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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Increased Graft Occlusion or String Sign in Composite Arterial Grafting for Mildly Stenosed Target Vessels

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Background. Composite grafting is a useful technique that avoids the need for aortic manipulation and enables a wide range of target vessels to be revascularized, effectively using the limited arterial grafts available. However, it has not been clarified whether composite grafting can achieve angiographic outcomes equivalent to those obtained with individual grafting for specific target vessels.

Methods. We retrospectively reviewed 830 distal arterial graft anastomoses in 256 patients who underwent off-pump coronary artery bypass surgery and also underwent 1-year follow-up coronary angiograms. Four hundred and ten anastomoses using a composite grafting technique were compared with 420 anastomoses using individual grafting.

Results. In target vessels with mild stenosis, the incidence of graft occlusion or string sign was significantly higher in composite internal thoracic arteries (ITA) than in individual ITA grafts (composite 20.3% versus individual 7.3%; $p = 0.018$) and showed a higher tendency in composite radial arteries (RA) than in individual RA grafts (59.3% versus 36.4%, $p = 0.09$). In contrast, the incidence was similar between composite and individual ITA grafts (5.7% versus 3.3%, $p = 0.278$) and composite and individual RA grafts (11.5% versus 29.6%, $p = 0.297$) in target vessels with severe stenosis.

Conclusions. The angiographic outcomes of composite grafts were closely related to the severity of stenosis of the target coronary artery. In target vessels with mild stenosis, composite grafting resulted in a higher incidence of graft occlusion or string sign than individual grafting did.

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Modern coronary artery bypass graft surgery (CABG) involves several sophisticated procedures developed to handle particular problems or improve the quality of treatment. The aortic "no-touch" technique is considered effective for reducing stroke risk in patients with the atherosclerotic ascending aorta, and multiple arterial grafting is usually preferred because it provides excellent long-term clinical outcomes. Composite grafting plays a crucial role in these procedures, because it eliminates the need for proximal anastomosis to the ascending aorta and conserves extra lengths of an arterial graft for additional grafting.

Although the prevalence of composite grafting is increasing, there have been few studies to support the feasibility of performing composite grafting for a particular target coronary artery. Several studies reported that the clinical and angiographic results of composite grafting were equivalent to those of individual grafting [1–3]. Conversely, some other studies reported that composite grafting may be susceptible to the detrimental effect of flow competition with native coronary artery when used for a mildly stenosed target vessel [4, 5]. The difference in angiographic outcomes between composite and individual grafting in target vessels with mild stenosis has not been clarified. Hence, the purpose of this study was to compare the angiographic outcomes between composite and individual grafts according to the severity of stenosis of the target coronary artery.

Material and Methods

Study Design

This was a retrospective cohort study to verify the hypothesis that angiographic outcomes of composite grafts

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Table 1. Patient Characteristics

	Total n = 256	Without Composite n = 108	With Composite n = 148	*p* Value*
Age, years	66.3 ± 8.1	66.3 ± 8.1	66.6 ± 7.3	0.776
Male (n)	85.6% (219)	85.2% (92)	85.8% (127)	1.000
Coronary risk factor (n)				
Hypertension	69.9% (179)	69.4% (75)	70.3% (104)	0.891
Diabetes mellitus	41.0% (105)	35.2% (38)	45.3% (67)	0.123
Hyperlipidemia	63.7% (163)	68.5% (74)	60.1% (89)	0.189
Smoking	57.0% (146)	57.4% (62)	56.8% (84)	1.000
Old cerebral infarction (n)	7.4% (19)	4.6% (5)	9.5% (14)	0.227
PVD (n)	6.3% (16)	3.7% (4)	8.1% (12)	0.194
Chronic hemodialysis (n)	3.5% (9)	1.9% (2)	4.7% (7)	0.310

* Comparison between patients with and without composite grafts.

PVD = peripheral vascular disease.

were inferior to those of individual grafts in target vessels with mild stenosis. One-year angiographic outcomes of arterial grafts were reviewed, and incidence of graft occlusion or string sign was compared between composite and individual grafts according to the severity of stenosis of the target coronary artery. Moreover, multivariate analysis was performed to identify the independent predictor of graft occlusion or string sign. The Ethics Committee of Sakakibara Heart Institute approved this study, waived the need for patient consent, and provided approval before the publication of the data.

Study Subjects and Data Collection

Between September 2004 and July 2007, 536 patients underwent isolated CABG in our institute. All patients were scheduled for off-pump CABG. Six patients who were converted to an on-pump CABG were excluded from the study. We routinely performed coronary angiograms 1 year after surgery in patients who have undergone off-pump CABG, regardless of the patient's symptoms. Patients who died, refused angiographic evaluation, were more than 75 years old, or had renal dysfunction (serum creatinine > 1.2 mg/dL) were excluded from the angiographic follow-up. Of the 536 patients, 256 patients (47.8%) underwent 1-year follow-up angiograms and were retrospectively reviewed. Preoperative characteristics of the study patients are shown in Table 1.

In the 256 study patients, there were 1,050 distal anastomoses, an average of 4.1 per patient. Of these, 830 anastomoses were constructed with arterial grafts and 220 were constructed with saphenous vein. All composite grafts were constructed with arterial grafts. Anastomoses constructed with saphenous vein were excluded from the analysis. Among the 830 anastomoses using arterial grafts, 410 anastomoses were constructed with composite graft (composite group) and 420 anastomoses with individual graft (individual group). Both groups included sequential grafting. Graft material and location and stenosis of the target coronary artery are shown in Table 2. Composite grafts were made using an "I" configuration in 37 anastomoses and a "Y" configuration in 373 anastomoses.

One physician initially reviewed all the coronary angiograms, and a consensus was reached after review. For native coronary arteries, mild stenosis was defined as a stenotic lesion producing luminal narrowing of 75% or less, and severe stenosis as narrowing of more than 75%. Distal anastomoses were assessed and classified as patent, focally stenosed, string sign, or occluded. Focally stenosed was defined as 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 more.

Operative Strategy

The surgical procedures and principles of off-pump CABG we used have been previously described [6]. The left-sided coronary arteries were revascularized with arterial grafts in most cases. The left anterior descending artery (LAD) was revascularized exclusively using the

Table 2. Graft Material and Location and Stenosis of Target Coronary Artery

	Composite n = 410	Individual n = 420	*p* Value
Graft material			<0.001
ITA	191 (46.6%)	336 (80.0%)	
RA	211 (51.5%)	49 (11.7%)	
GEA	8 (2.0%)	35 (8.3%)	
Location of target coronary artery			<0.001
LAD	34 (8.3%)	223 (53.1%)	
D	127 (31.0%)	51 (12.1%)	
LCX	234 (57.1%)	108 (25.7%)	
RCA	15 (3.7%)	38 (9.0%)	
Stenosis of target coronary artery			0.021
Mild, ≤ 75%	153 (37.3%)	125 (30.0%)	
Severe, > 75%	257 (62.7%)	295 (70.2%)	

D = diagonal branch; GEA = gastroepiploic artery; ITA = internal thoracic artery; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RA = radial artery; RCA = right coronary artery.

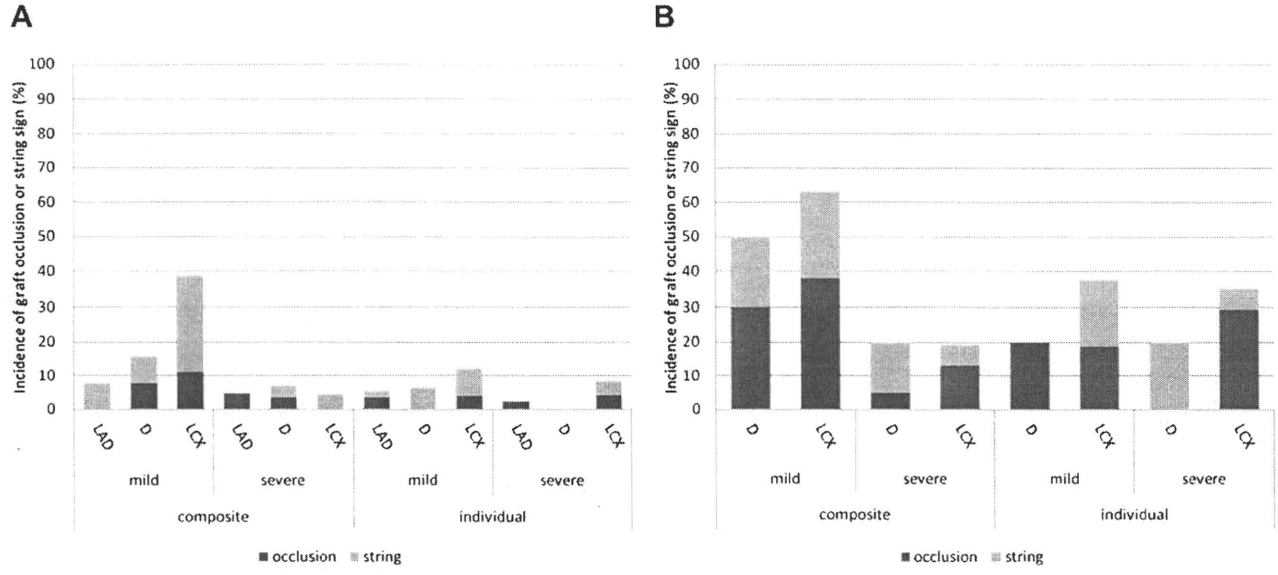

Fig 1. The incidence (%) of graft occlusion (dark gray shaded bar) or string sign (light gray shaded bar) according to graft material or location of target coronary artery. (A) internal thoracic artery (ITA). (B) Radial artery (RA). (D = diagonal artery; LAD = left anterior descending artery; LCX = left circumflex artery.)

internal thoracic artery (ITA), and the left ITA was preferably used. The right ITA was revascularized to the LAD only when the left ITA was required to bypass a remote anastomosis 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 (RA). In this arrangement, the right ITA was used as an in-situ graft for the diagonal artery, and the RA 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.

Statistical Analysis

Categorical variables are reported as percentages. To compare categorical variables, the χ^2 test was used to compare among three groups and the Fisher's exact test was used to compare between two groups. Student's t test was used to compare continuous variables. Multivariate analysis was performed to identify independent risk factors for graft occlusion or string sign. A generalized estimating equation method was used to account for within-patient correlation. Covariates included in the generalized estimating equation models were age, sex, hypertension, diabetes mellitus, hyperlipidemia, smoking history, peripheral vascular disease, graft material (ITA or non-ITA), target coronary artery (LAD or non-LAD), stenosis rate of target coronary artery (mild or severe), composite grafting, and sequential grafting. Odds ratios are presented with 95% confidence intervals. Statistical significance was accepted at p less than 0.05. All statistical analyses was performed with SPSS statistical software (SPSS version 17.0; SPSS Japan, Tokyo, Japan).

Results

Incidence of graft occlusion or string sign was compared between composite grafts and individual grafts according to graft material, location of target coronary artery, and stenosis of target coronary artery (Table 3). There were significant differences between composite and individual

Table 3. Incidence of Graft Occlusion or String Sign in Composite and Individual Grafts

	Composite	Individual	p Value
Graft material			
ITA	11.0% (21/191)	4.5% (15/336)	0.006
RA	34.6% (73/211)	32.7% (16/49)	0.868
GEA	12.5% (1/8)	22.9% (8/35)	1.000
Location of target coronary artery			
LAD	5.9% (2/34)	3.1% (7/223)	0.339
D	15.0% (19/127)	7.8% (4/51)	0.228
LCX	30.8% (72/234)	17.6% (19/108)	0.052
RCA	13.3% (2/15)	26.3% (10/38)	0.472
Stenosis of target coronary artery			
Mild, ≤ 75%	40.5% (62/153)	13.6% (17/125)	<0.001
Severe, > 75%	12.8% (33/257)	7.8% (23/295)	0.065
≤ 50%	66.7% (14/21)	57.1% (4/7)	0.674
> 50%, ≤ 75%	36.4% (48/132)	11.0% (13/118)	<0.001
> 75%, ≤ 90%	15.1% (23/152)	6.9% (13/188)	0.020
> 90%	9.5% (10/105)	9.3% (10/107)	1.000

D = diagonal branch; GEA = gastroepiploic artery; ITA = internal thoracic artery; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RA = radial artery; RCA = right coronary artery.

Table 4. Incidence of Graft Occlusion or String Sign According to Severity of Target Coronary Artery

	Composite	Individual	p Value
ITA			
Mild, ≤ 75%	20.3% (14/69)	7.3% (7/96)	0.018
Severe, > 75%	5.7% (7/122)	3.3% (8/240)	0.278
≤ 50%	14.3% (1/7)	60.0% (3/5)	0.222
> 50%, ≤ 75%	21.0% (13/62)	4.4% (4/91)	0.003
> 75%, ≤ 90%	5.6% (4/72)	3.2% (5/157)	0.473
> 90%	6.0% (3/50)	3.6% (3/83)	0.672
RA			
Mild, ≤ 75%	59.3% (48/81)	36.4% (8/22)	0.090
Severe, > 75%	11.5% (25/130)	29.6% (8/27)	0.297
≤ 50%	93.0% (13/14)	50.0% (1/2)	0.242
> 50%, ≤ 75%	50.7% (34/67)	35.0% (7/20)	0.308
> 75%, ≤ 90%	23.4% (18/77)	40.0% (6/15)	0.206
> 90%	13.2% (7/53)	16.7% (2/12)	0.667

ITA = internal thoracic artery; RA = radial artery.

grafts in ITA grafts and in the presence of mild stenosis of target coronary artery.

Incidence of graft occlusion or string sign in ITA and RA graft according to severity of target coronary artery is shown in Table 4. In target vessels with severe stenosis, there were no differences in the incidence of graft occlusion or string sign between composite and individual grafts in ITA (composite 5.7% versus individual 3.3%, $p = 0.278$) and RA (11.5% versus 29.6%, $p = 297$). But in target vessels with mild stenosis, the incidence of graft occlusion or string sign was significantly higher for composite grafts than for individual grafts in ITA (20.3% versus 7.3%, $p = 0.018$) and showed a lower tendency in RA (59.3% versus 36.4%, $p = 0.09$). The incidence of graft occlusion or string sign according to graft material, location and stenosis of the target coronary artery, and graft configuration is shown in Figure 1. The incidences of graft occlusion and string sign were particularly high when composite grafts were used for a mildly stenosed target vessel, irrespective of the graft material or location of the target coronary artery.

The results of multivariate analysis are shown in Table 5. The independent predictors of graft occlusion or string sign in total were non-ITA graft, mild stenosis of the target coronary artery, and peripheral vascular disease. Composite grafting was an independent predictor of graft occlusion or string sign only when grafted to the target vessels with mild stenosis.

Comment

Comparison of Composite and Individual Grafting

The present study revealed that the angiographic outcomes of composite grafts were closely related to the severity of stenosis of the target coronary artery. Several previous studies reported that the patency rate of composite grafts was equal to that of individual grafts [1–3]. However, none of them examined the patency rate in relation to stenosis of the target coronary artery. Suboptimum angiographic results of composited grafting for mildly stenosed target vessels have been reported by several studies. Pevni and colleagues [4] reported that a lower stenosis rate of the target coronary arteries was associated with a higher occlusion rate of composite ITA grafts. Gaudino and associates [5] reported that the threshold of stenosis for graft occlusion in a target coronary artery was higher in composite RA grafts than in individual RA grafts. Nakajima and associates [7] reported that 75% stenosis in the right coronary artery was an independent predictor of competitive flow and graft occlusion. From a practical standpoint, whether there is a difference in angiographic outcomes between composite and individual grafts for particular target vessels has been considered important, but none of these studies compared angiographic outcomes of composite and individual grafting. The present study is the first to demonstrate a higher incidence of graft failure in composite grafting for mildly stenosed target vessels. Moreover, in target vessels with mild stenosis, composite grafting has been shown to be an independent predictor of graft occlusion or string sign. Based on these results, we do not recommend composite grafting in target vessels with mild stenosis.

Mechanism of Graft Failure in Composite Grafts

The precise mechanism of graft failure in composite grafts has not been completely clarified. Arterial grafts are known to narrow diffusely or occlude when they are used in low-flow conditions [6, 8]. The susceptibility of composite grafting to low-flow conditions when used in target vessels with mild stenosis has been suggested by several studies. Studies examining the blood flow of composite grafts reported flow reduction of approximately 20% for composite grafting compared with the

Table 5. Multivariate Analysis of Risk Factors for Graft Occlusion or String Sign

Risk Factors	Odds Ratio	95% CI	p Value
Total			
Non-ITA	4.88	2.74–8.69	<0.001
Mild stenosis	3.61	2.29–5.70	<0.001
Composite grafting	1.37	0.70–2.68	0.362
Peripheral vascular disease	2.65	1.21–5.82	0.015
For mildly stenosed target vessels			
Non-ITA	5.80	2.64–12.71	<0.001
Composite grafting	2.73	1.17–6.40	0.021
For severely stenosed target vessels			
Non-ITA	4.26	1.83–9.90	<0.001
Composite grafting	0.72	0.27–1.91	0.509
Peripheral vascular disease	4.55	1.69–12.23	0.003

CI = confidence interval; ITA = internal thoracic artery.

sum of 2 individual grafts [9, 10]. Furthermore, the flow through a composite graft is strongly influenced by native coronary flow. Markwirth and colleagues [11] reported that in composite grafts anastomosed to a patent but stenosed target vessel, the graft flow is lower by 40% than that in grafts anastomosed to occluded target vessels. Nakajima and coworkers [7] reported the incidence of flow competition in composite grafts was as high as 14.6%. These findings suggest that composite grafting may be susceptible to the detrimental effect of flow competition with native coronary artery, resulting in a low-flow condition. This supposition is in agreement with the finding in the present study that mild stenosis of the target coronary artery is related to the incidence of graft occlusion or string sign in composite grafts.

Study Limitations

This study has several limitations. First, all data were retrospectively collected, which may have led to information bias. Second, a follow-up angiogram was performed in only 47.8% of the patients who underwent off-pump CABG during this study period. The angiogram was performed according to a protocol and was not symptom-directed. Third, composite grafting included both I and Y configurations. According to our data, there were no differences in patency rate between these configurations. Fourth, in some graft designs, the number of anastomoses was too small to perform statistical analysis. The number of gastroepiploic arteries was too small to draw any conclusion. The number of individual RA grafts was relatively small, which may have involved a wide variation of the data. Fifth, the graft occlusion and string sign may include intraoperative graft failure, because we did not perform early postoperative angiography in all patients.

In conclusion, the angiographic outcomes of composite grafts were closely related to the severity of stenosis of the target coronary artery. In target vessels with mild stenosis, angiographic outcomes of composite grafts were inferior to those of individual grafts.

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INVITED COMMENTARY

This report by Manabe and colleagues [1] provides a 1-year angiographic follow-up of coronary revascularization using composite grafting, which was compared with revascularization using individual grafting, and composite grafting in target vessels with mild stenosis is not recommended.

Greater freedom from reinterventions and enhanced long-term survival rates have been demonstrated when bilateral internal thoracic arteries (ITAs) are used rather than a single ITA graft in surgical revascularization for multi-vessel coronary disease. The superiority of one method in comparison to another has not been established for bilateral ITA grafting in an individual or composite configuration. A recent study by Kim and colleagues [2] demonstrated that perfusion improvements were similar for both bilateral individual ITA and composite grafts in terms of reversibility scores at 5 years postoperatively.

Revascularization of stenotic coronary lesions that induce myocardial ischemia can improve a patient's functional status and outcome. However, the benefit of revascularization is less clear for mildly stenotic coronary lesions that do not induce myocardial ischemia. Coronary angiography remains the most accurate morphologic assessment of lumen of the coronary arteries. However, angiographically, the degree of stenosis is a poor tool for gauging the functional significance of a specific coronary stenosis. Fractional flow reserve (ie, the ratio of maximal blood flow in a stenotic artery to normal maximal flow) is an index of the physiologic significance of a coronary stenosis, and this can easily be measured during coronary angiography. The combination of anatomic assessment and precise functional information is indispensable in tailoring the revascularization in angiographically dubious stenoses [3].

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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

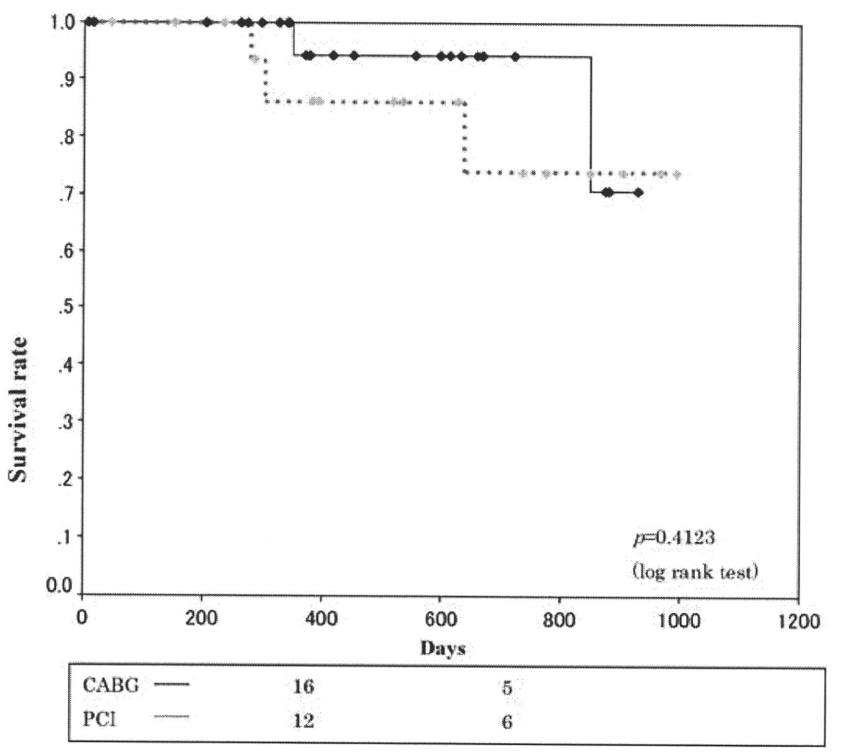

Figure 1. *Cumulative proportion of chronic hemodialysis patients free of death after coronary artery bypass grafting (CABG) or percutaneous coronary artery intervention (PCI). The curves were not significantly different between the two groups. p = 0.41.*

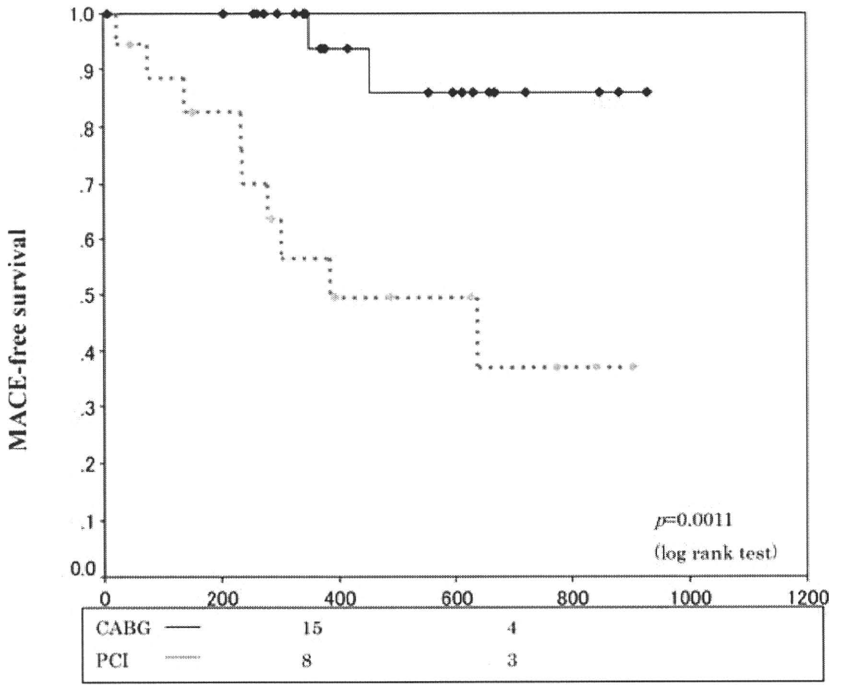

Figure 2. *Cumulative proportion of chronic hemodialysis patients free of major adverse cardiac events (MACE) after coronary artery bypass grafting (CABG) or percutaneous coronary artery intervention (PCI). The curves were significantly different between the two groups. p = 0.0011.*

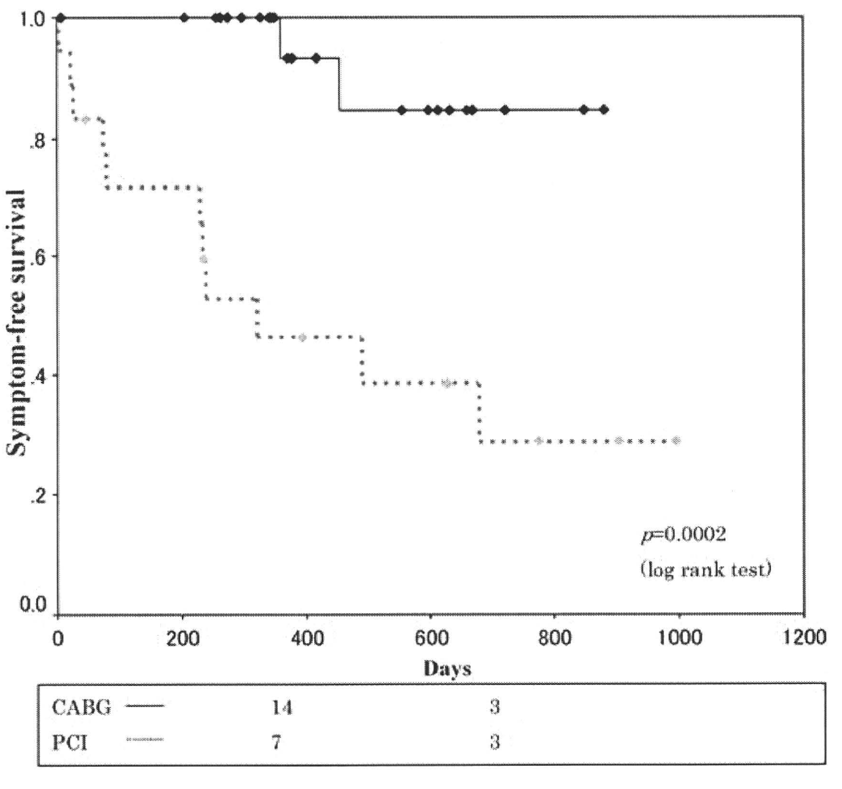

Figure 3. *Cumulative proportion of symptom-free chronic hemodialysis patients after coronary artery bypass grafting (CABG) or percutaneous coronary artery intervention (PCI). The curves were significantly different between the two groups. p = 0.0002.*

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.

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).

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 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

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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

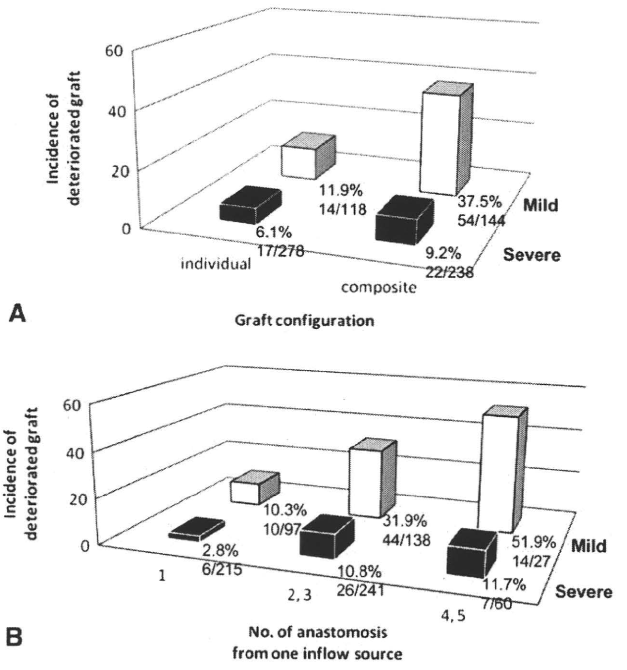

FIGURE 1. Effects of graft configuration (A) and number of distal anastomoses from single inflow source (B) on incidence of arterial graft deterioration according to severity of target coronary artery stenosis.

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 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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000 **Arterial graft deterioration one year after coronary artery bypass grafting**

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We investigated arterial graft deterioration in 243 patients at 1 year after off-pump coronary artery bypass grafting. Multivariate analysis revealed that non–internal thoracic artery graft, mild target stenosis, and multiple grafting were independent predictors of graft deterioration. Arterial graft deterioration was closely related to particular graft materials and designs.