From the Society for Vascular Surgery

Outcomes after early and delayed carotid endarterectomy in patients with symptomatic carotid artery stenosis

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ABSTRACT

Objective: The objective of this study was to define outcomes after carotid endarterectomy (CEA) in patients with symptomatic carotid artery stenosis (CAS) when patients are operated on within 14 days after onset of symptoms.

Methods: Clinical data of consecutive patients who underwent CEA between 2003 and 2012 for symptomatic CAS were reviewed. Patients were classified into group 1, CEA ≤14 days of minor stroke or transient ischemic attack, and group 2, CEA >14 days. Primary end point was stroke/death; secondary end points were stroke, death, and myocardial infarction.

Results: There were 233 patients (32% female; mean age, 72 ± 9.1 years) who underwent 238 CEAs. Group 1 included 57 CEAs in 56 patients; 11 CEAs were performed at 0 to 2 days, 23 at 3 to 7 days, and 23 at 8 to 14 days. Group 2 included 181 CEAs in 177 patients. One death (group 2) and five strokes (group 1, four; group 2, one) occurred at 30 days (stroke/death, 2.6%), more in group 1 vs group 2 (7.1% vs 1.1%; $P = .03$). In group 1, three strokes occurred when the patients were operated on within 2 days (27% [3/11]), more than at 3 to 7 days (0% [0/22]) or 8 to 14 days (4.3% [1/23]; $P = .008$). Patients operated on between days 3 and 14 had similar stroke/death rate to those operated on after 14 days (2.2% vs 1.1%; $P = .49$). Myocardial infarction occurred in six patients (2.5%; group 1, 0% [0/57]; group 2, 3.3% [6/177]; $P = .34$). Median follow-up was 7.0 years (interquartile range, 4.6-9.9 years). Freedoms from stroke/death were similar between groups (hazard ratio [HR], 1.22; 95% confidence interval [CI], 0.75-1.99; $P = .42$), 69% for group 1 and 76% for group 2 at 5 years. Age ≥80 years, high surgical risk, and no preoperative $P2Y_{12}$ antagonist use predicted stroke/death. Freedoms from any stroke were similar in groups (HR, 2.46; 95% CI, 0.95-6.41; $P = .06$); survivals were also similar (HR, 1.12; 95% CI, 0.67-1.87; $P = .67$) at 5 years.

Conclusions: In this single-center study, CEA in symptomatic patients had a 30-day stroke/death rate of 2.6%. Age ≥80 years and high surgical risk predicted late stroke or death; taking $P2Y_{12}$ antagonists was associated with late stroke. High stroke rates when patients were operated on immediately support CEA after 2 days in symptomatic patients with CAS. (J Vasc Surg 2018;67:1110-9.)

Stroke is the fifth leading cause of death and a major cause of long-term disability. In the United States, each year an estimated 800,000 people suffer from new or recurrent strokes.[1] Extracranial carotid artery stenosis (CAS) contributes to 20% to 30% of all strokes,[2-4] and patients with symptomatic high-grade CAS are at increased risk.[5,6] The role of carotid endarterectomy (CEA) in the management of symptomatic CAS has been established in the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[7,8] and European Carotid Surgery Trial (ECST).[9] The benefit of CEA was significant in patients with CAS between 70% and 99% and equally significant, although to a lesser degree, in patients with CAS between 50% and 70%.

The updated Society for Vascular Surgery guidelines recommend CEA as the first-line treatment for most symptomatic patients with carotid stenosis of 50% to 99%, a Grade 1A recommendation.[10] However, optimal timing of CEA after a recent neurologic ischemic event has been debated. The National Institute for Health and Care Excellence guidelines recommended that CEA be performed within 14 days after onset of symptoms[11]; the 14-day threshold was also adopted in the 2009 European Society for Vascular Surgery guidelines.[12] The 2011 American Heart Association/American Stroke Association guidelines advised that CEA within 14 days was a "reasonable" option.[13] Others also recommend revascularization within 14 days after nondisabling stroke or transient ischemic attack (TIA).[14,15] A recent review

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showed that 29 of 33 guidelines recommended CEA as soon as possible or within 2 weeks of symptoms.[16] Naylor emphasized that CEA can be performed safely within 7 days after onset of symptoms, although risks might be higher when it is performed within 48 hours.[17]

The purpose of this study was to review early outcomes after CEA in symptomatic CAS patients when they were operated on within 14 days after onset of symptoms or later at a tertiary medical institution. We also reviewed long-term results to compare outcomes in those operated on before and beyond 14 days after onset of symptoms.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective, single-center, cohort study
- **Take Home Message:** Carotid endarterectomy in 233 symptomatic patients resulted in a stroke or death rate of 27% if patients were operated on within 48 hours and 2.2% if they were operated on between 3 and 14 days.
- **Recommendation:** This study suggests that symptomatic patients should undergo carotid endarterectomy after 2 days following symptoms because of much higher stroke or death rate in the first 2 days.

METHODS

Clinical data of consecutive patients undergoing CEA between 2003 and 2012 for symptomatic CAS at Mayo Clinic, Rochester, Minnesota, were retrospectively reviewed. Symptomatic CAS was defined according to the Carotid Revascularization Endarterectomy vs Stenting Trial (CREST)[18] as the most recent TIA, amaurosis fugax, or minor stroke involving the ipsilateral carotid artery that occurred within 180 days preceding the index CEA. Demographics, comorbidities, preoperative chronic medication use (>30 days of aspirin, $P2Y_{12}$ antagonist, statins, or beta blockers), intraoperative data, strokes, deaths, complications, and reinterventions were documented. CAS measured by duplex ultrasound was recorded and categorized as 70% to 99% or 40% to 69% CAS. Primary end point was stroke/death; secondary end points were any stroke (minor or major stroke, ipsilateral ischemic stroke), death, and myocardial infarction (MI). Informed consent of the patients was obtained for the study. The study was approved by the Mayo Foundation Institutional Review Board.

Patients were classified into two groups based on the onset of symptoms: group 1, symptoms occurred within 14 days before CEA; and group 2, symptoms occurred beyond 14 days before CEA. Group 1 was divided into three subgroups: CEA performed within 2 days after onset of symptoms (0-2 days), at 3 to 7 days, and at 8 to 14 days.

Procedure. CEA included conventional and eversion endarterectomies. Conventional endarterectomy was performed using a synthetic or bovine pericardial patch angioplasty closure; some patients had polytetrafluoroethylene or autogenous vein patch closure. Primary closure was occasionally performed for a large carotid artery, usually >6.0 mm in diameter.

Follow-up. Patients were asked to return at 3 months for physical examination and for duplex ultrasound scanning at 3 months and annually afterward. Computed tomography angiography was indicated in cases of critical or symptomatic carotid restenosis; carotid angiography was considered when an endovascular reintervention was planned. Follow-up information was obtained from the available medical records. The patient's vital status was established from charts, a death certificate, or autopsy report.

Definition. Using definitions of the CREST trial,[18] TIA was a temporary focal brain or retina deficit caused by vascular disease that resolved in 24 hours. Amaurosis fugax, defined as temporary loss of vision in one eye (≤10 minutes) due to insufficient flow of blood to the retina, was included in TIAs. Stroke was an acute neurologic event with focal symptoms and signs lasting for 24 hours or more. Major stroke was defined on the basis of clinical data or if the National Institutes of Health Stroke Scale score was 9 or higher 90 days after the procedure; otherwise, it was classified as a minor stroke.[18] Ipsilateral ischemic stroke was an acute neurologic ischemic event of at least 24 hours in duration with focal symptoms and signs affecting the cerebral hemisphere supplied by the treated carotid artery. MI was defined by a creatine kinase MB or troponin level that was twice the upper limit of the normal range or higher in addition to either chest pain or symptoms consistent with ischemia or electrocardiographic evidence of ischemia, including new ST-segment depression or elevation of >1 mm in two or more contiguous leads.[18] Complications were identified using Vascular Quality Initiative criteria. High surgical risk included age >80 years, clinically significant cardiac disease (congestive heart failure, abnormal stress test results, or need for open heart surgery), severe pulmonary disease, contralateral carotid occlusion, contralateral laryngeal nerve palsy, previous radical neck surgery or radiation therapy to the neck, and recurrent stenosis after endarterectomy.[19] Reinterventions included new procedures because of vascular or nonvascular complications.

Statistics. Descriptive statistics were reported as number (percentage) and mean or median (range, interquartile range [IQR]) as appropriate. Differences between groups were assessed by χ^2 analysis or by Student *t*-test as appropriate. Thirty-day events were assessed using logistic regression, reporting odds ratio and 95% confidence interval (CI), assuming five patients