EDITORIAL

Endarterectomy, Stenting, or Neither for Asymptomatic Carotid-Artery Stenosis

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Important data from two large, randomized trials comparing early and late outcomes after carotid endarterectomy and carotid-artery stenting have now been published in the *Journal*.[1,2] In common with every other large, multicenter, randomized trial to date, the Asymptomatic Carotid Trial (ACT I) and the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) showed that after the perioperative period, there was no difference in the rate of late ipsilateral stroke after endarterectomy or stenting. In ACT I, which included asymptomatic patients who were deemed to be at average risk, the 5-year rate of ipsilateral stroke (excluding the perioperative period) was 2.2% after stenting (i.e., 0.4% per year) and 2.7% after endarterectomy (0.5% per year).[1] In CREST, which included symptomatic and asymptomatic patients who were deemed to be at average risk, the estimated 10-year rate of ipsilateral stroke (excluding the perioperative period) was 6.9% after stenting (i.e., 0.7% per year) and 5.6% (0.6% per year) after endarterectomy.[2]

The fact that there is near-unanimous consensus within randomized trials that after the perioperative period the rates of late ipsilateral stroke after stenting do not differ significantly from those after endarterectomy should dispel any lingering concerns about the durability of stenting. That issue has now surely been resolved. What has not been resolved, however, is the issue of the generalizability of randomized-trial findings into routine clinical practice, and, more importantly, the vexed question of how best to treat the asymptomatic patient. No one should harbor any illusions that ACT I and CREST have resolved the latter issue.

CREST and ACT I both used credentialing to ensure that only the best interventionists and surgeons performed stenting or endarterectomy within the trials. The commendably low rates of death and stroke during the procedure in ACT I and CREST attest to this. It therefore remains to be seen whether these findings can be translated into routine clinical practice, if guidelines are changed to further liberalize indications for stenting, especially in asymptomatic patients. This is an important point, because a recent systematic review showed that 9 of 21 large administrative data-set registries (43%) reported rates of death and stroke in excess of the 3% risk threshold that is recommended by the American Heart Association in asymptomatic patients undergoing stenting, as compared with 1 of 21 registries (5%) after endarterectomy.[3] Furthermore, the 3% risk threshold is clearly too high, given the reduction of risk with intensive medical therapy. Discrepancies between randomized-trial data (i.e., from ACT I and CREST) and real-world practice are nothing new and, in this case, are probably attributable to the fact that many real-world practitioners in the United States are performing two or fewer procedures annually in asymptomatic patients, with poorer outcomes than their more experienced colleagues.[4]

The magnitude of the initial procedural risk will ultimately determine whether endarterectomy or stenting is preferable in recently symptomatic patients, and this will be determined by recency of symptoms, age of the patient, and coexisting conditions. However, there is a major concern that the data from these two trials will be uncritically interpreted to mean that stenting is equivalent to endarterectomy and so further exacerbate the situation in the United States, where more than 90% of carotid-artery interventions are performed in asymptomatic patients,

even though evidence suggests that up to 90% of them will undergo an ultimately unnecessary and potentially harmful procedure.[5,6] By contrast, the percentage of interventions that are performed for asymptomatic stenoses is approximately 60% in Germany and Italy, 15% in Canada and Australia, and 0% in Denmark.[7] Such discrepancies call into question the appropriateness of advocating routine interventions for asymptomatic carotid-artery stenosis.

The ACT I authors conceded that in hindsight it would have been preferable to have included a medical group in their trial.[1] However, the debate about how improvements in modern medical therapy may have lowered the annual risk of stroke had not reached its zenith when ACT I was conceived. It is certainly a highly topical and controversial issue in the current era, because data from both randomized trials and nonrandomized studies suggest that the annual rate of stroke among medically treated asymptomatic patients has declined over the past two decades, regardless of the severity of stenosis at baseline.[8] Evidence now suggests that the annual rate of ipsilateral stroke may be as low as 0.5 to 1%[8] — a rate that is very similar to that observed in ACT I and CREST after successful stenting or endarterectomy.[1,2]

Accordingly, contemporary guidelines, which recommend that interventions may be appropriate if they can be performed with a risk of less than 3%, are based on historical data from randomized trials that were completed decades ago and that should now be considered obsolete. Outside clinical trials, endarterectomy and stenting should be reserved for patients with symptomatic severe stenosis or for asymptomatic patients who are shown to be at higher risk for stroke with medical therapy than with intervention. Such patients (approximately 10 to 15% of patients with asymptomatic stenosis of 70 to 99%) may be identified by an algorithm that incorporates information about microemboli detected by means of transcranial Doppler,[6,9,10] and in the future by imaging strategies that identify the vulnerable plaque.[11]

It is hoped that the Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial (CREST-2; ClinicalTrials.gov number, NCT02089217), which includes a medical group, will help settle this issue. Unfortunately, the Stent-Protected Angioplasty in Asymptomatic Carotid Artery Stenosis vs. Endarterectomy (SPACE-2; Current Controlled Trials number, ISRCTN78592017) trial (which also had a third group receiving medical therapy) has now been abandoned because of poor recruitment. Pending the completion of CREST-2, we think that it would be desirable for interventionists and surgeons to forgo stenting and endarterectomy in low-risk asymptomatic patients outside that trial. This restraint would not only spare patients from procedures that may be unnecessary, but it should also facilitate early completion of the trial (and so avoid the fate of SPACE-2), so that it may be possible to identify which patients will benefit from an intervention rather than medical therapy alone in an evidence-based rather than an eminence-based manner.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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