Effect of the Distal-Balloon Protection System on Microembolization During Carotid Stenting

Nadim Al-Mubarak, MD; Gary S. Roubin, MD, PhD; Jiri J. Vitek, MD, PhD; Sriram S. Iyer, MD; Gishel New, MD; Martin B. Leon, MD

Background—The distal-balloon protection system is being evaluated for its efficacy in preventing embolic neurological events during carotid stenting (CAS). We sought to determine the effect of this system on the frequency of Doppler-detected microembolic signals (MES) during CAS.

Methods and Results—Using transcranial Doppler, we compared the frequency of MES during CAS in 2 groups: 39 patients without distal protection and 37 who used the distal-balloon protection system (GuardWire). There were no significant differences in the clinical or angiographic characteristics between the 2 groups. Three phases with increased MES counts were identified during unprotected CAS: these were stent deployment, predilation, and postdilation (75±57, 32±36, and 27±25 METS, respectively). The distal-balloon protection significantly reduced the frequency of MES during CAS (MES counts: 164±108 in the control versus 68±83 in the protection group; P=0.002), particularly during these 3 phases. MES in the protection group were detected predominantly during sheath placement, guidewire manipulation, and distal-balloon deflation.

Conclusion—Three phases with increased MES counts were identified during unprotected CAS (eg, stent deployment, predilation, and postdilation). The distal-balloon protection system significantly reduced the frequency of MES during CAS, particularly during these 3 phases. (Circulation. 2001;104:1999-2002.)

Key Words: carotid arteries ■ angioplasty ■ stents ■ revascularization ■ embolism

Carotid stenting (CAS) has emerged as an endovascular treatment for obstructive extracranial carotid artery disease.1–3 Initial reports suggest favorable efficacy in preventing stroke, and randomized trials are being commenced to compare its outcome to carotid endarterectomy.4 Despite advanced stenting techniques, neurological events linked to the embolization of particulate material in the cerebral circulation occur in ≥5% of the cases.1–3,5 Efforts are ongoing to optimize the outcome of this treatment by developing strategies that eliminate the risk of embolic events.6 One such strategy is distal-balloon protection.6 By occluding the distal carotid artery with a balloon, embolic material released during the intervention is contained within the proximal blood column, which is subsequently aspirated before the protective balloon is deflated.

Transcranial Doppler studies have documented the prevalence of microembolization during unprotected CAS.7,8 Subclinical microemboli produce characteristic Doppler signals (microembolic signals, MES) that, in a variety of clinical conditions, correlate with increased risk for embolic neurological events.8–10 Thus, MES may serve as a surrogate marker of embolic events during CAS and facilitate the assessment of various distal-protection strategies. The higher frequency of MES compared with the clinical events in this setting allows such an assessment in a smaller number of patients.7,8 In this study, we evaluated the effect of distal-balloon protection on the frequency of the Doppler-detected MES during CAS.

Methods

Study Population
The frequency of MES during CAS was assessed in 76 patients undergoing the procedure; 39 had no distal protection (control group), and 37 were treated with distal-balloon protection (GuardWire, Percusurge; protection group). The control group included participants of a prospective registry investigating the efficacy of CAS (January 1999 to April 2000) and preceded the enrollment of the protection group (May 2000 to November 2000), which was part of a trial investigating the feasibility of the GuardWire system during CAS (Carotid Angioplasty Free of Emboli, CAFÉ-USA). The enrollment criteria for both groups were identical and included symptomatic or asymptomatic patients with a stenosis in the internal carotid artery of ≥60% or ≥80% diameter obstruction, respectively, as determined by quantitative angiography (Phillips Integris) using the methodology from the North American Symptomatic Carotid Endarterectomy Trial (NASCET).11 Consecutive patients enrolled into either of the 2 protocols at our institution who had an optimal Doppler insonation window and who were cooperative with the transcranial Doppler monitoring procedure were enrolled in the present study.

Stenting Protocol
All procedures were performed in accordance with the guidelines of the Institutional Review Board. CAS was performed using the
These phases were defined from the time the respective catheter was introduced into the guiding sheath until it was removed. These phases were (1) sheath placement, (2) wiring, (3) predilation, (4) stent deployment, (5) postdilation, (6) aspiration phase (protection group only), and (7) angiography.

A standard technique, as previously described, all patients were given 75 mg of clopidogrel (Plavix, Pfizer Inc) once a day and 325 mg of aspirin twice a day for 7 days before the procedure. A bolus of heparin (4000 U) was administered during the procedure. Glycoprotein IIb/IIIa antagonists were administered at the operator’s discretion. The GuardWire system was applied as previously described using a single-stage distal-balloon inflation with only-aspiration technique.

Transcranial Doppler Protocol
Transcranial Doppler signals, using a multichannel system (EME-Pioneer-4040, Nicollet-Vascular), were recorded from the ipsilateral middle cerebral artery via the transtemporal window. Monitoring was started before the procedure and continued for 10 minutes after the procedure whenever possible. Standard settings were used, with 2 sample volumes of 10-mm in diameter, each at a depth of 46 to 56 mm (4 to 6 mm apart). Data were stored on a hard disk using a coding system and were analyzed off-line on a later day by an investigator who was blinded to patient information. MES were identified according to the recommended guidelines. The procedure was divided into the following phases: (1) sheath placement, (2) wiring, (3) predilation, (4) stent deployment, (5) postdilation, (6) aspiration phase (protection group only), and (7) angiography. These phases were defined from the time the respective catheter was introduced into the guiding sheath until it was removed.

Statistical Analysis
MES counts are expressed as mean±SD. By convention, 1 second of microembolic shower signal is considered 10 MES. All MES recorded during contrast injections were excluded from the analysis because they may indicate microbubbles, which may be less hazardous than solids. Data were compared using χ² for categorical and Student’s t test for continuous variables.

Results
Table 1 summarizes the baseline clinical characteristics. Except for history of prior carotid endarterectomy (22% in the control group versus 3% in the protection group), there were no significant differences in the age, sex, or clinical comorbidities between the 2 groups. Symptoms attributable to the treated artery occurring within 3 months before CAS were present in 26% of the control group and 28% of the protection group (P=NS).

Table 2 summarizes the angiographic and procedural data. There were no significant differences in angiographic lesion characteristics or residual stenosis between the 2 groups. A bolus of a glycoprotein IIb/IIIa antagonist (Aggrastat, Pfizer Inc.) was administered to 4 patients in the control group and 1 patient in the protection group. Self-expanding stents were used in all patients. The Wallstent (Boston Scientific) was used exclusively in the protection group but in only 49% of patients in the control group.

Two procedural, nondisabling embolic strokes occurred, one in each group. Both improved completely within 3 days. One patient in the protection group died 2 days after CAS from a subarachnoid hemorrhage complicating hyperperfusion syndrome that developed immediately after intervention. His procedure was technically uncomplicated and notable for its low MES count. Baseline head MRI showed multiple lacunar infarctions but no acute ischemic changes. At 30 days, there have been no additional neurological events and no deaths in either group.

Microembolic Signals
MES were detected during all procedural phases in both groups (Table 3). Three phases with increased MES counts were identified in the control group; these were stent deployment, predilation, and postdilation (Figure 1). The GuardWire significantly reduced the total MES count compared with the control group (68±83 versus 164±108 MES; P=0.002), particularly during these 3 phases (Table 3). The combined MES count during the unprotected phases of the procedure (sheath placement and wire manipulation) was 30±24 in control group, and 34±41 in the protection group (P=NS). In the protection group, MES occurred predominantly during sheath placement, wire manipulation, and distal balloon deflation (Table 3). During the postprocedural observation period (mean, 9±5 minutes), no MES were detected in any of the patients.

On further analysis of the control group, there was no significant difference in the MES counts between the patients

<table>
<thead>
<tr>
<th>TABLE 1. Patient Clinical Characteristics</th>
<th>Control Group</th>
<th>Protection Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (mean±SD)</td>
<td>68±9</td>
<td>72±8</td>
<td>NS</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>28 (87)</td>
<td>30 (81)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>31 (80)</td>
<td>34 (92)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>12 (31)</td>
<td>13 (35)</td>
<td>NS</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>26 (67)</td>
<td>25 (68)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary artery disease, n (%)</td>
<td>21 (54)</td>
<td>16 (48)</td>
<td>NS</td>
</tr>
<tr>
<td>Prior neck radiation, n (%)</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SD or n (%). NS indicates not significant.

<table>
<thead>
<tr>
<th>TABLE 2. Procedural Data</th>
<th>Control Group</th>
<th>Protection Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stenosis severity, %</td>
<td>77±12</td>
<td>76±12</td>
<td>NS</td>
</tr>
<tr>
<td>Predilation</td>
<td>15±10</td>
<td>11±8</td>
<td>NS</td>
</tr>
<tr>
<td>Postdilation</td>
<td>14±7</td>
<td>15±6</td>
<td>NS</td>
</tr>
<tr>
<td>Angiographic characteristics, n (%)</td>
<td>16 (41)</td>
<td>15 (41)</td>
<td>NS</td>
</tr>
<tr>
<td>Ulceration</td>
<td>22 (56)</td>
<td>18 (49)</td>
<td>NS</td>
</tr>
<tr>
<td>Calcification</td>
<td>10 (26)</td>
<td>8 (22)</td>
<td>NS</td>
</tr>
<tr>
<td>Self-expanding stents, n (%)</td>
<td>39 (100)</td>
<td>37 (100)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SD or n (%). NS indicates not significant.

<table>
<thead>
<tr>
<th>TABLE 3. MES Counts</th>
<th>Control Group</th>
<th>Protection Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheath placement</td>
<td>11±7</td>
<td>16±24</td>
<td>NS</td>
</tr>
<tr>
<td>Wire manipulation</td>
<td>23±22</td>
<td>22±33</td>
<td>NS</td>
</tr>
<tr>
<td>Predilation</td>
<td>32±36</td>
<td>12±31</td>
<td>0.001</td>
</tr>
<tr>
<td>Stent deployment</td>
<td>75±57</td>
<td>17±22</td>
<td>0.004</td>
</tr>
<tr>
<td>Postdilation</td>
<td>27±25</td>
<td>5±9</td>
<td>0.002</td>
</tr>
<tr>
<td>Distal balloon deflation</td>
<td>NA</td>
<td>17±21</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>164±108</td>
<td>68±83</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Values are mean±SD. NS indicates not significant; NA, not applicable.
who had a Wallstent versus those who had other self-expanding stents (156±93 versus 170±101 MES, respectively; P=NS). A significant difference was absent throughout the various steps, including the stenting phase (67±55 versus 78±63 MES; P=NS). Both subgroups were matched in their clinical and angiographic characteristics.

Discussion
Preliminary results of the clinical evaluation of distal-balloon protection during CAS suggest that this strategy is associated with a favorable low rate of embolic stroke.6 In the present study, the use of distal-balloon protection during CAS was associated with significantly lower MES counts compared with no protection. This finding supports the clinical efficacy of this protection strategy. Further, the study defines the Doppler microembolic profile during CAS and describes the impact of distal-balloon protection on MES counts during the various procedural steps. Three critical phases are responsible for increased MES counts during the unprotected CAS: stent deployment, predilation, and postdilation, with the highest counts observed during stent deployment. This contradicts the general belief that stent deployment is associated with low embolic risk due to the scaffolding effect of the stent, which traps atherosclerotic debris against the arterial wall. It is possible that the sheer forces of the self-expanding stent, which is usually oversized to the artery, are responsible for the increased emboli release. In the protection group, MES counts were significantly reduced during these 3 critical phases. Our data also suggest that the unprotected phases (eg, sheath placement, wire manipulation, and the immediate postprocedural period) are associated with a relatively low risk of embolization.

Several factors may have contributed to the MES observed in the protection group. These include (1) a nonocclusive distal balloon; (2) embolization via the external carotid artery (Figure 2), which questions the suitability of the saline-flushing maneuver into the internal carotid artery before the distal-balloon deflation, diverting potential emboli into the external carotid artery; and (3) trapped emboli within the “shadow-zone” of the aspiration catheter that were inaccessible for removal.

Although the evidence that MES represent microemboli is well established, their use as a surrogate marker of embolic events during CAS may have a potential limitation.7,8 Although high MES counts correlate with an increased risk for embolic stroke in many clinical conditions, such a correlation during CAS has yet to be established. Because of the small number of clinical events, this correlation could not be examined in the present series. In addition, due to the logistics of enrolling consecutive patients into CAFE-USA when the technique became available at our institution, a randomized design of this study was not possible. However, the two groups were well matched in their clinical and angiographic characteristics. Subgroup analysis of the control group suggests that the difference in the stent type between the two groups did not seem to impact MES counts. Nevertheless, these data provide an important insight into the
embolization profile during CAS and into the performance of the distal-balloon protection.

References
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