Impact of Additional Lipid-Lowering Therapy on New Ischemic Lesions of Diffusion-Weighted Imaging in Carotid Artery Stenting

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Background: New ischemic lesions on diffusion-weighted imaging (DWI) are frequently found after carotid artery stenting (CAS) and sometimes cause neurologic deficit. We investigated the rate and the potential factor of new DWI lesions during the perioperative period of CAS in symptomatic patients at our institution. *Materials and Methods:* Of 187 consecutive patients who underwent CAS (April 2013-August 2016), we investigated 60 symptomatic patients with artery-to-artery embolism from carotid plaque. During hospitalization for ischemic stroke, patients with more than 120 mg/dL of plasma low-density lipoprotein cholesterol (LDL-C) level or more than 100 mg/dL of LDL-C level in case of coronary artery disease were administered additional lipid-lowering therapy (ALL therapy), for example, the same statin as patients took or evolocumab for patients with the maximum tolerated dose of statin. All patients were implanted the same type of carotid stent by the same procedure as we predefined. We implemented data analysis to identify factors on new DWI lesions. *Results:* New DWI lesions were observed in 17 patients (28%). Baseline plasma triglyceride level was found to be the factor of new DWI lesions. ALL therapy was administered to 26 patients, including 8 patients of evolocumab. The average period from the start of ALL therapy to CAS was 15 days. New DWI lesions occurred in 11.5% of patients with ALL therapy and 41.2% of patients without ALL therapy ($P = .019$). Multivariate logistic analysis showed that ALL therapy was an independent predictor of absence of new DWI lesions ($P = .029$). *Conclusions:* ALL therapy before CAS may reduce new DWI lesions. **Key Words:** Carotid artery stenting—diffusion-weighted imaging—additional lipid-lowering therapy—low-density lipoprotein cholesterol.

Introduction

Carotid artery stenting (CAS) is generally performed in patients with carotid artery stenosis. Even though periprocedural lesions on diffusion-weighted imaging (DWI) remain clinically silent, they may be associated with cognitive dysfunction as assessed on neuropsychometric evaluation. Increased lesion load might be responsible for the clinical impact.[1,2] In the International Carotid Stenting Study—Magnetic Resonance Imaging substudy, detection of new DWI lesions in 124 symptomatic patients treated with CAS was associated with increased risk of recurrent ischemic stroke or transient ischemic attack (TIA), especially within the first 6 months after CAS.[3]

To prevent perioperative cerebrovascular events and new DWI lesions, embolic protection devices and carotid stents have been developed. Statins have been documented to prevent cerebro- and cardiovascular events in

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Cholesterol Treatment Trialists' Collaboration[4] and the possibility for statins to decrease the risk of perioperative ischemic stroke in patients who underwent CAS in the single-center observational study might be shown.[5] It has recently become common for neurovascular physicians to prescribe statins in naïve patients before CAS procedure under the lipid management guideline.[6,7]

In this report, we show the ratio of new DWI lesions at our institute where the embolic protection devices and CAS procedure have been unified with strictly management on plasma lipid levels before CAS, and clarify factors associated with new DWI lesions in symptomatic patients treated with CAS.

Materials and Methods

Patient Population

Of 187 consecutive patients who underwent CAS between January 2013 and August 2016 in the Hyogo Brain and Heart Center at Himeji, 77 patients had symptomatic cerebral infarction or TIA. Of which, 15 patients with hemodynamic ischemic stroke and 2 patients with anatomically broad atherosclerotic lesions were excluded. Furthermore, 60 (54 men and 6 women; mean age: 74.4 years) patients in whom artery-to-artery embolism from carotid plaque was identified as the cause of symptoms were included in this analysis.

Clinical, radiological, and procedural data were obtained for each patient. Magnetic resonance imaging (MRI) was routinely performed 2 days before and after CAS. Findings about plaques on carotid ultrasonography (Aplio500, Toshiba, Tochigi, Japan) were evaluated as calcified, echogenic, or echolucent. The diagnosis and the indication for CAS were confirmed at a medical conference by neurologists and neurosurgeons at our center based on the criteria used in the Stenting and Angioplasty with Protection in the Patients at High Risk for Endarterectomy (SAPPHIRE) trial.[8] Except for at initial hospitalization, neurologic examination was performed at 3 time points: one day before CAS, on day 1 and on day 30 after CAS.

Medication: Additional Lipid-Lowering Therapy

All 60 patients were initially hospitalized at the Department of Neurology and received conservative treatment. After being diagnosed as symptomatic stroke due to internal carotid artery stenosis, the patients were referred to the Department of Neurosurgery. We decided whether additional lipid-lowering (ALL) therapy should be administered or not then, based on the plasma low-density lipoprotein cholesterol (LDL-C) levels. The Japan Atherosclerosis Society Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2012 shows that the LDL-C treatment target is less than 120 mg/dL for patients with stroke and less than 100 mg/dL for patients with coronary artery disease (CAD). So, ALL therapy was administered to patients with LDL-C level of greater than 120 mg/dL or 100 mg/dL if they had already taken a statin.

Statins for ALL therapy included atorvastatin, rosuvastatin, and pitavastatin. If they had been administered a statin, ALL therapy was the same statin as they had as possible.

Patients who already took the maximum tolerable dose of a statin at the time of admission were administered evolocumab, which is an antibody for proprotein convertase subtilisin/kexin type 9 subcutaneously every 2 weeks.

Medication: Other than Lipid-Lowering Therapy

Dual antiplatelet therapy with aspirin and clopidogrel and, if needed, medication for hypertension and diabetes were prescribed for each patient at admission.

CAS Procedure

Under local anesthesia, heparin (100 IU/kg) was administered intravenously; further doses were administered, if required, to maintain the activated clotting time (ACT) at ≥300 seconds. Vascular access was obtained via the femoral artery. An 8Fr Brite tip (Cordis Endovascular Systems, Miami Lakes, FL) was guided to the common carotid artery, and FilterWire EZ (Boston Scientific, Natick, MA) was deployed by crossing the lesion. Atropine sulfate 1A (.5 mg) was intravenously administered after angiography, and predilation, stent placement, and postdilation angiograms were obtained.

The open-cell stent Precise (Cordis, Johnson & Johnson, Fremont, CA) was used in all patients. Both predilation and postdilation were performed in all patients. Predilation was performed with a 3.5-mm balloon in all patients; postdilation was performed with the aim to achieve a 100% gain based on the diameter of the normal blood vessel just distal to the lesion. The dilation pressure was the nominal pressure specified for the balloon in all patients. After that, the filter was retrieved using a capture sheath.

When impaired flow (slow flow or no flow) was observed on angiography postdilation, blood aspiration in the proximal part of the FilterWire EZ was performed with the Export aspiration catheter (Medtronic, Minneapolis, MN) to reduce embolic lesions on the basis of a previous report.[9,10] Blood was aspirated using a 25-mL syringe until gross debris disappeared.

Magnetic Resonance Imaging

MRI (3 T, Intra; Philips Medical Systems, Best, The Netherlands) was performed 2 days before and 2 days after CAS. The presence or absence and the number of new ischemic lesions were evaluated on DWI (spin echo-echo planar imaging, repetition time/echo time and field of view) (TR/TE = 3545/70 milliseconds; slice thick-