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CLINICAL RESEARCH **Interventional Cardiology**

Effect of Two Different Neuroprotection Systems on Microembolization During Carotid Artery Stenting

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OBJECTIVES This study sought to compare the efficacy of two different cerebral protection systems for the prevention of embolization during carotid artery stenting (CAS) using a transcranial Doppler (TCD) monitoring with the detection of microembolic signals (MES).

BACKGROUND Despite the introduction of cerebral protection systems, neurologic complications during CAS cannot completely be prevented. Transcranial Doppler and detection of MES may aid in assessing the efficacy of different neuroprotection systems.

METHODS A total of 42 patients with internal carotid artery stenoses were treated by CAS using either a filter (E.P.I. FilterWire, Boston Scientific Corp., Santa Clara, California) (n = 21) or a proximal endovascular clamping device (MO.MA system, Invatec s.r.l., Roncadelle, Italy) (n = 21). Microembolic signal counts were compared during five phases: placement of the protection device, passage of the stenosis, stent deployment, balloon dilation, and retrieval of the protection device.

RESULTS There were no significant differences in clinical or angiographic outcomes between the two groups. Compared to the filter device, the MO.MA system significantly reduced MES counts during the procedural phases of wire passage of the stenosis, stent deployment, balloon dilation, and in total (MES counts for the filter device were 25 ± 22, 73 ± 49, 70 ± 31, and 196 ± 84 during the three phases and in total, MES counts for the MO.MA system were 1.8 ± 3.2, 11 ± 19, 12 ± 21, and 57 ± 41, respectively; $p < 0.0001$).

CONCLUSIONS In comparison to a filter device the MO.MA system led to significantly lower MES counts during CAS. The detection of MES by TCD may facilitate the evaluation and comparison of different neuroprotection systems. (J Am Coll Cardiol 2004;44:1966–9) © 2004 by the American College of Cardiology Foundation

Cerebral protection devices have proven to be safe and effective in preventing distal embolization, according to several uncontrolled studies. However, neurologic complications cannot be prevented completely by these devices (1,2).

The most common neuroprotection systems include distal filter devices or distal balloon protection systems. In contrast, proximal endovascular clamping devices such as the MO.MA system (Invatec s.r.l., Roncadelle, Italy) establish cerebral protection by endovascular occlusion of the external (ECA) and common (CCA) carotid artery, leading to a cessation of flow in the target vessel (1,2).

We used transcranial Doppler (TCD) monitoring for the detection of microembolic signals (MES) to evaluate and compare the efficacy of two different neuroprotection systems in preventing embolization during CAS.

METHODS

Study population. Between March 2002 and February 2003, MES counts were determined during CAS in 42 consecutive patients using either a FilterWire EX (E.P.I. FilterWire, Boston Scientific Corp., Santa Clara, California) (n = 21) or the MO.MA system (n = 21). All patients gave written informed consent for the intervention. Inclusion criteria were symptomatic stenoses of the internal carotid artery (ICA) ≥70% or asymptomatic stenoses ≥80%. Exclusion criteria for the use of the MO.MA system were a severely diseased ECA, which precluded a safe placement of the system, or an occlusion of the contralateral ICA. In all other cases the choice of the protection device was at the discretion of the interventionalist.

Stenting protocol. All procedures were performed via a femoral approach. In the filter group, after placement of a 90-cm 7F sheath (Super Arrow Flex Sheath, Arrow International Inc., Bernville, Pennsylvania) into the CCA, the stenosis was passed with the filter system and the filter was positioned in the distal portion of the ICA.

The MO.MA system integrates the functional aspects of a guiding catheter and cerebral protection incorporating two separately inflatable low-pressure elastomeric balloons for endovascular clamping of the ECA and CCA. An exit port (6-F) of the guiding catheter between the two occlusion balloons enables the introduction of the angioplasty devices (Fig. 1). After insertion of the MO.MA system over an 11-F sheath (Fig. 2A), the distal balloon was inflated in the ECA and the proximal balloon in the CCA, blocking the

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Abbreviations and Acronyms

CAS = carotid artery stenting
CCA = common carotid artery
ECA = external carotid artery
ICA = internal carotid artery
MES = microembolic signals
TCD = transcranial Doppler

antegrade flow across the target vessel (Fig. 2B). A 0.014-in guide wire (Galeo ES, Biotronik, Berlin, Germany) was used for wiring of the stenosis. In both groups, predilation or direct stent implantation (Carotid Wallstent Monorail, Boston Scientific Corp., Natick, Massachusetts) was performed. All stents were post-dilated with a 5.0- or 6.0-mm balloon (Submarine Rapido, Invatec s.r.l.), depending on the vessel size. A specially manufactured retrieval catheter was used for removal of the filter system. In the MO.MA group, potential debris was removed by blood aspiration of 40 to 60 ml via the guiding catheter before de-clamping of the protection device. All procedures were performed in accordance with the guidelines of the institutional review boards.

All patients received 75 mg clopidogrel and 100 mg aspirin daily at least three days before intervention, or 300 mg clopidogrel and 500 mg aspirin intravenously before the intervention. In addition, all patients received 10,000 U of heparin intravenously at the beginning of the procedure and 1 mg atropine before the first balloon dilation. An independent neurologic examination, including the National Institutes of Health Stroke Scale, was performed before and after all procedures.

Detection of microembolic signals. Microembolic signals were detected using a multichannel transcranial Doppler (Multi-Dop X4, DWL, Sipplingen, Germany). A 2.0-MHz transducer was fixed to the temporal bone for insonation of the ipsilateral middle cerebral artery. Microembolic signals were recorded during the whole procedure and analyzed offline by an experienced investigator according to recommended guidelines (3). Because the stenting protocol had to be provided to the investigator for matching the MES to the procedural steps, the reviewer could not be blinded to the different protection devices in use. Microembolic signals were summarized for the following procedural phases: 1) positioning of the protection device into the CCA, 2) passage of the stenosis, 3) stent deployment, 4) balloon dilation, and 5) retrieval of the neuroprotection system. Injection of dye invariably leads to shower of MES caused by microbubbles, which may be less hazardous then solid particles (4). Phases of contrast injection were therefore excluded from the analysis.

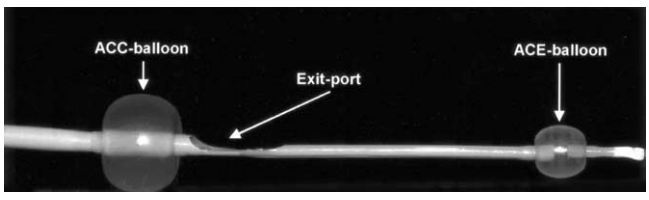

Figure 1. Tip of the MO.MA system. Inflated common and external carotid artery balloons for endovascular clamping and exit port of the guiding catheter. ACC = arteria carotis communis; ACE = arteria carotis externa.

Statistical analysis. Microembolic signal counts are given as mean values ± SD. Microembolic showers are considered 10 MES per one second (5). Comparison of data was performed using the Student *t* test for continuous and chi-squared test for categorical data.

RESULTS

Patient characteristics were not different between the two groups (Table 1). There were no significant differences in angiographic target lesion characteristics or angiographic outcomes after CAS between the two groups (Table 2). All CAS were successful, leaving no residual stenosis >30%. There were no post-procedural neurologic complications except one transient ischemic attack with temporal weakness of the right arm after CAS of a left ICA in the filter group. In one patient of each group, unconsciousness occurred during the intervention with immediate resolution after retrieval of the filter device or de-clamping of the MO.MA system. In both cases, CAS could be concluded under cerebral protection.

Microembolic signals. In the filter group, MES were detected in all patients during all phases, except for one patient during passage of the stenosis with the filter. In the MO.MA group, MES were detected in all patients during the first and last phase of the procedure, but in a significantly lower number of patients during wiring of the stenosis, stent deployment, and balloon dilation (Table 3). Angiography revealed a superior thyroid artery originating proximal of the ECA balloon in 11 patients of the MO.MA group. This anatomy did not correlate with the occurrence of MES during the clamping period. In the filter group, stent deployment and balloon dilation were associated with increased MES counts. Compared to the filter group, the MO.MA system led to similar MES counts during the first and last phase, but were significantly reduced during wiring of the stenosis, stent deployment, and balloon dilation and in total (Table 4).

DISCUSSION

In the present study, TCD monitoring with detection of MES was used to compare the efficacy of two different concepts of neuroprotection. Our study showed that CAS using the MO.MA system, a proximal endovascular clamping device, was accomplished with significantly lower MES counts compared to CAS using a filter system.

The first crucial step during CAS is the passage of the stenosis with a guide wire or a distal protection device. Transcranial Doppler and ex-vivo studies have shown that emboli are frequently provoked during this step of the

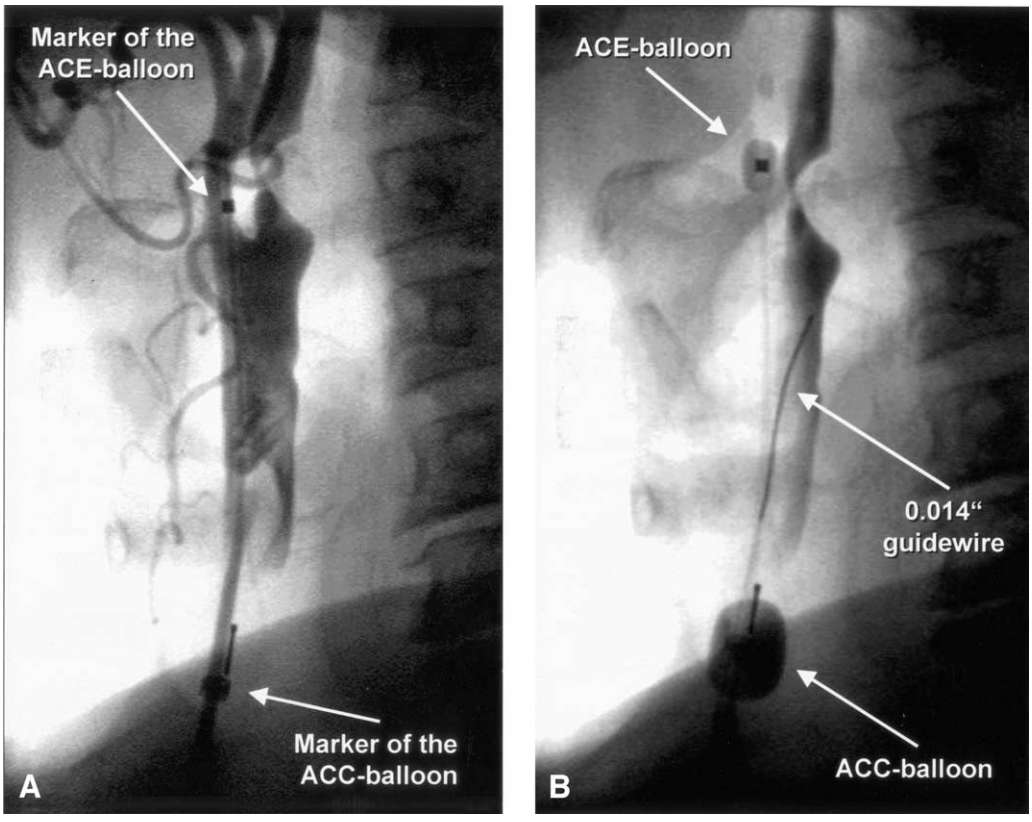

Figure 2. **(A)** MO.MA system placed into the external carotid artery (ECA) and common carotid artery (CCA); **(B)** 0.014-inch guidewire for passage of the stenosis after clamping of the ECA and CCA. Abbreviations as in Figure 1.

procedure (6,7). A potential advantage of proximal endovascular clamping over distal filter or balloon devices is that protection is established before the stenosis is passed. In our study, MES were highly significantly reduced during wiring of the lesion using the MO.MA system compared with the filter device.

Stent deployment and balloon dilation are the steps considered to have the highest risk for distal embolization during the intervention (5,7). In our study, the use of the MO.MA system significantly reduced MES counts during stent deployment and balloon dilation compared with a filter device.

Another finding is that MES counts in the filter group of our series detected during stent deployment, balloon dilation, and in total were of the same magnitude as the MES counts in unprotected CAS during the corresponding phases and in total reported in another TCD study (5). This finding could suggest that filters are not able to hold back emboli, either because of insufficient vessel wall alignment or because a considerable amount of emboli are too small to be captured by these devices. In fact, it was shown that hundreds of thousands of microemboli <100 μm in size can be shed during angioplasty with a potential to pass through the pores of filter devices that range from 80 to 130 μm, leading to neurologic complications in an animal model (7).

Published results of studies using diffusion-weighted magnetic resonance imaging after CAS are consistent with our findings. New cerebral lesions were seen in nearly 30% of patients after mostly uncomplicated CAS without pro-

Table 1. Patient Characteristics

	Filter Group	MO.MA Group	p Value
Age (yrs)	69 ± 9	70 ± 6	NS
Male gender, n (%)	16 (76)	18 (86)	NS
Hypertension, n (%)	19 (90)	19 (90)	NS
Diabetes, n (%)	9 (43)	9 (43)	NS
Hyperlipidemia, n (%)	10 (48)	10 (48)	NS
Coronary artery disease, n (%)	15 (71)	16 (76)	NS
Symptomatic stenosis, n (%)	6 (29)	7 (33)	NS

Data are mean values ± SD or n (%).
NS = not significant.

Table 2. Lesion Characteristics and Procedural Data

	Filter Group	MO.MA Group	p Value
Grade of stenosis (%)	85 ± 8	86 ± 9	NS
Lesion length (mm)	11 ± 5	13 ± 4	NS
Calcification, n (%)	15 (71)	16 (76)	NS
Eccentricity, n (%)	11 (52)	12 (57)	NS
Ulceration, n (%)	7 (33)	6 (29)	NS
Contralateral stenosis ≥70%, n (%)	6 (29)	0 (0)	0.008
Contralateral occlusion, n (%)	2 (10)	0 (0)	NS
Macroscopic evidence of debris, n (%)	14 (67)	18 (86)	NS

Data are mean values ± SD or n (%).
NS = not significant.

Table 3. Number of Patients (%) with Detectable MES During the Different Phases of CAS

	Filter Group	MO.MA Group	p Value
Sheath placement-protection device placement	21 (100%)	21 (100%)	NS
Wiring of the stenosis	20 (95%)	6 (29%)	< 0.0001
Stent deployment	21 (100%)	11 (52%)	0.0003
Balloon dilation	21 (100%)	15 (71%)	0.008
Retrieval of the protection device	21 (100%)	21 (100%)	NS

Data are mean values ± SD or n (%).
CAS = carotid artery stenting; MES = microembolic signals; NS = not significant.

tection devices (8). However, new lesions were also seen in up to 23% of the patients after protected CAS utilizing mostly filter devices (9).

Another explanation for the high MES counts in the filter group could be the inability of TCD to differentiate between gaseous and solid emboli (10). Although MES showers caused by contrast injection were excluded from the analysis, some MES could represent less hazardous gaseous emboli released from contrast or saline associated with the interventional equipment. Nevertheless, in a large registry with TCD performed in 263 CAS procedures, an association of high MES counts with neurologic complications was confirmed (6).

It is difficult to explain the occurrence of MES during protection in the MO.MA group. A nonocclusive balloon or a superior thyroid artery originating proximal of the ECA balloon may lead to a continuous antegrade flow in the target vessel during clamping. However, the latter condition seems unlikely, as we found no correlation between this anatomic constellation and MES counts.

Table 4. MES Counts During the Different Phases of CAS

	Filter Group	MO.MA Group	p Value
Sheath placement-protection device placement	20 ± 15	18 ± 10	NS
Wiring of the stenosis	25 ± 22	2 ± 3	< 0.0001
Stent deployment	73 ± 49	11 ± 19	< 0.0001
Balloon dilation	70 ± 31	12 ± 21	< 0.0001
Retrieval of the protection device	14 ± 15	19 ± 15	NS
Total	196 ± 84	57 ± 41	< 0.0001

Data are mean values ± SD or n (%).
Abbreviations as in Table 3.

Study limitations. Patient inclusion was nonrandomized. However, clinical and angiographic criteria were well matched between the two groups. Only one filter device was used in our study. Other types of filter devices with differences in pore size or alignment to the vessel wall may have generated different results. Because of the study size, no conclusions can be drawn about differences in clinical efficacy of the investigated protection devices.

Conclusions. The MO.MA system led to a significant reduction of MES compared with a filter device. This suggests that the concept of proximal endovascular clamping has the potential to increase the safety of carotid intervention.

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