Treatment of Aortocoronary Vein Graft Lesions With Membrane-Covered Stents
A Multicenter Surveillance Trial

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Background—Stent implantation in lesions of degenerated aortocoronary vein grafts is associated with a high risk of periprocedural thrombus embolization and in-stent restenosis.

Methods and Results—In a multicenter study, we followed up 109 consecutive patients (mean age 66±8 years, 12% female) who received polytetrafluoroethylene (PTFE) membrane–covered stents for 125 de novo stenoses in vein grafts 11±5 years after bypass surgery. Stent deployment was successful in all but 1 patient; 1 patient suffered from subacute stent thrombosis. Six-month cardiac mortality was 7% (8 patients), 3 patients (3%) underwent repeat bypass surgery, and 9 patients (8%) required target-lesion PTCA. Repeat angiography revealed vessel occlusions in 9% and in-stent restenosis in 8% of patients by the end of follow-up.

Conclusions—Membrane-covered stents appear to be a safe and efficient treatment strategy associated with a low incidence of restenosis and target-vessel revascularization. Compared with previous studies, the investigated device is not associated with an increase in mortality or late vessel occlusions. (Circulation. 2000;102:2024-2027.)

Key Words: grafting • stents • thrombosis • restenosis • polytetrafluoroethylene

Coronary artery bypass surgery is the established treatment strategy in patients with multivessel coronary disease. Ten years after bypass surgery, however, half of the vein grafts have been found to be occluded or showing obstructive disease.1 Because the operative risk of consecutive bypass surgery is substantially increased, PTCA has gained increasing importance for the treatment of bypass graft lesions.2

PTCA of venous bypass grafts is associated with a high risk of distal thrombus embolization and peri-interventional myocardial infarction.3 Moreover, the long-term results of venous grafts after PTCA are still unsatisfactory, considering a restenosis rate >45%.4 Remarkably, coronary stents, despite their proven benefit in native arteries, did not substantially reduce the incidence of restenosis in vein grafts.5,5

The investigated stent is covered by an expandable polytetrafluoroethylene (PTFE) membrane (Figure 1), which was suggested to diminish peri-interventional thrombus embolization and long-term luminal renarrowing. We report here the first major cohort of patients who received this device for de novo lesions in aortocoronary vein grafts.

Patient Population
The study included 109 consecutive patients (age 66±8 years, 88% male) who underwent stent implantation in 3 centers in Germany; 14 patients were reported previously in a descriptive pilot study.6 Fifty-one patients were enrolled prospectively; the analysis of the remaining patients was performed in retrospect.

Major coronary risk factors were diabetes mellitus (n=30; 28%), hyperlipoproteinemia (n=87; 80%), hypertension (n=72; 66%), and current or recently stopped smoking (n=49; 45%). Seventy percent (n=76) had previous myocardial infarctions; repeat bypass surgery had been performed in 8 patients (7%). The patients presented with stable (n=76, 70%) as well as unstable (n=25, 23%) angina; 8 patients (7%) underwent stent implantation within primary PTCA. The left ventricular ejection fraction was reduced to 35% to 25% in 20 and <25% in 7 patients.

In all, 125 de novo lesions in venous bypass grafts were treated 11±5 years (range 1 to 21 years) after bypass surgery. Lesions were localized in vein grafts to the left anterior descending coronary artery (n=52), the circumflex artery (n=47), and the right coronary artery (n=26). The mean lesion length was 12±7 mm, ranging between 3 and 37 mm. In 21 lesions, thrombotic debris was visualized angiographically before angioplasty; 8 vessels were occluded.

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**Stent Implantation Procedure**

A total of 125 stents (Jomed Coronary Stent Graft, Sitomed) between 9 and 26 mm (mean 17±8 mm) in length were implanted. The stents were mounted on semicompliant balloons ranging between 2.5 and 5.0 mm in diameter (mean 3.6±0.5 mm) and were deployed with a mean inflation pressure of 16±3 atm (range 10 to 22 atm). Thirty-one percent of the study population received glycoprotein (GP) IIb/IIIa receptor antagonists peri-interventionally (abciximab, n=26; tirofiban, n=5). Postprocedural medication included aspirin 100 mg/d and ticlopidine 500 mg/d. Ticlopidine was stopped 1 month after the procedure in the first 25 patients; the remaining patients received either ticlopidine 500 mg/d or clopidogrel 75 mg/d for 10 weeks.

**QCA Analysis**

Angiograms were obtained in 2 orthogonal projections. Quantitative analyses were performed offline at a core laboratory as described elsewhere.\(^7\) In-stent restenosis was defined as a reduction of 50% of the luminal diameter within 5 mm proximal and distal to the stent. In-stent restenosis was categorized as focal if its length was 10 mm and diffuse if it was >10 mm.

**Definitions**

Procedural success was defined as residual stenosis <50% of the reference diameter. Q-wave myocardial infarction was defined by new pathological Q waves in ≥2 contiguous leads and/or elevation in creatine kinase (CK) or its MB isoenzyme to ≥3 times the upper limit of normal. The latter was 80 U/L in all institutions; an increase of the CK-MB >10% of the CK was considered pathological. Cardiac death was defined as death that was proven or suspected to be due to myocardial infarction, malignant arrhythmias, or congestive heart failure. Major adverse cardiac events were defined as death, acute myocardial infarction, bypass surgery, and target-lesion PTCA.

**Results**

**In-Hospital Follow-Up**

Stent placement was successful for all but 1 lesion; loss of the stent within the graft led to its expansion proximal to the lesion. A second patient suffered from subacute stent thrombosis 1 day after incomplete expansion of the stent; the vessel was recanalized successfully. In 21 patients (19%), thrombotic debris was visualized before angioplasty; thrombus embolization was observed in 4 patients (4%). TIMI flow decreased from 3 to 2 in 1 patient and improved in 28 patients, yielding TIMI flow 3 in 104 patients (95%) by the end of the procedure. CK values are available for 86% of the study population. CK elevations between 86 and 219 U/L (median 146 U/L, 6% to 15% CK-MB) were observed in 5 patients (5%). One patient suffered from myocardial infarction the day after the procedure as a result of peripheral vessel occlusion; repeat PTCA was required in 1 patient after dissection distal to the target lesion. One ischemic stroke was observed on day 1 after the intervention.

**Six-Month Follow-Up**

Clinical follow-up was obtained for all patients after a median of 5.5 months (range 6 to 47 weeks). Major adverse cardiac events are displayed in Table 1. Eight patients died of definite or suspected cardiac causes within a median of 98 days (range 8 to 161 days) after implantation of stents with a mean length of 16±7 mm: 3 patients suffered fatal myocardial infarctions; 2 of them were located in the target territory, with angiographically proven in-stent vessel occlusion in 1 patient on day 124 after the procedure. Three additional patients died suddenly, 1 with an ejection fraction of 17% and another after proven patency of the target vessel. Two patients died of unknown causes. Nonfatal myocardial infarctions unrelated to the target lesion were observed in 3 patients; 14 patients underwent non–target-lesion PTCA.

**Quantitative Coronary Angiography**

Follow-up angiograms were available for 64 patients (59%) and 75 lesions (60%). Quantitative angiographic measurements are summarized in Table 2; the cumulative distribution functions of the minimal luminal diameter before treatment, after stent deployment, and at follow-up are displayed in Figure 2. Five patients (8%) had in-stent restenoses, which were categorized as diffuse in 2 patients. Four of the 5 patients underwent repeat PTCA. In 6 patients (9%), follow-up angiography revealed vessel occlusions; 2 lesions were recanalized by enrollment. Five patients had not received GP IIb/IIIa receptor antagonists peri-interventionally, and 4 of the 6 patients received ticlopidine for 10 weeks after the intervention.

**Discussion**

We report the first large series of patients who received PTFE membrane–covered stents for de novo lesions in aortocoronary vein grafts. Compared with previous reports, stent implantation was associated with a low rate of periprocedural complications and in-stent restenosis and no increase in late vessel occlusions or mortality.
The in-hospital event rates for death and myocardial infarction have been reported to be between 6% and 17%. A rate of postinterventional myocardial infarctions, 1% and a 6% incidence of minor CK elevations in this trial demonstrate a marked reduction compared with the 16% incidence of procedure-related Q-wave and non–Q-wave myocardial infarctions after vein graft stenting reported recently,9 suggesting a major reduction of thrombotic embolization by the PTFE membrane. To entrap debris at the lesion site, low inflation pressures during predilatation and consecutive high-pressure expansion of the stent (>14 atm) were demonstrated to be most effective.

A 11% rate of target-lesion revascularization during follow-up including 3% of patients undergoing bypass surgery represents a major decline compared with the 17% and 7% incidences in target-lesion revascularization and bypass surgery in the SAVED trial.4 Furthermore, the 17% rate of in-stent restenosis and vessel occlusion reflects a substantial reduction compared with in-stent restenosis in vein grafts reported to exceed 35%.4,8,10

The 6 observed vessel occlusions have to be analyzed carefully: Insufficient stent expansion may have caused 1 subacute stent thrombosis. Second, endothelialization of the PTFE membrane is known to be critical, as described previously in animal models investigating PTFE membranes.11 Vessel occlusion is a common limitation of percutaneous interventions in vein grafts, however: Implantation of conventional stents is associated with graft occlusion >10%.4 Moreover, balloon and laser angioplasty are complicated by long-term vessel occlusions in 13% and 24%, respectively,12,13 whereas recanalization per se bears an increased risk for vessel occlusion, suggesting that late vessel occlusion after interventions in vein grafts is lesion site–related rather than device-related.

Thus, we question whether the 8% mortality within the first 6 months inevitably reflects late in-stent thrombosis. The study population a priori has to be considered at high risk for cardiac death: The large number of acute coronary syndromes treated, the significantly impaired left ventricular function in nearly one third of the patients, and the treatment of predominantly degenerated vein grafts all are independent predictors of cardiac mortality.14 Periinterventional ischemia, an additional independent predictor of late mortality,15 might be further reduced by the use of aspiration systems16 as well as by routine administration of GP IIb/IIIa receptor antagonists.

Conclusions
Although the study lacks a randomized design, these data strongly suggest membrane-covered stents to be a superior treatment strategy for lesions in aortocoronary venous bypass grafts.

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