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PERIPHERAL

Cerebral Embolic Lesions Detected With Diffusion-Weighted Magnetic Resonance Imaging Following Carotid Artery Stenting

A Meta-Analysis of 8 Studies Comparing Filter Cerebral Protection and Proximal Balloon Occlusion

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ABSTRACT

OBJECTIVES The aim of this meta-analysis was to evaluate and compare the efficacy of the 2 different neuroprotection systems in preventing embolization during carotid artery stenting (CAS), as detected by diffusion-weighted magnetic resonance imaging (DW-MRI).

BACKGROUND Data from randomized and nonrandomized studies comparing both types of embolic protection devices revealed contrasting evidence about their efficacy in neuroprotection, as assessed by the incidence of new ischemic lesions detected by DW-MRI.

METHODS Eight studies, enrolling 357 patients, were included in the meta-analysis. Our study analyzed the incidence of new ischemic lesions/patient, comparing filter cerebral protection and proximal balloon occlusion.

RESULTS Following CAS, the incidence of new ischemic lesions/patient detected by DW-MRI was significantly lower in the proximal balloon occlusion group (effect size [ES]: −0.43; 95% confidence interval [CI]: −0.84 to −0.02, $I^2 = 70.08$, $Q = 23.40$). Furthermore, following CAS, the incidence of lesions at the contralateral site was significantly lower in the proximal protection group (ES: −0.50; 95% CI: −0.72 to −0.27, $I^2 = 0.00$, $Q = 3.80$).

CONCLUSIONS Our meta-analysis supports the concept that the use of proximal balloon occlusion compared with filter cerebral protection is associated with a reduction of the amount of CAS-related brain embolization. The data should be confirmed by a randomized clinical trial. (J Am Coll Cardiol Intv 2014;7:1177–83) © 2014 by the American College of Cardiology Foundation.

Carotid artery stenting (CAS) is a validated treatment to reduce the incidence of stroke among patients with moderate-to-severe symptomatic carotid stenosis (1,2), as well as among those with severe asymptomatic carotid stenosis (3,4). According to guideline recommendations, CAS has shown noninferiority to carotid endarterectomy in the prevention of stroke (5). However, because of the occurrence of periprocedural neurological ischemic events, current guidelines recommend the use of embolic protection devices (EPDs) during CAS (1).

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ABBREVIATIONS AND ACRONYMS

CAS = carotid artery stenting

CI = confidence interval

DW-MRI = diffusion-weighted magnetic resonance imaging

EPD = embolic protection device

ES = effect size

Among the EPDs that are in clinical use, proximal EPDs have the advantage of providing cerebral embolic protection during all phases of the endovascular intervention (6). The use of endovascular clamping, a proximal EPD, during CAS has been demonstrated to be particularly safe and efficient in large registries and clinical trials (7,8). Moreover, the use of proximal EPDs has been associated with a reduced amount of cerebral embolic signals when compared with distal protection devices (6).

Diffusion-weighted magnetic resonance imaging (DW-MRI) has been shown to be a sensitive tool in identifying new ischemic cerebral lesions caused by emboli during CAS. Data from randomized and nonrandomized studies comparing both types of EPDs revealed contrasting evidence about their efficacy in neuroprotection, as assessed by the incidence of new ischemic lesions detected by DW-MRI (9–16).

Therefore, the aim of this meta-analysis was to evaluate and compare the efficacy of the 2 different neuroprotection systems in preventing embolization during CAS, as detected by DW-MRI.

METHODS

STUDY SELECTION. The study was designed according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) requirements (17). MEDLINE, Cochrane (Cochrane Database of Systematic Reviews), Web of Science, and SCOPUS database were searched for studies published until December 2013. Studies were identified using the major medical subject heading "carotid artery stenting or CAS" AND "DW-MRI or magnetic resonance imaging" AND "distal embolic protection device or filter or distal cerebral protection" AND "proximal embolic protection device or flow reversal or proximal cerebral protection." Citations were screened at the title and abstract level, and retrieved as a full report if they reported data on the comparison of CAS outcomes, defined as new ischemic lesions detected at DW-MRI, between a filter cerebral protection group and a proximal balloon occlusion group. No language limitations were applied. The full texts and bibliography of all potential studies also were retrieved in detail to seek additional relevant studies.

INCLUSION CRITERIA. Studies were included if they:

1. Reported data on comparison of CAS outcomes, defined as the incidence of new ischemic lesions and number of new ischemic lesions per patient (lesions/patient), between a filter cerebral protection group and a proximal balloon occlusion group; and
2. New ischemic lesions were detected by DW-MRI.

EXCLUSION CRITERIA. Studies were excluded if any of the following criteria applied:

1. Duplicate publication, subgroup studies of a main study;
2. The outcome of interest was not clearly reported or was impossible to extract or calculate from the published results.

DATA EXTRACTION. Two reviewers independently screened studies for fulfilment of inclusion criteria. Reviewers compared selected trials, and discrepancies were resolved by consensus. The quality of the trials was not evaluated because this practice has been previously discouraged (18).

STUDY ENDPOINTS. The primary endpoint evaluated was the incidence of new ischemic lesions/patient during a CAS procedure with filter cerebral protection or proximal balloon occlusion. Publication bias was assessed by plotting the study results against the precision of the study (funnel plots) for each outcome. Symmetry of the funnel plots was tested using the trim and fill method. Of the 193 studies identified by the initial search, 12 were retrieved for more detailed evaluation, and 8 studies were included in the study (**Figure 1**).

STATISTICAL ANALYSIS. Mean, SD, and p values were used. Overall estimates of effect (effect size [ES]) were calculated with a random effects model (19). Statistical significance was set at $p < 0.05$ (2-tailed). Heterogeneity was assessed by a Q statistic and I^2 test. Significant heterogeneity was considered present for p values <0.10 or an I^2 >50%. Data analysis was performed using ProMeta 2.0 (Internovi, Cesena, Italy). For verification of the robustness of the results, sensitivity analyses were performed to test the influence of potential effect modifiers, including mean age, age >80 years, male sex, symptomatic carotid artery disease, smoking status, diabetes, coronary artery disease, chronic obstructive pulmonary disease, peripheral artery disease, hypertension, dyslipidemias, prior myocardial infarction, prior stroke, prior transient ischemic attack, and study publication year.

RESULTS

CHARACTERISTICS OF INCLUDED CLINICAL TRIALS. Of the 193 studies identified by the initial search, 12