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Clinical Research

Carotid Angioplasty With Stenting Versus Endarterectomy

10-Year Randomized Trial in a Community Hospital

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Objectives This single-center, randomized, clinical trial was designed to determine the 10-year comparative efficacy and durability of carotid angioplasty and stenting (CAS) versus carotid endarterectomy (CEA) in preventing ipsilateral ischemic stroke in symptomatic and asymptomatic patients with high-grade carotid artery stenosis.

Background Modern clinical trials with short-term follow-up indicate CAS and CEA are equivalent in reducing the risk for ipsilateral ischemic stroke secondary to carotid stenosis. A paucity of data exists regarding long-term outcomes.

Methods Patients of all surgical risks with symptomatic and asymptomatic carotid stenosis (>70%) were randomly selected for CEA or CAS and followed a minimum of 10 years.

Results Long-term follow-up was achieved in 173 patients (91%). Eighty-seven (50.2%) died within this period, most commonly of nonvascular causes. No difference in the risk of stroke ipsilateral to the treated artery was noted among treatment groups ($p > 0.05$). Restenosis determined by sequential ultrasound was assessed only in the CAS group (3.3%) and remained asymptomatic. The combined risk of fatal or nonfatal heart attack over the 10-year period was highest in individuals with symptomatic versus asymptomatic stenosis (27.5% vs. 11.0%; hazard ratio [HR]: 2.32, 95% confidence interval [CI]: 1.298 to 4.146, $p = 0.005$) and was higher in all patients treated with CEA (HR: 2.27, 95% CI: 1.35 to 3.816, $p = 0.002$).

Conclusions Long-term protection against ipsilateral stroke provided by CAS and CEA did not differ in this trial. The 10-year risk of fatal/nonfatal myocardial infarction was highest in all patients harboring symptomatic carotid stenosis at enrollment. The risk of fatal/nonfatal heart attack was significantly more prevalent in those symptomatic or asymptomatic patients randomized to CEA. (J Am Coll Cardiol Intv 2014;7:163–8) © 2014 by the American College of Cardiology Foundation

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The durability of carotid endarterectomy (CEA) for revascularization of high-grade carotid stenosis as defined by protection against ipsilateral stroke and absence of restenosis is well established through a series of randomized, controlled trials (1–5). The ECST (European Carotid Study Trial)

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observed the 10-year risk of stroke after CEA was approximately 2% per year. Less than one-half of these were related to residual or recurrent disease in the treated artery (5). The Mayo Clinic reported the restenosis rate following successful CEA was 0.1%, with no strokes at an average of 7 years of follow-up (6). Although CEA has long been considered the preferred intervention for carotid occlusive disease, recent randomized clinical trials (RCT) have indicated that carotid angioplasty and stenting (CAS) may serve as a minimally invasive alternative with equivalency in providing protection against ipsilateral stroke (7–11). Whereas these studies have reported favorable short- and mid-term (3 to 5 year) results, longer-term data, similar to that available for CEA, are lacking. Thus, despite the satisfactory early results, concern remains about the long-term durability of CAS.

Abbreviations and Acronyms

CAS = carotid angioplasty and stenting

CEA = carotid endarterectomy

CI = confidence interval(s)

DUS = duplex ultrasound

HR = hazard ratio(s)

RCT = randomized clinical trial(s)

The initial results of the Kentucky trial were presented over a decade ago (7,8). In this prospective, randomized trial, patients of all surgical risk categories with symptomatic or asymptomatic carotid artery stenosis were offered randomization into CEA versus CAS treatment groups. The results indicated that a clinical equipoise exists between the 2 revascularization strategies at 30 days and at 48 months. Extending our initial findings, the current report compares the long-term (≥10 years) durability and consequences of CAS with CEA in this randomized cohort of symptomatic and asymptomatic individuals with carotid artery stenosis.

Methods

The inclusion and exclusion criteria, methodology, and initial results of the Kentucky RCT comparing CEA with stenting have been published (7,8). Briefly, all patients presenting with symptomatic or asymptomatic carotid stenosis from 1998 through 2002 meeting the inclusion or exclusion criteria were offered enrollment. No anatomic risk factors or concurrent medical conditions other than those contained in the exclusionary criteria were considered in treatment assignment (7,8). Embolic protection devices were not available at the initiation of this trial and thus were not used. These RCT were approved by the institutional review board. A neurologist (T.C.C.) and research nurse coordinators (L.B., C.S.) provided independent oversight and neurological examination at specific prescribed intervals. Sequential independent neurological examinations and Rankin and Barthel scorings were performed concurrent with duplex scanning. This RCT was designed specifically to assess the initial (30 days), intermediate (48 months), and long-term (≥10 years) safety and efficacy of CAS and CEA in a community hospital.

The presence of extracranial atherosclerosis was established by a combination of duplex ultrasound (DUS) and cerebral angiography (7,8). Carotid DUS was assessed within 24 h of the index procedure and at 1, 3, 6, 12, and 24 months and thereafter at 12-month intervals for ≥10 years. The protocol for DUS included B-mode and angle-adjusted Doppler spectral imaging as standardized in the core ultrasound laboratory at Central Baptist Hospital, consistent with guidelines of the CREST (Carotid Revascularization Endarterectomy versus Stenting Trial) (9). Data were obtained from the treated and untreated carotid artery. Throughout this study, DUS accuracy and uniformity was confirmed by correlation with carotid angiography performed in individuals admitted to the stroke service but not enrolled in this RCT. Recurrent stenosis (>70%) was determined and defined as development of internal carotid artery peak velocities >300 cm/s and internal carotid artery/common carotid artery ratio of >3 subsequent to and compared with a previous ultrasound examination that showed no evidence of stenosis. All cases suspected of restenosis were confirmed by cerebral angiography.

A standardized pre-randomization assessment of risk factors and a post-procedural medical protocol were prescribed for all patients that included maintenance of systolic blood pressure at or below 140 mm Hg as recorded during each office visit; platelet inhibition with 325 mg of aspirin plus 75 mg of clopidogrel; encouragement for cessation of smoking, and prescribing statin therapy regardless of serum cholesterol levels. No specific pharmacological protocol for managing blood pressure was mandated. Post-procedural protocol compliance was based on patient and family self-report.

Adverse clinical events were defined as any stroke of any severity regardless of location, symptomatic ischemic heart disease, and/or death from any cause. The cause of death or morbidity was confirmed through family contact and review of medical records.

Statistical analysis. Kaplan-Meier survival curves were generated for all asymptomatic and symptomatic CAS and CEA groups as well as for combined CAS and CEA asymptomatic and symptomatic cohorts. For each subject, person-time days at risk were calculated for all strokes, ipsilateral stroke, all myocardial infarctions, and all combined vascular adverse events. Each of these variables included both fatal and nonfatal events. Values were