Carotid Artery Bypass Is Getting a Second Look

BY PATRICE WENDLING
Chicago Bureau

Long abandoned as ineffective at secondary stroke prevention, carotid artery bypass surgery for complete atherosclerotic occlusion is getting a second look.

Known as extracranial/intracranial (EC/IC) bypass, the procedure involves surgical anastomosis of the superficial temporal artery to the middle cerebral artery (STA-MCA). It is getting its second chance to prove its effectiveness in selected patients for complete carotid occlusion because technologic advances, such as refinement of PET, have made it possible to identify which patients are the best candidates for the procedure.

EC/IC bypass surgery has been shown in a series of small studies to normalize the oxygen extraction fraction (OEF), a marker of impaired cerebral blood flow in patients with carotid occlusion.

Whether that translates into a decreased stroke risk is the subject of the Carotid Occlusion Surgery Study (COSS), a $21 million, 7-year trial funded by the National Institutes of Health that is now underway in 28 U.S. centers.

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Dr. Colin Derdeyn is a coinvestigator on COSS, which will examine whether EC/IC bypass prevents subsequent stroke.

Candidates for the trial must be patients with symptomatic carotid occlusion and increased OEF on PET. To date, 169 patients have enrolled, and 38 patients have been randomized to treatment.

Enrollment in the nonblinded, controlled clinical trial has been slow, in part because few neurologists knew the option of bypass surgery existed, said Colin Derdeyn, M.D., principal investigator for the Washington University site in St. Louis.

The First EC/IC Bypass Study

STA-MCA surgical anastomosis was developed in 1967 and routinely performed on patients with carotid occlusion throughout the 1970s and mid-1980s.

However, data from the EC/IC Bypass Study showed no benefit for the prevention of subsequent stroke among 808 patients with symptomatic carotid occlusion, despite restoring blood flow to the carotid artery in 96% of cases (N. Engl. J Med. 1985;313:1191-200).

The researchers were unable to assess whether the procedure was more appropriate for one or another group of patients based on their cerebral hemodynamics because at the time the technology necessary to understand and measure cerebral blood flow had not been developed, according to M. Gazi Yasargil, M.D., professor of neurosurgery at the University of Arkansas, Little Rock, the Swiss neurosurgeon who pioneered the surgical procedure. "The time is ripe to work out a perfect indication for bypass surgery," he said.

Identifying Hemodynamics

PET has made it possible to measure OEF, a proven predictor of which patients have significantly decreased cerebral blood flow and are at increased stroke risk.

When there is unrestricted cerebral blood flow, the brain extracts about 40% of the oxygen delivered to it in the blood. Blood vessels dilate and constrict to maintain an equal OEF across the brain. When cerebral blood flow falls because of reduced perfusion pressure, the brain increases the fraction of oxygen extracted from the blood to 70% or 80% to support normal oxygen metabolism. This elevated OEF allows the brain to maintain normal function, but it puts patients at increased risk for stroke in the future.

Two prospective natural history studies, one conducted in the United States (JAMA 1998;280:1055-69) and the other in Japan (J. Nucl. Med. 1999;40:1992-8), have shown that having an increased OEF as measured by PET is an independent predictor of future stroke in medically treated patients with symptomatic carotid artery occlusion.

Depending on the precise clinical and PET criteria used, the 2-year ipsilateral stroke rates ranged from 26% to 57% in patients with an elevated OEF, compared with stroke rates of 5%-15% in patients with normal OEF, according to Dr. Derdeyn, coauthor of the U.S. study.

"The best information we have right now, as far as connecting an abnormality by physiologic imaging with a risk factor, is for increased oxygen extraction," Dr. Derdeyn told INTERNAL MEDICINE NEWS. OEF is a powerful and independent predictor of stroke. "It identifies a high-risk subgroup, without question," he said.

William J. Powers, M.D., principal investigator of COSS, agreed on the importance of identifying subsets of patients most likely to benefit from EC/IC. "It's absolutely clear that if [EC/IC bypass] is ever going to work, there has to be some more refined selection criteria to pick out the people, number one, who would be at particularly high risk if treated with medical therapy, and number two, in whom the subsequent risk of stroke seems to be related to a problem that the bypass would fix," he told this newspaper.

COSS is based on the hypothesis that surgical anastomosis of the superficial temporal artery to the middle cerebral artery, when added to the best medical therapy, can reduce subsequent ipsilateral ischemic stroke by 40% at 2 years' follow-up in this highly select patient population, despite perioperative stroke and death.

Investigators anticipate that the stroke rate in COSS will turn out to be 40% in the medically treated group and 24% in the surgically treated group, even taking into account a 12% perioperative stroke and mortality rate, as reported in the original EC/IC trial, said Dr. Powers, codirector of the Stroke Center at Barnes-Jewish Hospital and the Washington University School of Medicine.

Even if these reduced stroke rates are borne out by the study, EC/IC bypass surgery is unlikely to become as common as coronary artery bypass; elevated OEF occurs in only 30% of patients with carotid occlusion.The study's $21-million price tag over the next 5-7 years may prove to be money well spent if it settles the question of patient selection once and for all. A similar trial, the Japanese EC/IC Trial (JET), is also working on the question of patient selection. A third trial, the Randomized Evaluation of Carotid Occlusion and Neurocognition (RECON) study, was recently funded by NIH to examine the hotly debated question of whether carotid bypass surgery affects cognitive function. ■

EC/IC Bypass In a Nutshell

The 4-hour EC/IC procedure involves surgical anastomosis of the superficial temporal artery to the middle cerebral artery.

While the patient is under general anesthesia, an incision of several centimeters is made in the scalp on the side of the head where the diseased artery is located. A branch of the superficial temporal artery, generally the anterior division, is then identified and dissected using a surgical microscope.

A small craniotomy is then made beneath the temporalis muscle. A frontal branch of the middle cerebral artery is identified and isolated.

Once a suitable location for the anastomosis is determined, temporary clips are placed above and below the site. A slit is cut into this branch, and the previously dissected and prepared superficial temporal artery is sewn directly onto this middle cerebral artery branch for an end-to-side anastomosis.

The clips are then removed and blood flow restored.

Risks of the surgery include subsequent stroke as a result of temporary occlusion of the middle cerebral artery branch, thrombosis of the bypass graft, myocardial infarction during surgery, bleeding, and infection.

A retrospective analysis of EC/IC bypass surgery performed on 67 patients from 1986 to 2000 reported a perioperative morbidity rate of 3%, with no mortality (Acta Neurochir. [Wien] 2004;146:95-101).

Prednisone Associated With Increased Stroke in RA Patients

BY TIMOTHY F. KIRN
Sacramento Bureau

SAN ANTONIO — Prednisone treatment for rheumatoid arthritis patients was associated with an approximately 50% increased risk of stroke, according to figures from the National Data Bank for Rheumatic Diseases.

Treatment with infliximab was associated with a 50% decreased stroke risk. These findings don't in any way prove cause and effect, the study's lead investigator, Frederick Wolfe, M.D., cautioned in an interview. But they are suggestive of a trend.

They may also challenge some assumptions among providers. "There is a belief that low-dose prednisone is a benign drug treatment," said Dr. Wolfe of the National Data Bank. "I don't think it is."

Dr. Wolfe, who presented his findings in a poster presentation at the annual meeting of the American College of Rheumatology, said that his look at the incidence rate of stroke in rheumatoid arthritis (RA) patients was prompted by a request from investigators at the National Institutes of Health, who wanted to know about stroke risk and infliximab treatment. The study used data from 15,670 RA patients and 3,083 osteoarthritis patients, who were followed for a 3-year period ending in 2003.

RA patients had a higher incidence of stroke than did the osteoarthritis patients, with a hazard ratio of 1.26. This increased risk was independent of age, gender, diabetes, and hypertension. The incidence rate in the RA patients was equal to 8 cases per 1,000 patient-years.

Among the RA patients, stroke risk was increased in those on prednisone, with a hazard ratio of 1.52, and decreased in those on infliximab, with a hazard ratio of 0.49. Concurrent methotrexate therapy did not appear to have an impact on risk of stroke.

Sulfasalazine treatment was also found to be associated with a 50% decreased risk; however, there were too few patients in the group who took sulfasalazine for that finding to be considered statistically significant, Dr. Wolfe noted. ■