The Cart and The Horse

The Advancing Technology of Carotid Artery Stenting

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Endarterectomy is recommended in current clinical guidelines for selected patients with a significant symptomatic or asymptomatic extracranial carotid artery stenosis, provided that the operation can be performed with acceptable safety. These recommendations are based on the results of several controlled trials in which those randomized to have the operation had better clinical outcomes compared with those who did not, on a background of what at the time was considered to constitute best medical therapy. The advent of angioplasty/stenting offers the promise of a less invasive means of directly treating carotid artery steno-occlusive disease compared with endarterectomy. Unlike surgical procedures, however, pharmaceuticals, biologicals, and devices are subject to regulatory approval in the United States by the Food and Drug Administration. Placement of a carotid artery stent system was first approved by the Food and Drug Administration in 2004 for the treatment of patients deemed “at high risk for adverse events from carotid endarterectomy who require carotid revascularization [who have] neurological symptoms and ≥50% stenosis of the common or internal carotid artery by ultrasound or angiogram, or in patients without neurological symptoms and ≥80% stenosis of the common or internal carotid artery by ultrasound or angiogram” (http://www.fda.gov/cdrh/pdf4/p040012a.pdf).

Registries were developed to help assess the safety of stent systems as used in larger populations, in part to help identify risks that might not have been apparent based on the smaller numbers of subjects included in the randomized trial that compared stenting with endarterectomy in patients at high risk of postendarterectomy complications. In that trial, the postprocedural 30-day rate of stroke, myocardial infarction, or death was 2.1% with stenting versus 9.3% with endarterectomy (P=0.18) for symptomatic patients; for those with an asymptomatic carotid artery stenosis, the periprocedural rates (95% CI, 1.3% to 4.9%) for symptomatic and asymptomatic disease compared with endarterectomy. Unless surgical inaccessible stenosis, neck tumors, spine immobility, tracheostomy, and contralateral laryngeal nerve palsy). The complication rates found in these more recent registry studies, therefore, seem reassuring in that they generally compare favorably with those of the high carotid endarterectomy risk randomized trial, seem to reflect further temporal improvements as experience with the technique has increased (at least in those with asymptomatic disease) and tend to support the use of stenting in selected symptomatic patients who cannot have an endarterectomy because of anatomic features unfavorable for surgery.

Gray et al also note that the complication rates with carotid artery stenting that they report are within American Heart Association–recommended standards for endarterectomy as performed in average-risk patients (ie, <6% for symptomatic lesions and <3% for asymptomatic lesions). The direct application of these standards to the more recent carotid stenting data, however, may not be appropriate. The guideline recommendations are based on randomized trials with contemporaneous controls and are internally consistent. Acceptable complication rate thresholds might, however, be lower and absolute numbers of patients needed to treat to prevent a stroke increased if the event rates with medical therapy declined compared with when the trials were done. The results of the randomized trials of endarterectomy for high-grade symptomatic carotid artery stenosis were published almost 2 decades ago, with reports of trials for patients with a moderate symptomatic stenosis now more than 10 years old. Unlike these largely contemporaneous trials of endarterectomy for symptomatic stenosis, nearly a decade passed between the reports of the two, large randomized trials of endarterectomy for patients with a 60% to 99% asymptomatic carotid artery stenosis. The results of the Asymptomatic Carotid Atherosclerosis Study (ACAS) were published in 1995 and those of the Medical Research Council (MRC) Asymptomatic Carotid Surgery Trial (ACST) were published.
Any major stroke or perioperative death

ACAS 17.5 12.4 0.29 (0.11 to 0.44)
ACST 8.4 5.3 0.37 (0.18 to 0.52)

Any major stroke or death

ACAS 25.5 20.7 0.19 (0.03 to 0.32)
ACST 17.4 18.1 0.04 (0.01 to 0.21)*

Data are from the ACAS trial and calculated from data provided in the report of the ACST. ACAS: no immediate surgery, n=834; immediate surgery, n=825; ACST: no immediate surgery, n=1560; immediate surgery, n=1560. CEA indicates carotid endarterectomy; RRR, relative risk reduction.

RRR indicates Relative Risk increase for immediate versus no immediate carotid endarterectomy calculated based on the indicated data.

Asymptomatic carotid artery stenosis, may no longer be appropriate.

It is also important to reiterate that the comparability of carotid artery stenting and endarterectomy in patients at average risk of complications with endarterectomy has not been established. Three meta-analyses comparing carotid angioplasty (with or without stenting and with or without distal protection devices) with endarterectomy were published in 2008. Owing to differences in the trials that were included in each analysis, as well as variation in study end points and in the types of statistical analyses conducted, 1 meta-analysis concluded that there is no difference between stenting and endarterectomy in patients with symptomatic stenosis and 2 concluded that carotid artery stenting is neither safer nor as safe as endarterectomy. Yet, carotid endarterectomy is being performed less frequently and carotid artery stenting more frequently, at least among Medicare beneficiaries. Between 1998 and 2004, the rate of carotid endarterectomy decreased by 17% (P<0.01), whereas the rate of stenting increased by 149% (P<0.01). Analysis of the complication rates of 254,044 carotid endarterectomies and 14,035 stenting procedures from the US Nationwide Inpatient Sample from 2003 to 2004 found that, compared with endarterectomy, carotid artery stenting was associated with higher rates of both perioperative stroke (2.1% versus 0.9%, P<0.0001) and death (1.3% versus 0.4%, P<0.0001). After adjustment for confounders, carotid artery stenting was still associated with higher postprocedural odds of postprocedure stroke (odds ratio, 2.49; 95% CI, 1.91 to 3.25) and death in both symptomatic (odds ratio, 2.64; 95% CI, 1.89 to 3.69) and asymptomatic (odds ratio, 2.37; 95% CI, 1.46 to 3.84) patients.

The results of yet to be reported randomized trials comparing stenting with endarterectomy in average-risk patients, including the Carotid Revascularization Endarterectomy versus Stent Trial and the International Carotid Stenting Study, are desperately needed to help further inform clinical decision making. Even after these results become available, rigorous case selection and a realistic view of the comparable potential risks and benefits of the intervention need to be carefully assessed when considering whether to offer carotid revascularization to a particular patient, and if revascularization is appropriate, which procedure to recommend.

Disclosures

Dr Goldstein is the site investigator for CREST (National Institutes of Health), is a consultant for Johnson & Johnson, and serves on the Site Oversight Committee for ACT-I (Abbott).

References


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