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Remodeling of Reconstructed Left Anterior Descending Coronary Arteries With Internal Thoracic Artery Grafts

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Background. The internal thoracic artery (ITA) remodels its diameter in response to flow requirements. The objective of this study was to elucidate the remodeling capacity of the reconstructed coronary artery using the ITA.

Methods. We evaluated coronary angiograms in 63 patients who had left anterior descending artery (LAD) segmental reconstruction with or without endarterectomy after off-pump coronary artery bypass graft surgery. The diameters of the ITA and reconstructed coronary artery were measured early and at 1 year after surgery.

Results. The mean diameter of the reconstructed LAD was significantly larger than that of the ITA, but significantly decreased 1 year after surgery (2.69 ± 0.53 mm versus 1.87 ± 0.39 mm; $p > 0.0001$). The proximal ratio, the ratio of the ITA to proximal reconstructed coronary artery, and the distal ratio, the ratio of the distal LAD to distal reconstructed coronary artery, increased to a value of almost 1.0 (0.77 ± 0.11 versus 1.05 ± 0.18, $p < 0.0001$, and 0.77 ± 0.14 versus 0.92 ± 0.12, $p < 0.0001$, respectively). Based on the mean diameter of the reconstructed coronary artery, there were no relationships between the use of endarterectomy and the degree of native coronary stenosis. The proximal ratio in the group with severe stenosis was significantly greater than that in the group with mild stenosis (1.08 ± 0.18 versus 0.95 ± 0.16; $p = 0.036$), although the distal ratio was not different between the two groups.

Conclusions. Vascular remodeling of the coronary artery reconstructed with the ITA is observed within 1 year after surgery.

(Ann Thorac Surg 2009;88:54–8)

Coronary artery bypass graft surgery (CABG) using the internal thoracic artery (ITA) has been clearly recognized to provide an excellent long-term patency rate and survival benefit [1]; however, extensive and calcified atheromatous lesions cannot be treated by conventional CABG. The incidence of diffuse coronary artery disease is likely to increase because of increasing age, associated comorbidities, and the increased use of percutaneous interventions. Therefore, we have developed a technique of left anterior descending artery (LAD) reconstruction using the ITA in which atheromatous plaques are excluded or removed outside the lumen of the reconstructed vessel [2, 3].

Although there is abundant evidence that arterial conduits will adjust their caliber and wall structure by vascular remodeling to adjust to the flow requirements of the distal vasculature [4], changes of the LAD reconstructed with the ITA have not been reported. The objective of this study was to elucidate the remodeling capacity of the reconstructed LAD using the ITA by angiography early and at 1 year after surgery.

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Material and Methods

Patient Population

Between September 2004 and December 2006, isolated off-pump CABG was performed in 477 patients. Of these patients, 133 patients had segmental reconstruction (> 3 cm) of the LAD using the ITA. To evaluate the patency of the graft and anastomosis, 84 (63.2%) of 133 patients had postoperative coronary angiography before discharge and at 1 year of follow-up. Early angiography was not performed in 9 patients because of being elderly or having impaired renal function, and 40 patients declined 1-year follow-up angiography. For the purpose of this study, 17 patients with ITA-composite or sequential grafts and 4 patients with complications of the graft or segmental reconstruction were excluded. Finally, both the early (11.4 ± 7.2 days) and 1-year (373.3 ± 57.6 days) coronary angiograms in 63 patients were reviewed in this study. All angiograms were reviewed by a Board-certified cardiologist, and the patients were divided into two groups according to the degree of stenosis of the proximal native coronary artery: (1) a mild stenosis group with less than 90% stenosis, and (2) a severe stenosis group with 90% or greater stenosis. All patients signed informed consent forms before the operation and each angiography. The protocol of this study was approved by

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Table 1. Preoperative Patient Characteristics

Variable	Value	Percent
Age, years	66.5 ± 7.8	—
Male	58	92.1
CVA/TIA	7	11.1
Diabetes mellitus	35	55.5
Hypercholesterolemia	47	74.6
Hypertension	43	68.3
Current smoker	20	31.7
Unstable angina	19	30.2
Previous myocardial infarction	34	54.0
Three-vessel disease	45	71.4
Left main disease	13	20.6
Ejection fraction (%)	56.5 ± 12.4	—

CVA/TIA = cerebrovascular accident/transient ischemic attack.

the Institutional Review Board, and the necessity for patient consent regarding this study was waived.

The preoperative characteristics and operative data of the patients are shown in Tables 1 and 2. All patients had low-dose aspirin (81 mg/day) from the first postoperative day. Patients with extended segmental reconstruction (≥4 cm) were additionally given ticlopidine (200 mg/day) for 1 month and coumadin (maintained with a target international normalized ratio of 2.0 to 2.5) for 6 months after surgery.

Surgical Technique

Details of the surgical indication and technique of the segmental reconstruction were previously reported [2, 3]. The method of segmental reconstruction consisted of either coronary artery reconstruction with plaque exclusion or with endarterectomy. Coronary artery reconstruction without endarterectomy was performed by covering the arteriotomy with an ITA onlay graft to exclude atheromatous plaques from the lumen of the coronary artery. The ITA wall made up 75% of the reconstructed vessel, and the native artery formed the posterior wall that gave rise to septal and diagonal branch arteries. In case the needle could not be passed through calcified plaques, an endarterectomy was performed with distal intimal suture fixation. The majority of the reconstructed lumen consisted of intact intima of the ITA.

Angiographic Measurement

Coronary angiograms were analyzed at an institutional QCA core laboratory by means of the Clinical Measurements Solutions System (QCA-CMS, version 5.1; MEDIS Imaging Systems, Leiden, Netherlands) by experienced technicians. For serial measurement of the graft and reconstructed coronary artery, great care was taken to obtain similar projections for the measurements early and at 1 year of follow-up, and to use the projection that best visualized both the ITA and LAD. An automatic edge detection program determined the vessel contours by assessing brightness along scan lines perpendicular to the vessel center. Five coronary dimensions were measured referenced to catheter sizes, as shown in Figure 1. All measurements were carried out separately by two different observers blinded to each other's assessments. The proximal matching ratio was defined as the diameter ratio of the ITA to proximal reconstructed LAD, and the distal matching ratio was defined as the diameter ratio of the distal LAD to distal reconstructed LAD.

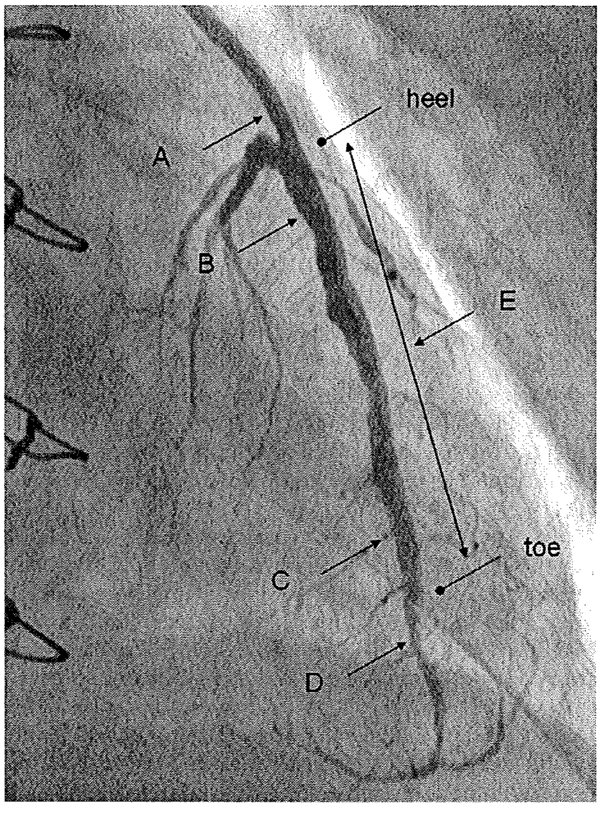

Fig 1. Five coronary dimensions were measured by the quantification system: A, the diameter of the internal thoracic artery about 5 mm proximal to the anastomosis; B, the diameter of the proximal reconstructed left anterior descending artery (LAD) approximately 5 mm from the heel; C, the diameter of the distal reconstructed LAD approximately 5 mm from the toe; D, the diameter of the distal LAD approximately 5 mm from the toe; and E, the mean diameter of the reconstructed LAD. (MRd = distal matching ratio [dashed line]; MRp = proximal matching ratio [solid line].)

Table 2. Operative Data of Left Anterior Descending Artery Segmental Reconstruction

Variable	Value	Percent
Without endarterectomy	40	63.5
Length (cm)	4.3 ± 1.1 (3.0–7.0)	
With endarterectomy	23	36.5
Length (cm)	5.8 ± 1.1 (4.5–9.0)	

Intraobserver and Interobserver Variability

Intraobserver and interobserver variability were assessed for the mean diameter of the reconstructed LAD. The

Table 3. Findings of Early and One-Year Angiography

	Early	One Year	p Value
Vessel diameter, mm			
Internal thoracic artery	2.36 ± 0.36	2.14 ± 0.35	0.001
Proximal reconstructed LAD	3.16 ± 0.71	2.09 ± 0.47	<0.0001
Distal reconstructed LAD	2.18 ± 0.50	1.66 ± 0.38	<0.0001
Distal LAD	1.66 ± 0.37	1.52 ± 0.38	0.037
Mean vessel diameter, mm			
Reconstructed LAD	2.69 ± 0.53	1.87 ± 0.39	<0.0001
Proximal ratio	0.77 ± 0.11	1.05 ± 0.18	<0.0001
Distal ratio	0.77 ± 0.14	0.92 ± 0.12	<0.0001

LAD = left anterior descending artery.

measurement of the mean diameter of the reconstructed LAD showed a high degree of intraobserver reproducibility (2.68 ± 0.53 mm versus 2.69 ± 0.55 mm, $r = 0.98$; $p < 0.0001$) and interobserver reproducibility (2.68 ± 0.53 mm versus 2.70 ± 0.54 mm, $r = 0.92$; $p < 0.0001$).

Statistical Analysis

Statistical analyses were performed using SPSS software (SPSS Inc, Chicago, IL). All data were expressed as the mean ± SD. Differences in the variables between early postoperative and 1-year angiography were determined by using a Wilcoxon test. Differences in the variables within a group or between two groups were determined by using a Mann-Whitney *U* test or Fisher's exact test for categorical variables. All p values were two-tailed, and values less than 0.05 were taken as significant.

Results

Early and 1-Year Angiography

In 63 patients, the diameter of the ITA and the mean diameter of reconstructed LAD were 2.36 ± 0.36 mm and 2.69 ± 0.53 mm, respectively. There were no significant differences in the diameters and ratios between the groups with mild and severe stenosis. At 1 year after surgery, the diameter of the ITA and the mean diameter of the reconstructed LAD were significantly decreased (2.36 ± 0.36 mm versus 2.14 ± 0.35 mm, $p < 0.0001$, and 2.69 ± 0.53 mm versus 1.87 ± 0.39 mm, $p < 0.0001$, respectively). The diameter of the ITA in the severe stenosis group was significantly larger than that in the mild stenosis group (2.21 ± 0.33 mm [n = 49], versus 1.88 ± 0.31 mm [n = 14], $p < 0.005$). However, the two groups showed no significant difference in the mean diameter of the reconstructed LAD (1.85 ± 0.33 mm versus 1.88 ± 0.41 mm, $p = 0.779$). Early and 1-year angiographic measurements are shown in Table 3.

The diameter of the ITA and reconstructed LAD showed no relationship with the application of endarterectomy, although the diameter of the proximal reconstructed LAD was significantly greater in patients with endarterectomy (3.40 ± 0.61 mm [n = 23] versus 3.02 ± 0.73 mm [n = 40], $p = 0.039$) at early angiography.

Change in Matching Ratio

During the 1-year follow-up, proximal and distal matching ratio significantly increased (0.77 ± 0.11 versus 1.05 ± 0.18, $p < 0.0001$, and 0.77 ± 0.14 versus 0.92 ± 0.12, $p < 0.0001$, respectively), as shown in Figure 2. At early angiography, there were no significant differences in either proximal or distal ratio between the two groups. However, proximal ratio of the severe stenosis group was significantly greater than that of the mild stenosis group at the 1-year follow-up angiography (1.08 ± 0.18 versus 0.95 ± 0.16, $p = 0.036$), although distal ratio was not different between the two groups (1.11 ± 0.17 versus 1.15 ± 0.20, $p = 0.667$).

Comment

The present study demonstrated following main findings: The diameter of the reconstructed LAD decreased to become equivalent to the diameters of the ITA and distal LAD at 1 year after surgery. Furthermore, the ratio of the ITA and proximal reconstructed LAD depended on the stenosis of the native coronary artery. These results suggest that the LAD reconstructed with the ITA remodels physiologically over time, in a manner similar to the ITA graft. This is a novel study demonstrating the remodeling capacity of the reconstructed LAD using the ITA.

Wall shear stress is the force induced by blood flow acting on the endothelium. This force modulates the levels of two potent endothelium-derived vasoactive mediators, the vasodilator nitric oxide [5] and the vasoconstrictor endothelin-1 [6]. Vascular remodeling of the arterial wall in response to changes in flow occurs over weeks to months and includes both cellular and noncellular elements. The end result of vascular remodeling is

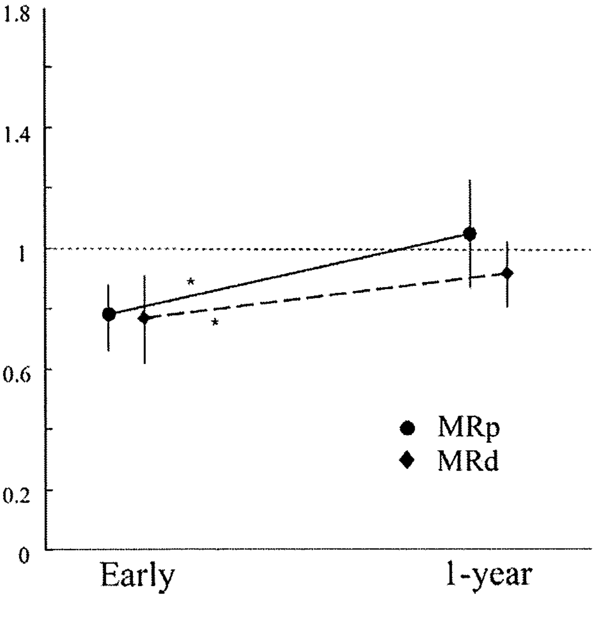

Fig 2. Changes in the matching ratio. The proximal ratio and distal ratio increased during the 1-year follow-up.

normalization of wall shear stress as detected by the endothelium. However, although healthy smooth muscle is highly responsive to dilators and constrictors, atherosclerotic vessels may not only have impaired endothelial responses but the smooth muscle can be destroyed or impaired by transmural sclerosis.

In this study, LAD reconstruction with endarterectomy was performed in 36.5% of the patients. Adaptive vascular remodeling after endarterectomy may be prevent by removal of the coronary endothelium and most of the smooth muscle, and is also influenced by inflammatory mediators, surface deposition of platelets and fibrin, occasional thrombosis, fibrosis, intimal hyperplasia, and endothelialization during the healing process. Moreover, nitric oxide, which has secondary effects on noncellular elements of the vessel wall, inhibits smooth muscle proliferation and neointimal hyperplasia. Despite of these situations, the diameter changes of the reconstructed LAD with endarterectomy were similar to those without endarterectomy. These responses must principally depend on the wall of the onlay grafting ITA. However, we guess that because the majority of the endarterectomized coronary arterial wall was excluded from the reconstructed coronary lumen in our technique, complete endothelial covering may be achieved rapidly and, thus, possibly decrease the risk of myofibrointimal proliferation.

Previous reports showed the ITA diameter had a particularly strong correlation with the degree of LAD stenosis within 1 month of CABG [7, 8]. In the present study, the stenosis of the native coronary artery significantly affected the proximal ratio but not affected the distal ratio. Moreover, the proximal ratio was larger at 1 year. There is substantial evidence that the reconstructed LAD dilate or narrow when flow dictates this response, although the posterior wall remains severely disease coronary artery. These findings suggest that shear stress in the entire reconstructed artery normalizes, and this may provide the best long-term patency, because lower shear stress is associated with the development of atherosclerosis.

There are a few limitations of this study that must be recognized. First, in our analysis, no data on flow velocity with a Doppler wire or intimal thickness measurements with an intravascular ultrasonography catheter were included. We only elucidated the anatomic change in the reconstructed LAD using the ITA early and at 1 year after surgery, and this anatomic change was defined as vascular remodeling. Second, long-term patency of the reconstructed LAD using the ITA has not been evaluated. There is some evidence that the patency rate ranged from 56% to 90% at 1 year using the vein graft with endarterectomy [9, 10]. Moreover, the patency rate was 92.5% using the ITA anastomosed to the vein patch [11], and ranged from 94.6% to 98.6% using the ITA in LAD reconstruction with or without endarterectomy [3, 12]. Third, the percent diameter stenosis is not always the best predictor of native coronary flow. Fourth, the number of patients enrolled was relatively small because the complexity of the study protocol made it difficult to recruit patients, especially the need for angiography at 1 year.

In conclusion, vascular remodeling of the reconstructed LAD is obtained angiographically within 1 year after segmental reconstruction using the ITA. Endarterectomy does not affect the remodeling. These results suggest that the LAD that has been reconstructed with the ITA over a long segment remodels over time, and that may provide the high long-term patency rate in the severely diseased coronary artery.

The authors thank Kazuya Takeda, RT, for radiographic contribution to this study.

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INVITED COMMENTARY

Shimokawa and colleagues [1] present a follow-up study of a technique for left anterior descending coronary artery (LAD) reconstruction using the internal thoracic artery (ITA). In this article, the diameter changes in

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Intermediate-Term Patency of Saphenous Vein Graft With a Clampless Hand-Sewn Proximal Anastomosis Device After Off-pump Coronary Bypass Grafting

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Background. To avoid complications related to aortic manipulation, devices were developed to perform clampless anastomosis. However, there are few studies concerning the late patency of the graft. The aims of this study were to investigate the patency rate of saphenous vein (SV) graft after off-pump coronary artery bypass grafting (OPCAB) and to evaluate the influence of a clampless hand-sewn proximal anastomosis on late graft patency.

Methods. Patients (n = 232) were enrolled who underwent OPCAB with SV grafts from 2004 to 2007 and had follow-up angiography. For proximal anastomoses, a clampless device was used in 73 (group A; HEARTSTRING [Guidant Corporation, Santa Clara, CA] in 54, Enclose II [Novare Surgical Systems, Inc, Cupertino, CA] in 19), and partial clamping was used in 159 (group B). The proximal anastomosis procedure was modified according to the results of epiaortic ultrasonography. Coronary angiography was performed early (11.8 ± 10.4 days) and one-year postoperatively (n = 180, 371.5 ± 102.6 days).

Results. There were no significant differences in patient characteristics between the two groups except for a higher reoperation rate in group A. The overall SV patency rate at the early and one-year postoperative angiography was 95.7% and 83.0%, respectively. The patency rates were similar between the two groups (early: 97.3% vs 98.1%, p = 0.729; 1 year: 87.0% vs 81.3%, p = 0.316). There was also no significant difference in the target vessel revascularization rate during follow-up (6.8% vs 10.1%, p = 0.623).

Conclusions. Intermediate-term angiographic follow-up demonstrate an acceptable SV patency rate after OPCAB. The SV patency rate with a clampless device for proximal anastomosis is comparable with that with partial clamping during the first postoperative year.

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Off-pump coronary artery bypass (OPCAB) has been suggested to reduce postoperative neurologic events. However, manipulation of the ascending aorta during construction of proximal aortocoronary bypass anastomosis may produce particulate cerebral emboli with adverse neurologic outcome [1]. To avoid this problem, devices were developed to perform clampless anastomoses. Recently, new proximal seal devices, the HEARTSTRING (Guidant Corporation, Santa Clara, CA) and Enclose II (Novare Surgical Systems, Inc, Cupertino, CA), were introduced to facilitate the creation of a clampless hand-sewn coronary artery bypass-to-ascending aorta anastomosis. The use of these devices yielded encouraging results in terms of neurologic complications and early patency [2, 3]. Nevertheless, there is concern about the late patency rate because the first-generation automatic anastomotic device provided unacceptable patency within 6 months [4, 5]. The aims of this study were to investigate the patency rate of saphenous vein (SV) graft after OPCAB and to demonstrate the influence of a clampless hand-sewn proximal anastomosis on late graft patency.

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Material and Methods

This study enrolled 232 consecutive patients with postoperative early angiography after isolated OPCAB surgery using SV grafts from September 2004 to March 2007. We compared the angiographic results with two techniques for creating anastomoses: a clampless device in 73 patients with 74 SV grafts (group A; HEARTSTRING device in 54, Enclose II device in 19), and partial clamping in 159 patients with 161 SV grafts (group B). During the same period, 288 patients underwent OPCAB with aortocoronary SV bypass. The patient exclusion criteria for postoperative angiography were age greater than 80 years in 38 patients, impaired renal function in 11, chronic obstructive pulmonary disease that required tracheostomy in 3, severe peripheral vascular disease in 2, and postoperative severe conditions in 2 (mediastinitis

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Table 1. Patient Characteristics

Characteristics	All (n = 232)	Group A (n = 73)	Group B (n = 159)	*p* Value
Age (years)	66.9±7.7	68.0±7.9	66.4±7.7	0.076
Male	180 (77.6%)	61 (83.6%)	119 (74.8%)	0.139
Weight (kg)	62.4±10.4	61.6±9.9	62.7±10.8	0.811
Smoking	75 (32.3%)	30 (41.1%)	45 (28.3%)	0.053
History of stroke	28 (12.1%)	12 (16.4%)	16 (10.1%)	0.166
Hypertension	176 (75.9%)	55 (75.3%)	121 (76.1%)	0.900
Diabetes	103 (44.4%)	28 (38.4%)	75 (47.2%)	0.210
Hyperlipidemia	151 (65.1%)	45 (61.6%)	106 (66.7%)	0.456
Creatinine (mg/dL)	0.89±0.26	0.93±0.32	0.88±0.22	0.666
Number of diseased vessels	2.8±0.4	2.9±0.4	2.8±0.2	0.097
Left main trunk	70 (30.2%)	19 (26.0%)	51 (32.1%)	0.351
Emergent or urgent surgery	25 (8.6%)	8 (11.0%)	17 (10.7%)	0.951
Reoperation	6 (2.5%)	5 (6.8%)	1 (0.6%)	0.013
Ejection fraction (%)	57.3±12.4	57.4±12.8	57.2±12.6	0.750
Operative time (minutes)	287.9±55.9	298.8±66.5	284.4±51.9	0.348
Number of distal anastomosis	4.5±1.2	4.5±1.2	4.6±1.2	0.133
SV graft				
Number of distal anastomosis	1.4±0.6	1.4±0.7	1.4±0.6	0.440
RCA territory	219/235 (93.2%)	66/74 (89.2%)	153/161 (95.0%)	0.160

RCA = right coronary artery; SV = saphenous vein.

and gastrointestinal bleeding). For all study patients early angiography was performed before discharge (11.8 ± 10.4 days) to evaluate the patency of the graft and anastomosis, and a follow-up study was planned for 1 year after surgery regardless of symptoms. A board-certified cardiologist reviewed all angiography results and graded the degree of stenosis. All patients signed informed consent forms before the operation and each angiography. The study protocol was approved by the Institutional Review Board and the necessity for patient consent regarding this study was waived.

The preoperative characteristics of the patients are shown in Table 1. Risk factors included diabetes mellitus (diet controlled, oral agent-treated, or insulin-treated), hyperlipidemia (total cholesterol ≥ 240 mg/dL or oral agent-treated), and hypertension (systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or oral agent-treated). Every patient was given an intravenous heparin injection 6 hours after surgery to prevent perioperative stroke and myocardial infarction. Most patients had low-dose aspirin (81 mg/day) from the first postoperative day. Coumadin was prescribed for at least 6 months and was maintained at a target international normalized ratio of 2.0 to 2.5. Target vessel revascularization was defined as repeat revascularization of the initial grafted vessel. The SV graft-related vessel revascularization was defined as repeat revascularization of the initial SV graft.

Surgical Technique

The technique of OPCAB has been described previously [6]. The SV graft was our first choice for revascularization of the right coronary artery territory, and bilateral internal thoracic artery (ITA) and radial artery (RA) grafting for the left coronary territory was the standard method. We used SV graft for the left coronary territory when arterial conduits were in poor preoperative condition on angiography and ultrasonography, arterial conduits had already been used in previous operations, or an emergency operation was necessary.

Full anticoagulation was achieved with heparin (3.0 mg/kg). We bypassed all significantly diseased coronary vessels with a diameter greater than 1 mm. After completion of the distal anastomoses, the proximal RA or SV graft anastomoses were performed on a disease-free segment of the aorta as assessed by epiaortic ultrasonography (Sonos 7500; Philips Medical Systems, Andover, MA). The proximal anastomosis procedure was modified according to the results of epiaortic scanning [7]. An anterior segment of normal or mildly diseased aorta entirely was required for the partial clamping technique, and a segment partially free of disease for the clampless device. The selection of the two anastomotic devices depended on the preference of each surgeon. In patients with severe aortic atherosclerosis, the operative procedure was modified to an aortic-no-touch technique. All proximal anastomoses were constructed manually with continuous 6-0 polypropylene using a blower-mister device to enhance visualization.

Statistical Analysis

Statistical analyses were performed with SPSS software (SPSS Inc, Chicago, IL). All data were expressed as means ± standard deviation. Univariate analysis was determined by a Mann-Whitney test for continuous variables or the Fisher 2-tailed exact test for categoric vari-

Table 2. Early Patency Rate

Variable	Group A (n = 73)	Group B (n = 159)	*p* Value
SV			
FG-A	95.9% (71/74)	95.0% (153/161)	
FG-B	1.4% (1/74)	0%	0.729
FG-O	2.7% (2/74)	5.0% (8/161)	
LITA	100% (73/73)	98.7% (155/157)	1.000
RITA	100% (65/65)	100% (132/132)	-
RA	96.7% (29/30)	98.9% (87/88)	0.445

FG = FitzGibbon grade; LITA = left internal thoracic artery; RITA = right internal thoracic artery; RA = radial artery; SV = saphenous vein.

ables. Multivariate analysis was performed using the logistic regression method. All *p* values less than 0.05 were taken as significant.

Results

There were no significant differences in patient characteristics between the two groups except for a higher rate of reoperation in group A than in group B (6.8% vs 0.6%, respectively, $p = 0.013$). The number of distal anastomoses and SV graft distal anastomoses were similar in both groups (4.4 ± 1.2 vs 4.6 ± 1.2, $p = 0.133$; 1.4 ± 0.7 vs 1.4 ± 0.6, $p = 0.440$, respectively). No patients had postoperative neurologic complications in this study. The incidence of postoperative heparin administration, aspirin intake, and Coumadin (DuPont, Wilmington, DE) intake were also similar in both groups (95.9% vs 95.6%, $p = 1.00$; 100% vs 99.4%, $p = 1.00$, 97.3% vs 96.2%, $p = 1.00$, respectively). Postoperative early angiography demonstrated a 97.3% graft patency rate of the SV (FitzGibbon grade A+B) in group A and 98.1% in group B ($p = 0.729$), as shown in Table 2. The ITA graft showed an excellent patency rate in both groups A and B, even though most of the LITA (left internal thoracic artery) grafts were anastomosed to the left anterior descending coronary artery. There was no significant difference between the two groups in the patency rate of the LITA (100% vs 98.7%), RITA (right internal thoracic artery; 100% vs 100%), and RA (96.7% vs 98.9%).

Among all enrolled patients, 53 patients declined one-year follow-up angiography because of noncardiac death in 2, cerebral infarction in 3, and no symptoms in 48 within one year after the operation. As a result, one-year angiography was performed in 180 patients with 182 SV grafts (group A, n = 53; group B, n = 127; 371.5 ± 102.6 days). The incidence of aspirin and Coumadin intake at one-year angiography were similar in both groups (100% vs 98.4%, $p = 0.100$; 39.6% vs 47.2%, $p = 0.412$, respectively). The overall SV graft patency rate decreased significantly during the first postoperative year (early 95.7% vs one-year 83.0%, $p < 0.0001$). Postoperative one-year angiography demonstrated an 87.0% patency rate of the SV graft (FitzGibbon grade A+B) in group A and an 81.3% rate in group B ($p = 0.316$), as shown in Table 3. There was also no significant difference between the two groups in the patency rate of the LITA (100% vs 97.6%), RITA (91.1% vs 91.6%), and RA (65.2% vs 83.1%). Univariate analysis demonstrated a higher incidence of hyperlipidemia (27 of 33, 81.8% vs 124 of 199, 62.3%, $p = 0.029$) and less Coumadin use (3/33, 9.1% vs 5/199, 2.5%, $p = 0.089$) in the occluded SV-graft group than in the patent SV-graft group. Multivariate logistic regression analysis showed hyperlipidemia (odds ratio [OR] 2.59, 95% confidence interval [CI] 1.02 to 6.6, $p = 0.046$) to be an independent predictor of SV-graft failure during the first postoperative year after OPCAB.

Twenty-one of 230 survivors underwent target vessel revascularization during the follow-up period at 21.7 ± 10.0 months. In group A, 2 of 7 target vessel revascularizations were related to vein graft occlusion, whereas 9 of 16 were related to occlusion in group B. There were no significant differences in the rate of target vessel revascularization and SV-related vessel revascularization rates between the two groups (6.8% vs 10.1%, $p = 0.623$; 2.7% vs 5.7%, $p = 0.510$, as shown in Table 4).

Comment

The present study demonstrated the following main findings. First, the overall SV graft patency rate decreased significantly during the first postoperative year. Second, the early and one-year patency rates were similar between patients with device and partial clamping. The use of a proximal hand-sewn device was not an independent predictor of graft failure during the first year after OPCAB. Third, there were also no significant differences in rate of all target vessel and SV graft-related target vessel revascularizations. To our knowledge, this is the novel study in OPCAB comparing the effect of a clampless hand-sewn proximal anastomosis device and partial clamping on intermediate-term SV graft patency rate.

Although the SV is still the most widely used graft because of its accessibility and ease of use, the surgical results of coronary artery bypass grafting (CABG) have demonstrated that SV long-term patency is lower than that of the ITA [8, 9]. Long-term angiographic studies of CABG grafts show occlusion rates of 15% to 20% at one

Table 3. One-year Patency Rate

Variable	Group A (n = 53, 74.0%)	Group B (n = 128, 80.5%)	*p* Value
SV			
FG-A	85.2% (46/54)	75.8% (97/128)	
FG-B	1.9% (1/54)	5.5% (7/128)	0.316
FG-O	13.0% (7/54)	18.8% (24/128)	
LITA	100% (52/52)	97.6% (123/126)	0.557
RITA	91.1% (41/45)	91.6% (98/107)	1.000
RA	65.2% (15/23)	83.1% (59/71)	0.083

FG = FitzGibbon grade; LITA = left internal thoracic artery; RITA = right internal thoracic artery; RA = radial artery; SV = saphenous vein.

Table 4. Target Vessel Revascularization

Variable	Group A (n = 73)	Group B (n = 159)	*p* Value
Rate of target vessel revascularization	6.8% (5/73)	10.1% (16/159)	0.623
Rate of SV-related vessel revascularization	2.7% (2/73)	5.7% (9/159)	0.510
Vein graft occlusion	2	9	
Arterial graft occlusion	2	5	0.804
Progression of native coronary disease	1	2	

SV = saphenous vein.

year, increasing to 40% at ten years [9, 10]. The SV patency after CABG is influenced by three processes: thrombosis, fibrointimal hyperplasia, and vein graft arteriosclerosis [11]. Thrombosis accounts for most graft failures within the first month, but continues to occur as long as one year after CABG. Fibrointimal hyperplasia occurs predominantly after one month to five years, and SV arteriosclerosis may begin as early as the first year but is fully developed only after about five years. Graft failure has consequences similar to those of native coronary artery disease: recurrent angina, myocardial infarction, additional revascularization procedures, and premature death [12]. Two meta-analyses using several randomized trials showed that OPCAB significantly increased the risk of graft failure within the first postoperative year [13, 14]. These results suggested that lower SV graft patency rates result from the type of graft, the exposure and quality of stabilization, and increased procoagulant activity in OPCAB patients. Procoagulant activity is a well-known phenomenon in major general surgery and is increased in the first 24 hours after OPCAB [15]. This phenomenon may increase the risk of venous thrombosis and potentially endanger the patency of coronary anastomoses. Therefore, perioperative anticoagulation for patients undergoing OPCAB should be more aggressive than that for patients undergoing conventional CABG. In this study, preoperative aspirin was discontinued before surgery. Postoperative intravenous heparin, oral aspirin, and Coumadin were given to all patients without side effects. Our results demonstrated that the overall SV patency rate at the early and one-year postoperative angiography was 94.2% and 84.8%, respectively. Those rates are similar to the SV patency rate after conventional CABG. Recently, Magee and colleagues [16] reported that the SV graft failure rate was 25% in both on-pump and off-pump CABG in a prospective randomized study [16]. Although we found hyperlipidemia as the only predictor of SV graft failure, they reported that target artery quality, length of surgery, sequential grafts, body weight, endoscopic harvest technique, and graft quality were all independent predictors.

Proximal anastomotic devices have been introduced to reduce aortic manipulation and therefore, associated complications. Devices have been classified as either automatic or manual. The automatic devices allow anastomoses between the conduit and aorta through automated connectors and deployment systems. Automatic anastomotic devices using connector technology are technically more complex, and problems regarding cost and early patency rates have been reported [17]. In a prospective randomized study comparing the Symmetry-supported anastomotic procedure with the conventional suture technique, a 38% stenosis rate was observed with the Symmetry device (St Jude Medical Inc, St. Paul, MN) versus 0% for hand-sewed anastomoses [18]. Because the observed rate of stenosis was not acceptable, many surgeons stopped further clinical use of the device. Lower patency rates have been attributed to the following causes: the 90 degree angulation of the venous graft with the ascending aorta may cause kinking and graft occlusion if an unsuitable site for proximal anastomosis is chosen; loading the vein onto the delivery system may produce intimal lesions and later intimal hyperplasia; and nitinol may play a role in the progression of neointimal hyperplasia [17, 18].

Although a new automatic device (CorLink device [Bypass Ltd, Herzelia, Israel] and PAS-Port device [Cardica, Inc, Redwood City, CA]) has recently been introduced [19, 20], we believe that hand-sewing using a running suture is the gold standard for creation of a vascular anastomosis because it is reliable and reproducible. The HEARTSTRING and Enclose II are simple manual anastomotic devices that allow the choice of performing distal or proximal anastomoses first, facilitating the proximal anastomosis. Early clinical results have been satisfactory in terms of ease of use, neurologic complications, and early graft patency [2, 3]. In our experience with 109 patients using the HEARTSTRING or Enclose II, no patients had difficulty achieving hemostasis. Furthermore, no hospital mortality or intraoperative stroke related to the device was observed [21]. The present study demonstrated a satisfactory intermediate-term SV patency rate with a proximal hand-sewn device. These results suggest these devices can be useful for CABG in case the ascending aorta shows atheromatous disease on epiaortic ultrasonography.

In this study most of the radial artery was used as a Y-composite graft and the patency rate of the radial artery was lower at one-year angiography. We guess the use of radial artery as a Y-composite graft to mild stenosed target coronary artery resulted in a poor prognosis. When performing a multiple arterial grafting, the selection of graft material and graft design is especially important to gain the advantages of arterial grafts.

There are a few limitations of this study that must be recognized. First, the present study was not performed in a randomized manner with regard to the conditions of the ascending aorta, the graft, and the target vessels, although the majority of veins were grafted to revascularize right coronary arterial territories. Patients with aortic atheromatous disease tended to avoid partial clamping, and this may have introduced bias into the patient selection process. Second, we might have overestimated the patency rates by selecting patients who survived and had angiograms performed both early and one year after surgery. We did not perform early postoperative angiography in patients greater than 80 years old, patients with impaired renal function, patients with severe peripheral vascular disease, or in patients in poor postoperative condition. It is possible that excluding these patients could have affected the difference between the two groups. Third, we used two different devices in the device group. It was difficult to assess which device was more useful in this study. Finally, this study was an observational study in a single institution. The size of the cohort was relatively small and the follow-up period was short. Further randomized, controlled studies with a larger sample size and a longer follow-up period will be mandatory to confirm the reliability of these devices and the factors associated with graft failure.

In conclusion, intermediate-term angiographic follow-up demonstrate an acceptable SV graft patency rate after OPCAB. The patency rate of SV graft with the clampless device for proximal anastomosis is comparable with that with partial clamping during the first postoperative year.

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Coronary Artery Bypass Surgery Versus Percutaneous Coronary Artery Intervention in Patients on Chronic Hemodialysis: Does a Drug-Eluting Stent Have an Impact on Clinical Outcome?

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ABSTRACT **Coronary revascularization methods continue to be refined, and the emergence of the drug-eluting stent (DES) has especially changed clinical practice related to ischemic heart disease. For chronic hemodialysis (HD) patients, however, the impact of DES on clinical outcome is yet to be determined. Forty-six consecutive chronic HD patients who underwent myocardial revascularization in our institute were retrospectively reviewed. Twenty-eight patients underwent coronary artery bypass surgery (CABG) and 18 patients underwent percutaneous coronary artery intervention (PCI). Patient characteristics were similar between the two groups. In the CABG group, bilateral internal thoracic artery (ITA) bypass grafting was performed in 27 patients and off-pump CABG was performed in 20 patients. In the PCI group, a DES was used in 12 patients. The number of coronary vessels treated per patient was higher in the CABG group (CABG: 4.25 ± 1.32 vs. PCI: 1.44 ± 0.78; $p < 0.001$). Two-year survival rates were similar between the two groups (CABG: 94.1% vs. PCI: 73.9%; $p = 0.41$), but major adverse cardiac event-free survival (CABG: 85.9% vs. PCI: 37.1%; $p = 0.001$) and angina-free survival (CABG: 84.9% vs. PCI: 28.9%; $p < 0.001$) rates were significantly higher in the CABG group. The one-year patency rate for the CABG grafts was 93.3% (left ITA: 100%, right ITA: 84.6%, sapenous vein: 90.9%, gastro-epiploic artery: 100%), and six-month restenosis rate for PCI was 57.1% (balloon angio-plasty: 75%, bare metal stent 40%, DES: 58.3%). Even in the era of DES, clinical results favored CABG. The difference in clinical results is due to the sustainability of successful revascularization.**
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According to the annual report of the US Renal Data System, annual mortality rates in chronic hemodialysis (HD) patients remains excessively high (19.5% per year).[1] Ischemic heart disease is a particular concern that profoundly affects the survival of chronic HD patients. Approximately 30% of new HD patients experience a myocardial infarction (MI) within five years,[1] and 26% of these MI result in in-hospital mortality.[2] MI also has great impact on long-term mortality in HD patients: mortality rate rapidly increases after the onset of MI; one-year mortality goes to 59%, and five-year mortality goes to 90%.[2] As a result, 44% of overall mortality is due to cardiovascular disease and 22% of mortality from a cardiac cause is due to MI.[1] The survival benefit of coronary revascularization is addressed by several studies,[3-5] but the implementation rate of invasive coronary procedure among HD patients is low. Procedure rate after diagnostic angiography is 70.1% among non-HD patients, whereas it is 46.4% among HD patients.[6] Therefore, aggressive implementation of coronary revascularization in HD patients may improve clinical outcomes, but the optimal approach to coronary revascularization in chronic HD patients remains to be determined.

Coronary revascularization methods continue to be refined. One of the most important technological innovations in percutaneous coronary artery intervention (PCI) is the emergence of the drug-eluting stent (DES). Meta-analysis of 14 randomized trials demonstrated that DES resulted in less need for re-intervention than did bare-metal stent (BMS),[7] and the large

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observational study based on New York Percutaneous Coronary Intervention Reporting System data demonstrated that the rate of nonfatal myocardial infarction was reduced after the introduction of DES.[8] Coronary artery bypass grafting (CABG) also has some innovations such as bilateral internal thoracic artery grafting and off-pump technique. But the efficacy of these new modalities for HD patients is yet to be determined. Hence, the purpose of this study is to survey the clinical results of the coronary revascularization with new modalities performed in HD patients.

MATERIALS AND METHODS

Patient population

The study was a retrospective single institute analysis of 46 consecutive patients who were on chronic HD and underwent coronary revascularization therapy in our institute between September 2004 and May 2007. CABG was performed in 28 patients and PCI was performed in 18 patients. Our institutional ethics committee waived the need for patient consent for this study, and approval was provided before publication of the data. Clinical follow-up was obtained through telephone interviews and hospital records.

CABG

All isolated CABG was performed with off-pump procedure. Off-pump CABG was performed in 20 patients, and on-pump CABG with concomitant procedure (mitral valve plasty in four, mitral valve replacement in one, left ventricle plasty in two, and aortic valve replacement in one) was performed in eight patients. Left internal thoracic artery (ITA) was used in all patients and right ITA was used in 27 patients. All ITAs were dissected as skeletonized vessels with a harmonic scalpel. In most cases, ITAs were used for left-sided (left anterior descending and circumflex artery) arterial revascularization. Bilateral ITAs were used as composite grafts in 14 patients and as individual in situ graft in 13 patients. Right coronary system revascularization was performed with saphenous vein in 20 patients and with gastroepiploic artery in four patients.

PCI

PCI was performed in 18 patients with 26 lesions. Lesions were treated using standard PCI techniques. Sixteen lesions were treated with DES, six lesions were treated with BMS, and four lesions were treated with balloon angio-plasty.

Definitions

Cardiac mortality was defined as death occurring in relation to MI, cardiac arrhythmia, sudden death, or congestive heart failure. Undetermined causes of death were regarded as cardiac. Major adverse cardiovascular events (MACE) were defined as the occurrence of a nonfatal MI, the need for revascularization, or cardiac mortality. Follow-up was obtained by means of telephone survey and medical records.

TABLE 1
Patient Characteristics

	CABG (n = 28)	PCI (n = 18)	p Value*
Age (years)	63.9 ± 8.9	61.2 ± 12.2	0.566
Male/female	23/5	17/1	0.380
Coronary risk factor			
Diabetes mellitus	18	9	0.373
Insulin-dependent	6	3	1.000
Hypertension	20	14	0.739
Hyperlipidemia	6	6	0.495
Smoking history	14	6	0.364
Peripheral vascular disease	3	3	0.666
Cerebral vascular disease	5	3	1.000
EF (%)	48.9 ± 15.8	52.8 ± 17.6	0.383
EF < 40%	9 (32%)	4 (22%)	0.5222
Emergency	4	2	1.000
HD duration (years)	6.3 ± 8.9	6.0 ± 8.0	0.250
HD etiology			0.560
Diabetes mellitus	18 (64%)	8 (44%)	
Hypertension	6 (21%)	5 (28%)	
Glomerular nephritis	2 (7%)	3 (17%)	
Others	2 (7%)	2 (11%)	

Data are presented as the mean ± SD.
CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; HD = hemodialysis; EF = left ventricular ejection fraction.

Statistical analysis

Continuous variables are reported as mean ± SD. Fisher's exact test was used to analyze group differences in categorical variables. The Mann-Whitney test

TABLE 2
Extent of Coronary Disease and Number of Vessels Treated

	CABG (n = 28)	PCI (n = 18)	p Value*
Left main disease	10 (35.7%)	0 (0%)	
Number of diseased vessels			0.001
One	0 (0%)	4 (22.2%)	
Two	7 (25.0%)	10 (55.6%)	
Three	21 (75%)	4 (22.2%)	
Mean number of diseased vessels	2.75 ± 0.44	2.00 ± 0.69	<0.001
Vessels treated			<0.001
One	0 (0%)	4 (22.2%)	
Two	2 (7.1%)	10 (55.6%)	
Three	5 (17.9%)	4 (22.2%)	
Four	12 (42.9%)	0 (0%)	
More than five	9 (32.1%)	0 (0%)	
Mean number of treated vessels	4.25 ± 1.32	1.44 ± 0.78	<0.001

Data are presented as the mean ± SD.
CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

TABLE 3
Mid-term Results

	CABG (n = 28)	PCI (n = 18)	p value*
Follow-up period (year)	1.29 ± 0.72	1.48 ± 0.81	0.50
Mortality	2	3	0.41
Cardiac	1	2	
Other	1	1	
Major adverse cardiovascular event	2	9	0.0011
Cardiac mortality	0	2	
Myocardial infarction	0	0	
Repeat revascularization	1	7	
CABG	0	0	
PCI	1	7	
New lesion	1	1	
Restenosis	0	6	
Recurrence of symptoms	2	11	0.0002
Angina	2	6	
Heart failure	0	5	

Data are presented as the mean ± SD.
CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

was used to analyze differences in continuous variables. Kaplan-Meyer curves were used to show freedom from time-related events. Statistical significance was accepted as $p < 0.05$. Statistical analysis was performed with SPSS statistical software (SPSS version 11.0; SPSS Japan, Tokyo, Japan).

RESULTS

Patient characteristics

Patient characteristics (Tables 1 and 2) were similar between the two groups. In the CABG group, the number of vessels was larger and left main disease was more prevalent. Treated vessels were also higher in the CABG group.

Short-term results

There was no in-hospital mortality in either group. There were two postoperative complications (mediastinitis in one and stroke in another) in the CABG group, and no postoperative complication in the PCI group.

Mid-term results

The follow-up period was similar between the two groups (Table 3). Survival is shown in Figure 1. There were two mortalities (one sepsis and one unknown) in the CABG group and three mortalities (one sudden death, one heart failure, and one cerebral infarction) in the PCI group. There was no significant difference between the two groups in mid-term survival. MACE free survival is shown in Figure 2. MACE occurred in two patients (one mortality due to an unknown cause and one PCI against new lesion) in the CABG group and in nine patients in the PCI group (two cardiac deaths, and seven repeat PCI). MACE free survival rate was significantly higher in the CABG group. Symptom-free survival was shown in Figure 3. Symptom-free survival

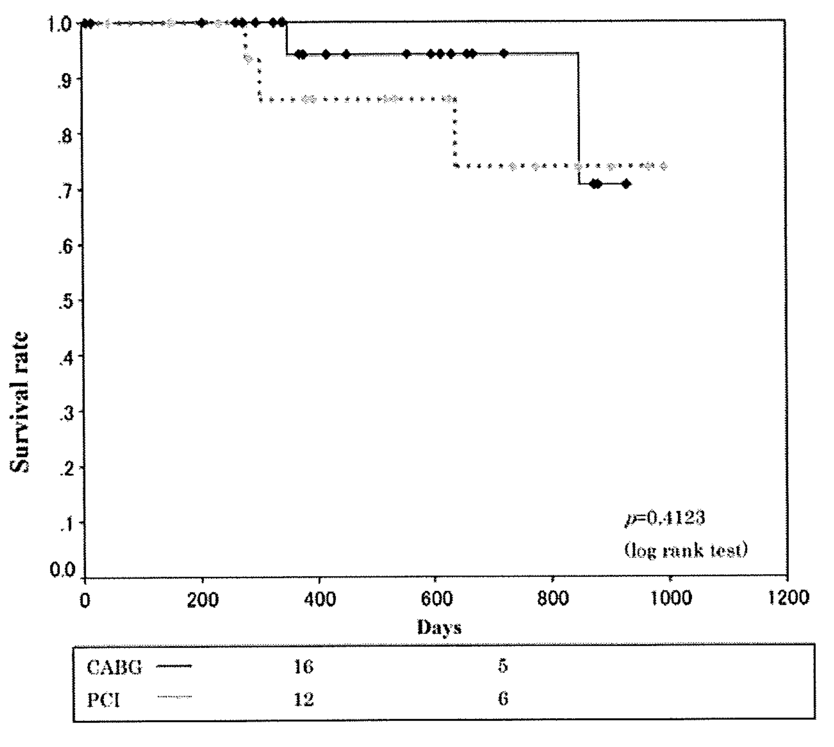

Figure 1. *Cumulative proportion of chronic hemodialysis patients free of death after coronary artery bypass grafting (CABG) or percutaneous coronary artery intervention (PCI). The curves were not significantly different between the two groups. p = 0.41.*

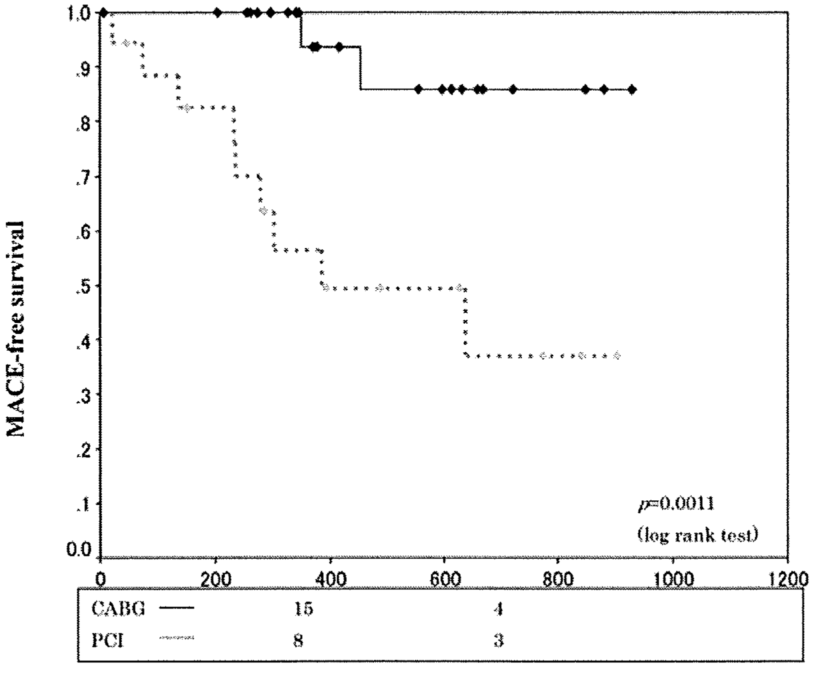

Figure 2. *Cumulative proportion of chronic hemodialysis patients free of major adverse cardiac events (MACE) after coronary artery bypass grafting (CABG) or percutaneous coronary artery intervention (PCI). The curves were significantly different between the two groups. p = 0.0011.*

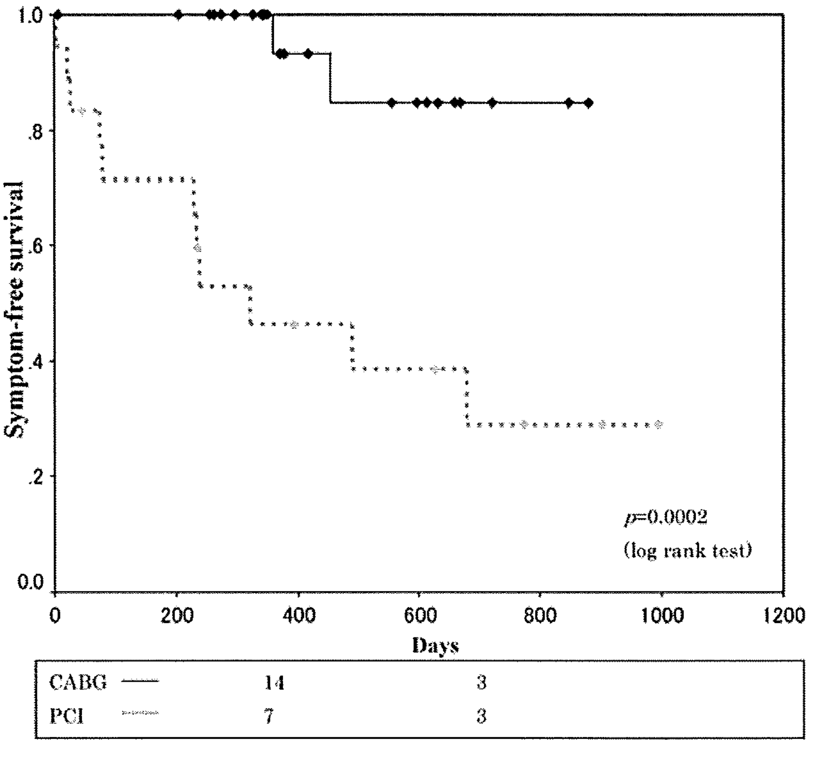

Figure 3. *Cumulative proportion of symptom-free chronic hemodialysis patients after coronary artery bypass grafting (CABG) or percutaneous coronary artery intervention (PCI). The curves were significantly different between the two groups. p = 0.0002.*

TABLE 4
Patency Rates of CABG Grafts and Restenosis Rates of PCI

	Early	One year
LITA	26/26 (100%)	14/14 (100%)
RITA	29/29 (100%)	11/13 (84.6%)
SV	17/19 (89.5%)	10/11 (90.9%)
GEA	10/10 (100%)	7/7 (100%)
RA	2/2 (100%)	
Total	84/86 (97.7%)	42/45 (93.3%)
	Six months	
POBA	3/4 (75%)	
BMS	2/5 (40%)	
DES	7/12 (58.3%)	
Total	12/21 (57.1%)	

rate was significantly higher in the CABG group. Patency rate of the CABG grafts and the restenosis rate of PCI are shown in Table 4

DISCUSSION

The present study compared mid-term clinical results of CABG and PCI in chronic HD patients. The majority of PCI was performed with DES, and most CABG was performed with bilateral ITA grafting. Although there was no difference in survival between the two groups, MACE-free survival and symptom-free survival were statistically higher in the CABG group. Angiographic studies revealed that these differences in clinical outcome were mainly due to the sustainability of successful revascularization. Most cardiac accidents in the PCI group were attributed to the restenosis of the target vessels; meanwhile, good clinical results in the CABG group were attributed to the high patency rate of the bypass graft, especially of ITA graft.

Coronary revascularization methods continue to be refined, and the emergence of DES has especially changed the clinical practice for treatment of ischemic heart disease. Our study is the first to compare the clinical outcomes of PCI including DES with CABG in chronic HD patients, but the results are almost consistent with the prior studies conducted before the emergence of DES.[3-5,9,10] Our study did not find a survival benefit with CABG, but this result may be due to the small patient number in our study. Other single institutional studies also found no survival difference between the two groups[4,5,9,10] in accordance with our results, but the multi-institutional study based on US Renal Data System data demonstrated a survival benefit with CABG.[3] Our study revealed that CABG has apparent superiority in relief of angina symptoms and avoidance of repeat revascularization. Rinehart et al. also reported that CABG is associated with a lower incidence of angina or MI.[10] The high incidence of repeat revascularization was also reported by two studies.[4,9]

The optimal approach to coronary revascularization in chronic HD patients remains to be determined. Renal insufficiency is closely related with advanced atherosclerotic coronary artery changes, and this is probably the major reason for poor PCI outcomes in patients on HD.[11] The impact of DES on clinical outcomes in chronic HD patients was reported in several studies[12-14] which revealed that restenosis rates for DES in HD patients remained high (22.2% to 41.2%). Nakazawa et al.[14] reported that neointimal growth after DES implantation was pronounced in chronic HD patients, resulting in a high restenosis rate. Aoyama et al.[12] and Ishio et al.[13] reported that there was no difference in restenosis rates between DES and BMS in chronic HD patients. Even in the era of DES, restenosis remains a major problem in HD patients and results in poor clinical outcomes.

The best strategy for bypass graft selection in chronic HD patients is yet to be determined. The feasibility of bilateral ITA grafting for patients on chronic HD has been reported,[15,16] and our strategy is to revascularize maximally with ITA. Bilateral ITA grafting was performed in all but one patient. In 14 patients, bilateral ITA was used as composite grafting. Sixty-five percent of total target lesion was grafted with ITAs (25% with saphenous vein, 8% with gastroepiploic artery, and 2% with radial artery). Furthermore, ITA was used in all left anterior descending territory, in 88% of diagonal territory, and in 79% of left circumflex territory. In CABG patients, therefore, the majority of left-sided target lesion was protected with ITA. In previous studies, angiographic results of ITA in HD patients were lacking. Our study revealed that the patency rate of ITA in HD patients was excellent and almost similar to that in non-HD patients. The potent resistance against atherosclerotic changes in ITA was also seen in HD patients, and we believe this is one of the most important reasons for the good mid-term results of the CABG group.

Efficacy of off-pump technique in HD patients remains unknown. Beckermann et al. conducted a large-scale study using data from the US Renal Data System and found survival benefit in off-pump CABG.[17] However, Dewey et al. reported that the survival benefit of off-pump CABG in HD patients was restricted to the short-term period.[18] Their poor long-term results may be due to a relatively small number of anastomosis and incomplete revascularizaion. We previously reported excellent clinical outcomes after complete revascularization in HD patients undergoing off-pump CABG.[19] But we are not able to discuss the superiority between off-pump and on-pump procedure because we routinely perform off-pump CABG in patients undergoing solitary CABG.

Study limitation

Limitations of the present study include its retrospective nature, a short follow-up time, and the possible impact of selection bias for choice procedure. Our patient sample was small and larger and longer follow-ups would be required to carry out further analysis.

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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;■:1-6)

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.

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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

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).

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

Conduit	Target coronary artery: 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.

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Clinical Outcomes

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

TABLE 4. Patient characteristics and postoperative medications Q3

	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.

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