Arterial Versus Venous Bypass Grafts in Patients With In-Stent Restenosis

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Background—In patients who develop in-stent restenosis, successful revascularization can be difficult to achieve using percutaneous methods. This study was designed to verify the surgical results in this setting and to evaluate the potential beneficial role of arterial bypass conduits.

Methods and Results—Sixty consecutive coronary artery bypass patients with previous in-stent restenosis and 60 control cases were randomly assigned to receive an arterial conduit (either right internal thoracic or radial artery; study group) or a great saphenous vein graft (control group) on the first obtuse marginal artery to complete the surgical revascularization procedure. At a mean follow-up of 52±11 months, patients were reassessed clinically and by angiography. Freedom from clinical and instrumental evidence of ischemia recurrence was found in 19 of 60 subjects in the study group versus 45 of 60 in the control series ($P=0.01$). The results of the arterial grafts were excellent in both the study and control groups (right internal thoracic artery patency rate, 19 of 20 for both, and radial artery patency rate, 20 of 20 versus 19 of 20; $P=0.99$). Saphenous vein grafts showed lower patency rate than arterial grafts in both series and had extremely high failure rate in the study group (patency rate, 10 of 20 in the study group versus 18 of 20 in the control group; $P=0.001$). Use of venous graft was an independent predictor of failure in the study group, whereas hypercholesterolemia was associated with graft failure in both series.

Conclusions—Venous grafts have an high incidence of failure among cases who previously developed in-stent restenosis, whereas the use of arterial conduits can improve the angiographic and clinical results. Arterial grafts should probably be the first surgical choice in this patient population. **(*Circulation.* 2005;112[suppl I]:I-265–I-269.)**

Key Words: coronary disease ■ restenosis ■ surgery

Subjects who develop in-stent restenosis represent a challenging patient population for both interventional cardiologists and cardiac surgeons. In fact, once the technical and anatomic factors have been ruled out, in-stent restenosis identifies a subgroup of cases with aggressive coronary atherosclerosis in whom a second failure of percutaneous interventions is more likely.[1–4]

To assess whether, in these cases, accelerated graft disease and failure occur also after surgical revascularization and to verify whether the use of arterial bypass conduits (known to be less susceptible to graft atherosclerosis) can improve the clinical and angiographic results, we designed the present study protocol.

Methods

This investigation received local Institutional Review Board approval, and each patient gave informed consent to participate in the protocol. All of the patient data were prospectively collected and stored in a computerized database.

Aim of the Study

This protocol was aimed at evaluating the angiographic results of arterial versus venous bypass conduits in a patient population at high risk for graft failure: patients in whom a technically correct percutaneous stent implantation resulted in restenosis or occlusion. In order to maximize homogeneity and reduce the minimum confounding factors, we decided to isolate a single target vessel for the study. Because of obvious ethical concerns related to the left-anterior descending artery (LAD), we chose the type I first obtuse marginal branch of the circumflex artery, which, in the majority of cases, is the second coronary vessel of importance.[5] Regarding the arterial conduits to be adopted, we used those that are usually grafted on the marginal branch and with which our institution is most familiar (the radial and right-internal thoracic artery).

Patient Population

We selected 120 consecutive patients referred for coronary artery bypass grafting (CABG) at our institution from January 1994 to October 1997 who fulfilled the following inclusion criteria at the time of surgery: (1) primary elective isolated CABG; (2) previous percutaneous coronary angioplasty with successful stent implantation in any coronary vessel ≥1.2 mm in diameter at least 1 month before surgery with preoperative angiographic demonstration of failed (n=60; study group) or patent (n=60; control group) intracoronary stent; (3) angiographic evidence of triple-vessel coronary artery disease with a diseased (ie, proximal stenosis ≥70%) graftable (ie, ≥1 mm in diameter) obtuse marginal artery (OM) type I according to the classification proposed by Mc Alpine et al[5]; (4)

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TABLE 1. Main Features of the 2 Patients Groups

Variables	Study Group	Control Group
Age	65±9	63±8
Males	35	31
Smokers	39	37
Hypercholesterolemia	38	35
Mean preoperative cholesterol level (mg/dL)	268±10	271±8
Hypertension	18	21
Diabetes	40	22*
Mean target OM diameter (mm)	1.2±0.2	1.15±0.1
Mean target OM stenosis (%)	78.6±5.9	80.1±3.4
Time from stent implantation (months)	38.9±8.8	40.3±2.2
No. of graft/patient	2.9±0.2	2.8±0.3
Mean cholesterol level at follow-up (mg/dL)	199±16	203±11

*P=0.001.

good preoperative left ventricular function (ejection fraction ≥0.50); and (5) no preoperative evidence or history of lateral or posterolateral myocardial infarction.

Subjects who underwent stent implantation <1 month before surgery were excluded, in the presumption that stent failure in such limited time frame could have been technically related. Stent failure was defined as intrastent restenosis ≥50% at the site of previous stent implantation.[4,6]

These 120 cases represent 5.4% of the totality of CABG cases operated at our institution in the study period. The main features of the patients are summarized in Table 1.

Surgical Technique

Surgical revascularization was performed following a standardized and previously described method and using median sternotomy, cardiopulmonary bypass, and cardioplegic arrest.[7] No major change in intraoperative and postoperative protocols was introduced during the study period.

Patients were randomly assigned according to a computer-generated sequence to receive a right internal thoracic artery (RITA; n=40, 20 for each group), a radial artery (RA; n=40, 20 for each group), or a great saphenous vein (GSV; n=40, 20 for each group) graft on the OM branch (Figure 1).

The left internal thoracic artery (LITA) was always used to graft the LAD, whereas the RA or the GSV were used to graft secondary non-OM target vessels. Complete anatomic revascularization was achieved in all of the cases.

The management of RA grafts followed the methods described in detail elsewhere.[7] All of the patients were treated with antiaggregants and statins since the early postoperative days.

Follow-Up

Each patient was followed up regularly at our institution 6 months after surgery and every year thereafter. At each time interval, clinical examination was performed, and the results of surface electrocardiography, stress Tl^{201} myocardial scintigraphy, 24-hour Holter monitoring, and transthoracic echocardiography were carefully reviewed. Angiographic control was considered in the case of scintigraphic evidence of inducible ischemia. For the aim of the present study, control coronary angiography was proposed to all of the patients at the fifth follow-up visit.

Graft morphology was graded according to the 4-grade scale in use at our institution:[7] perfectly patent graft, patent graft with irregularities, stringed graft, and occluded graft. All of the angiograms were reviewed blindly by 2 expert observers; in case of disagreement, a third external blinded review was requested.

Statistical Analysis

Statistical analysis comparing the 2 groups was performed with unpaired 2-tailed t testing for the means or χ^2 test for categorical variables. Univariate logistic regression analysis was performed in order to identify risk factors for graft malfunction (irregularity, string, or occlusion). Variables found to be significantly associated with graft failure at univariate analysis were, therefore, included in the multiple logistic regression model.

Statistical significance was set at the 0.05 level. Analysis was conducted by the software Statistica for Windows 4.1 (Statsoft Inc).

Results

There was no in-hospital death. Follow-up was 100% complete, and mean follow-up time was 52±11 months, without difference between the study and control group (53±9 versus 55±7 months; P=0.17)

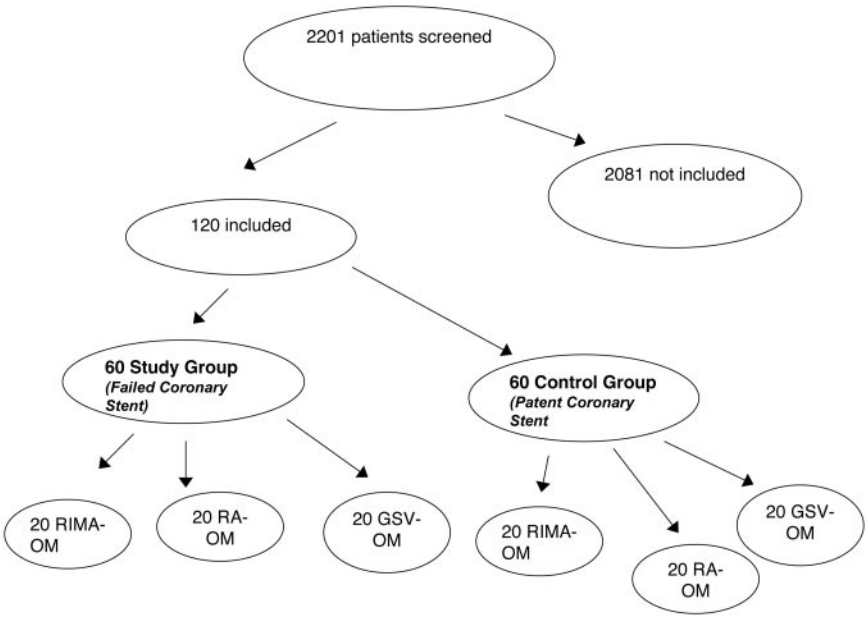

Figure 1. Trial design.

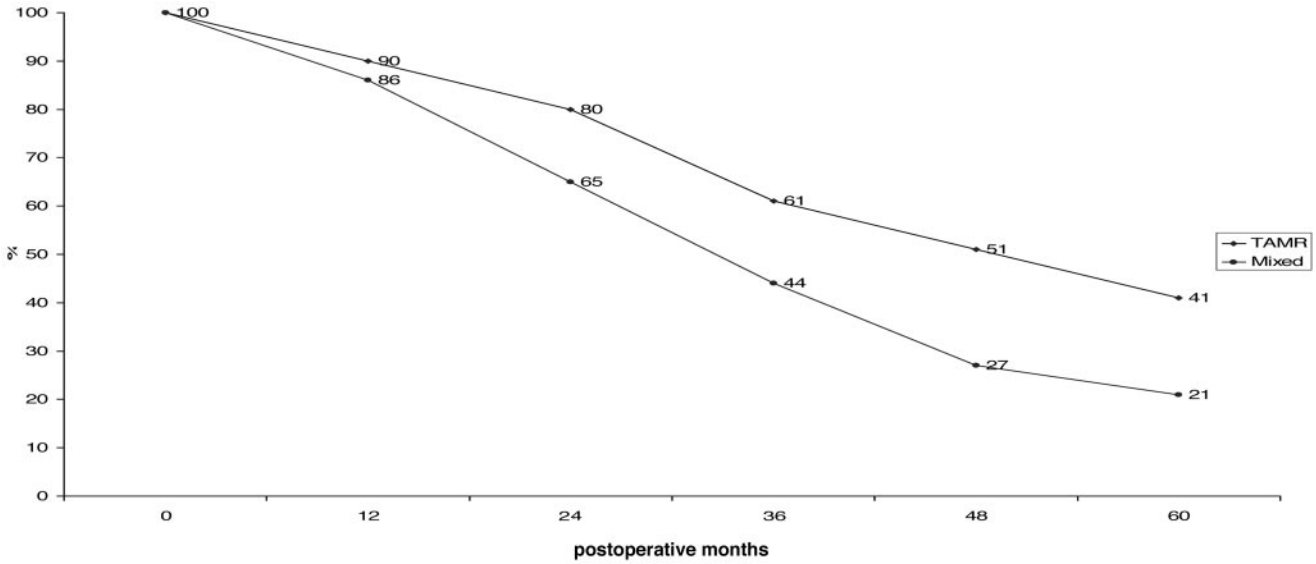

Figure 2. Event-free survival in the study group according to the revascularization strategy used. TAMR indicates total arterial myocardial revascularization.

Survival and Ischemia-Free Survival

No death occurred during the follow-up period. Freedom from clinical and instrumental evidence of ischemia recurrence was found in 19 of 60 subjects in the study group versus 45 of 60 subjects in the control series ($P=0.01$).

When evaluating the outcome of patients of the study group according to the type of revascularization used (totally arterial with both internal thoracic arteries (ITAs) and the RA or mixed arterial and venous), a trend was evident toward a lower incidence of clinical and instrumental evidence of ischemia recurrence for patients treated with only arteries, although the difference between the 2 subgroups did not reach statistical significance (Figure 2).

Angiographic Data

The main angiographic results are summarized in Tables 2 and 3. The patency rate of the ITA-LAD was 115 of 120 (57 of 60 versus 58 of 60 in the study group and control group, respectively; $P=0.94$); whereas the patency rate of grafts to secondary non-OM target vessels was 63 of 71 for the RA grafts (32 of 35 in the study group versus 31 of 36 among control group; $P=0.95$) and 100 of 165 for the GSV (38 of 84 in the study group versus 62 of 81 in the control group; $P=0.05$).

Regarding the graft constructed on the first OM, which was the subject of the study, the results of the arterial grafts (RITA and RA) were excellent in both groups (RITA patency rate, 19 of 20 in both groups and RA patency rate, 20 of 20 versus 19 of 20; $P=0.99$).

Saphenous vein grafts showed a lower perfect patency rate than arterial grafts in both groups (Table 3) and had an unacceptably high failure rate in the study group (perfect patency rate, 10 of 20 study versus 15 of 20 controls; $P=0.001$). Results of the univariate logistic and of the multiple logistic regression analysis are reported in Tables 4 and 5 (for grafts directed to all target arteries in study and control groups) and in Tables 6 and 7 (for grafts directed to the OM). The use of a venous graft was identified at multiple logistic analysis to be an independent predictor of failure in the study group, whereas hypercholesterolemia was significant at the 0.046 and 0.024 levels in the study group and at the 0.049 and 0.40 levels in the control group.

Discussion

Patients who develop in-stent restenosis constitute a peculiar technical challenge for both interventional cardiologists and cardiac surgeons. Indeed, once anatomical and technical factors have been ruled out, the occurrence of stent failure can

TABLE 2. Main Angiographic Results of ITA-Left Anterior Descending Grafts and Complementary Grafts to Non-OM Target Vessels in the 2 Patient Groups

	Study Group			Control Group		
Variables	ITA-LAD (n=60)	RA-NOMTA (n=35)	GSV-NOMTA (n=84)	ITA-LAD (n=60)	RA-NOMTA (n=36)	GSV-NOMTA (n=81)
Perfectly patent	56	31	28	58	29	50
Patent with irregularities	1	0	10	0	1	12
Stringed	0	1	0	0	1	0
Occluded	3	3	46	2	5	19

NOMTA indicates non-OM target coronary artery; LAD, left anterior descending.

TABLE 3. Main Angiographic Results Regarding the Graft Object of the Study in the 2 Patient Groups

	Study Group			Control Group		
Variables	RITA (n=20)	RA (n=20)	GSV (n=20)	RITA (n=20)	RA (n=20)	GSV (n=20)
Perfectly patent	18	19	10	19	17	15
Patent with irregularities	0	1	5	0	1	3
Stringed	1	0	0	0	1	0
Occluded	1*	0†	5	1*	1†	2

*P=0.90 compared with the RA and P=0.001 compared with the GSV in the same group.

†P=0.90 compared with the RITA and P=0.001 compared with the GSV in the same group.

identify a subset of patients with particularly aggressive coronary atherosclerosis in whom successful revascularization can be difficult to achieve using either percutaneous or surgical methods. In fact, in the cardiology literature, there is consistent evidence that the percutaneous retreatment of these cases leads to suboptimal clinical results and is associated with an high risk of additional restenosis or occlusion.[1–4] Although this issue has not been specifically investigated in surgical series, it is at least likely that even coronary bypass conduits can be damaged by the aggressive atherosclerotic process and develop accelerated graft disease and failure.

The present protocol was conceived to investigate the results of surgical revascularization in these patients and to verify whether the use of arterial bypass conduits can improve the clinical and angiographic results in this setting. At a mean follow-up of <5 years, we found that venous grafts have an unacceptably high incidence of failure in patients with previous in-stent restenosis. This incidence was significantly higher than that of the control group and was reported both for graft directed to the OM and for conduits anastomosed to other coronary vessels (Tables 2 and 3). In contrast, arterial grafts (LITA, RITA, and RA) showed similarly good results in both the study and control groups and were only minimally affected by graft disease, without differences between the different type of conduits used. This difference in angiographic patency was reflected also by the different clinical outcome of patients of the study and control groups and, to a lesser extent, by the enhanced rate of ischemia-free survival of patients in the study group submitted to totally arterial revascularization (although the limited sample size did not allow the achievement of statistical significance in this last case; Figure 2).

Up to now, the clinical benefits of total arterial grafting have not been definitely proven in the general population of patients referred for surgical myocardial revascularization.[8–11] On the basis of our data, it is tempting to speculate that cases who develop in-stent restenosis can represent a subset of patients at very high risk of failure using the

TABLE 4. Univariate Logistic Regression Analysis for Graft Malfunction (Irregularity, String, or Occlusion) for Grafts Directed to Both NOMTA and OM in the 2 Patient Groups

	Study Group		Control Group	
Variable	OR (95% CI)	P Value	OR (95% CI)	P Value
Age >65 years	0.43 (0.11–1.66)	0.22	0.65 (0.41–1.75)	0.28
Male sex	1.2 (0.40–2.58)	0.35	1.92 (0.62–3.34)	0.40
Cigarette smoking	3.1 (1.57–15.02)	0.09	3.8 (1.80–14.73)	0.11
Preoperative blood cholesterol level >270 mg/dL	9.03 (1.3–62.84)	0.012	5.9 (2.0–51.04)	0.019
Hypertension	2.08 (0.39–2.24)	0.072	1.08 (0.43–2.6)	0.061
Diabetes	4.16 (0.97–26.3)	0.09	3.88 (1.04–15.0)	0.075
Target OM diameter ≤1.2 mm	21.01 (1.78–116.7)	0.02	16.2 (0.98–93.4)	0.05
Target OM stenosis >80 %	4.2 (1.32–13.33)	0.03	3.5 (2.76–11.5)	0.044
Time from stent implantation >40 months	3.7 (2.9–16.7)	0.038	8.7 (1.61–87.21)	0.029
Blood cholesterol level at follow-up >200 mg/dL	32.6 (2.5–197.12)	0.011	28.0 (2.11–38.2)	0.018
Use of venous graft	52.1 (4.8–248.29)	0.004	1.88 (0.56–8.01)	0.046

NOMTA indicates non-OM target coronary artery; OR, odds ratio.

TABLE 5. Multiple Logistic Regression Analysis for Graft Malfunction (Irregularity, String, or Occlusion) for Grafts Directed to both NOMTA and OM in the 2 Patient Groups

	Study Group		Control Group	
Variable	OR (95% CI)	P Value	OR (95% CI)	P Value
Preoperative blood cholesterol level >270 mg/dL	3.71 (0.71–26.11)	0.084	3.4 (1.11–39.7)	0.076
Target OM diameter ≤1.2 mm	14.3 (2.30–46.8)	0.24	9.81 (0.54–63.9)	0.33
Target OM stenosis >80 %	1.1 (0.18–5.93)	0.24	2.3 (1.04–3.78)	0.35
Time from stent implantation >40 months	1.9 (0.52–9.7)	0.083	3.4 (0.92–61.33)	0.071
Blood cholesterol level at follow-up >200 mg/dL	19.9 (1.3–85.4)	0.046	2.0 (0.84–23.9)	0.049
Use of venous graft	35.4 (2.6–104.11)	0.025	0.21 (0.14–1.92)	0.73

NOMTA indicates non-OM target coronary artery; OR, odds ratio.

TABLE 6. Univariate Logistic Regression Analysis for Graft Malfunction (Irregularity, String, or Occlusion) for Grafts Directed to the OM in the 2 Patient Groups

	Study Group		Control Group	
Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age >65 years	0.63 (0.10–2.08)	0.31	0.71 (0.39–1.98)	0.29
Male sex	2.3 (0.62–2.85)	0.39	1.53 (0.68–4.67)	0.52
Cigarette smoking	5.2 (1.74–17.42)	0.07	5.8 (2.93–20.01)	0.09
Preoperative blood cholesterol level >270 mg/dL	27.03 (1.9–169.4)	0.008	19.1 (2.8–77.18)	0.013
Hypertension	9.13 (0.78–21.64)	0.041	3.95 (0.81–8.9)	0.055
Diabetes	2.09 (0.65–19.9)	0.12	3.21 (0.87–13.02)	0.068
Target OM diameter ≤1.2 mm	8.71 (0.98–78.0)	0.061	19.3 (1.8–73.5)	0.055
Target OM stenosis >80 %	4.5 (1.52–14.76)	0.03	5.7 (1.79–21.35)	0.039
Time from stent implantation >40 months	2.9 (1.0–14.8)	0.041	15.2 (3.11–114.89)	0.022
Blood cholesterol level at follow-up >200 mg/dL	18.5 (3.1–103.1)	0.023	26.0 (1.98–36.8)	0.016
Use of venous graft	44.7 (3.11–186.35)	0.010	0.72 (0.38–2.4)	0.057

NOMTA indicates non-OM target coronary artery; OR, odds ratio.

TABLE 7. Multiple Logistic Regression Analysis for Graft Malfunction (Irregularity, String, or Occlusion) for Grafts Directed to the OM in the 2 Patient Groups

	Study Group		Control Group	
Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Preoperative blood cholesterol level >270 mg/dL	18.53 (1.2–132.9)	0.024	9.6 (2.1–30.60)	0.040
Hypertension	3.55 (0.28–14.6)	0.29	1.53 (0.51–4.3)	0.19
Target OM stenosis >80 %	2.1 (0.37–5.06)	0.38	1.91 (0.89–13.5)	0.19
Time from stent implantation >40 months	0.92 (0.032–6.2)	0.13	12.9 (4.38–71.0)	0.09
Blood cholesterol level at follow-up >200 mg/dL	10.2 (2.7–77.9)	0.058	15.2 (1.08–31.4)	0.060
Use of venous graft	24.1 (2.81–102.45)	0.038	...	...

NOMTA indicates non-OM target coronary artery; OR, odds ratio.

traditional "mixed" grafting strategy in whom the use of all-arterial revascularization can improve the clinical outcome. Additional larger investigations are obviously needed to confirm these data, which are based on a limited number of observations. The role of medicated stents in the treatment of these cases and the comparison between the new surgical and percutaneous approaches will obviously be an additional object of extensive clinical research in this field.

At the moment, we can conclude that venous grafts have an unacceptably high incidence of failure among cases who previously developed in-stent restenosis and in whom the use of arterial conduits can improve the angiographic and clinical results in this patient population. The use of arterial conduits should probably be the first-line surgical option in these cases; saphenous grafts should be adopted only in extreme circumstances.

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