Comparison of Plaque Sealing With Paclitaxel-Eluting Stents Versus Medical Therapy for the Treatment of Moderate Nonsignificant Saphenous Vein Graft Lesions

The Moderate VEIn Graft LEsion Stenting With the Taxus Stent and Intravascular Ultrasound (VELETI) Pilot Trial

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Background—The presence of moderate saphenous vein graft (SVG) lesions is a major predictor of cardiac events late after coronary artery bypass grafting. We determined the effects of sealing moderate nonsignificant SVG lesions with paclitaxel-eluting stents (PES) on the prevention of SVG atherosclerosis progression.

Methods and Results—Patients with at least 1 moderate SVG lesion (30% to 60% diameter stenosis) were randomized either to stenting the moderate SVG lesion with a PES (n=30, PES group) or to medical treatment alone (n=27, medical treatment group). Patients had an angiographic and intravascular ultrasound evaluation of the SVG at baseline and at 12-month follow-up. The primary end points were (1) the ultrasound SVG minimal lumen area at follow-up and (2) the changes in ultrasound atheroma volume in an angiographically nondiseased SVG segment. Mean time from coronary artery bypass grafting was 12.6 years, and mean low-density lipoprotein cholesterol level was 73±31 mg/dL. A total of 70 moderate SVG lesions (39±7% diameter stenosis) were evaluated. Significant disease progression occurred in the medical treatment group at the level of the moderate SVG lesion (decrease in minimal lumen area from 6.3±3.0 to 5.6±3.1 mm²; P<0.001), leading to a severe flow-limiting lesion or SVG occlusion in 22% of the patients compared with none in the PES group (P=0.014). In the PES group, mean minimal lumen area increased (P<0.001) from 6.1±2.2 to 8.6±2.9 mm² at follow-up (P=0.001 compared with the medical treatment group at 12 months). There were no cases of restenosis or stent thrombosis. No significant atherosclerosis progression occurred at the nonstented SVG segments. At 12-month follow-up, the cumulative incidence of major adverse cardiac events related to the target SVG was 19% in the medical treatment group versus 3% in the PES group (P=0.091).

Conclusions—Stenting moderate nonsignificant lesions in old SVGs with PES was associated with a lower rate of SVG disease progression and a trend toward a lower incidence of major adverse cardiac events at 1-year follow-up compared with medical treatment alone, despite very low low-density lipoprotein cholesterol values. This pilot study supports further investigation into the role of plaque sealing in SVGs.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT002289835.

(Key Words: atherosclerosis ◼ coronary disease ◼ stents)

Approximately 350,000 coronary artery bypass graft (CABG) surgeries are performed annually in the United States. In addition to at least 1 arterial graft conduit, 1 or several saphenous vein grafts (SVGs) are used in most CABG surgeries. However, atherosclerotic disease starting as early as within the first year after the operation and progressing very rapidly occurs in a high proportion of SVGs, leading to the occlusion of 1 or more SVGs in up to 50% of patients at 10-year follow-up. Importantly, SVG obstruction frequently leads to a high-risk acute coronary syndrome with a high mortality rate and limited therapeutic options. Several predictive factors of such an accelerated atherosclerotic...
process were identified in the Post Coronary Artery Bypass Graft Trial, in which SVG maximum percent stenosis was found to be the most important predictor of SVG disease progression. In addition, several retrospective studies have identified the presence of moderate “nonsignificant” SVG lesions as the most important predictor of cardiac events at midterm follow-up. The incidence of death or myocardial infarction (MI) in patients with old SVGs with moderate lesions was as high as 17% to 25% at 2- to 3-year follow-up, a much higher rate than that observed in patients with moderate lesions in native coronary arteries.

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The use of drug-eluting stents in intermediate coronary artery lesions has been associated with a very low event rate at midterm follow-up, but difficulties in identifying the vulnerable plaques and the extremely low rate of cardiac events associated with moderate stenoses in the native coronary tree compared with SVGs have limited the use of such a technique for the prevention of atherosclerosis progression and cardiac events in native coronary arteries. We formulated the hypothesis that moderate SVG lesions are at high risk of significant progression within 12 months and that stenting moderate SVG lesions would be associated with a very low restenosis rate and no deleterious effects on the atherosclerotic process of nonstented SVG segments. This pilot study sought to evaluate the effects of sealing moderate nonsignificant lesions with paclitaxel-eluting stents (PES) on the prevention of atherosclerosis progression in SVGs at 12-month follow-up.

Methods

Study Design and Patients

The Moderate VEin Graft LESion Stenting With the Taxus Stent and Intravascular Ultrasound (VELETI) trial was a randomized, prospective, pilot study assessing the effects of stenting moderate nonsignificant SVG lesions with paclitaxel-eluting stents (PES) on the prevention of atherosclerosis progression in SVGs at 12-month follow-up. Restenosis was defined as the presence of in-lesion "in-stent" and "in-lesion" segments (including the stented segment and the proximal SVG lesion). The same measurements were obtained after stent implantation in both baseline and follow-up studies. Plaque, lumen, and total vessel measures were obtained for each SVG target lesion: minimal lumen diameter, reference diameter, and percent diameter stenosis. The final IVUS evaluation was performed before any intervention in the target SVG.

IVUS Procedures

The IVUS procedures were performed with the use of 40-MHz ultrasound catheters (Galaxy ultrasound system, Boston Scientific Inc). At least 1 automated pullback of ≥80 mm at 0.5 mm/s including the target SVG lesion(s) was obtained at baseline and follow-up studies. The ultrasound transducer was advanced at least 4 cm distal to the target lesion or up to the distal SVG anastomosis. The pullback ended at least 4 cm proximal to the target lesion or at the proximal vein graft anastomosis. The pullback sequence was recorded on super-VHS videotape for offline analysis. In those cases randomized to target lesion stenting, an IVUS automated pullback was obtained before the procedure and after stent implantation.

Clinical, Angiographic, and IVUS Follow-Up

Patients had clinical visits at 1-, 6-, and 12-month follow-ups, and all of them were asked to return for repeat SVG angiography and IVUS 12 months after enrollment. In case of clinical indication for coronary and SVG angiography before the planned 12-month follow-up, the final IVUS evaluation was performed before any intervention in the target SVG.

Quantitative Coronary Angiography

Quantitative measurements of the target SVG lesions were performed offline with the use of the CMS-Medis quantitative coronary angiography system (Medis, Leiden, Netherlands). The following measures were obtained for each SVG target lesion: minimal lumen diameter (MLD), reference diameter, and percent diameter stenosis. The same measurements were obtained after stent implantation in “in-stent” and “in-lesion” segments (including the stented segment and 5-mm segment proximal and distal to the stent). In-lesion measurements were taken for comparison with the medical treatment group. For the PES group, angiographic late loss was calculated as the difference between MLD after stent implantation and at follow-up. Restenosis was defined as the presence of in-lesion ≥50% diameter stenosis at follow-up.

IVUS Measurements

IVUS images were analyzed by 2 experienced technicians blinded to clinical data and supervised by a cardiologist using the CMS-IVUS system (CMS-Medis). Although it was not possible to blind IVUS assessment to treatment groups, all assessments were performed in a random sequence. The lumen and external elastic membrane borders were traced manually on digitized cross sections at every 1 mm at both baseline and follow-up studies. Plaque, lumen, and total vessel volumes were computed for the entire length of the analyzed segments by multiplying the corresponding areas of each cross section by the distance between neighboring slices and then adding all the products. With the use of the distal or proximal SVG anastomosis as landmark, the exact same segment length was analyzed at baseline and at follow-up. For both medical treatment and PES groups, the lumen area and plaque burden (plaque area/vessel area × 100) were noted at the tomographic section showing the
smallest lumen area (minimal lumen area [MLA]). After stent implantation, MLA was measured in “in-stent” and “in-lesion” segments (including the stented segment and 5-mm segment proximal and distal to the stent) in both baseline and follow-up studies. In-lesion measurements were used for comparison with the medical treatment group. In both groups, the atheroma volume (absolute value and percentage) of a 30-mm SVG segment with no angiographic moderate lesion was measured at baseline and at follow-up. This SVG segment had to be >5 mm from the proximal or distal edge of the moderate SVG lesion.

End Points
The primary end points were (1) the ultrasound MLA at the SVG tomographic section showing the most severe stenosis at 12-month follow-up and (2) the change in ultrasound atheroma volume (absolute and percent values) between baseline and follow-up in an angiographically nondiseased 30-mm SVG segment starting >5 mm proximal or distal to the target SVG lesion. Secondary angiographic and clinical end points were as follows: (1) angiographic SVG target lesion MLD and percent diameter stenosis at 12-month follow-up; (2) the incidence of lesion(s) ≥50% stenosis at the target SVG as evaluated by angiography at 12-month follow-up; (3) the cumulative incidence of major adverse cardiac events (MACE) (death, MI, revascularization); and (4) the cumulative incidence of MACE related to the target SVG. Any death was considered cardiac unless proven otherwise. Cardiac enzyme determination was systematically performed at 6 to 8 hours and at 24 hours after intervention, and periprocedural MI was defined as an elevation of serum creatine kinase–MB isoenzyme that was ≥3 times the upper limit of normal. MI after the periprocedural period was defined as any typical rise above the upper range limit and fall of biochemical markers of myocardial necrosis with at least 1 of the following: cardiac symptoms, development of Q waves on the ECG, or ECG changes indicative of ischemia. Stent thrombosis occurrence was defined and classified according to the Academic Research Consortium criteria.18

Statistical Analysis and Sample Size Calculation
With consideration of the lack of IVUS data in moderately diseased SVGs, the sample size calculation was performed on the basis of previous angiographic data.19 On the basis of a reference diameter of 3.59 ± 0.85 mm and a MLA of 2.29 ± 0.66 mm at the level of the moderate SVG lesion at baseline examination, we estimated a reduction in MLD of 0.35 ± 0.50 mm, leading to a MLD of 1.94 ± 0.70 mm at follow-up in the medical treatment group. In the PES group, we estimated a MLD poststent implantation of 3.26 ± 0.85 mm and a late loss of 0.39 ± 0.50 mm, leading to a MLD of 2.87 ± 0.70 mm at follow-up. With the assumption of a dropout rate of 15%, a total of 27 patients per group would provide 90% power to detect such differences in MLD between baseline and follow-up studies in the medical treatment group and >90% power to detect such differences in MLD between medical treatment and PES groups at follow-up, with a 2-sided significance level of 5%. The study was not powered to detect significant differences between groups relative to clinical end points.

Qualitative variables were expressed as percentages and numerical variables as mean (SD) values or median values (25% to 75% interquartile range). In patients with >1 moderate SVG lesion, the mean value of the angiographic and IVUS measurements obtained in all moderate lesions was used for analysis. Comparison of numerical variables was performed with the Student t test or Wilcoxon rank sum test depending on variable distribution. The x2 (if ≥5 events) or Fisher exact test (if ≤5 events) was used to compare qualitative variables. An ANOVA for repeated measurements was performed to compare changes in angiographic and IVUS variables in the same group at different points of time and between groups. The results were also adjusted for differences in clopidogrel treatment between groups at follow-up. Because the study had 2 primary study end points, a Bonferroni correction was applied to the a posteriori results to adjust for multiple testing. To implement this correction, P values were reported as calculated by the statistical model, but the level of significance was adjusted to a more stringent threshold of 0.025. The data were analyzed with the use of the statistical package program SAS version 9.1.3 (SAS, Cary, NC).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results
From February 2006 to October 2007, a total of 270 patients undergoing coronary and SVG angiography by clinical indication were screened and provided informed consent for participation in the study. Of these, a total of 57 patients presented at least 1 moderate SVG lesion and constituted the final study population. These patients were then randomized to either SVG lesion stenting with a PES (n=30) or medical treatment alone (n=27) (Figure 1). The clinical characteristics of the study population are shown in Table 1. Mean time from CABG was 12.6 years, and most patients were on intensive statin therapy, with mean LDL cholesterol levels of 73 ± 31 mg/dL.

Angiography and IVUS Data
Follow-up SVG angiography was performed in 51 patients (90%), and all but 2 also had an IVUS study (Figure 1). In 1 patient the IVUS study was not performed because of the occlusion of the SVG at follow-up, and difficulties in advancing the ultrasound catheter through a stent located at the SVG ostial anastomosis precluded performing the IVUS study in another patient. The angiographic characteristics of the study population are shown in Table 2. A total of 70 SVG lesions were evaluated (1.2 lesions per patient), with a mean percent diameter stenosis of 39 ± 7%. In the medical treatment group, there was significant atherosclerosis progression at the target SVG lesion, leading to a lower MLD (from 2.20 ± 0.57 to 1.90 ± 0.84 mm; P=0.007) and a higher percent diameter stenosis (from 40 ± 7% to 47 ± 18%; P=0.028) at follow-up. Cumulative frequency distribution curves of angiographic MLA are shown in Figure 2. Five of the 23 patients (22%) with SVG angiography at follow-up had a significant SVG disease angiographic progression leading to a percent diameter stenosis >60% (4 patients; mean percent diameter stenosis=70±6%) or SVG occlusion (1 patient) (P=0.014 versus PES group) (Figure 3). In the PES group, a total of 40 stents were used to treat 40 lesions (1.0 stents per lesion). No cases of in-stent or in-lesion restenosis, new angiographic lesions, or target SVG occlusion were observed at follow-up angiography.

IVUS data are shown in Table 3. There were no differences between groups relative to SVG target lesion severity and atheroma burden in the angiographically “nondiseased” SVG segment. At follow-up, MLA in the tomographic section showing the most severe stenosis was lower in the medical treatment group compared with the PES group (5.6±3.1 versus 8.6±2.9 mm2; P=0.001). In the medical treatment group, a significant reduction in ultrasound MLA (−0.73±0.88 mm2; P<0.001) and an increase in plaque burden (5.5±7.8%; P=0.003) were observed between baseline and follow-up studies. Cumulative frequency curves of ultrasound MLA are shown in Figure 2. SVG atheroma burden measurements in the SVG segments with no moderate stenosis (“angiographically nondiseased segment”) showed a
lack of significant atherosclerosis progression between baseline and follow-up studies in both medical treatment and PES groups.

Cardiac Events
The incidence of MACE according to randomization group is shown in Table 4. The cumulative incidence of MACE related to the target SVG tended to be higher in the medical treatment group than in the PES group (19% versus 3%; \( P = 0.091 \)). The only event related to the target SVG in the PES group consisted of a postprocedural non-ST-segment elevation MI secondary to transient no-reflow after stent implantation. In the medical treatment group, 5 patients (19%) had clinically driven target SVG lesion revascularization due to the progression of the disease to a severe SVG lesion or SVG occlusion at follow-up (\( P = 0.019 \) versus PES group). Three of these 5 patients presented with an acute coronary syndrome (1 non–ST-segment elevation MI, 2 unstable angina), and 2 patients had stable angina with a positive noninvasive functional test.

Discussion
The results of this study showed that atherosclerotic disease progressed very rapidly in old and moderately diseased SVG despite optimal control of LDL cholesterol levels with lipid-lowering therapy. Such an accelerated atherosclerotic process was related mainly to SVG sites with higher plaque burden leading to moderate SVG stenosis, and in up to one fifth of these patients SVG disease progression led to a severe lesion or SVG occlusion within 12 months. Sealing nonsignificant SVG lesions with PES was associated with a higher ultrasound SVG MLA and did not induce any deleterious effect on SVG atherosclerosis of the nonstented segment as evaluated by IVUS at 12-month follow-up. In addition, SVG stenting with PES was associated with a very low rate (3%) of procedural complications, and no cases of restenosis or stent thrombosis were observed at 12-month
Table 1. Clinical Characteristics of the Study Population According to Randomization Group

<table>
<thead>
<tr>
<th>Treatment</th>
<th>PES (n=30)</th>
<th>PES (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>69±7</td>
<td>69±9</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>26 (96)</td>
<td>25 (83)</td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>4 (15)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>15 (56)</td>
<td>16 (53)</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>24 (89)</td>
<td>29 (97)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>10 (37)</td>
<td>10 (33)</td>
</tr>
<tr>
<td>Prior MI, n (%)</td>
<td>15 (56)</td>
<td>16 (53)</td>
</tr>
<tr>
<td>No. of SVGs</td>
<td>2.7</td>
<td>3.8</td>
</tr>
<tr>
<td>No. of grafts</td>
<td>3.8</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Clinical indication for angiography, n (%) | 0.32

Stable angina pectoris | 7 (25) | 5 (17) | 0.005
Acute coronary syndrome | 17 (63) | 24 (80) | 0.67
Unstable angina | 13 (76) | 19 (79) | 0.47
Non-STEMI | 3 (18) | 5 (21) | 0.22
STEMI | 1 (6) | 0 | 0.00
Other | 3 (11) | 1 (3) | 0.00

Time from CABG, y | 11±6 | 12±6 | 0.54

SVG angiographic progression was associated with a higher rate of death and MI at 3-year follow-up.

Table 2. Angiographic Data According to Randomization Group

<table>
<thead>
<tr>
<th>Treatment</th>
<th>PES (n=30)</th>
<th>PES (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of moderate SVG lesions</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td>No. of lesions per patient</td>
<td>1.1±0.3</td>
<td>1.3±0.6</td>
</tr>
</tbody>
</table>

Baseline

Reference diameter, mm | 3.65±0.91 | 3.53±0.51 | 0.56
MLD, mm | 2.20±0.57 | 2.15±0.37 | 0.70
Percent diameter stenosis | 40±7 | 39±6 | 0.70
Lesion length, mm | 9.24±3.29 | 9.95±4.23 | 0.49

SVG stenting

No. of stents (total) | ... | 40 | ...
No. of stents (per patient) | ... | 1.3±0.6 | ...
Stent diameter, mm | ... | 3.9±0.4 | ...
Stent length, mm | ... | 18.9±4.7 | ...
Maximal balloon pressure, mm | ... | 17.4±2.7 | ...
Predilatation, n (%) | ... | 5 (17) | ...

Follow-up

In stent

MLD, mm | 3.64±0.34 | ...
Percent diameter stenosis | 3.8±6 | ...

In lesion

MLD, mm | 3.32±0.44 | ...
Percent diameter stenosis | 13±8 | ...

Follow-up

In stent

MLD, mm | 1.90±0.84* | 3.09±0.43 | <0.0001
Percent diameter stenosis | 47±18† | 16±10 | <0.0001
Late loss, mm | ... | 0.24±0.48 | ...
Net gain, mm | ... | 0.97±0.41 | ...
Percent diameter stenosis | 7 (30) | 0 | 0.003

*P=0.007 vs baseline.
†P=0.028 vs baseline.

follow-up. Finally, although the study was underpowered for clinical events, the SVG PES strategy was associated with a lower revascularization rate and a trend toward a lower rate of MACE at 12-month follow-up.

Significant SVG disease progression occurred in up to 39% of patients in the Post Coronary Artery Bypass Graft Trial despite optimal lipid control,22 and, of clinical relevance, SVG angiographic progression was associated with a higher rate of death and MI at 3-year follow-up.9 In a recent retrospective study, we have shown that significant atherosclerosis progression at 15-month follow-up occurred in approximately half of the patients with mild to moderately
diseased SGVs after a mean time of 8 years after CABG surgery despite mean LDL cholesterol levels of <90 mg/dL. The present study was the first to use both angiography and IVUS to determine prospectively the atherosclerosis progression rate in very old (average 12±6 years) and moderately diseased SVGs. Despite intensive lipid-lowering therapy with mean LDL cholesterol levels <75 mg/dL, significant atherosclerosis progression occurred in a period of only 12 months and was related mainly to the progression of the disease in the SVG segments with higher plaque burden leading to a moderate stenosis at baseline examination, with no significant atherosclerosis progression in the SVG segments with no moderate stenosis at baseline. Importantly, some increase in plaque burden occurred in most patients at moderate stenosis sites (Figure 2), leading to severe stenosis or occlusion of the SVG, which required a clinically driven revascularization in approximately one fifth of them. Ellis et al 7 first identified the presence of moderate SVG lesions as an important prognostic factor at midterm follow-up, with a cardiac event rate between 1- and 3-year follow-up of up to 45% in patients with moderate SVG lesions compared with 2% in patients without them. We also showed that the presence of such moderate SVG lesions in old SVGs remained the most important predictor of cardiac events at 20-month follow-up despite aggressive lipid-lowering therapy. 8 Ellis et al 7 had already suggested a strategy of sealing moderate SVG lesions with stents instead of conservative management to reduce cardiac events at midterm follow-up. However, SVG stenting has been associated with 2 important pitfalls that could preclude its potential use as a preventive strategy.
strategy: a high rate of periprocedural events and stent restenosis. Most cardiac events after SVG stenting are related to lesions with a high plaque burden or those associated with complex features such as thrombus or ulceration and to diffusely degenerated SVGs. Therefore, focal moderate SVG lesions as low as 3%, with 1 of 30 patients suffering a periprocedural non–ST-segment elevation MI. In recent years, several studies have shown that the use of PES for the treatment of SVG lesions was associated with a very low restenosis rate leading to a 5% to 13% target SVG revascularization rate at 6- to 12-month follow-up. Importantly, no cases of stent thrombosis were reported in any of these studies that included >500 patients treated with PES. The present study showed that PES for the treatment of moderate SVG lesions (average of 39±6% diameter stenosis) was associated with no in-stent or in-lesion restenosis and no stent thrombosis at 12-month follow-up. Treating lesions with a lower plaque burden might have influenced the low late loss and the absence of restenosis observed in the present study. In addition, the present study showed that those SVG segments without moderate lesions presented a similar nonsignificant mild increase in plaque burden as evaluated by IVUS at 12-month follow-up in both the medical treatment and PES groups, showing that SVG stenting with PES had no effect on the atherosclerotic process of the nonstented SVG segments. This study has limitations. This was a pilot study, and thus the number of patients included was small, and the follow-up period was limited to 12 months. Although some observational studies have shown a favorable long-term safety profile after SVG drug-eluting stenting, others have raised some concerns about the possibility of late stent thrombosis and higher mortality at long-term follow-up. This study was not powered for clinical end points, and further studies with a larger number of patients and longer follow-up are needed to provide clinical evidence of the benefits of plaque sealing with PES in old and moderately diseased SVGs. Although the use of clopidogrel in addition to aspirin failed to demonstrate any benefit in stable coronary patients, we cannot exclude an effect of the imbalance in clopidogrel use between the 2 study groups on atherosclerosis progression and MACE. Finally, and despite the fact that previous studies have shown the safety of IVUS for the evaluation of coronary atherosclerosis, a potential deleterious effect of IVUS on atherosclerosis progression of moderately diseased SVGs cannot be ruled out completely.

In conclusion, this was the first study evaluating the use of stenting as a preventive treatment for SVG atherosclerosis progression. The results showed that old and moderately diseased SVGs presented a significant and very rapid (within 12 months) disease progression at the sites exhibiting moderate lesions and that sealing such moderate lesions with PES prevented this process without inducing any deleterious effects on the atherosclerotic disease of nonstented SVG segments. This proof-of-concept study represents the first

Table 3. IVUS Data According to Randomization Group

<table>
<thead>
<tr>
<th>In lesion</th>
<th>Medical Treatment</th>
<th>PES</th>
<th>p</th>
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<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MLA, mm²</td>
<td>6.3±3.0</td>
<td>6.1±2.2</td>
<td>0.73</td>
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<tr>
<td>Plaque burden, %</td>
<td>61.2±16.3</td>
<td>63.5±11.8</td>
<td>0.59</td>
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<tr>
<td>Stent implantation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLA, mm² (in stent)</td>
<td>...</td>
<td>9.7±2.7</td>
<td>...</td>
</tr>
<tr>
<td>MLA, mm² (in lesion)</td>
<td>...</td>
<td>9.2±2.6</td>
<td>...</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLA, mm² (in stent)</td>
<td>...</td>
<td>8.8±2.9</td>
<td>...</td>
</tr>
<tr>
<td>MLA, mm² (in lesion)</td>
<td>5.6±3.1</td>
<td>8.6±2.9</td>
<td>0.001</td>
</tr>
<tr>
<td>MLA change (follow-up vs baseline)</td>
<td></td>
<td></td>
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<tr>
<td>Nominal change, mm</td>
<td>−0.73±0.88</td>
<td>2.51±2.67</td>
<td>&lt;0.0001</td>
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<tr>
<td>P (follow-up vs baseline)</td>
<td>&lt;0.001</td>
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<tr>
<td>Percent change</td>
<td>−14.1±17.9</td>
<td>54±55</td>
<td>&lt;0.0001</td>
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<td>&lt;0.0001</td>
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<tr>
<td>Plaque burden, %</td>
<td>66.7±16.1*</td>
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<td>...</td>
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<tr>
<td>SVG segment with no lesion</td>
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<td>Atheroma volume, mm³</td>
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<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>283.9±113.7</td>
<td>282.6±144.9</td>
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<tr>
<td>Follow-up</td>
<td>291.9±118.8</td>
<td>289.6±148.3</td>
<td>0.96</td>
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<tr>
<td>Absolute change</td>
<td>8.0±40.2</td>
<td>7.0±30.4</td>
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<tr>
<td>P (follow-up vs baseline)</td>
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<tr>
<td>Percent change</td>
<td>3.0±13.1</td>
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<tr>
<td>P (for % change)</td>
<td>0.29</td>
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<td>Percent atheroma volume</td>
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<td>Baseline</td>
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<tr>
<td>Follow-up</td>
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<tr>
<td>Absolute change, %</td>
<td>0.6±3.7</td>
<td>1.1±3.0</td>
<td>0.66</td>
</tr>
<tr>
<td>P (follow-up vs baseline)</td>
<td>0.40</td>
<td>0.17</td>
<td></td>
</tr>
</tbody>
</table>

*P=0.003 vs baseline.

Table 4. Cumulative Incidence of MACE at 12-Month Follow-Up According to Randomization Group

<table>
<thead>
<tr>
<th></th>
<th>Medical Treatment</th>
<th>PES</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>27</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Patients with MACE, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>8 (30)</td>
<td>5 (17)</td>
<td>0.35</td>
</tr>
<tr>
<td>MI</td>
<td>1 (4)</td>
<td>2 (7)</td>
<td>1.00</td>
</tr>
<tr>
<td>Clinically driven revascularization</td>
<td>8 (30)</td>
<td>4 (13)</td>
<td>0.20</td>
</tr>
<tr>
<td>Patients with MACE related to the target SVG, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>1 (4)</td>
<td>1 (3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Clinically driven revascularization</td>
<td>5 (19)</td>
<td>0</td>
<td>0.019</td>
</tr>
</tbody>
</table>
step toward a new treatment strategy for this highly challenging subset of patients and will need to be substantiated by a large randomized clinical trial.

Acknowledgments
We would like to thank Serge Simard for statistical analysis; Julie Robinson, RN, and Kathia Desmeules for their help in patient recruitment, patients’ follow-up, and database management; and Lyne Bouchard and Michèle Asselin for ultrasound measurements.

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Disclosures
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The presence of moderate saphenous vein graft (SVG) lesions is a major predictor of cardiac events late after coronary artery bypass grafting. We designed a pilot study to test the hypothesis of sealing moderate nonsignificant SVG lesions with paclitaxel-eluting stents (PES) to prevent atherosclerosis progression at the level of the moderate SVG lesion while not inducing any deleterious effect on the atherosclerotic process of the nonstented SVG segments. Patients with at least 1 moderate SVG lesion (30% to 60% diameter stenosis) were randomized either to stenting the moderate SVG lesion with a PES (n\textsuperscript{H11005}30, PES group) or to medical treatment alone (n\textsuperscript{H11005}27, medical treatment group). Patients had an angiographic and intravascular ultrasound evaluation of the SVG at baseline and at 12-month follow-up. Mean time from coronary artery bypass grafting was 12\textsuperscript{H11006}6 years, and mean low-density lipoprotein cholesterol level was 73\textsuperscript{H11006}31 mg/dL. Significant disease progression occurred in the medical treatment group at the level of the moderate SVG lesion as evaluated by angiography and intravascular ultrasound (P<0.01 versus baseline; P<0.01 versus PES group), leading to a severe flow-limiting lesion or SVG occlusion in up to 22% of the patients compared with none in the PES group (P=0.014). There were no cases of restenosis or stent thrombosis, and no significant atherosclerosis progression occurred at the nonstented SVG segments. At 12-month follow-up, the cumulative incidence of major adverse cardiac events related to the target SVG was 19% in the medical treatment group versus 3% in the PES group (P=0.091). In conclusion, old and moderately diseased SVGs presented a significant and very rapid (within 12 months) disease progression at the sites exhibiting moderate lesions despite optimal control of low-density lipoprotein cholesterol levels, and sealing such moderate lesions with PES prevented this process without inducing any deleterious effect on the atherosclerotic disease of nonstented SVG segments. This pilot study provides early evidence that plaque sealing as a new strategy for the treatment of a challenging subset of patients after coronary artery bypass grafting should be explored further.

CLINICAL PERSPECTIVE

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