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ORIGINAL INVESTIGATIONS

Ischemic Brain Lesions After Carotid Artery Stenting Increase Future Cerebrovascular Risk

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ABSTRACT

BACKGROUND Brain lesions on diffusion-weighted imaging (DWI) are frequently found after carotid artery stenting (CAS), but their clinical relevance remains unclear.

OBJECTIVES This study sought to investigate whether periprocedural ischemic DWI lesions after CAS or carotid endarterectomy (CEA) are associated with an increased risk of recurrent cerebrovascular events.

METHODS In the magnetic resonance imaging (MRI) substudy of ICSS (International Carotid Stenting Study), 231 patients with symptomatic carotid stenosis were randomized to undergo CAS (n = 124) or CEA (n = 107). MRIs were performed 1 to 7 days before and 1 to 3 days after treatment. The primary outcome event was stroke or transient ischemic attack in any territory occurring between the post-treatment MRI and the end of follow-up. Time to occurrence of the primary outcome event was compared between patients with (DWI+) and without (DWI–) new DWI lesions on the post-treatment scan in the CAS and CEA groups separately.

RESULTS Median time of follow-up was 4.1 years (interquartile range: 3.0 to 5.2). In the CAS group, recurrent stroke or transient ischemic attack occurred more often among DWI+ patients (12 of 62) than among DWI– patients (6 of 62), with a cumulative 5-year incidence of 22.8% (standard error [SE]: 7.1%) and 8.8% (SE: 3.8%), respectively (unadjusted hazard ratio: 2.85; 95% confidence interval: 1.05 to 7.72; p = 0.04). In DWI+ and DWI– patients, 8 and 2 events, respectively, occurred within 6 months after treatment. In the CEA group, there was no difference in recurrent cerebrovascular events between DWI+ and DWI– patients.

CONCLUSIONS Ischemic brain lesions discovered on DWI after CAS seem to be a marker of increased risk for recurrent cerebrovascular events. Patients with periprocedural DWI lesions might benefit from more aggressive and prolonged antiplatelet therapy after CAS. (A Randomised Comparison of the Risks, Benefits and Cost Effectiveness of Primary Carotid Stenting With Carotid Endarterectomy: International Carotid Stenting Study; ISRCTN25337470) (J Am Coll Cardiol 2015;65:521–9) © 2015 by the American College of Cardiology Foundation. Open access under CC BY license.

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ABBREVIATIONS AND ACRONYMS

ARWMC = age-related white matter changes

CAS = carotid artery stenting

CEA = carotid endarterectomy

DWI = diffusion-weighted imaging

FLAIR = fluid-attenuated inversion recovery

MRI = magnetic resonance imaging

TIA = transient ischemic attack

The occurrence of periprocedural ischemic brain lesions on magnetic resonance imaging (MRI) after revascularization of atherosclerotic stenosis of the internal carotid artery, either with stenting (CAS) or endarterectomy (CEA), has been commonly described (1). The randomized ICSS (International Carotid Stenting Study) compared CAS with CEA in patients with symptomatic carotid stenosis (2). In the MRI substudy of ICSS (ICSS-MRI), 50% of patients treated with CAS and 17% of those undergoing CEA had periprocedural ischemic brain lesions on diffusion-weighted imaging (DWI) on MRI scans obtained a median of 1 day after treatment (adjusted odds ratio 5.21; 95% confidence interval [CI]: 2.78 to 9.79; $p < 0.0001$) (3). However, the clinical significance of these lesions remains unclear. Previous research focused mainly on the persistence of lesions on follow-up imaging (4–7) and their effects on neuropsychological function (8–10).

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The goal of the present analysis of the ICSS-MRI substudy was to investigate whether the occurrence of periprocedural DWI lesions altered the risk of future cerebrovascular events during long-term follow-up.

METHODS

The prospective multicenter ICSS-MRI substudy included 124 patients randomly assigned to CAS and 107 patients randomly assigned to CEA in ICSS. The study design and the main short- and long-term results of ICSS and the ICSS-MRI substudy have been reported previously (2,3,11). Briefly, ICSS patients with recently symptomatic moderate or severe carotid stenosis (defined by a luminal narrowing of ≥50% according to the measurement of degree of stenosis used in the North American Symptomatic Carotid Endarterectomy Trial [12]) were randomized in a 1:1 ratio to receive CAS or CEA. Baseline imaging of the target artery was specified to require consistent findings on at least 2 noninvasive imaging modalities, including computed tomography angiography, magnetic resonance angiography, and duplex ultrasound; or intra-arterial digital subtraction angiography. Eight patients in the CAS group and 7 patients in the CEA group underwent digital subtraction angiography before the randomly allocated procedure, and the remainder received noninvasive imaging. The protocol recommended the use of a cerebral protection device during CAS whenever such a device could be safely deployed, but this action was not mandatory. The combination of aspirin and clopidogrel was recommended to cover the period of stenting and to be continued for a minimum of 4 weeks after the procedure.

If no contraindications to MRI were present, all patients included at 7 ICSS centers had the option of participating in the ICSS-MRI substudy (**Figure 1**). MRI scans at field strengths of 1.5- or 3-T (including DWI and fluid-attenuated inversion recovery [FLAIR] sequences) were specified to be conducted 1 to 7 days before treatment (pre-treatment MRI) and 1 to 3 days after treatment (post-treatment MRI). Assessment of MRI scans was performed through consensus reading by a neurologist (L.H.B.) and a neuroradiologist (L.M.J.) who were blinded to treatment allocation and clinical outcome. In cases of disagreement between

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