Role of the Distal Balloon Protection Technique in the Prevention of Cerebral Embolic Events During Carotid Stent Placement

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Background and Purpose—We sought to quantitatively and qualitatively evaluate the release of atheromatous plaque debris induced by carotid stenting procedures.

Methods—Eight patients with severe carotid atheromatous stenoses were treated by stent implantation under distal balloon protection. Blood samplings were obtained after stent deployment in the blood pooled below the inflated protection balloon. The samples were centrifuged and evaluated for plaque debris with the use of light microscopy. The debris release was quantitatively estimated by dividing the total volume of debris obtained by the mean debris size. Five patients without endovascular procedure were used as a control group.

Results—The 2 main debris types found were nonrefringent cholesterol crystals (4 to 389 $\mu$m; 115 to 8697 in number) and lipid masses (7 to 600 $\mu$m; 341 to 34,000 in number). There was a statistically significant difference compared with the samples obtained in the control group ($P=0.017$).

Conclusions—Blood samples collected during stent implantation procedures contain a large quantity of atheromatous plaque debris. This emphasizes the role of distal protection techniques in avoiding migration of this plaque material into the cerebral circulation. (Stroke. 2001;32:479-484.)

Key Words: atherosclerosis ■ carotid stenosis ■ protection device ■ stents

The carotid bifurcation is the most common location of craniocervical atheromatous disease,1 accounting for 20% to 30% of strokes.2 Carotid stenoses may result in brain ischemia either through direct hemodynamic impact on the cerebral blood circulation or as a source of thromboembolic material.3 The tendency of atheromatous lesions to produce thromboembolic events is linked to their morphological characteristics, in particular the presence of plaque ulceration.4 The benefits of carotid atheromatous disease treatment by carotid endarterectomy have been established by several large studies.5–7 Carotid angioplasty and stenting recently emerged as a therapeutic alternative derived from the extensive experience gained in peripheral endovascular procedures. Initially, carotid angioplasty was associated with embolic complication rates ranging from 4% to 33%.$^{8–17}$ This high propensity to produce embolic plaque debris led to the development of distal protection techniques to be used during endovascular procedures performed for lesions of the carotid bifurcation.$^{18}$ Balloon angioplasty with or without stent placement using a distal protection technique involving temporary balloon occlusion of the cervical internal carotid artery (ICA) has been shown to be safe and effective.$^{19}$ Diffusion of the balloon protection technique has been limited by the lack of device availability and large-scale studies. With the advent of commercially available protection devices, the role of protection techniques may rapidly increase.$^{20,21}$

The purpose of the present study was to prospectively evaluate the amount and type of plaque debris released during endovascular stent placement in patients with carotid bifurcation atheromatous disease.

Subjects and Methods

Carotid Stent Patients

Nine consecutive carotid bifurcation stent placements performed in 8 patients with severe carotid atheromatous disease were prospectively evaluated. In all cases, self-expandable stents (Wallstent, BSC) were deployed and performed after dilatation via a triple coaxial system.$^{19}$ Eight lesions were symptomatic, and 1 lesion, a postradiotherapy
stenosis with 95% lumen reduction, was asymptomatic (procedure 9 in the Table). Endovascular treatment was performed 1 to 5 months after presentation of neurological symptoms. The degree of stenosis ranged from 70% to 95%, with a mean percentage of stenosis measured at 84% according to the criteria of the North American Symptomatic Carotid Endarterectomy Trial. Plaque ulcers were found in 7 of 9 cases (procedures 1 to 4 and 6 to 8). One patient was treated for a recurrent stenosis secondary to neointimal hyperplasia after previous stent implantation (procedure 8). Protection was used in this case for a redilatation procedure without introduction of another stent.

All procedures were performed under distal balloon protection with the technique described by Théron et al.19 This technique involved temporary occlusion of the cervical ICA by a nondetachable latex balloon (BC 17, Nycomed) fixed on a 2.6F and 300-cm-long microcatheter (tubing with distal end collar, catalog No. 5RE-658, Cordis Europe N.V.) by latex ligatures (Nycomed). All stenotic lesions were passed with the protection balloon system and the stent delivery device together, with the deflated protection balloon system used as a guide. There was no need for predilatation in any of the procedures. After stent deployment, the stent delivery device was removed, and a postdilatation procedure with angioplasty balloons of 5 to 8 mm diameter and 2 cm in length (Smash, BSC) was performed. Subsequently, after removal of the dilatation balloon, the 9F guiding catheter (Vistabriteip, Cordis) was gently advanced under fluoroscopic control within the stent lumen to reach the level of angioplasty, and blood was aspirated with a 50-mL syringe. This aspiration occurred through the large side port of a valve adapter (adjustable hemostasis valve, Cordis) fixed to the hub of the 9F guide catheter, which allowed for easy withdrawal of large blood samples. The space between the 9F guide catheter lumen and the coaxial 2.6F microcatheter allows for unconstrained fluid exchange. The remaining blood pooled below the balloon was then flushed into the external carotid circulation by the injection of 30 mL saline at a rate of 2 mL/s with a power injector (Figures 1 and 2). The protection system was then withdrawn, and a postprocedural angiographic control was obtained (Figures 1 and 2). All patients received a bolus injection of heparin (150 IU/kg) at the beginning of the procedure for anticoagulation purposes. Atropine 1 mg IV was given immediately before angioplasty to prevent bradycardia. Aspirin 300 mg/d (Bayer) was started 3 days before the procedure and continued indefinitely. Ticiopidine 1 mg (Ticlid, Sanofi Winthrop) was given immediately before the procedure and continued for 3 months.

### Number and Size of Debris Aspirated During 9 Carotid Stent Procedures and During 5 Control Group Cases

<table>
<thead>
<tr>
<th>Procedure/Control No.</th>
<th>Crystal</th>
<th>Lipoid Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Maximum</td>
</tr>
<tr>
<td><strong>Stent</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5000</td>
<td>318</td>
</tr>
<tr>
<td>2</td>
<td>4620</td>
<td>348</td>
</tr>
<tr>
<td>3</td>
<td>5000</td>
<td>259</td>
</tr>
<tr>
<td>4</td>
<td>8697</td>
<td>389</td>
</tr>
<tr>
<td>5</td>
<td>115</td>
<td>111</td>
</tr>
<tr>
<td>6</td>
<td>3480</td>
<td>286</td>
</tr>
<tr>
<td>7</td>
<td>988</td>
<td>51.8</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>3100</td>
<td>213.88</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>220</td>
<td>193</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>130</td>
<td>74</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>70</td>
<td>53.4</td>
</tr>
</tbody>
</table>

Size values are expressed in micrometers.

**Figure 1.** To illustrate the procedure used for harvesting plaque debris, an endovascular carotid stenting procedure with distal balloon protection is shown. Left, Extensive atheromatous ICA stenosis of the cervical portion. Middle left, Stent dilatation (Wallstent, BSC/Smash balloon, BSC) using a distal protection balloon (level C1-C2). Middle right, After removal of the dilatation balloon, the 9F guiding catheter is advanced under continuous distal balloon protection to reach the level of stent dilatation. A cleaning procedure with aspiration and flush delivery was performed in this position through the guiding catheter after removal of the dilatation balloon (Smash, BSC). Right, Control after endovascular treatment.
inject 30 mL of saline at a rate of 2 mL/s with a power injector. advanced below the distal protection balloon and was used to external carotid artery territory; the 9F guiding catheter was plasty. g, Flush technique to eliminate remaining debris in the blood was aspirated. f, Blood aspiration at the level of angioplasty, and within the stent lumen to reach the level of angioplasty, and the 9F guiding catheter was gently advanced before deployment. c, Inflation of the distal protection balloon was performed. e, Subsequently, after removal of the dilatation balloon, the 9F guiding catheter was advanced below the distal protection balloon and was used to inject 30 mL of saline at a rate of 2 mL/s with a power injector.

Analysis of Blood Samples Obtained During Endovascular Procedures
All patients gave informed consent for blood analysis. The blood samples were obtained by aspirating a total of 30 to 50 mL with a 50-mL syringe, as described above, and were used systematically in our procedures. The blood was heparinized and centrifuged immediately after withdrawal. The sediment was separated and weighed with a micrometric scale. To evaluate the quality of the sediment, 3 samples were taken at 3 different gravity levels (top, middle, and bottom parts of the sediment) and evaluated under the microscope after coloration (Oil Red O and Papanicolaou). The quantity of material analyzed in the 3 samples was extrapolated to the total volume of the sediment, allowing for estimation of the total number of plaque debris collected.

Control Group
As control, we elected to sample blood aspirated from different patients of a similar age group, either with similar disease but no endovascular treatment or similar disease at another location receiving endovascular treatment. For the carotid stenosis lesions, 3 symptomatic patients with similar atheromatous lesions were sampled during diagnostic angiography evaluation before endarterectomy surgery. For the endovascular treatment group receiving a stent for another atheromatous lesion, we chose 2 patients with symptomatic lesions of the distal ICA and vertebral artery origin. The first patient underwent angioplasty and stenting of an atheromatous stenotic lesion at the C5 segment of the ICA siphon. The blood was collected after postdilatation of the stent with a coaxial guide catheter reaching above the carotid bifurcation. The second patient was treated for an atheromatous stenosis of the right vertebral artery origin by angioplasty followed by stenting. In this case, the blood was collected in the subclavian artery at the level of the atheromatous lesion, just after postdilatation.

The aspirated material was evaluated by the previously described quantification technique, ie, analysis of 3 samples of the sediment and extrapolation to the total sediment volume.

Statistical Analysis
The 2-sample unequal variance $t$ test, with a value of $P<0.05$ considered significant, was used to evaluate differences in material collected by aspiration during carotid stenting procedures (studied population) and during diagnostic angiograms (control group).

Results

Types of Plaque Debris Found
The types of plaque debris found included cholesterol crystals and lipid masses (Figures 3 and 4).

Carotid Stent Patients
Therapeutic carotid stent placement was successfully performed in the 8 patients (9 stents), without periprocedural or postprocedural complications (Table). No or minimal vasospasm (lumen reduction of $<50\%$) at the level of the protection balloon position was observed in 7 lesions, and a moderate vasospasm (lumen reduction of 50% to 70%) with flow reduction was observed in 2 lesions. The latter were treated with nimodipine (60 $\mu$m IA, Nimotop, Bayer), with relief of vasospasm and improvement of the circulation within a few minutes. The blood samples were positive for cholesterol crystal in 7 of the 9 procedures (procedures 1 to 7 in the Table) and positive for lipid masses in all instances. By extrapolating the values obtained with 3 samples to the total centrifuged material for each collected blood specimen, the number of cholesterol debris was found to range from 115 to 8697 (mean, 3100; SD, 3003; median, 3480). The size of the aspirated cholesterol debris varied from 3.7 to 389 $\mu$m (mean, 102.5 $\mu$m; SD, 81.5 $\mu$m). By the same technique, the number of calculated lipid masses ranged from 341 to 34 333 (mean, 9726; SD, 12 723; median, 3933). Their size varied from 7.4 to 594 $\mu$m (mean, 128 $\mu$m; SD, 90.7). The results are summarized in the Table.

Because of the small sample size, a correlation of the type and the number of debris observed with symptoms or imaging studies was not performed. It should be noted, however, that 6 of 7 ulcerated lesions showed cholesterol crystals in the debris (procedures 1 to 4, 6, and 7 in the Table). Another lesion with 90% stenosis had cholesterol crystals without visualization of ulceration (procedure 5).

No crystals were observed in 1 of the 7 ulcerated lesions with 70% stenosis (procedure 8 in the Table) and in 1 lesion with 80% stenosis without ulceration but occurring after radiotherapy (procedure 9).

Control Group
The blood specimens obtained in 2 of the 3 diagnostic angiographic control cases were negative (control cases 3 and 5 in the Table). In the third patient the sampling showed a small quantity of cholesterol crystals (number, 130; mean size, 51.3 $\mu$m; control case 4). The results are summarized in the Table. The 2 control patients treated for atheromatous stenoses by angioplasty and stenting underwent successful procedures without periprocedural or postprocedural complications. The sample obtained in the vertebral stent case was positive only for lipid masses (number, 364; mean size, 66.4 $\mu$m; control case 2). The sample obtained in the intracranial stent case was positive for both types of debris (220 chole-
terol crystals; mean size, 145.3 μm; 73 lipoid masses; mean size, 535 μm; control case 1).

**Statistical Analysis**
The statistical evaluation of the results revealed a significant difference for both types of debris between the samples obtained below the protection balloon during carotid stenting procedures and the samples obtained in the control group ($P=0.017$).

**Discussion**
Although the complication rate related to endovascular treatment methods of carotid stenosis has decreased with the evolution of therapeutic devices,8,10 the risk of cerebral embolic events secondary to plaque debris migration during angioplasty and stent deployment remains of concern.9,16 Previous in vitro experimentation on isolated specimens of carotid atheromatous plaques has demonstrated the fragility of the plaque and the risk of debris release during stent placement.22 In vitro studies have, on the other hand, emphasized the ability of the distal balloon technique to protect against migration of plaque debris into the cerebral circulation.23 The purpose of our study was to confirm in vivo the role of this technique by sampling and analyzing the blood pooled below the protection balloon in 9 carotid stenting procedures. Two types of debris (cholesterol crystals and lipoid masses) were found in these samples. Atheromatous plaques are composed of a mixture of cholesterol crystals and atheromatous material; both can be released in the circulation when the plaque is broken.24 Cholesterol crystals were defined as geometric, angulated unstained structures, and...
lipoid masses were identified as aggregates of amorphous, granular, compact material stained with Oil Red O coloration. The amount of collected debris was significantly higher in the carotid stent patients than in the 5 control patients ($P=0.017$), confirming that debris release occurs during angioplasty and stent deployment.

High numbers of cholesterol crystals were seen mostly with ulcerated plaques and tight atheromatous stenosis, which may allow us to postulate that ulceration and degree of squeeze of the plaque during endovascular treatment could be considered risk factors for expulsion of cholesterol crystals.

In the present investigation, debris was collected during only one of the protection maneuvers, ie, the aspiration of the blood pooled below the balloon with a 50-mL syringe. The protection methodology implies that after this initial aspiration, the stagnant blood is flushed away toward the external carotid circulation by a brisk saline injection. This second part of the cleaning procedure was not evaluated in our study, which therefore likely underestimates the total amount of released debris. Another source of underestimation of the material accumulated below the protection balloon lies in the handling of the blood specimens: immediate heparinization of the samples precluded evaluation of potentially present thrombogenic material, and centrifugation of the specimens probably fragmented the collected debris, explaining their relatively small size.

Although sampling below the carotid stenosis before treatment would have been a good option to perform control studies, we elected to use a different patient group for this purpose. Sampling in the control group was performed in less advanced or differently located vascular atheromatosis, which allowed for sampling in a proximity of the lesion that was similar to the one used after carotid stent implantation. This choice of control allowed us to avoid a potentially dangerous preprocedural catheter sampling close to the ulcerated carotid lesions.

This study did not evaluate the potential of plaque debris released during the first and last steps of the endovascular procedure, ie, during initial introduction of the protection balloon system through the stenotic lesion and during removal of the same system at the end of the procedure.

Continuous sonographic Doppler controls at the level of the middle cerebral artery have shown presence of embolic events for the first step of the procedure in previous studies. We have occasionally performed similar Doppler controls at the level of the middle cerebral artery, and during both of these procedural steps we have recorded a small number of Doppler signals, indicating embolic events that were asymptomatic. We believe that protection from embolic events is difficult to avoid during both of these steps. However, our observation during introduction of the protection system together with the stent delivery device indicates important flow reduction as soon as the stenotic segment is passed. This flow arrest keeps potential debris close to the lesion while the protection balloon is inflated higher up in the ICA.

Our study confirms that uncovered stents do not provide protection against plaque debris release. It is interesting to note that all the samples collected during carotid stenting procedures were positive for lipid masses. The case of intimal hyperplasia that developed over a previously placed stent and was treated by angioplasty and restenting was positive for lipid masses as well, showing that this particular indication carried comparable embolic risks.

Whether lipid masses or cholesterol crystals would have different embolic effects cannot be concluded from this study. The maximal sizes of 0.389 mm for crystals and 0.594 mm for lipid masses indicate that both may exist in sizes that are large enough to occlude small cerebral arteries. Depending on location, this might lead to a neurological event. If the high number of smaller pieces of debris observed in our study is representative of endovascular procedures, then there needs to be an explanation for the few symptomatic events observed in the clinical cases treated without protection. It may be that the cerebral circulation tolerates a high number of silent embolic events if they are small enough to permit collateral supply.

The study shows that there are a significant number of large pieces of debris produced during endovascular stent application; however, the period when most debris is produced cannot be indicated because the samples were not drawn in a fractionated manner over the different steps of the procedure. We currently believe that the steps most likely to produce larger pieces of debris are during stent postdilatation procedures with balloon squeeze of the plaque and during shear forces of stent struts produced by secondary stent deformation in contact with the atheromatous wall.

Although more serious damage of the arterial wall due to application of a protection balloon may occur, such complications can be avoided by adequate training.

**Conclusion**

Our in vivo study clearly indicates that a large amount of plaque debris, probably underestimated in both size and number by our methodology, is released during the placement of a carotid stent. It is our belief that this debris accounts for most of the embolic complications related to carotid angioplasty and stenting. In the 9 uncomplicated carotid procedures reported here, potential embolic material was collected in the blood pooled below the protection balloon before it was washed out toward the external carotid circulation. Our findings emphasize the capacity of the distal protection technique to increase the safety of carotid angioplasty and stenting by preserving the cerebral circulation from plaque debris migration.

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**References**


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