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A Randomized Trial of Polytetrafluoroethylene-Membrane-Covered Stents Compared With Conventional Stents in Aortocoronary Saphenous Vein Grafts

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OBJECTIVES We compared a conventional stent (Jostent Flex, Jomed GmbH, Rangendingen, Germany) with a polytetrafluoroethylene (PTFE)-membrane-covered stent (Jostent Stentgraft) in patients undergoing intervention of a stenosis in an obstructed vein graft.

BACKGROUND The use of stents improved results of percutaneous revascularization of obstructed vein grafts, but did not demonstrate the reduced elevated restenosis rate. In addition, long-term clinical event rate is still high compared with intervention in native vessels. Observational studies suggested that stents covered with a PTFE membrane might be associated with a low complication and restenosis rate in venous bypass grafts.

METHODS This prospective multicenter study included a total of 211 patients who were randomly assigned to receive either a Flex stent or Stentgraft. The primary end point was binary restenosis rate at six months by core lab quantitative coronary angiography.

RESULTS Acute success and procedural events were comparable between the two groups. Restenosis rate was not significantly different between the Flex (20%) and the Stentgraft (29%) groups ($p = 0.15$), although there was a nonsignificant trend toward a higher late occlusion rate in the Stentgraft group (7% vs. 16%, $p = 0.069$) at follow-up. Likewise, after a mean observation period of 14 months, cumulative event rates (death, myocardial infarction, or target lesion revascularization) were comparable in the two groups (31% vs. 31%, $p = 0.93$).

CONCLUSIONS This controlled trial does not indicate a superiority of the PTFE-membrane-covered Stentgraft compared with a conventional stent with respect to acute results, restenosis, or clinical event rates. (J Am Coll Cardiol 2003;42:1360–9) © 2003 by the American College of Cardiology Foundation

Saphenous vein graft coronary artery bypasses degenerate in about one out of two patients within a decade after coronary surgery (1). Because repeat surgery is associated with substantial risk, percutaneous interventional revascularization seemed to be preferable. Furthermore, with the use of intracoronary stents, major cardiac events, especially procedure-related complications, could be substantially reduced compared with pure balloon angioplasty (2), but no effect was obtained with respect to the high restenosis rate of 37% in bypass grafts. Likewise, long-term clinical outcome is still poor despite the use of stents for interventional treatment of obstructed bypass grafts (3,4). In addition, elevation of creatine kinase (CK)-MB resulting from embolization of atheromatous debris of the obstructed graft is a strong independent predictor of late mortality—even in otherwise uncomplicated interventions of venous bypass grafts (5).

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These findings provided the rationale to develop a stent covered by a membrane in order to seal the lumen to reduce microembolization and to reduce restenosis by preventing protrusion of proliferating plaque material through the stent mash. Initial experiences using the Jostent Coronary Stentgraft (Jomed GmbH, Rangendingen, Germany), which has a sandwich-like design with a biocompatible distensible polytetrafluoroethylene (PTFE) membrane between two stainless steel stents, were promising, when used in saphenous vein grafts (6), and are a valuable bail-out anchor for

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Abbreviations and Acronyms

CK = creatine kinase
MI = myocardial infarction
PTCA = percutaneous transluminal coronary angioplasty
PTFE = polytetrafluoroethylene
STING = Stents IN Grafts trial

treatment of percutaneous transluminal coronary angioplasty (PTCA)-related vessel rupture (6,7). Results of a German multicenter registry suggested that the PTFE-membrane-covered stent appears to be a safe and efficient treatment strategy for obstructed vein grafts with restenosis rates of about 17% (8). The present study, Stents IN Grafts (STING), was designed as a prospective, randomized multicenter trial to compare the Jostent Coronary Stentgraft with a conventional stent with respect to restenosis and secondary cardiovascular events in patients undergoing percutaneous intervention of obstructed coronary vein grafts.

METHODS

Patient population. Patients were eligible in the study when they presented with angina pectoris or documented myocardial ischemia and had by visual estimation a hemodynamically significant de novo lesion in an aortocoronary saphenous vein bypass graft with a lesion length between 5 and 45 mm and a reference diameter between 3.0 and 5.0 mm, accessible to percutaneous revascularization. The main exclusion criteria were myocardial infarction (MI) <14 days before intervention, Thrombolysis In Myocardial Infarction (TIMI) flow 0 in the target vessel, restenotic lesion, distal ostial lesion (≤5 mm), multiple lesions within the target vessel, which cannot all be treated by the same stent type, scheduled for surgery, severe hypertension, severe liver or renal failure.

The study was performed in 12 centers in Germany and Austria (see Appendix). The study protocol was approved by the local ethics committee at each center. Written informed consent was obtained before the procedure from all patients.

Protocol. Patients were randomly assigned before the start of the procedure to treatment with either Jostent Coronary Stentgraft (hand-mounted) (Jomed GmbH, Rangendingen, Germany) or Jostent Flex Coronary Stent by phone call to a central office. Both stents have a Certificate of the European Union and were available in the lengths 9, 16, and 26 mm. Patients were pretreated with aspirin (100 mg per day). Heparin and abciximab (bolus and infusion over 12 h) were recommended for all patients. Stent implantation technique was performed at the discretion of the investigator. Ticlopidine (500 mg per day) or clopidogrel (75 mg per day) were started after loading doses at the day of the procedure and continued for three months. Control angiography was scheduled after six months. A final interview to assess clinical events was intended to be obtained after one year (12 ± 3 months). A clinical follow-up was available in all patients intended to treat. However, in 15 patients (6 randomized to Flex and 9 to Stentgraft), a final interview could only be obtained at the time of control angiography at 6 months.

Angiographic analysis. After intracoronary nitroglycerin, coronary angiography was performed in two projections before angioplasty, and identical projections were repeated after the stent implantation procedure as well as at follow-up. All angiograms were analyzed at the Frankfurt University Core Laboratory using a validated computer-assisted quantitative angiography system (Medis-CMS, Leiden, The Netherlands). Treatment allocation was not reported to the analysts. Stenosis morphology and procedural events were classified according to Ellis et al. (9) and Lincoff et al. (10), and flow was determined according to the TIMI study group (11). Procedural success was defined as a residual stenosis after intervention <20% in the absence of periprocedural events (death, MI).

End points. Primary end point was binary restenosis rate (>50% diameter stenosis) at six months follow-up. Late occlusion was defined as a TIMI status ≤1 at follow-up and counted also as restenosis. If repeat angiography was prematurely performed before 100 days for recurrence of symptoms, it served as control angiography only if restenosis was present. Secondary end point was a composite of clinical events assessed after one year: occurrence of either death, MI (CK elevation ≥3× upper normal limit with significant MB fraction >6%), or target lesion revascularization (PTCA at the site of the study stent or coronary artery bypass grafting with new graft to target vessel). In addition, target vessel revascularization (PTCA at any site of the target bypass graft or coronary artery bypass grafting) and non-target vessel revascularization were assessed.

Statistical analysis. We assumed a restenosis rate of 37% in the conventional stent (Flex) group (2) and a restenosis rate of 15% in the Stentgraft group (8). Using an α error of 0.05 and a power of 90%, a sample size of 210 patients is required (164 patients with control angiography taking into account a loss of follow-up). All analyses were reported according to the intention-to-treat principle. Results were reported as means (± SD) for continuous variables and as percentage for categorical variables. For continuous variables, normal distribution was tested by Kolmogorov-Smirnow test. Differences between the two groups were tested by Student *t* test for normally distributed variables, respectively by Mann-Whitney *U* test for non-normally distributed variables. For categorical variables, chi-square test or two-sided Fisher exact test (in case of 2 × 2 comparison with <5 expected observations in a cell) were used. A p value of ≤0.05 was considered to be statistically significant. All reported p values are two-sided. A stepwise logistic regression analysis was performed to determine independent predictors of late occlusions at six months. We included in the model all clinical and angiographic variables

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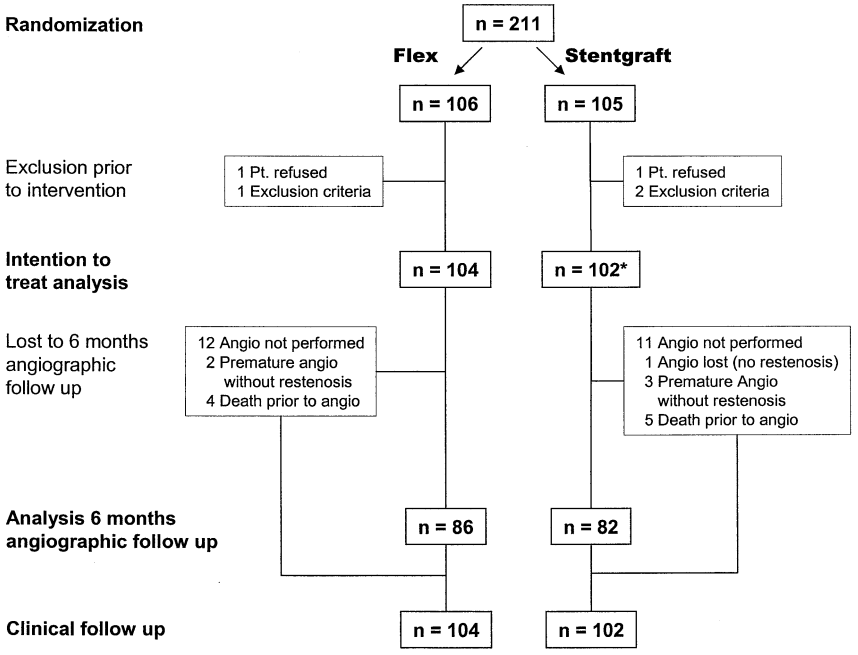

Figure 1. Trial profile. *Index angiogram was not suitable for quantitative analysis in one patient. Angio = coronary angiogram; pt. = patient.

that obtained a p value of <0.1 by univariate analysis. Event-free survival curves were estimated according to the Kaplan-Meier method and compared by the log-rank test. For composite end points, the first event was counted.

RESULTS

Patient characteristics. Between April 1999 and January 2001, a total of 211 patients were randomized at 12 centers. Five patients were excluded before intervention (Fig. 1), and stent implantation was performed outside of the protocol. Of those, one patient in the Flex group experienced periprocedural resuscitation without MI and was discharged alive; there were no clinical events in the other four patients at long-term follow-up.

In the 206 patients included in the intention-to-treat analysis, there were no differences between the Flex and the Stentgraft group except the incidence of diabetes, which was significantly more frequent in the Stentgraft group (Table 1).

Stent implantation procedure. There were no significant differences with respect to lesion characteristics between the two groups except calcification, which was significantly more frequent in stenosis of patients in the Stentgraft group. A significantly higher maximal balloon pressure was used in patients in whom a stent graft was implanted compared with the Flex group (Table 2), whereas balloon size, number, and length of stents was similar between the groups.

Of 102 patients assigned to the Stentgraft group, two patients with distal occlusion after predilation or a very proximal lesion did not receive any stent. In one patient with a tortuous vessel, the assigned Stentgraft could not be implanted, but conventional stents were successfully applied (cross-over). No stent was lost during implantation. Complete stent coverage of the stenosis was obtained in 99% in the Flex and 96% in the Stentgraft group (p = 0.21, Fisher exact). Postprocedure minimal luminal diameter by quantitative coronary angiography was comparable between the two groups (Fig. 2A). Mean percent stenosis after the intervention was 7.3 ± 13% in the Flex and 6.6 ± 14% in the Stentgraft group (p = 0.32, Mann-Whitney *U*). Periprocedural events during the intervention were similar between the groups (Table 3). There was one periprocedural death in the Flex group (subsequent to periprocedural infarction) and two deaths in the Stentgraft group (one patient during the procedure due to a no-reflow phenomenon with ST elevation and complete AV block after stent

Table 1. Baseline Patient Characteristics

Characteristics	Flex (n = 104)	Stentgraft (n = 102)	p Value
Age (yrs)	68 ± 7.5	67 ± 7.4	0.44†
Male gender	96 (92%)	88 (86%)	0.16‡
Unstable angina	21 (20%)	23 (23%)	0.68‡
Previous myocardial infarction	46 (44%)	42 (41%)	0.66‡
Left ventricular ejection fraction (%)*	54 ± 16	55 ± 14	0.91†
Age of vein graft (yrs)	10.6 ± 4.8	9.5 ± 5.1	0.12†
Hypercholesterolemia	77 (74%)	72 (71%)	0.58‡
Hypertension	73 (70%)	73 (72%)	0.83‡
Diabetes mellitus	20 (19%)	33 (32%)	0.031‡
Smoker	55 (53%)	42 (41%)	0.092‡
Beta-blocker	74 (71%)	75 (74%)	0.70‡
ACE inhibitor	56 (54%)	59 (58%)	0.56‡

*Visual estimation, determined in 66 Flex and 55 Stentgraft patients; †*t* test; ‡chi-square test.
ACE = angiotensin-converting enzyme.

Table 2. Lesion and Procedural Characteristics

	Flex (n = 104)	Stentgraft (n = 102)	p Value
Lesion			
Target bypass distribution			0.46†
LAD	38 (37%)	40 (39%)	
RCX	44 (42%)	35 (34%)	
RCA	22 (21%)	27 (27%)	
Sequential bypass	9 (8.7%)	8 (7.8%)	0.83‡
Multiple dilations			
Same vessel	8 (7.7%)	14 (14%)	0.16‡
Other vessel	7 (6.7%)	2 (2.0%)	0.17§
Stenosis morphology			
Calcification	4 (3.8%)	12 (12%)	0.034‡
Complex morphology	29 (28%)	29 (28%)	0.93‡
Bending >45°	13 (13%)	17 (17%)	0.40‡
TIMI status before intervention			0.98‡
0	1 (1%)	1 (1%)	
1	3 (2.9%)	4 (3.9%)	
2	17 (16%)	17 (17%)	
3	83 (80%)	80 (78%)	
Procedure			
Balloon size (mm)	3.9 ± 0.50	3.8 ± 0.52	0.37†
Maximal balloon pressure (atm)	15.0 ± 2.7	16.4 ± 2.6	< 0.001†
Balloon/reference ratio	1.15 ± 0.17	1.16 ± 0.20	0.62*
Stent lengths (Σ in mm)	19.0 ± 8.3	18.4 ± 8.4	0.53†
Number of stents implanted			0.38‡
0	0	2 (2%)	
1	83 (80%)	85 (83%)	
2	20 (19%)	14 (14%)	
3	1 (1%)	1 (1%)	
Crossover	0	1 (1%)	0.50§
Protection device used	10 (9.6%)	9 (8.8%)	0.84‡

*t test; †Mann-Whitney U test; ‡chi-square test; §Fisher exact test.
LAD = left anterior descending coronary artery; RCA = right coronary artery; RCX = right circumflex artery; TIMI = Thrombolysis In Myocardial Infarction.

implantation and one patient on day 2 due to pulmonary bleeding related to glycoprotein IIb/IIIa receptor blockade).

Angiographic outcome. In 82% of the 206 patients (n = 168), where a timely follow-up angiography (181 ± 39 days after stent implantation) was available, baseline and postintervention quantitative measurements were comparable between the Flex and Stentgraft groups (Table 4). At follow-up, there were no statistically significant differences in minimal luminal diameter or percent stenosis between the groups. With respect to the primary end point restenosis rate at six months, there was also no significant difference between the Flex (20%) and Stentgraft groups (29%) (p = 0.15). Angiographic pattern of restenosis differed between the groups; excluding late occlusions, minimal luminal diameter was more frequently within the medial part of the stent body (vs. the edges) in the Flex group (7 of 11) compared with the Stentgraft group (1 of 11; p = 0.024, Fisher exact test).

In patients with angiographically documented absence of restenosis at 6 months, subsequent target vessel revascularization during the clinical follow-up period (median, 14 months) was infrequently necessary in 3 patients (1 Stentgraft, 2 Flex) by percutaneous intervention and 2 patients (Stentgraft) by bypass surgery.

There was a tendency toward a higher occlusion status at follow-up in the Stentgraft group versus the Flex group (n = 13 vs. 6) (Table 4). However, this difference did not reach statistical significance by univariate as well as multivariate analysis (Table 5). One patient in the Stentgraft group suffered subacute stent thrombosis and MI two days after the procedure (Stentgraft) without subsequent intervention, and one patient in the Flex group experienced subacute stent thrombosis undergoing successful reintervention without MI. However, both patients demonstrated late occlusion at six months angiography. Two additional patients experienced CK elevation in association with occlusion of the study vessel of 117 U/l 121 days (Flex), respectively 250 U/l 125 days (Stentgraft), after stent implantation, and re-PTCA was performed. Interestingly, in none of the other 16 patients with late occlusion seen by angiography >150 days after stent implantation was an MI documented. In these patients, target vessel revascularization was performed in four (Stentgraft), respectively five (Flex), patients. One patient with documented late occlusion subsequently died during clinical follow-up from cardiovascular cause (Flex) and one patient died from noncardiovascular cause (Stentgraft).

In five patients (three Stentgraft, two Flex), only a premature angiogram was obtained demonstrating no reste-

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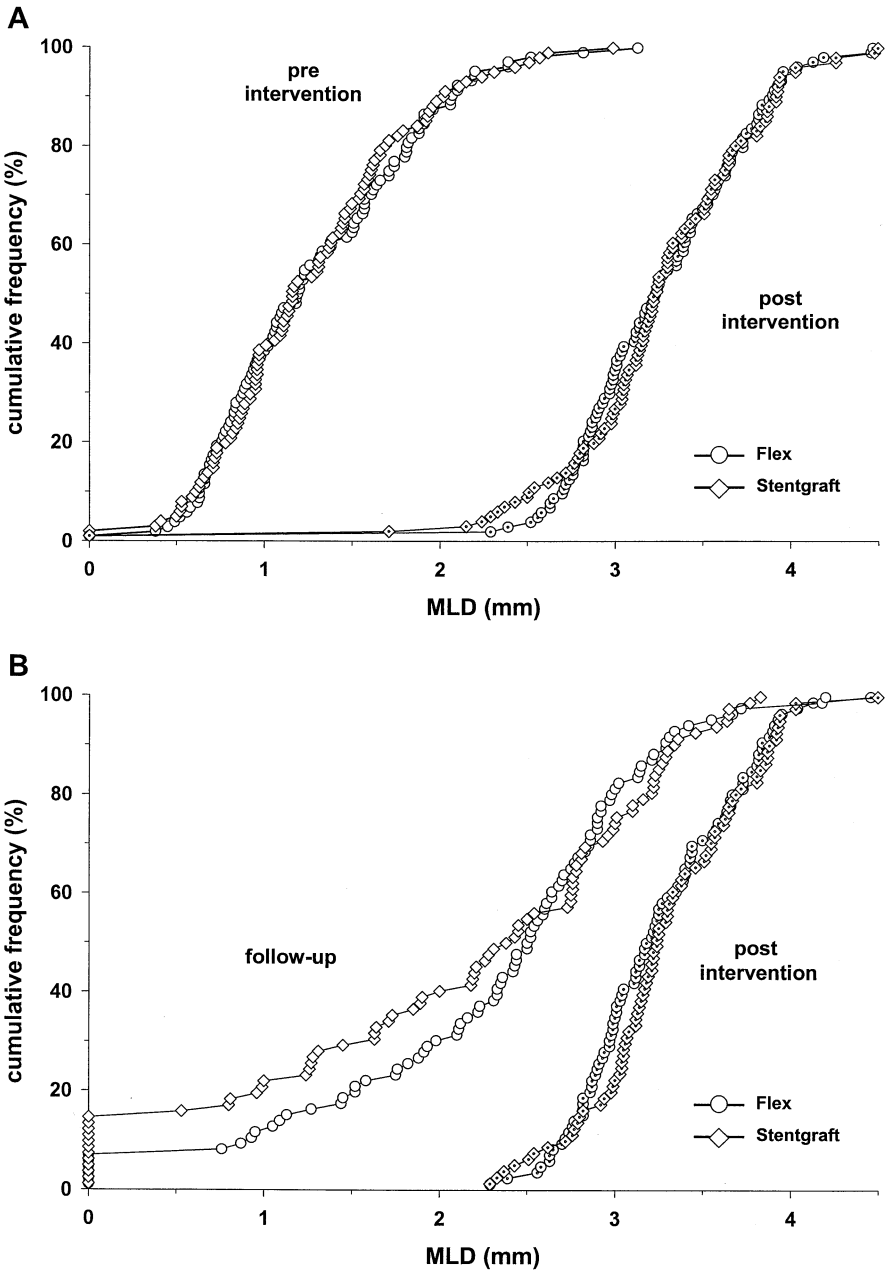

Figure 2. Cumulative distribution of minimal luminal diameter (MLD) assessed by quantitative coronary angiography. **(A)** Patients intended to treat: MLD before intervention and after intervention. **(B)** Patients undergoing follow-up angiography: MLD after intervention and at follow-up. **Diamond** = Stentgraft; **circle** = Flex; **dotted** = after intervention.

nosis. There were no deaths, MIs, or target vessel revascularizations at follow-up in these patients.

Clinical outcome. There were no statistically significant differences in individual or combined clinical events at 30 days or 6 months (Table 6).

Long-term clinical follow-up was obtained after a mean of 14 ± 2.1 months in the Flex group and 14 ± 2.8 months in the Stentgraft group. There was no difference in the secondary end point of cumulative event rate (death, MI, or target lesion revascularization) between the Flex and Stentgraft group by chi-square test (Table 6) or Kaplan-Meier analysis (Fig. 3A). In addition, there was no significant difference with respect to the components of the end points between the two groups (Table 6, Figs. 3B and 3C). The cause of death in the Flex versus Stentgraft group was cardiovascular death in four versus five patients with sudden death occurring in three out of four patients versus one patient out of five, respectively; noncardiovascular death in one versus two patients and unknown cause of death in one versus two patients, respectively. Because some patients with late occlusion did not undergo revascularization, a combined end point of death, MI, or angiographically documented restenosis was calculated. There was a tendency, albeit statistically not significant, toward a higher

Table 3. Periprocedural Events

	Flex (n = 104)	Stentgraft (n = 102)	p Value
Procedural dissection	16 (15%)	15 (15%)	0.89‡
Abrupt closure	7 (6.7%)	3 (2.9%)	0.33§
Distal embolization	5 (4.8%)	5 (4.9%)	0.98§
TIMI status postintervention			0.78‡
0	1 (1%)	1 (1%)	
1	1 (1%)	0	
2	6 (6%)	5 (5%)	
3	96 (93%)	96 (94%)	
Periprocedural death	1 (1%)	2 (2%)	0.62§
Periprocedural myocardial infarction	6 (5.6%)	5 (4.9%)	0.78‡
CK_{max} (U/I)	486 ± 210	398 ± 107	0.40*
Procedural success	93 (89%)	89 (87%)	0.63‡
Days postprocedure intensive care unit	0.35 ± 0.67	0.36 ± 0.73	0.93†

*t test; †Mann-Whitney U test; ‡chi-square test; §Fisher exact test.
CK = creatine kinase; TIMI = Thrombolysis In Myocardial Infarction.

event rate in the Stentgraft group (26% vs. 37%, p = 0.081, chi-square test).

DISCUSSION

Despite the fact that stents have improved the outcome of percutaneous intervention of obstructed vein grafts (2,3), prognosis of patients undergoing this procedure is still poor (4,12). Targets to improve intervention in saphenous vein grafts are to inhibit distal embolization of atherosclerotic debris (13) and to reduce restenosis rate, which is elevated compared with native vessels (2,4,14). Thus, it was intriguing to hypothesize that a stent covered with a membrane would seal the lumen and prevent protrusion of proliferating tissue and, thereby, reduce microembolization and restenosis rate. However, the present trial does not reveal a benefit of the PTFE-membrane-covered Jostent Stentgraft compared with the conventional stent used (Jostent Flex); restenosis rate, the primary end point, did not significantly differ between the Stentgraft (29%) and the conventional

Table 4. Quantitative Coronary Angiography of Patients With Angiographic Follow-Up

Characteristics	Flex (n = 86)	Stentgraft (n = 82)	p Value
Minimal lumen diameter (mm)			
Before	1.27 ± 0.59	1.26 ± 0.54	0.79†
After	3.25 ± 0.44	3.29 ± 0.45	0.53*
Follow-up	2.29 ± 0.96	2.10 ± 1.17	0.24†
Reference diameter (mm)			
Before	3.42 ± 0.59	3.32 ± 0.61	0.16†
After	3.50 ± 0.52	3.48 ± 0.59	0.71†
Follow-up	3.46 ± 0.50	3.31 ± 0.62	0.05†
Percent stenosis			
Before	64 ± 15	63 ± 14	0.48†
After	6.6 ± 9.0	4.5 ± 9.8	0.17*
Follow-up	33 ± 26	36 ± 34	0.81†
Acute gain (mm)	2.0 ± 0.57	2.0 ± 0.63	0.61†
Late loss (mm)	0.95 ± 0.97	1.17 ± 1.07	0.29†
Net gain (mm)	1.03 ± 0.96	0.87 ± 1.05	0.26†
Restenosis rate (>50% diameter stenosis)	17 (20%)	24 (29%)	0.15‡
Occlusion at follow-up	6 (7.0%)	13 (16%)	0.069‡

*t test; †Mann-Whitney U test; ‡chi-square test.

Table 5. Variables Associated With Late Occlusion at Follow-Up Angiography

	Univariate Analysis p Value	Multivariate Regression Analysis	
		Standardized Coefficient	p Value
Stent graft	0.069§	0.12	0.095
Diabetes mellitus	0.007‖	−0.18	0.011
Unstable angina	0.22‖		–
Low TIMI status before intervention	< 0.001§	−0.29	< 0.001
Intermittent vessel occlusion	0.032‖	0.16	0.021
Residual dissection	0.032‖	−0.12	0.10
Stent length	0.56‡		–
Percent stenosis after intervention	0.47†		–
Left ventricular ejection fraction*	0.30†		–
		R	0.46
Model summary		Adjusted R^2	0.19
		Significance (ANOVA)	p < 0.001

*Available in 99 patients; †t test; ‡Mann-Whitney U test; §chi square test; ‖Fisher exact test.
ANOVA = analysis of variance; TIMI = Thrombolysis In Myocardial Infarction.

Table 6. Occurrence of Clinical Events During Follow-Up

Characteristics	Flex (n = 104)	Stentgraft (n = 102)	p Value
30 days			
Death	1 (1%)	3 (2.9%)	0.37†
Myocardial infarction	6 (5.8%)	5 (4.9%)	0.78†
TLR	1 (1%)	0	0.99†
Cumulative death, MI, or TLR	7 (6.7%)	8 (7.8%)	0.76*
6 months			
Death	3 (2.9%)	7 (6.9%)	0.21†
MI	8 (7.7%)	8 (7.7%)	0.97*
TLR	13 (13%)	7 (6.9%)	0.17*
Cumulative death, MI, or TLR	22 (21%)	20 (20%)	0.78*
Up to 15 months			
Death	6 (5.8%)	9 (8.8%)	0.40*
MI	8 (7.7%)	10 (9.8%)	0.59*
Site of revascularization			
TLR	22 (21%)	17 (17%)	0.41*
TVR	25 (24%)	20 (20%)	0.44*
Nontarget vessel	10 (9.6%)	12 (12%)	0.62*
Revascularization (TVR or nontarget vessel)	34 (33%)	29 (28%)	0.51*
PTCA	33 (32%)	25 (25%)	0.25*
CABG	1 (1%)	5 (5%)	0.12†
Secondary end point: Cumulative death, MI, or TLR	32 (31%)	32 (31%)	0.93*

*Chi-square test; †Fisher exact test.
CABG = coronary artery bypass grafting; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; TLR = target lesion revascularization; TVR = target vessel revascularization.

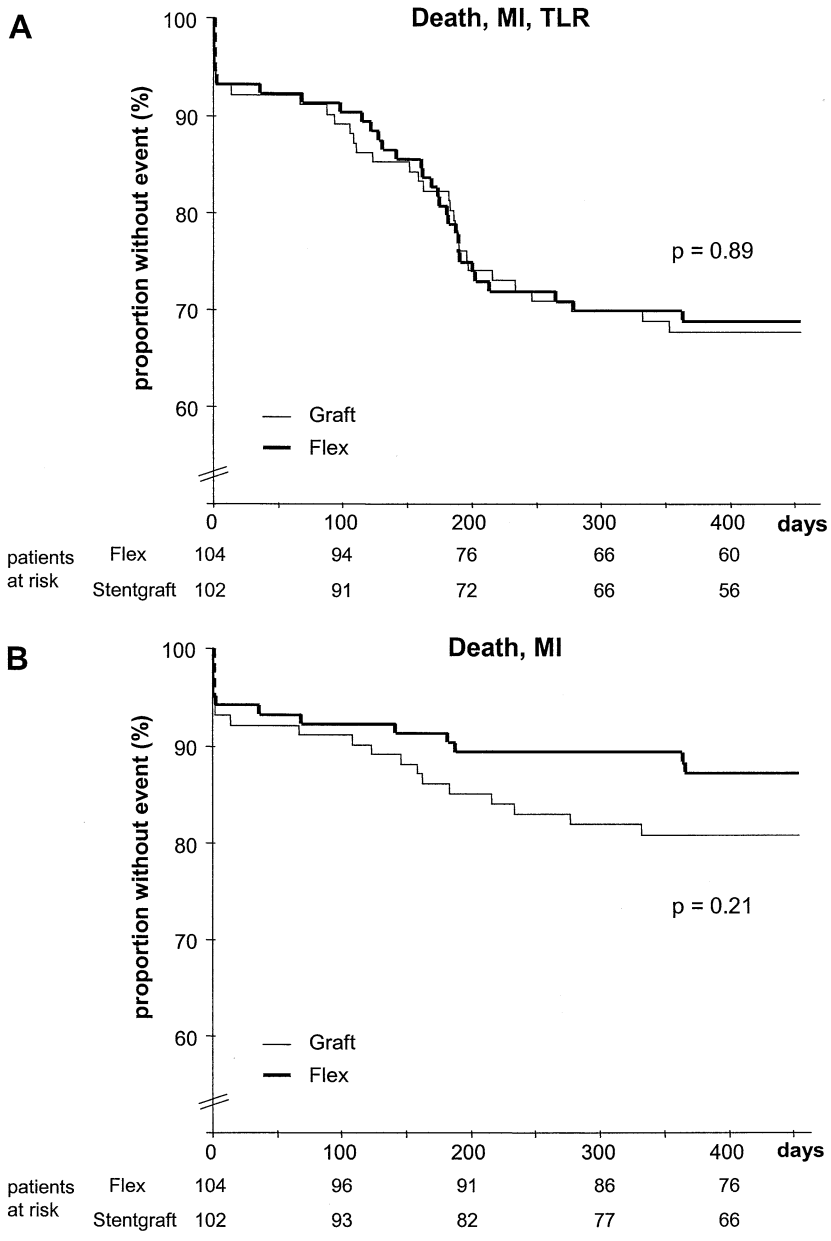

Figure 3. Kaplan-Meier analyses of cumulative event rates. **(A)** Cumulative event rate of secondary end point: death, myocardial infarction (MI), or target lesion revascularization (TLR). **(B)** Cumulative event rate: death or MI. *Continued on next page.*

stent group (20%). In addition, acute complications and long-term clinical event rate up to 15 months were comparable between the two groups.

Important to note is that the restenosis rate in both groups was lower in the present study than recently reported from vein graft stenting ranging from 34% to 43% (2,4,14). Patients in the conventional stent group had a most favorable angiographic outcome, making it unlikely to demonstrate a superiority of the Stentgraft. These favorable results might be related to patient selection, because the present study did not intend to treat stenosis at an ostial or distal anastomosis location as well as total occlusion, all known to be associated with a less favorable outcome (13,15), and reference vessel diameter was approximately 0.2 mm larger than in recent studies (2,14). In addition, acute angiographic success was advantageous in both groups of the present trial compared with the previous studies (2,14), with minimal luminal diameter after intervention being more than 0.4 mm larger and a residual percent stenosis being less, with 6.6% compared with 12% in previous studies (2,14).

The comparable results between the Stentgraft and the conventional stent were obtained despite the fact that baseline characteristics were unfavorable for the Stentgraft

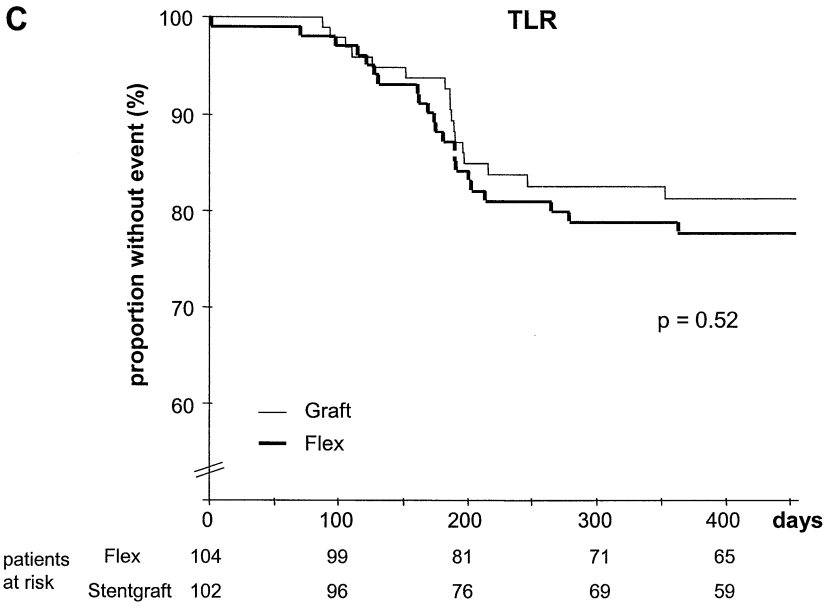

Figure 3 Continued. **(C)** Cumulative event rate: TLR.

group with a significantly higher rate of lesion calcification and patients with diabetes mellitus (33% vs. 19%). The latter is known to be a powerful predictor, not only for restenosis, but also for adverse acute and long-term clinical events in patients undergoing percutaneous intervention of obstructed vein grafts (14,16). Nevertheless, the outcome of the Stentgraft group was worse than the expectations resulting from a previous surveillance trial of 109 patients with 17% restenosis and 11% target lesion revascularization compared with 29% restenosis and 24% target vessel revascularization in the present study. Despite similar minimal lumen diameter after stent implantation, late loss was 0.4 mm higher in the present study compared with the registry. This phenomenon of discrepancy between the results of a registry and the subsequent randomized trial has also been made in previous studies assessing stent implantation in native vessels (18% vs. 28% restenosis in Stent Restenosis Study [STRESS]) (17,18) or saphenous vein grafts (22% vs. 37% restenosis in Saphenous Vein De Novo Trial [SAVED]) (2,19).

The rate of major adverse clinical events, which predominantly occurred during the first nine months, did not significantly differ between patients randomized to Stentgraft versus the conventional stent and were comparable to the stent group in the randomized SAVED trial reporting 7% death, 11% MI, and 17% target lesion revascularization up to 240 days after the procedure (2). However, a noticeable finding is that the rate of late occlusion was doubled in the Stentgraft group compared with the conventional stent group (13% vs. 6%), even though this difference did not reach statistical significance by univariate as well as multivariate analysis in the tested sample size. Late occlusion is a known problem associated with stenting of obstructed vein grafts reported to occur in 4% (14) to more than 10% (2) of the cases receiving a conventional stent and 9% in the recent registry of the Jostent Stentgraft (8). In most patients in the present study, late occlusion was documented beyond the three-month period, in which case therapy with ticlopidine or clopidogrel was intended by the protocol. Thus, one might speculate whether a postponed re-endothelialization or enhanced thrombogenicity of the PTFE membrane might predispose for late thrombotic occlusions. However, the clinical course of most documented late occlusions was surprisingly benign, with only few cases associated with an MI. Obviously, the present study cannot disclose whether a prolonged therapy with thienopyridines would have had an impact on late occlusions. However, the fact that late occlusions >150 days were not associated with MI might indicate that progressively proliferating restenosis, rather than acute thrombosis, might be the mechanism of late occlusion in these patients.

Study limitations. Although the study was prospective and randomized, patients as well as investigators were not blinded with respect to the treatment group, which might have influenced the results. Indeed, reluctance to revascularize a restenotic lesion after 6 months was 1 (occluded) restenosis out of 17 in the Flex group versus 11 out of 24 in the Stentgraft group. In the latter group, especially occluded vessels were not repeatedly revascularized (8 of 13 not treated), which might have obscured target lesion revascularization rate in favor of the Stentgraft group. However, the findings of the study are additionally based on the objective analysis of quantitative angiographic parameters using a standardized automatic edge detection system by a central core lab as well as hard end points such as death or MI, which are in line with the overall finding of the study.

The study was not powered to detect a difference in death or MI rates itself. In addition, a larger population might be needed to definitely disclose a potential impact of a PTFE-membrane-covered stent on the incidence of restenosis and

late occlusions. The results of two further studies ongoing in Italy (Randomized Evaluation of Polytetrafluoroethylene Covered Stent in Saphenous Vein Grafts [RECOVERS]) and the U.S. (BARRICADE) will probably add the desired information in conjunction with the present study.

The equivalence between the conventional stent and the Stentgraft cannot be transferred to other PTFE-membrane-covered stents. By design—having a PTFE-membrane fixed between two stainless steel stents—the Stentgraft in the present study is somewhat bulky, which is reflected by the fact that a higher balloon pressure was used compared with the conventional stent group in order to completely expand the stent. Future refinements of the Stentgraft design might be associated with a more favorable clinical outcome.

After completion of the inclusion into this trial, the results of the Saphenous Vein Graft Angioplasty Free of Emboli Randomized Trial (SAFER) (20) were published, demonstrating a reduction of major cardiovascular events by 42% with a protection device, which was used in less than 10% of the cases in the present study. However, there was no evidence that the Stentgraft substantially reduces the risk of atheromatous microembolism because the angiographically visible embolism, abrupt vessel closure, TIMI status after intervention, and the rate of postprocedural MIs were comparable between the two groups. Thus, it cannot be expected that the routine use of protection devices will uncover a difference between the two tested stent types. In addition, even though the effect of the glycoprotein IIb/IIIa inhibitor on microembolism in vein graft stenting is under debate (21,22), routine use of abciximab was mandatory in the present study.

Meanwhile, intracoronary brachytherapy has been proven to reduce restenosis rates and cardiovascular events by approximately 50% when treating an in-stent restenosis in an obstructed vein graft (23). It is not known whether this beneficial therapy might be used with the same success for treatment of restenosis of a PTFE-membrane-covered stent.

Furthermore, the double layer of PTFE may be disadvantageous for neointimal growth. Recent designs use a porous single membrane or provide a collagen-like matrix for endothelial cell growth (24). In addition, antiproliferative agents may be added to achieve better results in the future (25).

Conclusions. The present STING study does not indicate a superiority of stent grafts compared with conventional stents with respect to restenosis or clinical events, as it has been suspected by the previous retrospective data. Two additional findings were striking; first, restenosis rate in the conventional stent group was lower than expected from previous studies, making it unlikely to demonstrate a difference between the two stents. Second, there was a tendency—albeit statistically not significant—toward a higher rate of total occlusions at follow-up in the stent graft group compared with the conventional stent. However, before a final assessment of the role of membrane-covered stent grafts in the treatment of aortocoronary venous grafts can be made, final analysis of all ongoing studies should be awaited.

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APPENDIX

In addition to the authors, the following institutions and investigators participated in the STING trial:

Steering Committee: Ch. Hamm (chairman), A. M. Zeiher, J. Berger (statistics).

Safety Monitoring Board: B. Meier, H. J. Rupprecht.

Coronary Angiography Core Lab: A. M. Zeiher, V. Schächinger.

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