Carotid endarterectomy for symptomatic low-grade carotid stenosis

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Objective: **Although the management of carotid disease is well established for symptomatic lesions ≥70%, the surgical treatment for a symptomatic ≤50% stenosis is not supported by data from randomized trials. Factors other than lumen narrowing, such as plaque instability, seem to be involved in cerebral and retinal ischemic events. This study analyzes the early-term and long-term outcomes of carotid endarterectomy (CEA) performed in patients with low-grade (≤50% on North American Symptomatic Carotid Endarterectomy Trial criteria) symptomatic carotid stenosis.**

Methods: **The study involves 57 consecutive patients undergoing CEA for symptomatic low-grade carotid disease at our institution over 5 years, and 21 (36.8%) had experienced more than one ischemic event. Overall, 48 (84.2%) had a minor stroke, and nine (15.8%) had an episode of retinal ischemia. Diagnosis was made by a vascular neurologist based on an ultrasound examination combined with noninvasive imaging studies, after ruling out other possible causes of embolization. Before CEA, all patients were receiving antiplatelet treatment, and 87% were taking statins. All patients underwent eversion CEA under general deep anesthesia, with selective shunting. All carotid plaques were examined histologically. Long-term follow-up (median, 28 months; mean, 32 ± 5 months; range, 3-56 months) was obtained for 55 patients.**

Results: **No 30-day strokes or deaths occurred, and no patients had recurrent neurologic events related to the revascularized hemisphere during the follow-up. No late carotid occlusions were detected, but one asymptomatic moderate restenosis was documented. There were seven late deaths (12.7%), none of which were stroke-related. Survival rates were 98% at 1 year and 90% at 3 years. All removed carotid plaques showed different features of ulceration or rupture, with underlying hemorrhage associated with a thrombus.**

Conclusions: **This study shows that CEA is a safe, effective, and durable treatment for patients with symptomatic low-grade carotid stenosis associated with unstable plaque. Patients had excellent protection against further ischemic events and survived long enough to justify the initial surgical risk. Plaque instability seems to play a major part in the onset of ischemic events, regardless the entity of lumen narrowing. (J Vasc Surg 2014;59:25-31.)**

Carotid disease accounts for 10% to 20% of all ischemic strokes,[1,2] and generally speaking, the pathogenetic substrate of stroke attributable to carotid pathology is a plaque that causes hemodynamic turbulences ascribable to area reduction and with a complicated structure and surface generating emboli or determining occlusion. Guidelines for the best management of symptomatic internal carotid artery stenosis are based mainly on the conclusions of large randomized clinical trials (RCTs) such as the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[3] and the European Carotid Surgery Trial (ECST).[4] Pooled data from these RCTs demonstrated that carotid endarterectomy (CEA), compared with best medical management, is highly beneficial for individuals with cerebrovascular symptoms attributable to a carotid luminal narrowing ≥69% on angiography, with a 16% lower 5-year absolute risk of ipsilateral ischemic stroke. For symptomatic patients with moderate (50%-69%) carotid stenosis, the risk reduction is only 4.6%, and the benefit of CEA is minimal for symptomatic patients with mild (30%-49%) carotid stenosis.[5]

There is a consensus that medical therapy is as efficient as surgery for symptomatic patients with ≤50% carotid stenosis, but the presence of a vulnerable plaque, confirmed by well-established ultrasound criteria, might place these patients at a higher risk of cerebral ischemic events recurrence. As determined from results of RCTs, surgery does little to reduce the risk of ipsilateral ischemic stroke for low-grade (≤50%) symptomatic stenosis, not because patients are risk-free but because the surgical risk exceeds the stroke risk with medical management. Stroke risk and the benefits of CEA both increase with higher degrees of stenosis; thus, carotid narrowing is nowadays the most validated stroke risk parameter on which management decisions are based.[6]

The optimal approach for managing lower degrees of carotid disease remains unclear, however.[7] Several studies have shown that severe stenotic lesions might remain asymptomatic for many years on best medical treatment,[8]

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Author conflict of interest: none.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214/$36.00

http://dx.doi.org/10.1016/j.jvs.2013.06.079

whereas lower degrees of stenosis might progress and lead to a cerebral ischemic event over a short period of time due to plaque complication.[9-11]

In the last few years, progressive improvement has occurred in ultrasound B-mode imaging and in ultrasound contrast agents, and ultrasound B-mode is presently the best method for demonstrating low-grade carotid stenosis.[12] Although velocity measurements rule out a more severe stenosis, B-mode imaging in the longitudinal and cross-sectional planes is more relevant than velocity values in low-grade disease. Furthermore, the measurement of area reduction is more accurate than diameter reduction, especially when confronted with plaques with an irregular surface.[13,14]

In recent years, there has been a growing interest in multiparameter carotid plaque assessment, placing less emphasis on the degree of stenosis and more on its morphology, mobility, and composition. Intraplaque hemorrhage (IPH) and thin, ulcerated, or ruptured fibrous caps seem to be associated with higher stroke risk,[15-20] supporting the hypothesis, as in coronary artery disease, that many cerebral infarctions result from distal embolization,[21-23] not hypoperfusion, as it occurs distally to severe lesions or occlusions.[24,25]

This study was conducted to prospectively analyze the early-term and long-term outcomes of CEA performed outside the current guidelines in symptomatic patients with low-grade carotid lesions, assessing the morphologic and histologic features of the removed carotid plaques.

METHODS

The University of Padua, School of Medicine Ethics Committee approved the study. All patients gave their written informed consent to analyzing their records and publishing the findings.

Patients. A prospectively compiled computerized database was queried concerning all patients undergoing CEA at our tertiary referral center between January 2008 and December 2012 for recently symptomatic (<2 months) carotid plaque causing a ≤50% stenosis according to the NASCET criteria.[3] All patients were already receiving antiplatelet treatment, and most were taking statins before they were enrolled.

After their first ever ipsilateral or recurrent cerebral ischemic event, or plaque progression/instability, they entered the study and underwent CEA. Patients were routinely monitored for the first 3 days of their hospital stay. They underwent transthoracic and transesophageal echocardiography and were finally examined by a consultant cardiologist to rule out any cardiac source of embolization. A vascular neurologist attributed all cerebral or retinal ischemic events to embolization from an ipsilateral carotid stenosis. All patients were diagnosed with symptomatic carotid lesions ≤50% based on velocity criteria (peak systolic velocity <125 cm/s) on preoperative duplex ultrasound performed by two experienced neurosonographers.[26]

Carotid plaque morphology and characteristics were analyzed using contrast-enhanced carotid ultrasonography. Plaque morphology in terms of echogenicity, defined with reference to the sternocleidomastoid muscle, was assessed in a modified version of the classification proposed by Gray-Weale et al[27] and graded from 1 to 4 as echolucent, predominantly echolucent, predominantly echogenic, or echogenic.[19] Unstable plaque was defined on carotid ultrasound as echolucent or heterogeneous plaque, with surface irregularities, ulcer, or rupture. Plaque inflammation, adventitial vasa vasorum, intimal angiogenesis, and plaque neovascularization were identified on contrast-enhanced carotid ultrasonography as potential indicators of atheroma instability.

All patients underwent additional noninvasive imaging,[28] including magnetic resonance imaging (MRI)/angiography, computed tomography angiography, or digital subtraction angiography, to exclude tandem lesions (ie, a second intracranial lesion on the same vessel) and to confirm the decision to perform CEA. Transcranial color-coded Doppler sonography was also performed in all patients to assess vasomotor reactivity and any intracranial atherosclerotic lesions or intracranial compensatory collaterals.

The patients' demographic and clinical data were recorded on a standardized form, including potential atherosclerotic risk factors, several risk-related characteristics, such as cholesterol, high-density lipoprotein cholesterol, triglycerides, or homocysteine, anatomic and clinical variables, preoperative medication, details of surgery, and all perioperative outcomes. The consultant neurologist assessed all patients preoperatively, on waking from the anesthesia, before discharge from the hospital, and during the follow-up. All patients with diabetes or hyperlipidemia, or both, and those with prior ischemic events were receiving statin therapy.

Surgical procedure. All surgical procedures were eversion CEAs performed by the same surgeon, with patients under general anesthesia, and routine intraoperative electroencephalographic monitoring was used for selective intraluminal shunting. The technical details of the surgical procedure have been described elsewhere.[29] Shunting depended exclusively on electroencephalographic changes consistent with cerebral ischemia occurring during carotid cross-clamping and unrelated to any bradycardia or arterial hypotension. Patients were administered intravenous unfractionated heparin (5000 U) before carotid clamping. Heparinization was never reversed with protamine up until December 2009; from January 2010 onward, all patients had partial (half-dose) heparin reversal. No completion angioscopy or imaging studies were performed.

Patients were usually monitored in the recovery room for 2 hours until their blood pressure and neurologic status were judged acceptable and then were transferred to a nursing unit specialized in vascular care for 12 to 24 hours. Patients with severe headache were closely monitored for hyperperfusion syndrome, and hypertension was treated aggressively. Most patients were discharged 48 to 72 hours after CEA.