

Abstract

Background: In arterial conduits, graft flow is one of the major determinants of durable patency. We sought to delineate the effect of strategy for graft arrangement to three-vessel disease by evaluation of the dominant flow direction in the bypass conduit.

Methods: Coronary angiograms of 1967 bypass grafts in 481 patients who underwent totally arterial off-pump complete revascularization (CR) for three-vessel territories since December 2000 were studied. The graft flow was graded as A(antegrade), B(competitive), C(reverse), and O(occlusion), and recorded for each target branch. Group S consisted of 197 patients who had a single in-situ internal thoracic artery(ITA) as a composite graft. Group B consisted of 284 patients with the bilateral in-situ ITAs. Group B-1 consisted of 82 patients until March 2003, and Group B-2 consisted of 202 patients since March 2003. Current graft arrangement, which has been applying in Group B-2, consists of the in-situ ITA to the anterior descending artery and the composite I-graft of the right ITA and radial artery to the left circumflex and right coronary artery territories, and its orientation is selected to achieve a sufficient antegrade flow.

Results: The number of distal anastomoses was 3.54 ± 0.63 in Group S, and 4.47 ± 0.86 in Group B, respectively ($p<0.0001$). The overall graft patency rate was 98.4% (1935/1967). Grade A in Group B was (1175/1269; 92.6%), and was significantly higher ($p=0.02$) than that in Groups S (624/698; 89.4%). The rate of the patients, who had at least one grade A bypass graft to each of the three major vascular regions; i.e. physiological CR, in Group B was 83.5% (237/284), and was significantly higher than that of Group S (145/197, 73.6%). The grade A bypasses in Group B-2 was 862/921 (93.6%), and was significantly higher ($p=0.03$) than that in Group B-1 (313/348; 89.9%). The multivariate Cox-regression analysis remonstrated that the early period ($p=0.03$) and physiological incomplete revascularization (0.03) were the significant predictors of cardiac events.

Conclusion: The use of bilateral ITAs and radial artery in the appropriate configurations, which maximize the antegrade bypass flow, improved the clinical outcomes. "Flow-conscious" graft arrangement may enhance the advantage of total arterial CR.

Introduction

Completeness of revascularization is considered as the most important determinant of lower incidence of adverse cardiac events in the follow-up period. Fewer bypass grafts and more incomplete revascularization may explain the increased recurrence of angina and repeated coronary intervention associated with off-pump surgery. Currently, complete revascularization may be essential for justifying coronary surgery without cardiopulmonary bypass (1,2,3).

The arterial grafts are commonly used because of its beneficial characteristics in terms of expectancy of graft patency and improved late outcome (4,5,6). Regarding the arterial grafts, the circumstances of the blood flow in the graft lumen may be an important determinant of the patency. It has been reported that occlusion or string sign in the arterial grafts closely correlates with insufficiency of the bypass flow, which can typically occur when the pressure capacity of the bypass graft is not sufficiently higher than the intraluminal pressure in the native coronary artery with moderate stenosis. In the intermediate-term period, the patency rate of bypass grafts with reverse or competitive flow is significantly lower than that of bypass grafts with sufficient antegrade flow (7). We previously reported that reverse flow in the sequential or composite graft was commonly associated with the presence of moderately stenotic right coronary artery (RCA) and more than four target coronary branches for an in-situ internal thoracic artery (ITA) (8). In addition, the management of a coronary branch with critical stenosis and the strategy for the graft arrangement played definitive roles in the blood flow distribution (9).

The objectives of this study were to evaluate the effects of bilateral ITAs versus a single ITA and flow-conscious graft arrangement, and to delineate the advantage of completeness of total arterial coronary revascularization with sufficient antegrade flow toward three vessel territories in the early and intermediate-term outcomes.

Materials and methods

The definitions of terms used in the present study are as follows. The in-situ ITA graft is ITA which was divided only at its distal portion. A composite graft is a bypass

conduit consisting of one in-situ graft and a free graft anastomosed to it (in an end-to-end, end-to-side, or side-to-side fashion). An individual bypass is defined as a bypass conduit having one distal anastomosis and one in-situ graft. This includes the straight composite grafts; i.e., I-graft, to one target coronary branch. A bypass conduit having two or more distal anastomoses, such as a composite Y-(or K-) graft, is defined as non-individual.

The pre- and postoperative coronary angiograms of 1967 bypass grafts in 481 consecutive patients, who underwent off-pump complete revascularization for three-vessel disease using only ITA with or without radial artery between December 2000 and May 2006, were studied. The patients who had a bypass of the in-situ gastroepiploic artery or the saphenous vein, those with individual grafts only, and those who did not undergo postoperative coronary angiography were excluded. There were 397 men and 84 women with a mean age of 66.1 ± 9.1 years.

Coronary angiography was performed about 2 weeks after surgery. The native coronary artery stenosis and the graft patency were independently evaluated by cardiologists. The maximal severity of stenosis was recorded for all target branches. The detailed definitions were mentioned previously. In brief, a patent graft meant that the graft had a complete continuity of the graft lumen throughout its entire length from the subclavian artery to the target coronary branch, irrespective of the flow direction. Whenever the continuity of the graft lumen from an in-situ ITA graft to the anastomosis with the target coronary branch was interrupted at any level, it was defined as Grade O (occlusion). Grade A was defined as a situation in which antegrade graft flow was found in most of the multi-plane ITA angiographs. Grade B (competitive) was defined as a situation in which the target vessel was slightly opacified from the ITA graft injection, and the bypass graft did fill by retrograde flow from the native coronary injection. Grade C (reverse flow) was defined as a situation in which the distal anastomotic site was not opacified from the ITA graft injection at all, but it did fill clearly by retrograde flow from the native coronary injection. Flow grade was recorded for each target coronary branch.

We considered that the graft arrangement was successful, when the bypass flow was graded as A, when the bypass conduit provided grade A bypass flow to all target coronary

branches, when at least one bypass graft to each of the three major vascular regions was patent; i.e., angiographically confirmed complete revascularization (CR), or when at least one bypass graft with the antegrade bypass flow was achieved in each of the three major coronary regions; i.e., physiological CR.

Graft selection and arrangement

Total arterial CR was performed in all of our 481 patients. The arrangement of the bypass conduits was primarily determined by the operative risk and positional relationship of the target sites. As shown in Table 1, Group S consisted of 197 patients with single in-situ ITA graft as the Y- or K-graft. In Group B, 284 patients had bilateral in-situ ITAs in the combination of individual, Y-, K- or I-graft. Group B was divided into two groups by the date of surgery, because our current standard strategy was introduced in March 2003, aiming at preventing high-risk situations of reverse and competitive flow (9). Group B-1 consisted of 82 patients until March 2003, and Group B-2 consisted of 202 patients between March 2003 and May 2006 (Table 2). In the current standard technique since March 2003, one in-situ ITA, usually the left, supplies the left anterior descending artery (LAD) territory and an I-graft of the contralateral ITA, usually the right, and the radial artery supply the circumflex (LCX) and the right coronary artery (RCA) in a clockwise orientation, via a side-to-side anastomosis with the LCX branch and an end-to-side anastomosis with the RCA branch (Figure 1). The counterclockwise orientation was occasionally chosen to avoid grafting to the RCA branch with 75% stenosis at the end of the conduit, because reverse flow was commonly found at the distal end of the conduit (8,9). Before introduction of this strategy, the I-graft was used only in a counterclockwise orientation for the safety of redo operation in the future.

The details of our technique in off-pump coronary artery bypass grafting (CABG) were described previously. In the present series, all ITA grafts were larger than 1.5 mm in diameter at the distal portion. The radial artery was harvested from the non-dominant forearm irrespective of the patient's age, and was divided into two pieces when necessary. In the side-to-side anastomosis, we made a longitudinal arteriotomy both on the native

coronary artery and the arterial graft long enough for anastomosis without turbulence, and the angle of the graft placement was adjusted between 0 to 90 degrees to save the length and avoid kinking.

The mean follow-up period was 28 ± 18 months.

Statistical analysis

The continuous variables are expressed as the mean values \pm standard deviation (SD). These variables were compared by Mann-Whitney U-test between the two groups. The data of two independent groups were compared by Fisher's exact probability test. Cox regression analysis was used to examine the significance of the clinical and angiographic variables in predicting the cardiac event-free time. The differences in the outcomes were considered statistically significant when the p value was less than 0.05.

Results

The overall graft patency rate was 98.4% (1935/1967). The number of distal anastomoses in Group B was 4.47 ± 0.86 , and was significantly greater than that in Group S (3.54 ± 0.63) ($p < 0.0001$) (Table 3). In Group S, 624 (89.7%) bypasses were grade A, whereas 24 (3.4%), 40 (5.7%), and 10 (1.4%) were grade B, C, and O, respectively. The graft patency rate in Group B was 1247/1269 (98.3%), and was comparable with that in Group S (688/698; 98.6%). However, the rate of grade A bypass flow in Group B was 1175/1269 (92.6%), and was significantly higher than that in Groups S (624/698; 89.7%) ($p = 0.02$). In Group B, the number of bypass conduits which had the grade A bypass flow to all target coronary branches that was considered as a successful graft configuration, was 480/568 (84.5%), being significantly higher than that in Group S (131/197; 66.5%) ($p < 0.0001$). Angiographically confirmed CR was achieved in 189 (95.9%) patients in Group S and 271 (95.4%) patients in Group B, and the difference was not significant ($p = 0.79$). The success rate of physiological CR in Group B was (237/284; 83.5%), and was significantly higher than that in Group S (145/197; 73.6%) ($p = 0.009$).

As presented in Table 4, the rate of grade A in Group B-2 was 93.6% (862/921), and was significantly higher than that in Group B-1 (313/348; 89.9%) ($p=0.03$). In Group B-2, the number of bypass conduits with the grade A bypass flow to all target coronary branches was 350/404 (86.6%), and was significantly higher than that in Group B-1 (130/164; 79.3%) ($p=0.03$). The difference in the success rate of angiographically confirmed CR and physiological CR between Group B-1 and Group B-2 was not statistically significant.

During the follow-up period, 6 patients in Group S and 1 in Group B-1 died (sudden cardiac death in 3, cerebrovascular accident in 2, renal failure in 1, and sepsis in 1). Twelve patients in Group S, 16 in Group B-1, and 5 in Group B-2 underwent percutaneous coronary intervention for recurrent angina or myocardial infarction. The multivariate Cox regression analyses demonstrated that physiological incomplete revascularization ($p=0.03$; HR=2.12) and the early period; December 2000 ~ March 2003 ($p=0.03$ HR=2.61) were the significant predictors of the occurrence of cardiac events in the intermediate term (Table 5).

Discussion

The radial artery is useful as a free graft for CABG. Since its patency rate mostly depends on the severity of the native coronary stenosis, rather than on the proximal anastomotic site (10,11), the radial artery has been increasingly used as a part of the composite graft with the in-situ ITA. A composite graft allowed total arterial revascularization with excellent graft patency rate and lower incidence of cardiac and cerebrovascular events (12,13). Although various arrangements of the in-situ and free arterial grafts have already been reported (6,14,15), no optimal strategy for graft arrangement has been established yet. The decision of the configuration actually depends on the surgeon's preference or the custom of each group. To optimize the graft arrangement, the patency rate is not useful, because an excellent anatomical graft patency rate can be highly expected whenever arterial graft materials are exclusively used. In our present series, the graft patency rate and the success rate of angiographically confirmed CR were similar in these groups, and not useful for comparison.

Previously, the grading system of the luminal size at the narrowest portion, and intimal irregularity was reported (16,17). The grading system predicted the late occlusion, and was considered useful for assessment of graft degeneration, which was emerging as the major determinant of the long-term patency of the venous grafts. However, the luminal size of the anastomotic site is not precisely measurable in the sequential fashion, especially when the angle between the graft and the coronary branch is near 90 degrees, or when the contrast medium does not fill completely due to mixture with the blood flow from the native coronary artery. Moreover, the regression of stenosis and the increase or growth of the diameter were relatively common findings in the arterial materials (18,19). Therefore, the luminal size or the anatomical graft patency may not be relevant for comparison of the arterial graft arrangements.

Reversal flow, which means blood flow in the bypass graft dominantly from one coronary branch to the other, is a relatively common finding in the composite and sequential grafts. The bypass grafts with reverse flow do not contribute to the coronary perfusion in the grafted territory, even when the bypass graft is anatomically patent. A previous study

demonstrated that the patency rate of the grafts with sufficient antegrade bypass flow was significantly higher than that of the grafts with reverse and competitive flow (7). These physiologic changes in the luminal diameter were manifested within about 2 years (20,21,22,23). The arterial grafts without a sufficient antegrade flow may not be advantageous regarding the long-term patency rate, as compared with the venous grafts.

We previously reported that reverse flow in the composite graft had significant correlations with the moderately stenotic RCA and the number of distal anastomotic sites for an in-situ ITA (8). The interactions of the coronary branches, which were connected to each other by a sequential or composite graft, and the management of the coronary branch not only with moderate stenosis but also with critical stenosis played crucial roles in the occurrence of competitive and reverse flow. On the contrary, the kind of graft materials and the size of the target branch did not correlate with the dominant flow direction (9).

We consider that the appropriate pressure slope in each segment of the bypass conduit, highest at the proximal and lowest at the end of the conduit, was the most important for achievement of antegrade flow. The composite I-graft is useful, because the target coronary branch at the end of the conduit can be chosen by simply determining its orientation. On the other hand, the Y-graft is advantageous in terms of increased flow capacity (24) and availability to the distant target branches. In the Y-graft, an adequate pressure slope to both ends must be made, and therefore, the indication for Y- or K-graft should be more carefully decided. The Y- or K-graft may be preferred when all target branches have severe stenosis, the target diagonal branch is located at the anteroapical portion, or remarkable cardiomegaly exists.

In the present study, the graft arrangements were compared by the dominant flow direction in the arterial composite and sequential grafts, the success rate of conduit design and the achievement of antegrade bypass flow to all three territories; i.e., physiological CP. The use of bilateral in-situ ITAs provided a higher rate of antegrade flow in the bypass graft and enabled achievement of successful conduit design and physiological CP as compared with the use of single in-situ ITA, irrespective of the similar anatomical graft patency rate. Moreover, "flow-conscious" graft arrangement improved the antegrade bypass flow and

decreased the conduits causing reverse and competitive flow. In the late results, physiological CP and the current arrangement inversely correlated with the occurrence of cardiac events. Interestingly, the use of bilateral in-situ ITAs did not independently correlate with the cardiac event. These results suggested that the advantage of the use of bilateral in-situ ITAs was settled exclusively by prevention of competitive and reverse flow.

We consider that selection of patient suitable for this procedure would be a next concern. It has been undoubtedly accepted that the patients who have severe atherosclerosis of the ascending aorta are the most suitable candidates for this procedure, because of the reduced operative risk (12,13). In our experience, half of the patients with three-vessel disease would be good candidates for our technique. In these patients, the risky situations could be avoided by simple maneuvers during operation, and consequently, grade A rate of more than 98% can be expected. On the other hand, when graft non-function or occlusion during the relatively early postoperative period is highly predicted, alternative strategy, such as the aortocoronary bypass, which provides the highest bypass pressure, less invasive surgery or hybrid therapy using drug-eluting stent implantation and conservation of the arterial graft for the redo operation in the future, may be reasonable.

The present study had some limitations. First, this study was not randomized. Second, the peripheral vascular resistance in the myocardial tissue, which has an important role in the coronary perfusion, was not taken into account. Grade B probably includes both flow insufficiencies due to the strength of the native coronary flow and poor vascularity with high resistance. Although no bypass graft may be required for the latter, we could not assess the bypass flow separately. The third limitation may be regarding the learning curve of the off-pump CABG. It may influence the periodical increase in the number of distal anastomotic sites. However, on the contrary, the incidence of competitive and reverse flow significantly decreased and the graft patency rates were comparable in these groups. Therefore, we consider that improvement of the flow characteristics in the bypass conduit is due to evolvement in the strategy for graft arrangement. At last, the capacity of the ITA graft was not considered. The pressure capacity of the graft and

potentiality of growth or thinning and adaptability to the graft flow may also play important roles in the occurrence of insufficient flow and the resultant occlusion.

In conclusion, the use of bilateral ITAs increased the bypass grafts with antegrade flow and provided physiological CR, and the achievement of the antegrade bypass flow improved the clinical outcome after CABG. Consciousness of the anticipated bypass flow may be necessary to enhance the advantage of complete revascularization using exclusively arterial materials.

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Table 1

Baseline characteristics			
	Group S	Group B	p value
In-situ ITA	Single	Bilateral	
No. of patients	197	284	
Age (yrs)	70.4±7.3	63.5±8.9	<0.0001
Male/Female	152 / 45	245 / 39	0.01
Hypertension	116 (59%)	146 (51%)	0.11
Hyperlipidemia	99 (50%)	149 (52%)	0.63
Diabetes	84 (43%)	113 (40%)	0.53
End-diastolic volume index of LV (ml/m ²)	83.2±23.8	86.0±31.9	0.82
Ejection fraction of LV (%)	48.1±10.7	46.6±12.3	0.36
EF<40	35 (17.8%)	54 (19.0%)	0.73
Total distal anastomoses	698	1269	
Bypass conduits used	197	568	
in situ ITA	0	221	
composite Y-graft	172	102	
composite K-graft	25	15	
composite I-graft	0	230	

ITA; internal thoracic artery LV; left ventricle EF; ejection fraction

Table 2

Baseline characteristics			
	Group B-1 (~ Mar. 2003)	Group B-2 (Mar. 2003~)	p value
No. of patients	82	202	
Age (yrs)	60.6±8.2	64.6±8.9	<0.0001
Male/Female	70 / 12	175 / 27	0.78
End-diastolic volume index of LV (ml/m ²)	94.3±37.5	81.6±27.7	0.004
Ejection fraction of LV (%)	46.3±13.9	46.8±11.4	0.89
EF<40	22	32	0.03
Total distal anastomoses	349	920	
Bypass conduits used	164 (100%)	404 (100%)	
in situ ITA	38 (23.2%)	183 (45.3%)	
individual	28 (17.1%)	141 (34.9%)	
sequential	10 (6.1%)	42 (10.4%)	
composite Y-graft	50 (30.5%)	52 (12.9%)	
composite K-graft	14 (8.5%)	1 (0.2%)	
composite I-graft	62 (37.8%)	168 (41.6%)	
individual	18 (11.0%)	4 (1.0%)	
sequential	44 (26.8%)	164 (40.6%)	
ITA-RA-LCX-RCA (clockwise)	0	125 (30.9%)	
ITA-RA-RCA-LCX (counterclockwise)	44 (26.8%)	39 (9.7%)	

ITA; internal thoracic artery LV; left ventricle EF; ejection fraction

Table 3

Angiographic results				
		Group S (Single ITA)	Group B (Bilateral ITAs)	p value
Distal anastomoses		3.54±0.63	4.47±0.86	<0.0001
Total distal anastomoses		698	1269	
Flow grade	A	624 (89.7%)	1175 (92.6%)	
	B	24 (3.4%)	24 (1.9%)	
	C	40 (5.7%)	48 (3.8%)	
	O	10 (1.4%)	22 (1.7%)	
Antegrade flow rate	A	624 (89.4%)	1175 (92.5%)	0.02
Patency rate	A+B+C	688 (98.6%)	1247 (98.3%)	0.61
Bypass conduits		197	568	
Flow grade in the bypass conduits				
	grade A only	131 (66.5%)	480 (84.5%)	<0.0001
	non-A (+)	66 (33.5%)	88 (15.5%)	
No. of patients		197	284	
Angiographically confirmed CR		189 (95.9%)	271 (95.4%)	0.79
Physiological CR		145 (73.6%)	237 (83.5%)	0.009

CR; complete revascularization

Table 4

Angiographic results				
		Group B-1 (~ Mar. 2003)	Group B-2 (Mar. 2003~)	p value
Distal anastomoses		4.26±0.83	4.55±0.86	0.009
Total distal anastomoses		348	921	
Flow grade	A	313 (89.9%)	862 (93.6%)	
	B	8 (2.3%)	16 (1.7%)	
	C	19 (5.5%)	29 (3.1%)	
	O	8 (2.3%)	14 (1.5%)	
Antegrade flow rate	A	313 (89.9%)	862 (93.6%)	0.03
Patency rate	A+B+C	340 (97.7%)	907 (98.5%)	0.34
Bypass conduits		164	404	
Flow grade in the bypass conduits				
	grade A only	130 (79.3%)	350 (86.6%)	0.03
	non-A (+)	34 (20.7%)	54 (13.4%)	
No. of patients		82	202	
Angiographically confirmed CR		77 (93.9%)	194 (96.0%)	0.43
Physiological CR		68 (82.9%)	169 (83.7%)	0.88

CR; complete revascularization

Table 5
 Predictors of cardiac event in 481 patients with three-vessel disease

Variables	Hazard ratio	95% CI	p value
<i>Univariate analysis</i>			
Age	0.97	(0.94 - 1.001)	0.06
Female	0.81	(0.313 - 2.08)	0.66
Diabetes	1.97	(0.93 - 4.20)	0.08
Hypertension	1.44	(0.74 - 2.77)	0.28
Hyperlipidemia	0.70	(0.36 - 1.36)	0.29
Ejection Fraction < 40%	1.80	(0.92 - 3.52)	0.09
Bilateral in situ ITA	1.32	(0.67 - 2.58)	0.42
Early Period; Dec.2000~March 2003	3.29	(1.39 - 7.69)	0.007
Physiological incomplete revascularization	2.26	(1.16 - 4.42)	0.02
<i>Multivariate analysis</i>			
Age	0.97	(0.94 - 1.004)	0.09
Diabetes	1.88	(0.88 - 4.22)	0.10
Ejection Fraction < 40%	1.81	(0.91 - 3.57)	0.09
Early Period; Dec.2000~March 2003	2.61	(1.10 - 6.21)	0.03
Physiological incomplete revascularization	2.12	(1.07 - 4.22)	0.03

ITA; internal thoracic artery

Figure Legends

Figure 1

A composite I-graft in the clockwise (*right*) and counterclockwise orientation (*left*).

The overall graft arrangement for a given patient should be designed to create a favorable pressure slope from the proximal to the distal end. The distal end of the bypass conduit, which was connected with a moderately stenotic target coronary branch, was commonly associated with competitive or reverse flow, and the presence of the anastomosis with a branch having critical stenosis at the middle of the conduit would provoke these flows at the end. Selecting an appropriate orientation of the composite I-graft can be simple and effective for accomplishment of such a slope.

Figure 2

Comparison of the proportions of bypass conduits used in the early and the late periods, and the rate of the conduits having only grade A, in various configurations.

(*Left*) In the early period, we decided the configuration of the grafts only for the positional relationship of the target sites. (*Right*) Since March 2003, we have designed the configuration to achieve smooth pressure slope from the proximal to the distal end or ends of the conduit. Since it was difficult to achieve a favorable pressure slope to all distal ends in the Y- and K-graft as compared with the I-graft, we carefully decided the indication of these grafts. As shown in the figure, the proportion of the Y-graft and K-graft decreased. The I-graft was placed in either clockwise or counterclockwise orientation. Consequently, the bypass conduits with competitive or reverse flow significantly decreased, in spite of the increased distal anastomotic sites.

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