[Original article]

Long-term follow-up after percutaneous coronary intervention with polytetrafluoroethylene-covered Symbiot™ stents compared to bare metal stents, with and without FilterWire™ embolic protection, in diseased saphenous vein grafts

The randomized STROMBOLI (Symbiot and FilterWire in the prevention of embolization during percutaneous treatment of coronary vein grafts) trial

Johan BENNETT¹, MD; Jo DENS², MD, PhD; Francis STAMMEN³, MD, PhD; Patrick COUSSEMENT⁴, MD; Luc JANSSENS⁵, MD; Marc CLAEYS⁶, MD, PhD; Mathias VROLIX², MD; Peter SINNAEVE¹, MD, PhD; Christophe DUBOIS¹, MD, PhD; Walter DESMET¹, MD, PhD

¹Department of Cardiovascular Diseases, University Hospitals Leuven, Leuven, Belgium; ²Department of Cardiology, Hospital Oost-Limburg, Genk, Belgium; ³Department of Cardiology, Heilig-Hart Hospital Roeselare-Menen, Belgium; ⁴Department of Cardiology, General Hospital Sint-Jan, Brugge, Belgium; ⁵Department of Cardiology, Imelda Hospital, Bonheiden, Belgium; ⁶Department of Cardiology, University Hospital Antwerpen, Antwerpen, Belgium.

Objectives The long-term clinical outcome of covered stents in the percutaneous treatment of diseased saphenous vein graft (SVG) has been disappointing. The single self-expanding polytetrafluoroethylene (PTFE)-covered Symbiot stent with a unique profile may present advantages that translate into superior long-term clinical outcomes. This study evaluated the safety, effectiveness and clinical outcome of the Symbiot™ covered stent system (Boston Scientific, Natick, Mass.) and FilterWire™ EX (Boston Scientific, Natick, Mass.) versus bare metal stents (BMS) in SVG intervention.

Methods and results Between January 2003 and August 2005, 90 patients with degenerative SVG lesions were prospectively randomized at 6 study sites to Symbiot implantation (n = 30), BMS with FilterWire as embolic protection device (EPD, n = 30), or BMS without EPD (control group, n = 30). The primary end point was reduction in peri-procedural cardiac enzyme rise. The major secondary end points were in-hospital, 6-month and long-term target vessel failure rates, defined as the cumulative of death, myocardial infarction and clinically driven target lesion revascularization. There was no significant reduction in median [IQR] post-procedural troponin-I rise in the Symbiot group compared to the FilterWire or the control group (0.08 [0-1.40] µg/l; 0.06 [0-0.28] µg/l; and 0.04 [0-0.31] µg/l, *P* = 0.58). At 7.4 ± 1.3 (mean ± SD) years, there were numerically less deaths in the Symbiot group, although this did not reach statistical significance (*P* = 0.20). There was no significant difference in TVF-free survival between the treatment groups (*P* = 0.98).

Conclusion This study failed to show a procedural or long-term clinical advantage for the Symbiot PTFE-covered stent in the treatment of degenerated SVG.

Keywords Covered stent – saphenous vein graft intervention – embolic protection device – percutaneous coronary intervention.

Address for correspondence:

Johan Bennett, MD, Department of Cardiovascular Diseases, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium.
E-mail: johan.bennett@uzleuven.be

Received 18 October 2012; accepted for publication 7 November 2012.

INTRODUCTION

Aortocoronary saphenous vein grafts (SVG) are marked by general attrition and accelerated atherosclerosis, with a failure rate of 2% per annum between 1 and 6 years after surgery, followed by 5% from 6-10 years. At 10 years, only 35-45% of the SVG are patent¹⁻³. Percutaneous coronary intervention (PCI) in SVG remains one of the most challenging subsets of all percutaneous interventions due to higher rates of death, peri-proce-

dural myocardial infarction (MI), and an increased incidence of clinical and angiographic restenosis in comparison to native vessel PCI⁴⁻⁷. Several studies have shown that the routine use of embolic protection devices (EPD) improves the peri-procedural safety of PCI in SVG by reducing the amount of atherothrombotic material embolized and therefore, the severity of distal microvascular occlusion⁸. Whether the use of drug-eluting stents (DES) in SVG provides improved clinical outcomes compared with bare metal stents (BMS) remains controversial. The recently published results of the long-term follow-up of the SOS (Stenting of Saphenous Vein Grafts) trial suggest that the use of DES in PCI of SVG is associated with significantly better clinical outcomes when compared to BMS⁹. There remains a need to further investigate both the short- and long-term clinical outcomes after DES in SVG and several large trials, including the ISAR-CABG, BASKETSAVAGE and DIVA trials, are ongoing.

About 8-10 years ago, there was considerable interest in the potential use of membrane-covered stents in SVG intervention as there was a proposed benefit of trapping the friable degenerated plaque against the graft wall, thereby reducing the probability of distal embolization and hence reducing the incidence of peri-procedural MI. A further rationale for the use of covered stents in SVG was an expected reduction in the degree of neointimal proliferation and subsequent in-stent restenosis by serving as a barrier preventing smooth muscle cell proliferation and migration¹⁰⁻¹². Several polytetrafluoroethylene (PTFE)-covered stents were developed and investigated. The two main PTFE-covered stents are the JOSTENT coronary stent graft (Jomed GmbH, Ransgendingen, Germany) and the SymbiotTM Covered Stent System (Boston Scientific Corporation, Natick, MA).

In two large, randomized controlled trials, STING and RECOVERS, the Jostent failed to reduce distal embolization and peri-procedural major adverse cardiac events^{13,14}. Moreover, the use of the Jostent in SVG PCI was associated with an increased risk of non-Q-wave MI compared to BMS¹⁴ and, in the recently published BARRICADE study, resulted in inferior long-term clinical outcomes compared with BMS, with a significantly higher rate of target vessel failure (TVF)¹⁵. The SymbiotTM covered stent system, a single self-expanding, nitinol, multi-segmented stent encased within a thin (13 µm), porous, polytetrafluoroethylene (PTFE) polymer membrane was designed to achieve a lower profile, thereby enhancing deliverability and reducing embolization while crossing the lesion. Despite the favourable profile of the Symbiot stent, the results of the large 400-patient randomized, controlled Symbiot III trial showed that the Symbiot stent failed to reduce the rate of peri-procedural MACE, including non-Q-wave MI when compared to

a conventional BMS during SVG PCI¹⁶. Furthermore, the Symbiot stent failed to significantly reduce the rates of in-stent binary restenosis (29.1% Symbiot, 21.9% BMS, $P=0.17$) at 8 months post PCI and actually resulted in greater rates of proximal stent edge restenosis (9.0% Symbiot, 1.8% BMS, $P=0.02$). The long-term (> 8 months) performance of the Symbiot stent has not been previously evaluated, but remains of interest as the concept of a unique, self-expanding multi-segmented stent encased within a porous PTFE-polymer membrane, designed to maintain the viability of the adjacent tissues, is attractive.

METHODS

The Stromboli study is a randomized, controlled, multicentre, prospective trial designed to evaluate the safety, efficacy and clinical outcome of the SymbiotTM Covered Stent System as compared to a conventional BMS (Express II, Boston Scientific), with or without a FilterwireTM Distal Protection Device (Boston Scientific, Natick, MA) for the treatment of diseased coronary vein grafts. The local ethics committees in the involved study sites approved the study design and all enrolled patients provided written informed consent before the index procedure.

The trial was single-blinded in that the patients and outcome assessors were blinded, but the interventional cardiologists and treating physicians were not. The study was performed at 6 different clinical sites in Belgium: the UZ Leuven, Leuven (coordinating site); Heilig-Hartziekenhuis, Roeselare-Menen; Algemeen Ziekenhuis Sint-Jan, Brugge; Imeldaziekenhuis, Bonheiden; Universitair Ziekenhuis Antwerpen; Ziekenhuis Oost-Limburg, Genk.

Patients. The inclusion criteria for the study were: (1) age ≥ 21 years; (2) clinical evidence of ischaemia or a positive functional test; (3) one or two 50% to 99% de novo or re-stenotic lesions in a SVG with reference diameter ≥ 3.5 mm and ≤ 5.5 mm by visual estimation; (4) target lesion(s) involving less than half of the entire graft length or ≤ 50 mm; (5) ability to position a Filter-Wire at least 15 mm distally to target lesion site, in a non-bended segment; (6) Thrombolysis In Myocardial Infarction flow grade ≥ 2 ; (7) negative pregnancy test in women with child-bearing potential. All patients had to provide informed, written consent and agree to the follow-up procedures which consisted of follow-up MACE evaluations (by telephone contact) at 1 month, 6 months and at long term (5-7 years). Exclusion criteria were: (1) contraindications or allergy to aspirin, heparin, clopidogrel, nitinol, stainless steel or other stent materials; (2) left ventricular ejection fraction $< 30\%$;

(4) MI within 24 hours before procedure or any creatine kinase or troponin ≥ 2 times normal at the time of treatment; (5) patients requiring PCI in > 1 vessel during the index hospitalization; (6) target lesion < 1.5 cm from distal anastomosis or in an arterial conduit; (7) previous cerebrovascular accident within the past 2 months; (8) inability to tolerate heparin administration during the procedure sufficient to maintain an activated clotting time ≥ 200 seconds; (9) current participation in another investigational drug or device trial.

Protocol. After eligible patients provided written consent, they were randomized in a 1:1:1 ratio to treatment with Symbiot stent, BMS with FilterWire, or conventional unprotected BMS using sealed envelopes.

The Symbiot stent was available in 2 diameters (4.0 and 5.0 mm) and three lengths (20, 31 and 45 mm) for use in vessels ranging from 3.5 to 5.5 in diameter. A FilterWireTM EX distal protection device was used in the FilterWire group. If there was difficulty in passing the target lesion with the FilterWire, the use of a “buddy” guidewire and, if necessary, low-pressure balloon predilatation was permitted. Balloon dilatation before stent placement was not required, with direct stenting being recommended. Post-dilatation was performed in all Symbiot patients as recommended by the manufacturer, and according to operator preference in the other groups. If a second stent was required for a clinically relevant edge dissection or suboptimal result, a stent of the assigned type was used. An EPD was not used in the Symbiot or control group. The total creatin kinase (CK), myocardial band isoenzyme (CK-MB) and troponin I were measured at baseline, and at 6–8 hours, 12–16 hours and 18–24 hours post procedure. If any enzyme elevation was present, repeated measurements were taken every 8 hours until a decline was noted. An electrocardiogram was obtained at baseline, immediately post-procedure, at discharge and with any suspicious ischaemic episode.

Study treatment. Before intervention, all patients were treated with oral aspirin (325 mg). Patients who had not been on chronic therapy with clopidogrel or ticlopidine received a loading dose of ticlopidine (500 mg) or clopidogrel (300 mg) before or, at the latest, immediately after the procedure. Anticoagulation during PCI was achieved with a heparin loading dose of 70 U/kg aiming for an activated clotting time (ACT) of ≥ 200 seconds, with repeated ACT measurements taken every 30 minutes during the procedure. Heparin was discontinued immediately after the procedure. The use of the intravenous glycoprotein IIb/IIIa inhibitor abciximab (bolus and infusion over 12 hours) was highly recommended but left at the discretion of the operator. Post PCI, all patients received ≥ 160 mg aspirin daily indefinitely and ticlopidine (250 mg) or clopidogrel (75 mg) for at least 1 month.

Quantitative coronary angiography. Quantitative coronary analysis was performed at the Angiographic Core Laboratory in Leuven by experienced assessors blinded to the patient’s identity, treatment group, type of stent used and clinical outcome. The minimal lumen diameter (MLD) and nearest normal reference vessel diameter (RVD) were measured (in mm) by using the guiding catheter as a scaling factor and were calculated as the average from two orthogonal views and the average of normal segments proximal and distal to target lesions, respectively. Percent diameter stenosis was calculated as $100 \times (1 - (\text{MLD}/\text{RVD}))$. Acute gain was defined as the post-procedure MLD minus the pre-procedure MLD.

End points and definitions. The primary end point was a reduction of $\geq 50\%$ in maximal release of troponin-I during the first 24 hours after treatment in the protection (Symbiot or FilterWire) group versus the control (BMS only) group. The secondary end points were changes in Thrombolysis in Myocardial Infarction (TIMI) flow grade from before to after the procedure, incidence of “no reflow” (a reduction of ≥ 1 TIMI flow grade to TIMI grade 2 without angiographic evidence of mechanical vessel obstruction), technical device success (defined as successful delivery and deployment of the device to target site and intact device retrieval), and major adverse cardiac events (MACE, defined in this study as TVF, a composite end point of all-cause death, Q-wave or non-Q-wave MI, or target lesion revascularization (TLR)) at hospital discharge, 1 month, 6 months and at long-term follow-up.

Non-Q-wave MI was defined as elevation of post-procedure CK-MB fraction $\geq 3 \times$ the upper limit of normal in the absence of pathological Q waves. A Q-wave MI was defined as the development of new, pathological Q waves in 2 or more contiguous leads with post-procedure CK-MB levels elevated above normal. TLR was considered as any clinically driven PCI or bypass surgery performed on the target lesion after documentation of recurrent angina and/or evidence of myocardial ischaemia by stress testing. Lesion success was defined as attainment of $< 30\%$ residual stenosis of the target lesion, by angiographic core lab QCA determination, using the assigned device or any percutaneous method. Procedural success was defined as the successful implantation of the study device, achievement of $< 30\%$ residual in-stent stenosis by angiographic core lab QCA determination, and freedom from in-hospital TVF, or in-hospital major bleeding event (defined as any intracranial bleeding, cardiac tamponade, bleeding events associated with either a decrease in haemoglobin ≥ 5.0 g/dl, transfusion or surgical repair).

Stent thrombosis was defined as composite thirty-day ischaemic end point including death, Q-wave MI, or

sub-abrupt closure requiring revascularization. After successful stent deployment, stent thrombosis was defined as angiographic thrombus within the stented segment at the time of the clinically driven angiographic restudy for documented ischaemia, representing abrupt or sub-abrupt closure. Any death not attributed to a non-cardiac cause in the first 30 days, or any Q-wave MI in the territory of the stented vessel in the first 30 days was considered a surrogate for stent thrombosis.

Statistical analysis. This study was a pilot evaluation of the SYMBIOT stent. At the time the study was conceived, no data regarding biomarker levels after SYMBIOT implantation in SVG was available. For this reason, no definite sample size could be formally calculated to establish a powered analysis to compare the different devices studied. We felt that an initial evaluation performed in 90 SVGs could be adequate to provide valuable information to be used to plan future studies. Continuous data are presented as means $\pm$ standard deviation or medians [interquartile range] as appropriate, and compared by analysis of variance. Categorical data are summarized as frequencies and compared by the chi-square test. Adverse event analyses were carried out with time-to-event data, were

compared with the log-rank test and were displayed with Kaplan-Meier methodology. All data are presented in the intent-to-treat population, consisting of all patients randomized, regardless of which treatment the patient actually received. A *P* value of ≤ 0.05 was considered statistically significant. Statistical analyses were performed by SPSS (version 20, SPSS Inc. Chicago, Illinois).

RESULTS

Patient and lesion characteristics

Between January 2003 and August 2005, 90 patients were enrolled at 6 clinical sites and were randomized to the Symbiot group (*n* = 30), FilterWire group (*n* = 30), or conventional BMS group (*n* = 30). As shown in table 1, the treatment groups were well matched for baseline characteristics. Overall, 88% of patients were male, and 21% had diabetes. The average age of the target SVG was 13.3 ± 5.9 years.

Baseline lesion characteristics (table 1) and angiographic measures (table 2) were similar between groups. The mean lesion length was 13.2 ± 8.3 mm, with a mean

Table 1 Baseline characteristics

	Symbiot group (<i>n</i> = 30)	FilterWire group (<i>n</i> = 30)	Control group (<i>n</i> = 30)	<i>p</i> value
Patient characteristics				
Age (yrs)	70 $\pm$ 7	69 $\pm$ 8	71 $\pm$ 8	0.74
Male	26 (87)	27 (90)	26 (87)	0.90
Previous myocardial infarction	16 (53)	9 (30)	14 (47)	0.17
Peripheral vascular disease	6 (20)	8 (27)	6 (20)	0.77
Diabetes mellitus	6 (20)	7 (23)	6 (20)	0.94
Dyslipidaemia*	24 (80)	19 (63)	18 (60)	0.21
Hypertension	17 (57)	18 (60)	18 (60)	0.96
Current or ex-smoker	20 (67)	15 (50)	19 (63)	0.38
Familial premature CAD	9 (30)	13 (43)	15 (50)	0.28
Age of graft (yrs)	13.4 $\pm$ 5.2	13.3 $\pm$ 6.9	13.5 $\pm$ 6.2	0.98
Medication				
Beta blocker	24 (80)	20 (67)	23 (77)	0.47
Aspirin	18 (60)	17 (57)	18 (60)	0.96
Statin	19 (63)	16 (53)	17 (57)	0.73
Lesion characteristics				
Number of lesions	31	30	31	
Target graft distribution				
LAD	3 (10)	5 (17)	2 (6)	0.43
Circumflex	17 (55)	12 (40)	15 (48)	0.51
RCA	9 (29)	13 (43)	12 (39)	0.50
Ramus	1 (3)	-	-	0.37
Sequential	-	-	1 (3)	0.37
Target vessel diameter (mm)	4.0 $\pm$ 0.4	4.0 $\pm$ 1.8	4.8 $\pm$ 5.6	0.59
Lesion length (mm)	15.0 $\pm$ 9.8	12.9 $\pm$ 9.0	11.4 $\pm$ 6.2	0.32
Lesion stenosis (%)	71.6 $\pm$ 14.9	69.4 $\pm$ 14.6	69.5 $\pm$ 14.6	0.52

Values are mean $\pm$ SD or *n* (%), *total cholesterol ≥ 250 mg/dl or LDL ≥ 160 mg/dl, or treated dyslipidaemia.

Table 2 Quantitative coronary angiography

	Symbiot group (n = 31)	FilterWire group (n = 30)	Control group (n = 31)	p value
Minimal lumen diameter (mm)				
Before	1.03 ± 0.63	1.09 ± 0.64	1.03 ± 0.51	0.91
After	3.42 ± 0.73	3.33 ± 0.75	3.32 ± 0.66	0.84
Reference diameter (mm)				
Before	3.48 ± 0.65	3.45 ± 0.60	3.35 ± 0.55	0.68
After	3.56 ± 0.57	3.44 ± 0.58	3.42 ± 0.58	0.60
Percent stenosis (%)				
Before	71.6 ± 14.9	69.4 ± 14.6	69.5 ± 14.6	0.83
After	7.1 ± 6.6	9.6 ± 9.6	7.7 ± 9.6	0.52
Acute gain (mm)	2.39 ± 0.76	2.24 ± 0.58	2.29 ± 0.53	0.65

Values are mean ± SD.

Table 3 Procedural characteristics

	Symbiot group (n = 31)	FilterWire group (n = 30)	Control group (n = 31)	p value
Glycoprotein IIb/IIIa inhibitor	24 (77)	27 (90)	23 (74)	0.26
Pre-dilatation	11 (35)	9 (30)	12 (39)	0.77
Device success	30 (97)	27 (90)	31 (100)	0.15
Embololic material capture	-	9 (30)	-	
No reflow	1 (3)	1 (3)	3 (10)	0.44
Lesion success	31 (100)	30 (100)	31 (100)	1.00
Procedure success	26 (84)	26 (87)	26 (84)	0.94
Total No. of stents per lesion	1.2 ± 0.5	1.3 ± 0.6	1.1 ± 0.3	0.39
Total stent length (mm)	32.7 ± 17.6	24.8 ± 13.0	19.8 ± 6.3	0.004
Stent diameter (mm)	4.1 ± 0.3	3.8 ± 0.7	3.7 ± 0.5	0.04
Maximum inflation pressure	11.8 ± 5.8	14.6 ± 2.2	14.3 ± 2.8	0.62
Post-dilatation	28 (90)	6 (20)	3 (10)	< 0.001
Mean pressure (atm)	13.5 ± 3.9	16.0 ± 3.3	21.0 ± 4.2	0.005
Peri-procedural MI *	5 (16)	3 (10)	5 (16)	0.70
Non-Q-wave MI	5 (16)	3 (10)	3 (10)	0.66
Q wave MI	0 (0)	0 (0)	2 (7)	0.13
Median CK-MB rise (µg/l)	0.9	0.5	0.3	0.50
Interquartile range (µg/l)	[0-4.9]	[0-2.9]	[0-1.1]	
Median troponin I rise (µg/l)	0.08	0.06	0.04	0.58
Interquartile range (µg/l)	[0-1.40]	[0-0.28]	[0-0.31]	

Values are mean ± SD or n (%), *defined as elevated CK-MB fraction ≥ 3 X the upper limit of normal.

vessel reference diameter of 4.3 ± 3.4 mm. The lesions were most commonly present in grafts to the circumflex (48%) and RCA (37%), and were located in the proximal section of the graft in 97% of cases.

Procedural characteristics (table 3)

The procedural success rate was comparable between groups (Symbiot 84%, FilterWire 87%, and control 84%, $P=0.94$). The FilterWire could not be correctly positioned in 3 patients and therefore PCI was performed without EPD, whilst in the Symbiot group there was failure to deliver 1 Symbiot stent in the target lesion and

a BMS was deployed instead. Lesion success was 100% in all groups. Angiographic results, including post-PCI residual stenosis and acute gain were similar between the groups (table 2). The protocol required post-dilatation when using the Symbiot stent, and therefore a significantly larger number of patients had post-dilatation in the Symbiot group (90% versus 20% in the FilterWire group and 10% in the control group, $P<0.001$), although at significantly lower inflation pressures ($P=0.005$). The incidence of “no reflow” was low throughout the treatment groups. There was no significant difference in the incidence of peri-procedural MI ($P=0.70$). There was a non-significant trend to higher post-PCI median

Fig. 1 Kaplan-Meier analyses of cumulative event rates.

(A) Estimates for survival by study group, (B) estimates for survival free of MI by study group, (C) estimates for survival free of TLR by study group, (D) estimates for survival free of TVF by study group. MI = myocardial infarction, TVF = target vessel failure, TLR = target lesion revascularization.

CK-MB (0.9 [0-4.9] $\mu\text{g/l}$ vs 0.5 [0-2.9] $\mu\text{g/l}$ vs 0.3 [0-1.1] $\mu\text{g/l}$, $P=0.50$) and median troponin-I (0.08 [0-1.40] $\mu\text{g/l}$ vs 0.06 [0-0.28] $\mu\text{g/l}$ vs 0.04 [0-0.31] $\mu\text{g/l}$, $P=0.58$) levels in the Symbiot group compared to the FilterWire and control groups. There were no major bleeding events post procedure.

Clinical outcomes

In-hospital MACE rates were similar between the groups (table 4). Two cases of stent thrombosis occurred

within 30 days, one in the Symbiot group on day 1 post procedure treated successfully with urgent PCI and another in the FilterWire group on day 22 post PCI, with the patient suffering a fatal cardiac arrest during renal dialysis therapy.

The clinical outcomes at 6 months post index PCI and at long term, mean 7.4 ± 1.3 years, are presented in table 4 and figure 1. Overall, 52 of 90 patients who participated in the STROMBOLI trial experienced at least 1 MACE during long-term follow-up: 17 of 30 Symbiot patients, 17 of 30 FilterWire patients, and 18 of

Table 4 Clinical events at longest available clinical follow-up

	Symbiot group (n = 30)	FilterWire group (n = 30)	Control group (n = 30)	p value
Long-term follow-up (years)	7.3 ± 1.6	7.6 ± 0.9	7.4 ± 1.6	0.68
Death, all cause				
In-hospital	1 (3)	1 (3)	0	0.60
6 months	3 (10)	2 (7)	1 (3)	0.58
Long-term	6 (20)	13 (43)	11 (37)	0.20
Myocardial infarction				
In-hospital	2 (7)	1 (3)	1 (3)	0.76
6 months	2 (7)	2 (7)	2 (7)	1.00
Long-term	7 (23)	5 (17)	7 (23)	0.69
Target lesion revascularization				
In-hospital	1 (3)	0	0	0.37
6 months	3 (10)	2 (7)	1 (3)	0.59
Long-term	8 (27)	5 (17)	10 (33)	0.32
Target vessel failure				
In-hospital	3 (10)	1 (3)	1 (3)	0.42
6 months	6 (20)	4 (13)	3 (10)	0.33
Long-term	17 (57)	17 (57)	18 (60)	0.98

Values are mean ± SD and event rates are Kaplan-Meier estimates (number of events (%)).

30 control patients. Six patients in the Symbiot group died during follow-up compared to 13 patients and 11 patients in the FilterWire and control groups, respectively. Although numerically less deaths occurred in the Symbiot group, this did not reach statistical significance ($P=0.20$) (figure 1). The cause of death in the Symbiot group was cardiac in 1 patient, non-cardiac in 3 patients and unknown in 2 patients. In the FilterWire group, death was cardiac in origin in 5 patients, non-cardiac in 3 patients, and unknown in 5 patients. Cause of death in the control group was cardiac in 3, non-cardiac in 2, and unknown in 6.

A total of 18 patients (7 in the Symbiot group, 5 in the FilterWire group and 6 in the control group) experienced an MI during follow-up. At 6 months and at long-term follow-up, there was no significant difference in the incidence of TLR between the treatment groups (table 3). At long-term follow-up, TVF had occurred in 57% of patients treated with the Symbiot, versus 57% of patients treated with the FilterWire and 60% of patients treated with BMS only ($P=0.98$).

DISCUSSION

The prognosis of degenerated SVG is extremely poor and the percutaneous treatment remains unsatisfactory, mainly due to the high risk of procedural complications and the poor long-term clinical outcomes following PCI. The employment of a more contemporary PCI approach

to SVG lesions, consisting of prolonged dual anti-platelet therapy and use of DES with adjunctive embolic protection, has improved the short- and long-term outcome considerably¹⁷. The targets to improve intervention in SVG are to reduce distal embolization of atherosclerotic debris and to reduce restenosis rates. As we have seen in this study, there does not appear to be a beneficial role for the covered stent in reaching either of these targets.

During active patient enrolment for the STROMBOLI study, the provisional results of other studies, mainly the large Symbiot III trial, were made known, and consequently there was a shift away from the use of covered stents in vein graft PCI. Nevertheless, long-term follow-up of the Symbiot PTFE-covered stent, currently no longer commercially available, has not been published, and this is only the second study, after the BARRICADE study, to systematically follow up patients after SVG intervention for more than 5 years.

Primary end point

The findings of this study confirm that the Symbiot covered stent does not reduce peri-procedural MI during SVG intervention when compared to a conventional BMS, hereby supporting the findings of several previous studies^{16,18}. The failure of the Symbiot stent to reduce peri-procedural MI is likely explained by the failure to reduce distal embolization, which appears to occur almost exclusively after the mandatory post-dilatation¹⁸.

Likewise, in the FilterWire group there was also no significant reduction in the rate of post-procedural cardiac enzyme rise, although there were numerically less peri-procedural MIs (3, 10%) compared to the Symbiot (5, 17%) and the control (5, 17%) groups ($P=0.70$).

Clinical outcomes

In terms of clinical follow-up, there was no significant difference in the incidence of TVF between the Symbiot and the BMS, with or without FilterWire. In the recently published 5-year follow-up of the BARRICADE study, use of the Jostent in SVG PCI resulted in significantly higher rates of TVF (68.3%) after 5 years of clinical follow-up compared to BMS (51.8%). The SymbiotTM covered stent system therefore appears to compare favourably to the Jostent coronary stent graft with TVF rates of 57% at 7 years, a finding that could be related to differences in design. The Jostent has a sandwich-like design and consists of a distensible PTFE membrane between two 316 L stainless steel slotted tube, balloon-expandable stents making it more bulky, which is reflected by the requirement for higher balloon pressures to completely expand the stent¹⁹. In contrast to the Jostent, the SymbiotTM covered stent system consists of a single self-expanding, nitinol, multi-segmented stent encased within a thin (13 μ m), porous, polytetrafluoroethylene (PTFE) polymer membrane designed to maintain cellular viability of the adjacent tissue. It is conceivable that the double stent layer in the Jostent may be disadvantageous for neo-intimal growth, thereby increasing the risk of restenosis.

In the Symbiot III trial, the 30-day and 8-month overall MACE rates and stent thrombosis rates were similar for the Symbiot and BMS groups suggesting that the Symbiot stent demonstrated an acceptable safety profile. At 8 months, however, there was a significantly higher rate of TLR in the Symbiot group over the BMS group (17.9% vs 10.4%, $P=0.04$), with the authors suggesting the greater stent-to-lesion length ratio for the Symbiot stent versus BMS as a possible explanation. We did not encounter similar higher rates of TLR with the Symbiot stent with 6-month TLR rates of 10% and 7%, in the Symbiot and BMS groups, respectively. At long-term follow-up, the TLR rates were 27%, 17% and 33% in the Symbiot, FilterWire and control groups, respectively, confirming that the Symbiot stent had no long-term clinical advantage, but also no inferior performance, compared to the conventional BMS.

Interestingly, during follow-up there were approximately half the number of deaths in the Symbiot Group (6) compared to the FilterWire (13) and control (11) groups. Although statistically not significant ($P=0.20$) and likely a result of small sample sizes, it is nevertheless an intriguing finding and again indicates that the Symbiot stent has a satisfactory safety profile.

In summary, the following are the findings of this randomized study: (1) the Symbiot PTFE-covered stent is safe and effective for the treatment of degenerated SVGs, (2) there are no short- or long-term clinical advantages in using the Symbiot stent compared to BMS, suggesting that PTFE covering does not prevent intimal hyperplasia, (3) when observing the long-term follow-up results of the Jostent in the BARRICADE study, the Symbiot appears to have a more favourable long-term clinical outcome.

Study limitations

The primary limitation of this study is its size and therefore no definite judgement can be made from this study on the effects of the Symbiot or FilterWire on clinical outcomes, for which the study was not powered to assess. The recruitment for this trial stopped approximately 7 years ago, and consequently the use of drug-eluting stents in SVG PCI was not investigated. The majority of SVG lesions in this study were short (all ≤ 25 mm long) and therefore long-term clinical outcomes may have been worse had severe diffuse or occluded SVG been included in the study. Finally, although the study was prospective and randomized, the investigators were not blinded to the treatment assignment of individual patients.

CONCLUSIONS

The randomized STROMBOLI study failed to show a procedural or long-term clinical advantage for the Symbiot PTFE-covered stent in the percutaneous treatment of degenerated SVG. It adds further weight to the evidence that there is no beneficial role for the routine use of covered stents in SVG PCI.

FUNDING: Boston Scientific Belgium supplied Symbiot stents and FilterWire devices only.

CONFLICT OF INTEREST: none declared.

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