



ADULT CARDIAC SURGERY:

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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 partic-

ular 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.

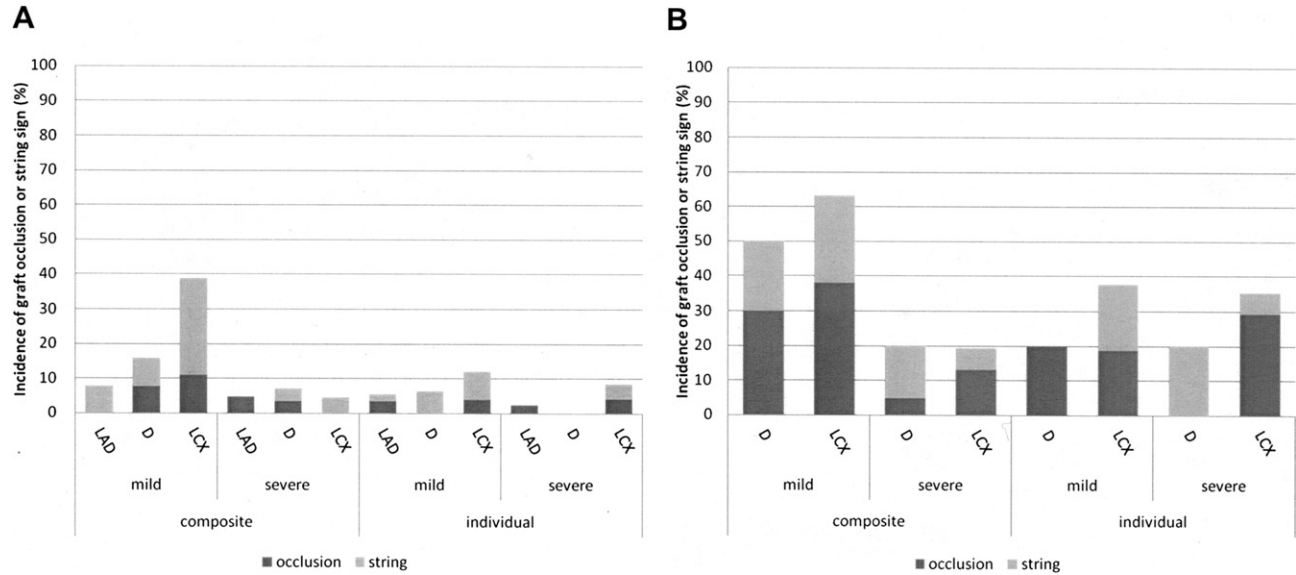


Fig 1. The incidence (%) of graft occlusion (dark gray shaded bar) or string sign (light gray shaded bar) according to graft material or location of target coronary artery. (A) internal thoracic artery (ITA). (B) Radial artery (RA). (D = diagonal artery; LAD = left anterior descending artery; LCX = left 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	<i>p</i> 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, $\leq 75\%$	40.5% (62/153)	13.6% (17/125)	<0.001
Severe, $> 75\%$	12.8% (33/257)	7.8% (23/295)	0.065
$\leq 50\%$	66.7% (14/21)	57.1% (4/7)	0.674
$> 50\%, \leq 75\%$	36.4% (48/132)	11.0% (13/118)	<0.001
$> 75\%, \leq 90\%$	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	<i>p</i> 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	<i>p</i> 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].