JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 6, NO. 11, 2013

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcin.2013.07.006

Randomized Comparison of Distal and Proximal Cerebral Protection During Carotid Artery Stenting

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Objectives This study sought to randomly compare cerebral protection with ANGIOGUARD (Cordis Corporation, Bridgewater, New Jersey) with Mo.Ma (Invatec/Medtronic Vascular Inc, Santa Rosa, California) during carotid artery stenting (CAS), using diffusion-weighted magnetic resonance imaging (DW-MRI) to detect new ischemic cerebral lesions. The number, size, and location of lesions were analyzed.

Background The choice of the type of cerebral protection during CAS is controversial.

Methods From July 2008 to July 2011, 60 patients undergoing CAS were randomized to ANGIOGUARD or Mo.Ma, distributed by chance, 30 patients for each group. All patients underwent DW-MRI before and after CAS. An independent neuroradiologist blinded to the cerebral protection used analyzed the images. Univariate and multivariate logistic models were fitted to analyze new ischemic lesions. Alternatively, a propensity score approach was used to reduce the bias due to differences between the groups. For the number of lesions, we used Poisson regression models.

Results New ischemic lesions seen on DW-MRI were present in 63.3% of the ANGIOGUARD group versus 66.7% of the Mo.Ma cohort ($p = 0.787$). The number of ischemic cerebral lesions per patient, when present, was significantly lower in the Mo.Ma group (a median of 6 lesions per patient vs. a median of 10 in the ANGIOGUARD, $p < 0.001$). Most lesions were small (<0.5 mm) and localized in the ipsilateral territory. One patient in the ANGIOGUARD group had a minor stroke during CAS (1.66%).

Conclusions New ischemic lesions seen on DW-MRI were present in both groups in >60%, but the number of lesions per patient was greater in the ANGIOGUARD group. No death or disabling stroke occurred during at least 1 year of follow-up in both cohorts. (J Am Coll Cardiol Intv 2013;6:1203–9)

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Manuscript received March 7, 2013; revised manuscript received June 7, 2013, accepted July 3, 2013.

In recent years, carotid artery stenting (CAS) has become an alternative to surgery, especially in high-risk patients (1). The CREST (Carotid Revascularization Endarterectomy vs. Stenting) trial (2) showed that carotid endarterectomy (CEA) and CAS were comparable treatments, and the differences between the methods (more infarction and cranial nerve injury with CEA and increased risk of minor ipsilateral stroke with CAS) are counterbalanced.

In the Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Unanticipated or Rare Events (CAPTURE) registry, the authors analyzed timing, location, severity, and types of strokes after protected CAS in 3,500 patients (3). Stroke occurred in 168 (4.8%) patients (4% ipsilateral and 2% major stroke). The incidence of major stroke was greater in symptomatic than in asymptomatic patients (4.6% vs. 1.6%, respectively). This registry also revealed that the majority of symptoms occurred during the procedure (22.3%) or during hospitalization (57.7%), but 20% developed after discharge, aiding in the understanding of the different mechanisms of stroke.

The use of cerebral protection devices (CPDs) during CAS began with Theron et al. (4), who placed a distal balloon occlusion system during a carotid intervention. In a meta-analysis comparing CAS and CEA (5), the authors found that the CPDs did yield significant improvements in the occurrence of disabling stroke or death after CAS in 30 days, with a lower incidence in those patients with a CPD. Additionally, Bersin et al. (6), in a meta-analysis of 2,397 patients, showed that the benefits of proximal CPD extended to various subgroups of patients undergoing CAS, including symptomatic patients and octogenarians.

Abbreviations and Acronyms

CAS = carotid artery stenting

CEA = carotid endarterectomy

CPD = cerebral protection device

DW-MRI = diffusion-weighted magnetic resonance imaging

In the present study, the authors aimed to compare 2 different principles of CPD during CAS, using a surrogate imaging endpoint diffusion-weighted magnetic resonance imaging (DW-MRI) to assess the effectiveness of the devices.

Methods

Study design and population. This was a prospective, randomized, open-label, single-center trial in patients with symptomatic and asymptomatic carotid stenosis who underwent CAS with a proximal or distal CPD.

From July 2008 to July 2011, 60 patients with severe carotid lesions (symptomatic and asymptomatic), with indications for CAS in whom both distal filter ANGIOGUARD (Cordis Corporation, Bridgewater, New Jersey) or proximal occlusion Mo.Ma Ultra (Invatec/Medtronic Vascular Inc, Santa Rosa, California) could be used, were selected according to the inclusion and exclusion criteria and randomized to 1 of the CPDs. Table 1 presents the main inclusion/exclusion criteria.

Four cervical vessels angiography performed before randomization allowed us to classify whether patients with tight lesions >80% had collateral circulation. When cerebral circulation ipsilateral to the lesion was visualized during angiography of the contralateral carotid artery, or when the anterior communicating artery, was opacified during angiography, we considered the presence of collateral circulation.

Plaque characteristics were analyzed regarding the location, eccentricity, the presence of an ulcer, smoothness of its surface (i.e., regular vs. irregular) eccentricity, and the degree of calcification and tortuosity. Those patients with severe angulation between the carotid internal artery and common carotid artery (tortuosity index) (7) were excluded from randomization because greater tortuosity and angulation impaired the effectiveness of using a distal ANGIOGUARD CPD as well as increased complications (8).

During the randomization period, 250 carotid stenting procedures were performed at our institution, and 67 patients met the inclusion/exclusion criteria and were enrolled in the study. During the study, 2 patients withdrew their consent to participate in the study, and in 5 patients at the time of the procedure, the operators deemed their anatomy more suitable for 1 or the other CPD, violating the inclusion criteria. These patients were excluded for the final analysis.

Randomization was performed before the beginning of the procedure and done electronically using the complex samples module of SPSS for Windows, version 19.0 (SPPS, Inc., Chicago, Illinois). Block randomization of 6 patients (3 patients for ANGIOGUARD and 3 patients for Mo.Ma) was used to ensure a periodic balance in the number of patients assigned to each group.

The study protocol was in accordance with the Declaration of Helsinki for human research and was approved by the Ethics in Research Committee of our institution. The entire supporting infrastructure for conducting the research and monitoring the patients enrolled was offered by the hospital, and all patients gave their written informed consent. There was no sponsoring for this study.

CAS procedure. CAS was performed according to the service routine, already described by Costa (9) and Cano (16) and followed international guidelines (10,11). For uniformity of the procedure, 1 type of carotid stent was used (PRECISE PRO RX carotid stent, Cordis Bridgewater, New Jersey), the same stent that was previously evaluated in the SAPPHIRE (Stent and Angioplasty with Protection in Patients at High Risk for Endarterectomy) trial (1). For the same reason, 1 type of distal CPD was chosen (ANGIOGUARD, Cordis). At the time of recruitment, a single type of proximal CPD was available for clinical use in our country (Mo.Ma, Invatec).

All patients were pre-medicated with clopidogrel 75 mg/day and aspirin 100 mg/day, at least 3 days before the

Table 1. Study Inclusion and Exclusion Criteria

Inclusion criteria
1. Male and female patients 40 years of age and older.
2. Asymptomatic patients with internal carotid artery stenosis ≥80% on angiography.
3. Symptomatic patients with internal carotid artery stenosis ≥50% on angiography.
4. Anatomic characteristics of the lesions that made it possible to use either type of cerebral protective device (proximal or distal).
5. The patient or legally authorized representative has been informed of the nature of the study, agrees to its provisions, and has provided written informed consent, approved by the appropriate Medical Ethics Committee, Institutional Review Board, or Human Research Ethics Committee.
Exclusion criteria
1. Extensive ipsilateral or disabling stroke.
2. Ischemic ipsilateral stroke progressing to hemorrhagic within 60 days.
3. Decreased brain reserve defined as extensive previous stroke, dementia, multiple lacunar infarcts.
4. Severe common carotid or intracranial artery lesion.
5. Occlusion of ipsilateral external carotid artery.
6. Occlusion of the target vessel occurred after indication of carotid artery stenting.
7. Occlusion of contralateral carotid artery.
8. Severe or obstructive lesion in vertebrobasilar segments.
9. Extremely calcified aortic arc that compromised the origin of the common carotid artery or the brachiocephalic trunk.
10. Chronic or paroxysmal atrial fibrillation treated with oral anticoagulation.
11. Acute coronary syndrome in the 30-day period before the procedure.
12. Contraindication to magnetic resonance examination (e.g., claustrophobia, pacemaker).
13. Patient has a history of bleeding diathesis within 1 month or coagulopathy or patients in whom antiplatelet and/or anticoagulant therapy is contraindicated.
14. Patient has a known hypersensitivity or contraindication to aspirin, heparin, and clopidogrel/ticlopidine, stent, and/or contrast sensitivity/allergy that cannot be adequately pre-medicated.

intervention. Clopidogrel was continued for at least 1 month after CAS and aspirin indefinitely. Betablockers were discontinued at least 24 h before the procedure and other medications used were at the discretion of the referring physician.

Cerebral DW-MRI was performed before and 48 h after CAS on 3-T unit (Excite HD, GE Medical Systems, Milwaukee, Wisconsin) with a head coil of 8 channels. All imaging was performed at the Hospital do Coração and analyzed by an independent neuroradiologist blinded to the CPD used.

Study endpoints. The primary endpoint of this study was comparison of the incidence, number, size, and location of new cerebral ischemic lesions using DW-MRI in patients treated with a distal (ANGIOGUARD) versus a proximal (Mo.Ma) CPD. Secondary endpoints included device success rate and the rate of major clinical events (death, major stroke, and myocardial infarction) up to 1 year.

Study definitions. Patients were considered symptomatic if they had an ipsilateral neurological ischemic event within 180 days before the procedure. The procedure was considered successful when residual stenosis after CAS was ≤30% without neurological complications. The ischemic lesions were considered ipsilateral when they occurred in the hemisphere supplied by the target vessel; otherwise they were contralateral. A transient ischemic attack was defined as a temporary alteration of the blood supply to an area of the brain, resulting in a sudden and brief (<24 h, usually <1 h) decrease in brain function. Symptoms varied depending on the area of the brain affected (12). Stroke was defined as a new focal neurological deficit with symptoms and signs consistent with focal ischemia lasting >24 h with the deficit corresponding to a vascular territory. The modified Rankin Scale score >2 was used to define classification as major and as minor when the score was ≤2. A minor stroke causes a neurological deficit that resolves completely within 30 days, whereas a major stroke causes a neurological deficit that does not resolve completely within 30 days and leads to a worsening of performance of daily activities (13,14).

Statistical analysis. Categorical variables were presented as frequency and percentage and quantitative variables were summarized as mean and SD, when normally distributed, or as median and interquartile range otherwise. The groups were compared using the Student *t* or Mann-Whitney test and the Pearson chi-square or Fisher exact test for numerical and categorical variables, respectively. To control the influence of confounding factors on the presence of new cerebral ischemic lesions, we used 2 approaches: conventional covariance analysis by simple and multiple logistic regression models (univariate and multivariate) (15) and propensity scores (16).

The multivariate model included variables with $p < 0.10$ in the univariate analysis and those with significant (or marginal) differences between groups. The same variables were selected for a logistic regression with group as a dependent variable to estimate the probability that a patient would be assigned to the ANGIOGUARD or Mo.Ma CPD. Inverse estimated probabilities (propensity

scores) were used as individual weights in a weighted logistic regression model. Alternatively, the propensity score was included as a covariate in the unadjusted regression model.

For the number of new ischemic lesions (total and ipsilateral), we used the Poisson regression model (17). The propensity score approach (as a weighted model or as a covariate) was also applied.

The level of significance was $p = 0.05$. The statistical programs used were SPSS for Windows, version 19.0 (SPPS, Inc., Chicago, Illinois) and R software version 16.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Between July 2008 and July 2011, 60 patients were randomized to receive either an ANGIOGUARD or Mo.Ma CPD.

Clinical and angiographic characteristics of the enrolled patients are summarized in Table 2. The majority of patients were male (67%), and >20% in both groups had undergone a previous carotid intervention (7 [23%] patients in the ANGIOGUARD group vs. 6 [20%] in the Mo.Ma group, $p = 0.753$). Most previous carotid interventions (12 of 13) were performed in the contralateral carotid artery. Also, previous coronary revascularization was performed in 25% of the total number of study patients with no significant difference between groups (30% of the patients with distal CPD vs. 20% of the patients with proximal CPD [$p = 0.371$]).

The groups were also similar with regard to the lesion characteristics, except for the amount of calcified lesions, which were more prevalent in the ANGIOGUARD cohort ($p = 0.004$). Of the total study population, 22 (36.7%) patients had bilateral carotid lesions, equally divided in both groups.

DW-MRI performed before the procedure found no difference between the groups with regard to cerebral atrophy, leukoaraiosis, or the presence of previous cerebral microinfarction (Table 3).

The number of old infarcts per patient ranged from 1 to 9 in the ANGIOGUARD group and from 1 to 7 in the Mo.Ma group. Regarding the size of the old infarcts, most were <1.5 cm (90.5% in ANGIOGUARD and 74.4% in Mo.Ma). All 15 patients with a previous stroke (7 Mo.Ma, 8 ANGIOGUARD) were classified according to both modified Rankin Scale score and Barthel Index of Activities of Daily Living score, and most of them had no significant disability and were able to carry out all usual activities, with a modified Rankin Scale score between 0 and 1, and in five patients a score of 2; the Barthel Index score of all 15 patients was 100 points before CAS.

Only 1 patient in the ANGIOGUARD group and 2 in the Mo.Ma cohort had acute hyperintense Cerebral images

Table 2. Baseline Clinical and Angiographic Characteristics

	Cerebral Protection		
	ANGIOGUARD (n = 30)	Mo.Ma (n = 30)	p Value
Men	19 (63.3)	21 (70.0)	0.584
Age, yrs	68.5 ± 7.5	67.0 ± 9.3	0.493
Age ≥80 yrs	2 (6.7)	1 (3.3)	>0.999
Symptomatic	6 (20.0)	9 (30.0)	0.371
Previous carotid disease*	15 (50.0)	19 (63.3)	0.297
Hypertension	28 (93.3)	28 (93.3)	>0.999
CAD	24 (80.0)	18 (60.0)	0.158
Dyslipidemia	24 (80.0)	23 (76.7)	0.754
Diabetes mellitus	12 (40.0)	12 (40.0)	>0.999
Peripheral vascular disease	11 (36.7)	18 (60.0)	0.071
COPD	2 (6.7)	2 (6.7)	>0.999
Chronic renal insufficiency	4 (13.3)	8 (26.7)	0.197
Aortic arch classification, type			0.437
I	19 (63.3)	17 (56.7)	
II	5 (16.7)	9 (30.0)	
III	6 (20.0)	4 (13.3)	
Aortic characteristics			
Calcified	8 (26.7)	3 (10.0)	0.095
Elongated	1 (3.3)	1 (3.3)	>0.999
Bovine arch	2 (6.7)	4 (13.3)	0.671
Contralateral lesion or previous stent	11 (36.7)	11 (36.7)	>0.999
Characteristics of treated lesion			
Localization			0.472
Carotid bifurcation	24 (80.0)	27 (90.0)	
Distal to bifurcation	6 (20.0)	3 (10.0)	
Plaque characteristics			0.791
Regular	19 (63.3)	18 (60.0)	
Irregular	11 (36.7)	12 (40.0)	
Degree of calcification			0.004
Absent or very little	5 (16.7)	17 (56.7)	
Moderate	10 (33.3)	7 (23.3)	
Severe	15 (50.0)	6 (20.0)	
Tortuosities			0.511
Absent	13 (43.3)	18 (60.0)	
Proximal	1 (3.3)	2 (6.7)	
Middle	6 (20.0)	3 (10.0)	
Distal	10 (33.3)	7 (23.3)	
Ulcerated	3 (10.0)	1 (3.3)	0.612
Eccentric	22 (73.3)	23 (76.7)	0.766
Stenosis, %	82.8 ± 5.4	84.4 ± 7.0	0.327
Lesion length, mm	13.1 ± 8.6	14.6 ± 9.3	0.537
Collateral contralateral circulation	22 (73.3)	15 (50.0)	0.063
Middle cerebral artery	30 (100)	30 (100)	N/A
Anterior cerebral artery	24 (80.0)	18 (60.0)	0.091

Values are n (%) or median ± SD. *Transient ischemic attack or stroke >180 days.
CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; N/A = not applicable.

Table 3. Diffusion-Weighted Magnetic Resonance Imaging Before Carotid Artery Stenting

	Cerebral Protection		
	ANGIOGUARD (n = 30)	Mo.Ma (n = 30)	p Value
Cerebral atrophy			
Absent	8 (26.7)	6 (20.0)	0.920
Minimum (sulci ≤3 mm)	—	—	
Moderate (sulci >3 to ≤5 mm)	19 (63.3)	21 (70.0)	
Intense (sulci >5 mm)	3 (10.0)	3 (10.0)	
Leukoaraiosis			
Absent/minimum, rare foci	22 (73.3)	22 (73.3)	>0.999
Moderate, numerous foci but narrow	6 (20.0)	5 (16.7)	
Severe, wide, and diffuse	2 (6.7)	3 (10.0)	
Old infarction	14 (46.7)	13 (43.3)	0.795
New microinfarction	1 (3.3)	2 (6.7)	>0.999
Microhemorrhages	14 (46.7)	14 (46.7)	>0.999

Values n (%).

on DW-MRI that probably occurred because of particles released either during or after diagnostic carotid angiography done a few days before CAS or spontaneously, although the patients remained completely asymptomatic.

Carotid angioplasty results. Clinical and procedural successes were achieved in 98.3% of the patients; 1 patient experienced a minor stroke during the procedure. In all of the patients, it was possible to complete CAS with the CPD according to randomization. There was no crossover between groups. Despite randomization, in the ANGIOGUARD group, a greater proportion of patients, the left carotid artery was treated (60% vs. 33% in the Mo.Ma group), with statistical significance (p = 0.038) (Table 4).

The procedure duration tended to be longer in the Mo.Ma group (29.5 min) compared with the distal CPD cohort (Δ24.2 min, p = 0.051).

There were no immediate deaths or major strokes. There were a low incidence of other complications, such as hypotension and bradycardia, and no statistical difference between groups. One patient (1.66%) required vascular surgery to stop bleeding at a puncture site. There was a late retinal infarction in a patient in the ANGIOGUARD group, and a patient with hyperperfusion syndrome in the Mo.Ma group, both of whom recovered quickly.

Results of DW-MRI after CAS. The findings of DW-MRI after CAS are shown in Table 5. The incidence of new microischemic lesions did not differ between groups (63.3% for the ANGIOGUARD group vs. 66.7% for the Mo.Ma group, p = 0.787).

CPD analysis according to the subgroups of interest did not point to any significant difference between the devices. However, when the number of new lesions per patients was analyzed, there was a statistically significant association between symptoms and the number of new lesions. Symptomatic patients had a greater number of lesions, with a significant p value = 0.001 for the whole group and for those with a the ANGIOGUARD CPD, and less significance with the Mo.Ma CPD (p = 0.039).

Table 4. Procedure Characteristics

	Cerebral Protection		
	ANGIOGUARD (n = 30)	Mo.Ma (n = 30)	p Value
Treated artery			
Right internal carotid artery	12 (40.0)	20 (66.7)	0.038
Left internal carotid artery	18 (60.0)	10 (33.3)	
Duration of CAS, min	24.2 (10.4)	29.5 (10.3)	0.051
Total contrast, ml	97.5 (70–100)	80.0 (60–100)	0.319
Residual lesion	14 (0–20)	10.0 (0–17)	0.244

Values are n (%) or median (interquartile range).
CAS = carotid artery stenting.

The majority of the new lesions were <0.5 cm, and >70% of the lesions were in a cortical location. There were no differences between groups with respect to lesion size (p = 0.950), anatomic location (p = 0.360), and vascular distribution (p = 0.915).

The total number of lesions seen on DW-MRI was significantly higher among patients with a distal CPD (424 lesions/19 patients vs. 167 lesions/20 patients in the Mo.Ma cohort, p < 0.001) as well as the number of lesions per patient (a median of 10 in the distal CPD group vs. a median of 6 in the proximal CPD group, p < 0.001). Overall, most new lesions were ipsilateral (>90% in both groups).

There were no independent predictors of acute ischemic event among these patients, regardless of the statistical model or correction (propensity score) applied.

Discussion

Our results showed that regardless of the CPD used during CAS, new cerebral lesions developed in >60% of patients as seen on DW-MRI, but the number of lesions per patient was greater in the ANGIOGUARD group. Fortunately, most DW-MRI–detected embolizations did not have immediate clinical translation, even though the effect on cognitive function is still debated (18). The majority of lesions (>90%) were smaller (<0.5 mm). There was no major stroke or death during hospitalization and at least 1 year of follow-up.

The recently published PROFI (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid Artery Stenting) trial (19), which also compared distal and proximal protection during CAS (n = 62), showed a higher incidence cerebral ischemic

Table 5. DW-MRI After Carotid Artery Stenting

Characteristics on DW-MRI	Cerebral Protection		
	ANGIOGUARD (n = 30)	Mo.Ma (n = 30)	p Value
Patients with new lesions	19 (63.3)	20 (66.7)	0.787
Patients with new ipsilateral lesions	17 (56.7)	19 (63.3)	0.598
Patients with new lesions >1 cm	3 (10.0)	2 (6.7)	>0.999
Patients with new ipsilateral lesions >1 cm	2 (6.7)	2 (6.7)	>0.999
Vascular distribution			
Ipsilateral	17 (56.7)	19 (63.3)	0.598
Contralateral	11 (36.7)	8 (26.7)	0.405
Supratentorial vertebrobasilar	7 (23.3)	7 (23.3)	>0.999
Infratentorial vertebrobasilar	3 (10.0)	2 (6.7)	>0.999
No. of new lesions per patient*	10 (3–42)	6 (2–8)	<0.001
Total no. of new lesions	424 (19p)	167 (20p)	
No. of new ipsilateral lesions*	12 (3–41)	6 (1–8)	<0.001
Total no. of new ipsilateral lesions	395 (17p)	145 (19p)	

Values are n (%) or median (interquartile range). *Only patients with new lesions (excluding those with no lesions).
DW-MRI = diffusion-weighted magnetic resonance imaging; p = patients.

events after the use of a distal filter (87.1% vs. 45.2%, p = 0.001). Although in our study the number of ischemic events was insufficient to determine the difference between the groups, the number of particles per patient undergoing CAS was significantly lower in the proximal CPD group than in the distal CPD group (167 in 20 patients vs. 424 in 19 patients, respectively), which is in accordance with the PROFI trial findings, which also pointed to a significant reduction in the incidence, number, and volume of new cerebral ischemic lesions in patients who underwent CAS with a proximal balloon as compared with distal (filter) protection.

As previously demonstrated, microparticles embolized during CAS might be generated during all of the steps of the procedure. Montorsi et al. (20) compared the frequency of microparticles generated during CAS with the proximal Mo.Ma CPD and the distal FilterWire EZ Embolic Protection System (Boston Scientific, Natick, Massachusetts) in lipid-rich atherosclerotic plaques by transcranial Doppler imaging during the various phases of stenting: 1) lesion wiring; 2) pre-dilation; 3) stent crossing; 4) stent deployment; 5) stent dilation; and 6) device retrieval/deflation. The authors reported fewer signals (microembolic signals) detected by transcranial Doppler imaging in the Mo.Ma group compared with FilterWire EZ Embolic Protection System group in phases 3, 4, and 5 (27% vs. 100%, p < 0.0001) and higher in phase 6 (8.5% vs. 2%, p = 0.0036) with no difference in phase 2. Patients in the Mo.Ma group had a decrease in the number of microembolic signals compared with the FilterWire EZ, with statistical significance in patients with high-risk, lipid-rich plaque undergoing CAS.

In our study, ipsilateral lesions after CAS were observed in 395 of 424 patients (93%) with the ANGIOGUARD CPD and 145 of 167 patients (87%) with the Mo.Ma CPD. The presence of ipsilateral lesions can be attributed to the release of particles from the treated plaque during CAS. Stojanov et al. (21) assessed the correlation between carotid plaque composition and the risk of distal embolization during CAS. They studied a group of 50 patients using a distal CPD filter. Plaque morphology was differentiated by sonography as fibrolipid or fibrocalcific. They found 14.89% of new lesions on DW-MRI, 8.51% in the ipsilateral territory, and those with fibrolipid plaques had significantly more new lesions compared with fibrocalcific plaques (p = 0.041). The absolute risk of new lesions in the fibrolipid group was 18.18%. Most of the patients with lesions had no clinical symptoms, and no significant relationship was found between new lesions and factors related to CAS.

The source of contralateral lesions was described by Barbato et al. (22), who showed that the occurrence of microemboli during CAS was not prevented by the use of distal filter, and in one fifth of patients, embolization occurred in the contralateral hemisphere. They found a correlation between age, increasing amount of calcium in the aortic arch, and the presence of aortic arch type II and the occurrence of new lesions. Other previous studies have also shown that both aortic arch anatomy and a tortuous carotid artery proximal to a plaque significantly increased the risk of technical failure and neurological complications during CAS (7,23).

Major technical and technological advances are taking place with the introduction of appropriate dedicated stents, better patient selection, improvement in physicians expertise and new cerebral protection devices (24). Even though we believe that CPDs have made a great contribution to the development of carotid intervention, we cannot forget that CAS still has the inherent risk of potential stroke.

Study limitations. The relatively small sample size might preclude definite conclusions about the efficacy of the tested devices in this clinical scenario. Also, only 2 types of CPDs were tested, and, therefore, the results do not apply to the various proximal and distal CPDs currently available.

Conclusions

New ischemic lesions seen on DW-MRI were present in >60% of both groups, but the number of lesions per patient was greater in the ANGIOGUARD than in the Mo.Ma cohort. There were no deaths or disabling strokes in the one-year follow-up of the entire population.

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REFERENCES

1. Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004;351:1493–501.
2. Brott TG, Hobson RW 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med 2010;363:11–23.
3. Fairman R, Gray WA, Scicli AP, et al. The CAPTURE registry: analysis of strokes resulting from carotid artery stenting in the post approval setting: timing, location, severity, and type. Ann Surg 2007; 246:551–6; discussion 556–8.
4. Theron JG, Payelle GG, Coskun O, Huet HF, Guimaraens L. Carotid artery stenosis: treatment with protected balloon angioplasty and stent placement. Radiology 1996;201:627–36.
5. Liu ZJ, Fu WG, Guo ZY, Shen LG, Shi ZY, Li JH. Updated systematic review and meta-analysis of randomized clinical trials comparing carotid artery stenting and carotid endarterectomy in the treatment of carotid stenosis. Ann Vasc Surg 2012;26:576–90.
6. Bersin RM, Stabile E, Ansel GM, et al. A meta-analysis of proximal occlusion device outcomes in carotid artery stenting. Catheter Cardiovasc Interv 2012;80:1072–8.
7. Faggioli G, Ferri M, Gargiulo M, et al. Measurement and impact of proximal and distal tortuosity in carotid stenting procedures. J Vasc Surg 2007;46:1119–24.
8. Wang Q, Liu C, Yan B, et al. Correlation of extracranial internal carotid artery tortuosity index and intraprocedural complications during carotid artery stenting. Eur Neurol 2012;68:65–72.
9. Costa JR, Oliveira DC, Cano MN, et al. Percutaneous implantation of endoprostheses in the carotid arteries. Arq Bras Cardiol 2003;80:71–6.
10. Naylor AR. What is the current status of invasive treatment of extracranial carotid artery disease? Stroke 2011;42:2080–5.
11. Kakisis JD, Avgerinos ED, Antonopoulos CN, Giannakopoulos TG, Moulakakis K, Liapis CD. The European Society for Vascular Surgery guidelines for carotid intervention: an updated independent assessment and literature review. Eur J Vasc Endovasc Surg 2012;44:238–43.
12. Siket MS, Edlow JA. Transient ischemic attack: reviewing the evolution of the definition, diagnosis, risk stratification, and management for the emergency physician. Emerg Med Clin North Am 2012;30:745–70.
13. Fischer U, Baumgartner A, Arnold M, et al. What is a minor stroke? Stroke 2010;41:661–6.
14. Breuer L, Blinzler C, Huttner HB, Kiphuth IC, Schwab S, Kohrmann M. Off-label thrombolysis for acute ischemic stroke: rate, clinical outcome and safety are influenced by the definition of 'minor stroke'. Cerebrovasc Dis 2011;32:177–85.
15. David W. Hosmer, Stanley Lemeshow. Model-Building Strategies and Methods for Logistic Regression. Second Edition. Hoboken, NJ: John Wiley & Sons, Inc., 2005.
16. Cano MN. A randomized study comparing two cerebral protection devices in carotid artery stenting: Evaluation of new ischemic lesions through the sequence of diffusion weighted magnetic resonance imaging (Thesis). Brazil: University of São Paulo, 2012.
17. Kirkwood B. Poisson regression. B K, editor. Malden, MA: Blackwell Science, 2003:249–62.
18. Maggio P, Altamura C, Landi D, et al. Diffusion-weighted lesions after carotid artery stenting are associated with cognitive impairment. J Neurol Sci 2013;328:58–63.
19. Bijuklic K, Wandler A, Hazizi F, Schofer J. The PROFI study (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid Artery Stenting): a prospective randomized trial. J Am Coll Cardiol 2012;59: 1383–9.
20. Montorsi P, Caputi L, Galli S, et al. Microembolization during carotid artery stenting in patients with high-risk, lipid-rich plaque. A randomized trial of proximal versus distal cerebral protection. J Am Coll Cardiol 2011;58:1656–63.
21. Stojanov D, Ilic M, Bosnjakovic P, et al. New ischemic brain lesions on diffusion-weighted MRI after carotid artery stenting with filter protection: frequency and relationship with plaque morphology. AJNR Am J Neuroradiol 2012;33:708–14.
22. Barbato JE, Dillavou E, Horowitz MB, et al. A randomized trial of carotid artery stenting with and without cerebral protection. J Vasc Surg 2008;47:760–5.
23. Bazan HA, Pradhan S, Mojibian H, Kyriakides T, Dardik A. Increased aortic arch calcification in patients older than 75 years: implications for carotid artery stenting in elderly patients. J Vasc Surg 2007;46: 841–5.
24. Bijuklic K, Tubler T, Wandler A, Goossens-Merkt H, Schofer J. Carotid artery stenting, what can be learned after more than 1,000 patients: a single centre single operator experience. EuroIntervention 2011;7:820–7.

Key Words: carotid artery stenting ■ cerebral protection device ■ diffusion-weighted MRI.