TPA Safe, Effective for Stroke After Cardiac Cath

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW ORLEANS — Thrombolysis was safe and effective for treating acute ischemic stroke in patients who recently underwent cardiac catheterization in a review of 48 cases.

Many physicians have been reluctant to use thrombolysis in such patients because of the erroneous presumptions that the intracranial thrombus would not be dissolved by treatment and that post-catheterization patients are especially vulnerable to intracranial hemorrhage. But these concerns were not borne out by this case review, Pooja Khatri, M.D., said while presenting a poster at the 30th International Stroke Conference.

"This is a great population of patients to treat," said Dr. Khatri, a neurologist at the University of Cincinnati.

Because these patients are still hospitalized when their strokes occur, they can be quickly diagnosed and treated, she explained.

Dr. Khatri and her associates collected case information on 48 consecutive, eligible patients who were treated at several U.S. academic centers since 2001. All patients had an ischemic stroke within 36 hours of cardiac catheterization. Of them, 10 were treated with tissue plasminogen activator (TPA), and the other 38 received only supportive care.

By 7 days after diagnosis, NIHSS scores had improved by a median of 6.5 points in those who got TPA and by a median of 2 points in those who did not.

The median National Institutes of Health Stroke Scale (NIHSS) score at the time of diagnosis was 12 in the patients treated with TPA and 6 in those who did not receive thrombolytic therapy. The study's primary outcome was the median improvement in the NIHSS score at 24 hours after initial diagnosis. The median improvement in NIHSS score was 6 points in the patients who got TPA, compared with 0 points in those who did not, a statistically significant difference, reported Dr. Khatri at the conference, which was sponsored by the American Stroke Association.

By 7 days after diagnosis, scores had improved by a median of 6.5 points in those who got TPA and by a median of 2 points in those who did not, also a statistically significant difference.

Substantially better improvement was seen in patients treated with TPA even when the analysis excluded patients with mild strokes, defined as a NIHSS score of 5 or lower at the time of diagnosis. "This will hopefully lead to a substantial change in patient treatment," she told CARDIOLOGY NEWS.

None of the 48 patients in the study had a symptomatic, intracranial hemorrhage. Six patients had minor, asymptomatic, intracranial hemorrhages, three in the group that received TPA and three in the group that did not get thrombolysis. A total of five patients had minor bleeding at their catheterization puncture sites; one of these patients had received TPA.

None of the patients in either group required a transfusion. No patient had a retroperitoneal hemorrhage, hemopericardium, or other sites of bleeding, Dr. Khatri said. ■

Advances in Imaging Renew Interest in Carotid Bypass Surgery

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 normalizes the oxygen extraction fraction, an important marker of impaired cerebral blood flow in carotid occlusion.

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.

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).

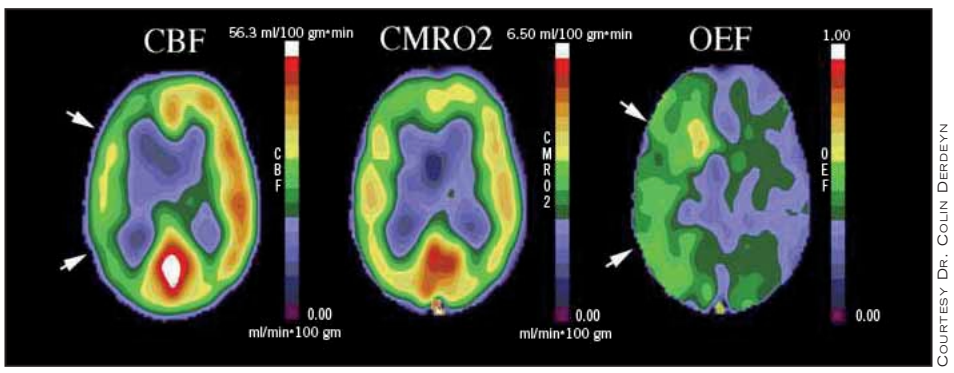
The researchers were unable to assess whether the procedure was more appropriate for one or another group of patients based on their cerebral hemodynamics because at the time the technology necessary to understand and measure cerebral blood flow had not been developed, according to M. Gazi Yasargil, 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.



COURTESY DR. COLIN DERDEYN

Stroke is more likely in brains that respond to reduced perfusion (left) with higher OEF (right) in order to support normal oxygen metabolism (middle), some say.

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. ■