

There is no consensus regarding the clinical significance of graft deterioration, especially of a graft showing string sign. There have been several case studies[19,20] in which arterial grafts showing string sign regained patency after progression of native coronary artery stenosis. Furthermore, arterial grafts showing string sign can increase graft flow in response to a hyperemic situation, which suggests the capacity to meet the blood flow demand and to function as a bypass conduit.[21,22] Several studies, however, have suggested poor angiographic outcomes of grafts showing string sign. Kim and colleagues[12] reported that among 20 grafts initially FitzGibbon grade B, 12 grafts remained grade B and 3 grafts were occluded 3 years after surgery. Nakajima and coworkers[7] reported that 71.4% of the bypasses with competitive or reversed flow at early angiography were occluded 3 years after surgery. Our study revealed that patients with deteriorated grafts were more likely to have ischemic symptoms. There have been no reports investigating the long-term consequences of grafts showing string signs, and further investigation is required.

Mechanism of Graft Deterioration

The mechanism of arterial graft deterioration is suggested by several previous studies. Arterial remodeling is a well-known physiologic adaptation that occurs in response to long-term changes in blood flow to normalize shear stress.[23] For ITA grafts, animal studies have demonstrated that a low-flow condition results in a decreased diameter of the artery accompanied by medial thickening within several months.[24] These findings suggest that the deterioration of an arterial graft may be induced by a low-flow condition, and several clinical studies supported this hypothesis. Akasaka and associates[21] investigated the flow dynamics of the ITA graft showing string sign by use of a Doppler guide wire and demonstrated to and fro signals with systolic reversal and diastolic antegrade flow. Shimizu and coworkers[25] demonstrated decreased graft diameter in a graft with low-flow condition. Tokuda and colleagues[26] reported that a lower mean graft flow and a higher percentage of backward flow as measured by intraoperative transit time flow were independent risk factors for arterial graft deterioration. The results of our study are in agreement with these findings. Graft designs that might decrease the flow at distal anastomoses were revealed to be risk factors for arterial graft deterioration. Mild stenosis of the target coronary artery promotes flow competition. Multiple grafting from a single inflow source may limit the inflow volume and result in decreased graft flow. These findings suggest that a certain amount of graft flow is required to maintain the function of the arterial graft.

Study Limitations

This study has several limitations. First, all data were retrospectively collected, which may have led to information bias. Second, follow-up angiography was performed for only 47.8% of the patients who underwent off-pump CABG during this study period. Angiography was performed according to a protocol and was not symptom directed. We cannot eliminate the possibility that there was a bias in the patient selection. The patient characteristics and the midterm clinical results are compared between the study patients and the excluded patients in Table 3. The differences need to be considered in the interpretation of our data. Importantly, the survival of the study patients was significantly higher than that of the excluded patients. This finding suggests that the rate of arterial graft deterioration may have been understated in our cohort, which was biased toward healthier patients. Third, the study patients included those with arterial grafts showing focal stenosis (11 instances of distal stenosis in 9 patients) on early angiography. The 11 grafts with focal stenosis seemed to have good graft flow on early angiography. At 1-year angiography, stenosis had disappeared in 5 grafts, and 6 grafts continued to show focal stenosis. None of the grafts with focal stenosis had graft deterioration. Fourth, the use of secondary preventive medication in the study patients was relatively low. Although postoperative medication was not statistically associated with the development of graft deterioration, it is possible that this low use of secondary prevention medication enhanced the development of graft deterioration.

CONCLUSIONS

Arterial graft deterioration 1 year after CABG occurred in 13.8% of all distal anastomoses in arterial grafts. The graft deterioration was closely related to particular graft materials and designs. The incidence of graft deterioration was higher for non-ITA grafts, non-LAD anastomoses, mild ($\leq$75%) stenosis of target coronary arteries, composite grafting, and multiple anastomoses from a single inflow source. The incidence was particularly high when composite or multiple grafting from a single inflow source was performed to a target coronary artery with mild stenosis. When performing multiple arterial grafting, careful attention to the selection of graft material and design is important to gain the full advantage of arterial grafts.

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ORIGINAL ARTICLE

Comparison of the waveforms of transit-time flowmetry and intraoperative fluorescence imaging for assessing coronary artery bypass graft patency

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Abstract
Purpose. An intraoperative fluorescence imaging (IFI) system, which can provide visual images, could be the common method for assessing graft patency intraoperatively. We conducted a prospective comparison of the diagnostic accuracy of both the fast Fourier transformation (FFT) analysis of transit-time flowmetry (TTFM) waveform and the IFI system to determine graft failure.
Methods. The study included 10 saphenous vein grafts (SVGs), all of which were aortocoronary grafts. Each patient underwent isolated coronary artery bypass grafting (CABG), including conventional CABG or off-pump CABG, and then underwent X-ray angiography after CABG. When intraoperative hemodynamics had stabilized, the grafts were evaluated with both the IFI system and TTFM. Based on the obtained flow profile of TTFM, certain variables were calculated. The waveforms of TTFM were analyzed with the FFT series. Harmonic distortion (HD) was calculated from the amplitudes, and the fundamental frequency was thus determined using the FFT series.
Results. The IFI system demonstrated a satisfactory flow of all grafts. X-ray angiography demonstrated that one SVG was 75% stenosed, and the others were patent. The mean graft flow (MGF) and the pulsatility index (PI) of the patent SVGs were not significantly different from those of the stenosed SVG. The HD of the patent SVGs was significantly different from that of the stenosed SVG.
Conclusion. The HD of the TTFM waveform can provide better diagnostic accuracy for detecting clinically significant grafts than MGF and PI of TTFM and the IFI system.

Key words Coronary artery bypass grafting · Ultrasound · Imaging · Ischemic heart disease

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Introduction

Graft failure is associated with several adverse consequences such as perioperative myocardial infarction, a need for repeated intervention, and symptoms. Early graft failure is a major cause of cardiac morbidity and mortality after coronary artery bypass grafting (CABG), occurring in up to 3% of grafts (8% of patients).[1] It is the common cause of perioperative myocardial infarction, which is detectable in up to 9% of patients before hospital discharge.[2] Postoperative angiography, used to assess graft patency before hospital discharge, has resulted in reoperation in some patients.[3,4]

Consequently, several techniques have been employed to assess intraoperative graft patency. These have included electromagnetic study,[5] transit-time flowmetry (TTFM),[6] Doppler velocity waveform,[7] epicardial echocardiography,[8] and conventional[9] and thermal[10] coronary angiography techniques. All techniques have limitations and frequently provide indirect or poor-resolution definition of grafts and flow. Recently, it was reported that the intraoperative fluorescence imaging

(IFI) system could evaluate the patency of bypass grafts[11] and that it provided better diagnostic accuracy for detecting clinically significant graft failure than does TTFM.[12] However, it has some limitations. First, it is not quantitative. Second, it does not allow precise definition of anastomotic quality. Finally, it is useful only with a skilled operator to estimate the quality of grafts.

We have previously reported that when using a fast Fourier transformation (FFT) analysis the waveform of TTFM was useful for estimating the quality of grafts.[13] Therefore, we describe our preliminary experience with analysis of the waveform of TTFM using FFT compared with the IFI system.

Material and methods

The IFI system (SPY; Novadaq Technologies, Toronto, Canada) is based on the fluorescence properties of indocyanine green (ICG). When illuminated with 806-nm light, ICG fluoresces and emits light at 830 nm. This fluorescent light is captured by a charged couple device (CCD) video camera at 30 frames per second and displayed on a computer monitor. The imaging head is positioned over the exposed heart, and the laser is activated before the first pass of a bolus of ICG through the field of view. After analyzing the sequence, the images are saved to the computer in audio-video interleave movie format.

Six patients underwent isolated CABG, including one with conventional CABG and five with off-pump CABG; all had postoperative coronary angiography. The patients received 10 saphenous vein grafts (SVGs) and 8 internal thoracic arteries (ITAs). The SVGs were aortocoronary bypass grafts, and the ITAs were in situ grafts. All of the anastomoses were performed by one surgeon (Y.O.) in the same fashion.

Graft flow tracing was obtained intraoperatively using a transit-time flowmetry (BF 1000; Medi-Stim AS, Oslo, Norway). This machine is to be able to measure graft flow and directly calculate a power of harmonics from the waveform of the flow using FFT. A flow probe to fit each SVG or ITA (between 3 and 4 mm) was placed around the graft when the hemodynamic condition had stabilized after the cardiopulmonary bypass was weaned, and all grafts were anastomosed.

Based on the obtained flow profile, the following variables were calculated: mean graft flow (MGF), pulsatility index (PI), and FFT of the flow waveform. The theoretical basis and the procedure for TTFM measurement have already been reported.[13] Harmonics of FFT analysis by the flowmeter existed at frequencies that were multiples of the frequency of the original waveform and were described in terms of amplitude and phase (Fig. 1A). In the present study, we defined F_0 as a power of the fundamental frequency, H_1 as a power of the first harmonic, H_2 as a power of the second harmonic, and so on for H_3, H_4, H_5, H_6, H_7, H_8, H_9, H_{10} (Fig. 1B). Ha (= $H_5 + H_6 + H_7 + H_8 + H_9 + H_{10}$) was then calculated.

After completion of the distal coronary artery anastomosis, 1 ml of ICG dye was injected through the central venous line and flushed through with 5 ml of natural saline. Screening was started at the time of injection and continued throughout them. Images were then recorded on a computer hard drive. The procedure takes 3–4 min per anastomosis. Images were assessed offline to determine surgeon-specified image quality and

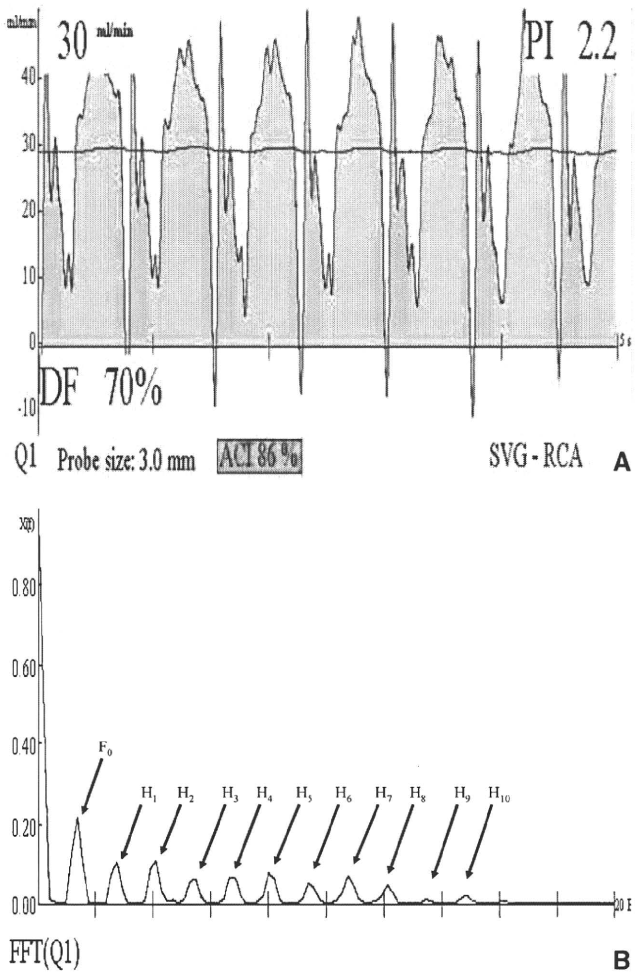


Fig. 1 **A** Typical waveform of a saphenous vein graft (SVG) (aortocoronary bypass). This graft was deemed to be patent on X-ray angiography after coronary artery bypass grafting (CABG). *RCA*, right coronary artery; *DF*, diastolic filling; *PI*, pulsatility index; *ACI*, acoustic insufficiency. **B** Typical power spectrum of the waveform (**A**) of SVG using a fast Fourier transform (*FFT*) analysis. We defined F_0 as a power of the fundamental frequency, H_1 as a power of the first harmonic, H_2 as a power of the second harmonic, and so on for H_3, H_4, H_5, H_6, H_7, H_8, H_9, and H_{10}

interrater agreement. The IFI system was used on all grafts. All patients underwent X-ray coronary angiography 1–2 months after leaving the hospital.

All data are expressed as the mean ± SD. The data were compared using the Grubbs-Smirnov test. $P < 0.05$ was considered statistically significant.

Results

All patients experienced an uneventful postoperative course. Intraoperative graft flow was visualized in all grafts, including SVGs and ITAs, confirming patency by an IFI system. Then, all grafts were patent in the operating room by an IFI system. In all patients, X-ray angiography was performed at a mean of interval 44.8 ± 13.7 days after CABG. One SVG, which went from the aorta to the no. 4 posterior descending branch, was deemed to be 75% occluded on X-ray angiography. Other grafts were patent.

The SVG was demonstrated to be patent with the IFI system in the operating room (Fig. 2A). However, the SVG was found to be 75% occluded with X-ray angiography after CABG (Figure 2B). The Ha of this graft was significantly higher than that of the other SVGs ($P <$ 0.05) (Fig. 3). The MGFs and PIs of this graft were not significantly different from those of the other SVGs (Fig. 4).

All ITA grafts were deemed to be patent with the IFI system and X-ray angiography. There was no significant difference in the Ha, MGF, or PI among all ITA grafts.

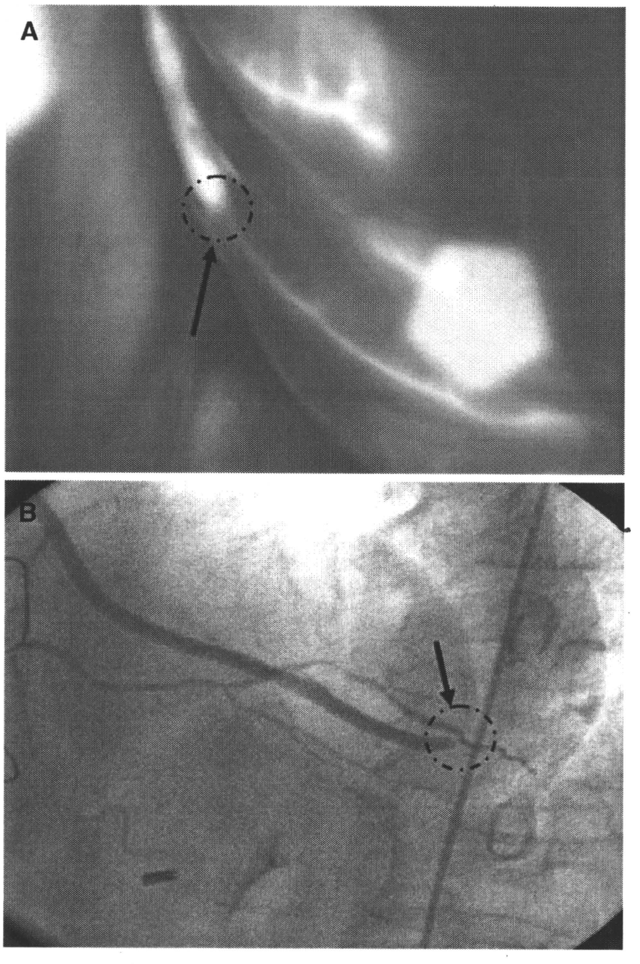


Fig. 2 **A** Intraoperative fluorescence imaging (IFI) system reveals patency of the SVG to the no. 4 posterior descending branch (PD) at the anastomosis. The IFI system captured the proximal coronary open. *Arrow* shows the anastomosis in the *circle*. **B** After CABG, angiography reveals stenosis of the SVG to the no. 4 PD at the anastomosis. *Arrow* shows the anastomosis in the circle

Discussion

We demonstrated that the waveform of TTFM might be more useful than the IFI system for estimating the quality of grafts. In our estimation, graft assessment of the TTFM waveform using FFT analysis suggested stenosis, whereas the IFI system did not.

Among graft assessment techniques currently available, contrast X-ray coronary angiography remains the gold, or reference, standard. Hybrid operating rooms with either ceiling-mounted or floor-mounted angiography equipment are becoming a reality owing to the advances in percutaneous and minimal access valvular surgery and endovascular surgery. This room is not yet popular, however. It is generally not available in the cardiac operating room because of logistical difficulties incorporating bulky equipment and safety concerns regarding contrast-induced renal insufficiency and aortoembolic and bleeding complications.[14] Although graft patency assessment techniques such as thermal angiography, Doppler flow measurement, and electromagnetic flow measurement have been attempted in the operating room, such techniques generally do not provide high-fidelity angiographic information and have not gained implementation in routine surgical practice.[5,9,15–17]

Our previous article noted that using FFT analysis the waveform of TTFM was useful for estimating the quality of grafts.[13] In this study, we indicated that the waveform of the occluded grafts had more high-frequency components than did the waveform of patent grafts. In the present study, the power of Ha in the patent grafts was lower than that in the stenotic graft. The powers of Ha are components of a high-frequency TTFM waveform. Thus, we demonstrated that Ha could be an index for assessing the quality of grafts in the future.

Some authors have reported that the IFI system provides better diagnostic accuracy for detecting graft errors

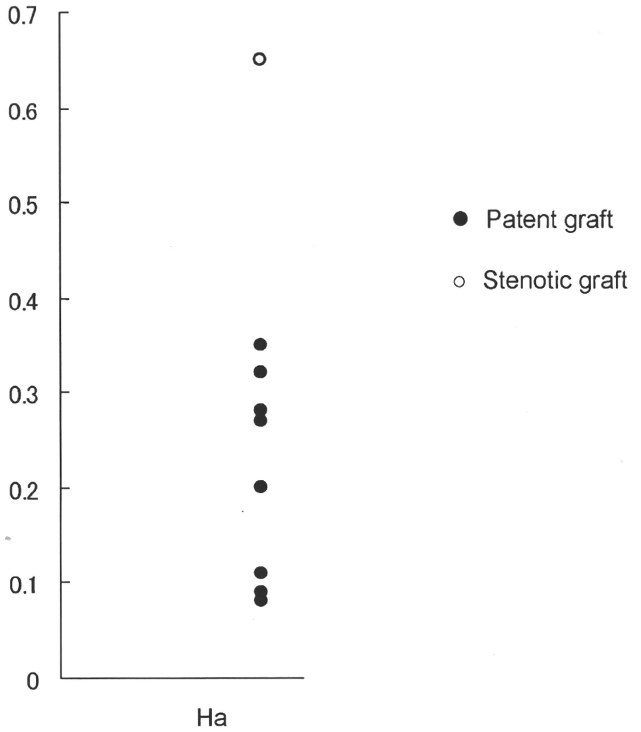
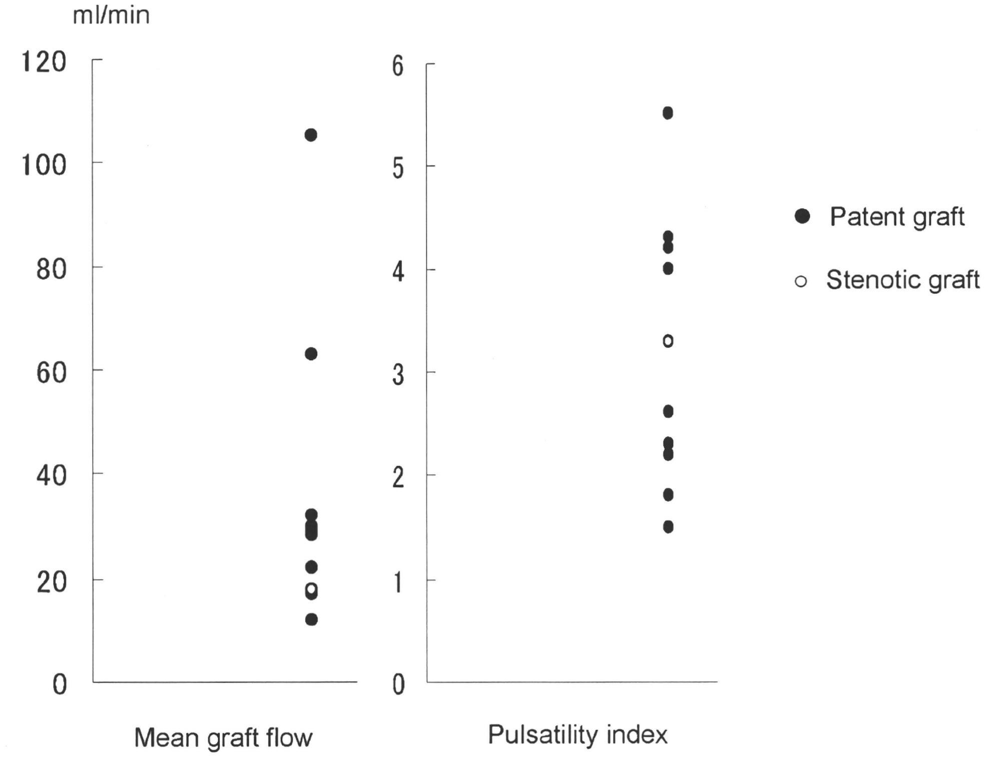


Fig. 3 The Ha (= $H_5 + H_6 + H_7 + H_8 + H_9 + H_{10}$) of this graft was significantly higher than that of the other SVGs ($P < 0.05$). *Filled circles*, patent SVGs; *open circles*, 75% stenosis of the SVG at the anastomosis

than does TTF[11,12,18] and that the limitation of wider use of TTF technology has been the lack of clear-cut values.[19,20] However, the IFI system is dependent on the surgeon's skill and the method for injecting ICG to assess the quality of grafts. It is sometimes difficult to detect anastomosis of coronary arteries behind the heart (e.g., right coronary distal branches or left circumflex distal branches) using the IFI system. Furthermore, the technique allows precise definition of the quality of the anastomosis in only about three-fourths of grafts. This is because the depth of penetration of the laser beam is only around 1 mm, which therefore precludes is use for greater depths of the native coronary artery. For the same reason, pedicled conduits are less well visualized than skeletonized ones.[11] The view with the IFI system could not be determined objectively. In contrast, the method using TTFM is easy to handle, not time-consuming, minimally invasive, easily meaningful and objective, and relatively inexpensive. However, the site of graft failure cannot be detected using TTFM, whereas the IFI system can detected it. Perhaps, the best method to assess graft quality should be a combined TTFM and IFI system.

This study was a preliminary one to compare a new technique using FFT and the IFI system in a small number of patients. It is a first report to compare our method with IFI system. In this study and the study we

Fig. 4 Mean graft flow and pulsatility index of this graft were not significantly different from those of the other SVGs. *Filled circles*, patent SVGs; *open circles*, 75% stenosis of the SVG at the anastomosis



reported elsewhere,[13] the cutoff values were unclear. We need to increase the number of cases and investigate such problems as whether the kind of graft (e.g., venous or arterial grafts; in situ or free grafts; grafts to the left anterior descending coronary artery, left circumflex coronary artery, or right coronary artery) affects the waveform of the graft and the cutoff values.

Conclusion

We compared the waveforms of TTFM with the view of IFI system for assessing CABG graft patency. We demonstrated that the waveform of TTFM using FFT analysis could be more useful than the IFI system for assessing the quality of the graft. We also found that the Ha value was higher in nonpatent grafts, including occluded or stenotic grafts, than that in patent grafts. This study was a pilot study. We need to increase the number of patients examined with the FFT and IFI system.

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