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5-Year Follow-Up of Polytetrafluoroethylene-Covered Stents Compared With Bare-Metal Stents in Aortocoronary Saphenous Vein Grafts

The Randomized BARRICADE (Barrier Approach to Restenosis: Restrict Intima to Curtail Adverse Events) Trial

Gregg W. Stone, MD,* Sheldon Goldberg, MD,† Charles O'Shaughnessy, MD,‡ Mark Midei, MD,§ Robert M. Siegel, MD,‖ Ecaterina Cristea, MD,* George Dangas, MD,* Alexandra J. Lansky, MD,* Roxana Mehran, MD*

New York, New York; Philadelphia, Pennsylvania; Elyria, Ohio; Towson, Maryland; and Phoenix, Arizona

Objectives We sought to evaluate the utility of the JOSTENT polytetrafluoroethylene (PTFE) stent-graft (Jomed GmbH, Rangendingen, Germany) in patients with diseased saphenous vein grafts (SVGs)
undergoing percutaneous coronary intervention (PCI).

Background Prior trials of the JOSTENT stent-graft did not mandate high-pressure implantation or prolonged dual antiplatelet therapy, and were limited by short-term follow-up.

Methods A total of 243 patients at 47 centers with 1 to 2 discrete lesions in SVGs were prospectively randomized to JOSTENT implantation (≥18 atm.) versus bare-metal stents (BMS). The JOSTENT patients were treated with aspirin indefinitely and clopidogrel for ≥8 months. Routine angiographic follow-up was performed at 8 months, and all patients were followed for 5 years.

Results The primary end point of in-lesion binary restenosis occurred in 31.8% of lesions treated with the JOSTENT versus 28.4% of lesions treated with BMS (relative risk: 1.12, 95% confidence interval [CI]: 0.72 to 1.75, p = 0.63). At 9 months, the major secondary end point of target vessel failure (death, myocardial infarction, or clinically driven target vessel revascularization) occurred in 32.2% of patients treated with the JOSTENT versus 22.1% of patients treated with BMS (hazard ratio: 1.54, 95% CI: 0.94 to 2.53, p = 0.08). During long-term follow-up, significantly more events accrued in the JOSTENT arm such that by 5 years target vessel failure had occurred in 68.3% of JOSTENT patients versus 51.8% of BMS patients (hazard ratio: 1.59, 95% CI: 1.13 to 2.23, p = 0.007).

Conclusions The long-term prognosis for diseased SVGs requiring PCI is dismal. The JOSTENT PTFE stent-graft results in inferior outcomes compared with BMS, despite high-pressure implantation and prolonged dual antiplatelet therapy, a finding that becomes more evident with longer-term follow-up. (J Am Coll Cardiol Intv 2011;4:300–9) © 2011 by the American College of Cardiology Foundation

From the *Department of Medicine, Division of Cardiology, Columbia University, Medical Center/New York-Presbyterian Hospital and the Cardiovascular Research Foundation, New York, New York; †Hahnemann University Hospital, Philadelphia, Pennsylvania; ‡EMH Regional Medical Center, Elyria, Ohio; §St. Joseph's Medical Center, Towson, Maryland; and the ‖Phoenix Memorial Hospital, Phoenix, Arizona. Dr. Stone reports receiving research grants from Jomed, and serving on the scientific advisory board for and receiving honoraria from Abbott Vascular and Boston Scientific. Dr. Goldberg reports receiving research grants from Jomed. Dr. O'Shaughnessy reports receiving research support from Abbott Vascular and serving on their advisory board. Dr. Dangas reports that his spouse has received speaker honoraria from Abbott Vascular. Dr. Mehran reports serving as a consultant/advisory board member for Abbott Vascular, AstraZeneca, Cardiva, Cordis, The Medicines Company, and she received research grants from Bristol-Myers Squibb/Sanofi-Aventis. Drs. Midei, Siegel, Cristea, and Lansky report that they have no relationships to disclose.

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As many as 25% to 30% of saphenous vein grafts (SVGs) fail within 12 to 18 months after coronary artery bypass graft surgery (CABG) (1), a proportion that increases to >50% beyond 10 years (2,3). Compared with treatment of native coronary arteries, percutaneous coronary intervention (PCI) of diseased SVGs is associated with higher rates of periprocedural complications and an increased incidence of clinical and angiographic restenosis (4,5). Distal protection devices improve the procedural safety of PCI in SVGs (6,7), whereas bare-metal stents (BMS) improve event-free survival compared with balloon angioplasty (8). Recently, 2 small randomized trials have provided conflicting results as to whether drug-eluting stents (DES) further improve outcomes after PCI of SVGs (9,10). Novel approaches are needed to further improve the prognosis of diseased SVGs.

The JOSTENT stent-graft (Jomed GmbH, Rangendingen, Germany) consists of a distensible polytetrafluoroethylene (PTFE) membrane sandwiched between 2 316L stainless steel slotted tube, balloon-expandable stents (Fig. 1) (11). This device is currently available in the U.S. as the GraftMaster (Abbott Vascular, Santa Clara, California) under a Humanitarian Device Exemption for treatment of life-threatening coronary perforations (12). Hypothetical benefits of elective use of the JOSTENT PTFE stent-graft in SVGs include reduced periprocedural myocardial infarction (MI) (by trapping potentially embolic degenerated atherosclerotic debris behind the PTFE membrane) and decreased restenosis (by serving as a barrier isolating the lumen from smooth muscle cell proliferation, migration, and extracellular matrix production arising from the media) (13). After favorable results from a multicenter registry (14), 2 trials were performed in which the JOSTENT was randomized to BMS in diseased SVGs, demonstrating comparable or increased rates of MI, restenosis, and late occlusion with the stent-graft (15,16). However, neither of these trials mandated high-pressure balloon inflation or prolonged dual antiplatelet therapy, measures that might be necessary to mechanically optimize the implant and facilitate endothelialization without thrombosis. Moreover, follow-up was limited to only 6 and 12 months in these studies, precluding the opportunity to determine whether there are late benefits (or harm) from this device—a salient issue, because the time course of both target lesion revascularization (TLR) and target vessel revascularization (TVR) might be protracted in SVGs compared with native coronary arteries (17).

Therefore, we performed a prospective, multicenter, randomized, controlled trial termed BARRICADE (Barrier Approach to Restenosis: Restrict Intima to Curtail Adverse Events) to evaluate the utility of the JOSTENT PTFE stent-graft for the treatment of discrete atherosclerotic lesions in diseased SVGs. JOSTENT post-dilation to ≥18 atm was mandated to overcome limitations of prior studies, as was use of dual antiplatelet therapy for ≥8 months, and all patients were followed for a total duration of 5 years. The present report represents the principal and final analysis from the BARRICADE trial.

Methods

Enrollment criteria. To be eligible for the BARRICADE trial, patients ≥18 years of age with clinical evidence of ischemia or a positive functional study had to have 1 or 2 SVG lesions eligible for PCI with either both lesions in 1 SVG or 1 lesion in each of 2 SVGs. Lesion eligibility required all the following to be present: visually estimated diameter stenosis of ≥50% and <100%; target vessel diameter ≥3.0 mm and ≤5.0 mm; lesion length ≤25 mm; and Thrombolysis In Myocardial Infarction flow grade ≥1 after successful wire passage. All patients had to agree to all follow-up procedures and provide informed, written consent. Patients were excluded from randomization if any of the following were present: contraindication to aspirin, heparin, clopidogrel, stainless steel, PTFE, or contrast media that could not be adequately pre-medicated; MI within 24 h before the procedure or any creatine phosphokinase (CPK)-myocardial band (MB) greater than normal; left ventricular ejection fraction <25%; PCI in a nonstudy vessel required ≤24 h before or during the index procedure or after (if staged procedure earlier, all other entry criteria must be met, including normal baseline creatine kinase-MB); unprotected left main disease; target lesion involving the distal anastomosis; presence of a ≥50% untreated stenosis proximal or distal to the target lesion; stent(s) located within 5 mm of the target lesion borders; excessive proximal tortuosity or lesion angulation; current participation in another investigational drug or device trial that had not completed the entire follow-up period; comorbidity with anticipated life expectancy to ≤12 months; liver function tests >3× normal; serum creatinine ≥2.0 mg/dl; platelet count <100,000 cells/mm^3; hemoglobin <10.0 g/dl; history of stroke or transient ischemic attack within 6 months; gastrointestinal bleeding within 6 months; history of bleeding diathesis or coagulopathy or will refuse blood transfusions; and active pregnancy or lactation.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CABG = coronary artery bypass graft surgery
CPK = creatine phosphokinase
DES = drug-eluting stent(s)
IVUS = intravascular ultrasound
PCI = percutaneous coronary intervention
PTFE = polytetrafluoroethylene
MB = myocardial band
MI = myocardial infarction
QCA = quantitative coronary angiography
SVG = saphenous vein graft
TLR = target lesion revascularization
TVF = target vessel failure
TVR = target vessel revascularization

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Figure 1. The JOSTENT Coronary Stent Graft

The JOSTENT coronary stent graft (Jomed GmbH, Rangendingen, Germany) combines 2 laser-cut 316L slotted-tube balloon-expandable stainless steel stents with polytetrafluoroethylene graft material. The polytetrafluoroethylene material is wrapped around the inner stent (approximately 2.5×) and sandwiched between the 2 stents.

Protocol and randomization. Direct stenting without pre-dilation was not permitted. Before randomization, treatment with any U.S. Food and Drug Administration-approved distal protection and/or thrombectomy device was permitted at the discretion of the operator, followed by pre-dilation with an undersized balloon catheter. If all eligibility criteria were present after pre-dilation, patients were randomized 1:1 in open-label fashion to the JOSTENT versus any U.S. Food and Drug Administration-approved BMS. Randomization was performed in random blocks of 4 to 6, stratified by the prior use of distal protection and/or thrombectomy. For patients randomized to the JOSTENT, the device was implanted at a nominal pressure, after which post-dilation with a noncompliant balloon was mandatory at a 1 to 1.1:1 balloon/artery ratio, to ≥18 atm. The JOSTENT was pre-mounted and available in lengths ranging from 9 to 29 mm and in diameters ranging from 3.0 to 5.0 mm. Only 1 JOSTENT was intended for a single lesion, by intent; however, additional JOSTENTs were permitted as necessary to treat residual diseased segments or edge dissections. The BMS were implanted according to standard of care.

Before the procedure patients received aspirin ≥325 mg, and clopidogrel 300 mg was recommended. Procedural anticoagulation was achieved with intravenous heparin, with the activated clotting time maintained at ≥300 s (200 to 250 s, if a glycoprotein IIb/IIIa inhibitor was used per investigator discretion). After the procedure all patients were administered aspirin 325 mg daily indefinitely. Patients who received a JOSTENT were administered clopidogrel 75 mg daily for at least 8 months, whereas clopidogrel was recommended for at least 1 month in patients treated with BMS. The CPK and CPK-MB levels were measured at baseline and every 8 h 3× within 24 h after the procedure. An electrocardiogram was obtained at baseline, immediately after the procedure, at discharge, and additionally for any recurrent symptoms.

Clinical follow-up visits were planned at the time of discharge, 1 month, 8 months, 9 months, 12 months, and then yearly through 5 years. In addition, follow-up angiography was planned in all patients at 8 months after discharge, unless angiography performed before 8 months showed restenosis of the target lesion.

Data management. Study monitors verified all case report forms data on-site. Major adverse cardiac events were adjudicated by an independent committee blinded to treatment allocation. Quantitative coronary angiography (QCA) analyses were performed at an independent core angiographic laboratory by technicians blinded to treatment assignment and clinical outcomes as previously described (18). Intravascular ultrasound (IVUS) guidance was not required but, if performed, was analyzed at an independent core ultrasound laboratory.

End points and definitions. The primary end point was the rate of binary angiographic restenosis in the target lesion at 8 months, defined as a >50% diameter stenosis within the stent or the 5-mm proximal or distal stent margins. The secondary end point was target vessel failure (TVF) at 9 months, defined as the composite of all-cause death, MI, or clinically driven TVR. Myocardial infarction was diagnosed by a rise of CPK-MB to >3× normal. Target vessel revascularization was defined as repeat PCI or CABG of the target lesion (TLR) or vessel (TVR) containing the target lesion and was considered clinically driven if signs or symptoms of ischemia were present referable to the target vessel with an in-lesion diameter stenosis ≥50% by QCA or with an in-lesion diameter stenosis ≥70% by QCA in the absence of ischemia. Stent thrombosis was defined as thrombus or subacute closure within the stented vessel at the time of a clinically driven angiographic repeat study for documented ischemia or any death not attributed to a noncardiac cause within the first 30 days in the absence of documented angiographic stent patency.

Sample size and statistical analysis. One hundred eighty-four patients/arm would provide 90% power to demonstrate superiority with a 2-sided $\alpha = 0.05$, on the basis of published nonrandomized data with the JOSTENT (14)—assuming a binary restenosis rate at 8 months after BMS of 35% from the SAVED (Saphenous Vein De Novo) trial (8) and anticipating a reduction in restenosis to 20%. Two hundred fifty patients/arm (500 total) were planned for enrollment, assuming an angiographic follow-up rate of 75%.

Categorical data were compared by chi-square or Fisher exact tests. Continuous data were expressed as mean ± SD and compared by unpaired *t* tests. Lesion level

variables, whether continuous or categorical, were compared with Generalized Estimating Equations to accommodate correlated data. Adverse event analyses were performed with time-to-event data, are displayed with Kaplan-Meier methodology, and were compared with the log-rank test. All data are presented in the intent-to-treat population, consisting of all patients randomized, regardless of treatment actually received. A p value of 0.05 was required for statistical significance. Statistical analyses were performed by SAS (version 9.1, SAS, Cary, North Carolina).

Results

Patients and procedures. Between August 9, 2001 and August 28, 2003, 243 patients were randomized at 38 U.S. centers. The manufacturer Jomed was acquired by Abbott Vascular in August 2003, after which the trial was suspended for performance of a futility analysis. It was determined, on the basis of this analysis, that the trial would not be positive, and the study was terminated. Follow-up continued, however, for the full 5 years for all randomized patients.

The baseline demographic and clinical characteristics were well matched between the 2 groups (Table 1). As shown in Table 2, mean graft age was 10 years; 90% of lesions arose from the body of the SVG. Multiple SVG lesions were treated in 23% of patients. Distal protection devices were used in 43% of cases, and thrombectomy was rarely used. The maximal stent implantation pressure was significantly higher for the JOSTENT than for BMS. Aspirin use was high in both arms throughout the study. Thienopyridine use was more frequent in the JOSTENT group at 8- and 9-month follow-up (Table 1).

Angiographic results. The baseline angiographic measures in the 2 groups were well matched, except that the reference vessel diameter in the BMS group was slightly larger (Table 3). After PCI, the rates of Thrombolysis In Myocardial Infarction flow and angiographic complications were comparable in the 2 groups. At 8-month follow-up, late loss and the rates of binary restenosis and vessel occlusion were not statistically different between the JOSTENT and BMS groups (Table 3). The primary end point of in-lesion binary restenosis occurred in 31.8% of lesions treated with the JOSTENT versus 28.4% of lesions treated with BMS (relative risk: 1.12, 95% CI: 0.72 to 1.75, p = 0.63).

IVUS. Intravascular ultrasound after PCI was performed in 23 JOSTENT patients and 11 BMS patients. The minimal luminal area was comparable in both groups (8.61 ± 3.27 mm^2 vs. 8.76 ± 3.63 mm^2, respectively, p = 0.91), as was the average reference lumen area (11.83 ± 4.66 mm^2 vs. 11.27 ± 3.86 mm^2 respectively, p = 0.73).

Table 1. Baseline Characteristics and Medication Use

	JOSTENT (n = 115)	Bare-Metal Stent (n = 128)	p Value
Age (yrs)	67.9 ± 9.7	68.8 ± 8.9	0.46
Male	90 (78.3%)	108 (84.4%)	0.22
Current smoker	13 (11.3%)	18/127 (14.2%)	0.50
Diabetes mellitus	44 (38.3%)	54 (42.2%)	0.53
Hypertension	97 (84.3%)	107 (83.6%)	0.87
Hypercholesterolemia	108 (93.9%)	117 (91.4%)	0.46
Prior myocardial infarction	49/114 (43.0%)	63/125 (50.4%)	0.25
Prior percutaneous coronary intervention	64/114 (56.1%)	64 (50.0%)	0.34
Prior coronary artery bypass graft surgery	115 (100%)	128 (100%)	—
Prior stroke or transient ischemic attack	17 (14.8%)	20 (15.6%)	0.86
Prior congestive heart failure	17 (14.8%)	26 (20.3%)	0.26
Canadian Cardiovascular Society class III/IV	47 (40.9%)	49 (38.3%)	0.68
Left ventricular ejection fraction (%)	50.5 ± 12.5	49.3 ± 12.5	0.48
Aspirin use			
Discharge	113 (98.3%)	128 (100.0%)	0.22
8 months	101/108 (93.5%)	110/124 (88.7%)	0.20
9 months	101/108 (93.5%)	108/124 (87.1%)	0.10
Thienopyridine use			
Discharge	113 (98.3%)	125 (97.7%)	1.0
8 months	87 (75.7%)	77 (60.2%)	0.01
9 months	78 (67.8%)	72 (56.3%)	0.06

Values are mean ± SD or n (%).

Table 2. Procedural Data

	JOSTENT (n = 115 Patients, 139 Lesions)	Bare-Metal Stent (n = 128 Patients, 154 Lesions)	p Value
Number of vein grafts treated			
1	109 (94.8%)	119 (93.0%)	0.56
2	6 (5.2%)	9 (7.0%)	0.56
Number of lesions treated			
1	88 (76.5%)	99 (77.3%)	0.88
2	25 (21.7%)	28 (21.9%)	0.98
3	2 (1.7%)	1 (0.8%)	0.60
Graft age (yrs)	10.2 ± 5.1	9.5 ± 5.3	0.26
Vein graft lesion location: aorto-ostial	13 (9.4%)	17 (11.0%)	0.63
Vein graft lesion location: body	126 (90.6%)	137 (89.0%)	0.63
Vein graft coronary artery distribution			
Left anterior descending	30 (21.6%)	26 (16.9%)	0.31
Right	45 (32.4%)	57 (37.0%)	0.41
Left circumflex	64 (46.0%)	71 (46.1%)	0.99
Glycoprotein IIb/IIIa inhibitors used	63 (54.8%)	62 (48.4%)	0.31
Distal protection used	48 (41.7%)	55/127 (43.3%)	0.81
Thrombectomy used	2/114 (1.8%)	1/127 (0.8%)	0.60
Total number of stents	1.37 ± 0.65	1.36 ± 0.61	0.97
Total stent length (mm)	20.7 ± 7.3	21.8 ± 13.0	0.36
Maximum device size (mm)	4.0 ± 0.6	4.0 ± 0.7	0.97
Maximum inflation pressure (atm)	18.5 ± 2.9	15.3 ± 3.3	<0.0001

Values are n (%) or mean ± SD.

Clinical outcomes. After PCI, the peak CPK (106.2 ± 107.1 IU/l vs. 91.9 ± 79.3 IU/l, p = 0.26) and CPK-MB levels (3.7 ± 8.3 IU/l vs. 3.9 ± 9.9 IU/l, p = 0.84) were comparable in the JOSTENT and BMS groups, respectively. Similarly, there were no significant differences between groups in the rates of MI, stent thrombosis, or other adverse events at 30 days (Table 4). At 9 months, the major secondary end point of TVF occurred in 32.2% of patients treated with the JOSTENT versus 22.1% of patients treated with BMS (hazard ratio: 1.54, 95% CI: 0.94 to 2.53, p = 0.08). Significant differences between the 2 stents in the rates of any of the components of TVF at 9 months were not apparent (Table 4).

Table 5 shows the annual rates of adverse cardiovascular events between 1 and 5 years. Events continued to accrue in both arms over time but more so in the JOSTENT arm, such that by 2 years and beyond TVF occurred more frequently in patients assigned to the JOSTENT. At the end of the 5-year follow-up period, TVF had occurred in 68.3% of patients treated with the JOSTENT versus 51.8% of patients treated with BMS (hazard ratio: 95% CI: 1.59 1.13 to 2.23, p = 0.007) (Fig. 2). This difference was driven primarily by more rapidly increasing TLR rates in JOSTENT-treated patients. Although there were no statistically significant differences between the 2 stent types in the rates of MI or stent thrombosis, target vessel occlusion was noted more frequently in the JOSTENT arm during long-term follow-up.

Discussion

The present study was designed to overcome several potentially important limitations from prior randomized trials of the JOSTENT PTFE stent-graft in diseased SVGs. Notably, the JOSTENT—consisting of 2 balloon-expandable stents containing a PTFE membrane—is frequently underexpanded unless high-pressure inflations are performed (19), which was not mandated in previous studies. Moreover, it has been hypothesized that delayed endothelialization of the PTFE material might explain the observed tendency toward thrombotic occlusion of the JOSTENT. Because prior studies required dual antiplatelet therapy for only 1 to 3 months (15,16), a more prolonged course might result in greater long-term graft patency. Finally, follow-up was truncated at 6 to 12 months in earlier trials (15,16), a duration insufficient to characterize the late prognosis after SVG intervention (17).

In the present trial, high-pressure (≥18 atm) inflations were performed in the JOSTENT with noncompliant balloons; dual antiplatelet therapy was prescribed for ≥8 months; and follow-up was continued for 5 years. Nonetheless, recruitment in the trial was terminated after enrollment of approximately 50% of the planned sample size for futility. The 8-month rates of late loss and restenosis were not superior to BMS (with high restenosis rates observed in both groups), even though angiog-

Table 3. Quantitative Coronary Angiography

	JOSTENT	Bare-Metal Stent	p Value
Vessel-level analysis			
Baseline	(n = 118 vessels)	(n = 132 vessels)	
TIMI flow grade: 0/1	2 (1.7%)	7 (5.3%)	0.18
TIMI flow grade: 2	18 (15.3%)	13 (9.8%)	0.20
TIMI flow grade: 3	98 (83.1%)	112 (84.8%)	0.70
Immediate post-PCI	(n = 118 vessels)	(n = 132 vessels)	
TIMI flow grade: 0/1	1 (0.8%)	3 (2.3%)	0.62
TIMI flow grade: 2	1 (0.8%)	1 (0.8%)	1.0
TIMI flow grade: 3	116 (98.3%)	128 (97.0%)	0.69
8-month follow-up	(n = 75 vessels)	(n = 90 vessels)	
TIMI flow grade: 0/1	12 (16.0%)	8 (8.9%)	0.16
TIMI flow grade: 2	3 (4.0%)	3 (3.3%)	1.0
TIMI flow grade: 3	60 (80.0%)	79 (87.8%)	0.17
Lesion-level analysis			
Baseline	(n = 125 lesions)	(n = 130 lesions)	
Reference vessel diameter (mm)	3.30 ± 0.64	3.48 ± 0.68	0.03
Minimal luminal diameter (mm)	1.19 ± 0.58	1.27 ± 0.59	0.27
Diameter stenosis (%)	63.8 ± 15.5	63.8 ± 13.8	1.0
Lesion length (mm)	11.9 ± 6.5	11.8 ± 6.9	0.94
Immediate post-PCI	(n = 125 lesions)	(n = 130 lesions)	
Reference vessel diameter (mm)	3.38 ± 0.61	3.54 ± 0.71	0.06
Minimal luminal diameter, in-stent (mm)	3.31 ± 0.53	3.34 ± 0.61	0.67
Diameter stenosis, in-stent (%)	1.0 ± 12.5	4.5 ± 12.5	0.02
Minimal luminal diameter, in-lesion (mm)	2.92 ± 0.58	2.99 ± 0.60	0.33
Diameter stenosis, in-lesion (%)	13.6 ± 8.0	15.0 ± 9.6	0.18
Thrombus	3 (2.4%)	1 (0.8%)	0.36
No reflow	1 (0.8%)	1 (0.8%)	1.0
Dissection	2/124 (1.6%)	4 (3.1%)	0.68
Distal embolization	0 (0%)	1/129 (0.8%)	1.0
8-month follow-up	(n = 85 lesions)	(n = 95 lesions)	
Reference vessel diameter (mm)	3.29 ± 0.68	3.50 ± 0.63	0.03
Minimal luminal diameter, in-stent (mm)	2.41 ± 1.36	2.32 ± 1.21	0.63
Diameter stenosis, in-stent (%)	25.8 ± 40.3	34.4 ± 31.8	0.12
Late loss, in-stent (mm)	0.89 ± 1.32	1.06 ± 1.09	0.35
Binary restenosis, in-stent	22 (25.9%)	25 (26.3%)	0.95
Minimal luminal diameter, in-lesion (mm)	2.04 ± 1.24	2.18 ± 1.16	0.42
Diameter stenosis, in-lesion (%)	38.6 ± 341	38.6 ± 29.6	1.0
Late loss, in-lesion (mm)	0.87 ± 1.12	0.82 ± 1.05	0.78
Binary restenosis, in-lesion	27 (31.8%)	27 (28.4%)	0.63

Values are n (%) or mean ± SD.
PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

raphy and IVUS demonstrated adequate stent expansion of the JOSTENT. Although IVUS was not performed at follow-up, these data suggest that either the porous PTFE membrane is not sufficiently restrictive to prevent neointimal hyperplasia from accumulating within the lumen or restenosis might also arise from circulating cellular mechanisms (20,21). Chronic recoil of the JOSTENT as an alternate mechanism in selected patients cannot be excluded without follow-up IVUS. Whether the trend toward increased late vessel occlusion with the JOSTENT is due to thrombosis or progressive hyperplasia also cannot be answered by this study, although it is clear that the 8-month use of dual antiplatelet therapy in most patients was insufficient to extend stent-graft patency.

The present study is the first to systematically follow all patients for 5 years after SVG intervention. In this regard, long-term follow-up serves to emphasize the bleak prognosis that can be expected after PCI of diseased SVGs with either the JOSTENT or BMS. Five years after treatment with BMS, TVF occurred in more than one-half of all

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Table 4. Clinical Outcomes at 30 Days and 9 Months

	JOSTENT (n = 115)	Bare-Metal Stent (n = 128)	p Value
30-day events			
Target vessel failure	8.7% (10)	7.0% (9)	0.63
Death, all-cause	0.9% (1)*	0.0% (0)	0.29
Myocardial infarction	7.0% (8)	7.0% (9)	0.99
Q-wave	2.6% (3)	1.6% (2)	0.57
Non–Q-wave	4.3% (5)	5.5% (7)	0.69
Target vessel revascularization	0.9% (1)†	0.8% (1)†	0.94
Percutaneous coronary intervention	0.9% (1)	0.8% (1)	0.94
Coronary artery bypass graft surgery	0% (0)	0% (0)	—
Stent thrombosis	1.7% (2)	0.8% (1)	0.50
9-month events			
Target vessel failure	32.2% (37)	22.1% (27)	0.08
Death, all-cause	6.1% (7)	3.3% (4)	0.31
Cardiac	5.3% (6)	2.5% (3)	0.27
Noncardiac	0.9% (1)	0.8% (1)	0.96
Myocardial infarction	10.6% (12)	10.4% (13)	0.96
Q-wave	3.5% (4)	2.4% (3)	0.61
Non–Q-wave	7.0% (8)	8.0% (10)	0.78
Target lesion revascularization	15.6% (17)	13.5% (16)	0.66
Percutaneous coronary intervention	14.7% (16)	13.5% (16)	0.81
Coronary artery bypass graft surgery	0.9% (1)	0.8% (1)	0.96
Target vessel revascularization	21.8% (24)	15.1% (18)	0.20
Percutaneous coronary intervention	20.9% (23)	15.1% (18)	0.26
Coronary artery bypass graft surgery	0.9% (1)	0.8% (1)	0.96
Stent thrombosis	3.6% (4)	2.5% (3)	0.61

Event rates are Kaplan-Meier estimates (number of events). *Adjudicated as a cardiac death. †Each was adjudicated as a target lesion revascularization.

patients; MI, stent thrombosis, and vessel occlusion had occurred in 17.4%, 5.6%, and 7.8% of patients, respectively; TLR and TVR were required in 29.6% and 33.3% of patients, respectively; and 22.3% of patients had died. Five years after treatment with the JOSTENT, TVF had occurred in more than two-thirds of patients, with worse outcomes in every component measure compared with BMS. Use of the stent-graft also did not prevent acute angiographic complications such as distal embolization or periprocedural MI. Lower pressure inflations or less aggressive implantation technique might have prevented complications from the "toothpaste" effect but would likely have negatively affected late outcomes. Freedom from early thrombosis or late occlusion was not enhanced in a prior study by adding a heparin coat to the JOSTENT (22). A different, totally encapsulated PTFE stent-graft has similarly failed to prevent periprocedural complications or late restenosis after SVG intervention (23). Clearly, novel strategies are required for diseased SVGs. Registry studies have suggested that DES might be more efficacious than BMS (24,25), although the 2 small randomized trials that have been completed to date in this population were inconclusive (9,10). Double-stranded oligonucleotide E2F decoys to transcription factors implicated in the upregulation of several genes involved in neointimal hyperplasia have also failed to prolong SVG patency (26). Pan-arterial CABG and hybrid PCI/CABG procedures should be increasingly employed to reduce the use of SVGs as bypass conduits.

Study limitations. Recruitment was stopped early after a futility analysis. However, examination of the CIs around the final clinical and angiographic end points provides reassurance that a possible beneficial effect of the JOSTENT is unlikely to have been missed. IVUS guidance during the index procedure was used in a minority of patients, although it is uncertain whether acute procedural results would have been improved with IVUS, given the requirement to dilate all JOSTENTs to ≥18 atm with a noncompliant balloon. Only 76% of patients randomized to the JOSTENT were adherent with dual antiplatelet therapy at 8 months. It is doubtful that the results would have been meaningfully different had clopidogrel compliance been higher. Distal protection devices

Table 5. Clinical Outcomes Annually Through 5 Years

	JOSTENT (n = 115)	Bare-Metal Stent (n = 128)	p Value
Target vessel failure			
1 yr	39.2% (45)	28.0% (34)	0.07
2 yrs	51.6% (59)	33.3% (40)	0.008
3 yrs	60.2% (68)	37.0% (44)	0.001
4 yrs	63.1% (71)	46.0% (53)	0.006
5 yrs	68.3% (76)	51.8% (59)	0.007
Death, all-cause			
1 yr	7.0% (8)	5.0% (6)	0.51
2 yrs	12.3% (14)	9.4% (11)	0.47
3 yrs	18.8% (21)	11.2% (13)	0.13
4 yrs	23.5% (26)	17.2% (19)	0.22
5 yrs	29.8% (32)	22.3% (24)	0.20
Myocardial infarction			
1 yr	14.2% (16)	11.3% (14)	0.53
2 yrs	18.9% (21)	13.1% (16)	0.27
3 yrs	21.0% (23)	14.1% (17)	0.21
4 yrs	22.2% (24)	16.2% (19)	0.27
5 yrs	26.2% (27)	17.4% (20)	0.16
Target lesion revascularization			
1 yr	20.9% (23)	16.9% (20)	0.46
2 yrs	32.1% (35)	19.7% (23)	0.06
3 yrs	37.4% (40)	21.8% (25)	0.02
4 yrs	39.8% (42)	26.2% (29)	0.04
5 yrs	43.9% (45)	29.6% (32)	0.04
Target vessel revascularization			
1 yr	28.2% (31)	21.1% (25)	0.22
2 yrs	36.6% (40)	23.8% (28)	0.05
3 yrs	41.9% (45)	26.8% (31)	0.03
4 yrs	44.2% (47)	31.2% (35)	0.04
5 yrs	48.2% (50)	33.3% (37)	0.04
Stent thrombosis			
1 yr	5.4% (6)	3.4% (4)	0.44
2 yrs	7.3% (8)	3.4% (4)	0.20
3 yrs	8.3% (9)	3.4% (4)	0.13
4 yrs	9.5% (10)	5.6% (6)	0.24
5 yrs	10.9% (11)	5.6% (6)	0.16
Target vessel occlusion			
1 yr	5.4% (6)	1.6% (2)	0.12
2 yrs	9.1% (10)	3.5% (4)	0.08
3 yrs	11.2% (12)	3.5% (4)	0.03
4 yrs	11.2% (12)	6.9% (7)	0.18
5 yrs	14.0% (14)	7.8% (8)	0.13

Event rates are Kaplan-Meier estimates (number of events).

were used in only 43% of enrolled patients, despite their documented ability to reduce periprocedural embolization and no reflow (6,7). This percentage, however, is higher than their contemporary use in SVG intervention. In this regard, although recruitment in this trial occurred more than 7 years ago, the tools for and technique of SVG PCI have not materially changed since then (other than the availability of DES). Finally, only SVGs with discrete (≤25 mm long) lesions were enrolled in the present trial. The long-term outcomes in both arms would likely have been even worse had severely degenerated or occluded SVGs been included (27).

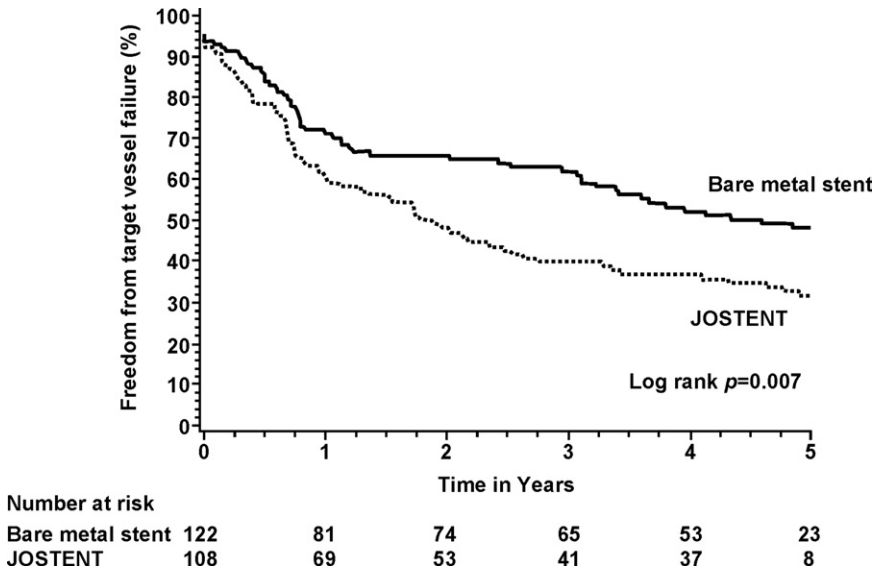

Figure 2. Target Vessel Failure Through 5 Years After Randomization

Target vessel failure (death, myocardial infarction, or target vessel revascularization) through 5 years after randomization in the 2 study groups.

Conclusions

The present trial underlines the dismal long-term prognosis of patients with diseased SVGs requiring PCI. Polytetrafluoroethylene-covered stent-grafts have a greater failure rate when used for this application than BMS and, therefore, should be reserved for life-threatening perforations of the coronary vasculature (12). The results of this study also emphasize the need for breakthrough strategies to prevent and treat SVG degeneration or preferably revascularization approaches that involve leaving saphenous veins undisturbed in the legs whenever possible.

Reprint requests and correspondence: Dr. Gregg W. Stone, Columbia University Medical Center, New York Presbyterian Hospital, The Cardiovascular Research Foundation, 111 East 59th Street, 11th Floor, New York, New York 10022. E-mail: gs2184@columbia.edu.

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Key Words: bypass graft ■ coronary artery disease ■ stent.

APPENDIX

For a list of the BARRICADE trial organization and participating sites and investigators, please see the online version of this article.