Surgical procedure does not appear to reduce risk of subsequent stroke after 'mini-stroke'

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Patients with thickening and blockage of the internal carotid artery (supplies blood to the brain) and hemodynamic cerebral ischemia (insufficient blood flow to the brain, sub-type of stroke) who had a surgical procedure performed to improve blood flow in the artery did not have a reduced rate of stroke after 2 years compared to similar patients who received medical therapy alone, according to a study in the Nov. 9 issue of *JAMA*.

"Atherosclerotic internal carotid artery occlusion (AICAO) causes approximately 10 percent of transient ischemic attacks [TIAs; temporary cessation or reduction of blood supply to part of the brain, resulting in brief neurologic dysfunction that usually persists for less than 24 hours; often referred to as 'mini-stroke'] and 15 percent to 25 percent of ischemic strokes in the carotid territory. The 2-year risk of subsequent ipsilateral [on the same side of the previous stroke] ischemic stroke while a patient receives medical therapy is 10 percent to 15 percent," according to background information in the article. Extracranial-intracranial (EC-IC; outside, within the skull) arterial bypass surgery was developed to prevent subsequent stroke by improving blood flow to the blocked artery with revascularization. A previous trial regarding use of this surgery failed to demonstrate benefit, though "this trial was criticized for failing to identify the subgroup of patients with hemodynamic cerebral ischemia due to poor collateral circulation for whom surgical revascularization might be of greatest benefit."

William J. Powers, M.D., of the University of North Carolina School of

Medicine, Chapel Hill, and colleagues conducted the Carotid Occlusion Surgery Study (COSS) to determine whether EC-IC bypass surgery, added to best medical therapy, reduces subsequent ipsilateral ischemic stroke at 2 years in patients with recently symptomatic AICAO and hemodynamic cerebral ischemia identified by positron emission tomography (PET). Of 195 patients who were randomized, 97 were randomized to receive surgery and 98 to no surgery. Antithrombotic therapy and risk factor intervention were recommended for all participants. The randomized trial was conducted from 2002 to 2010 at 49 clinical centers and 18 PET centers in the United States and Canada.

The primary measured outcome for all participants randomized to the surgical group who received surgery was the combination of (1) all stroke and death from surgery through 30 days after surgery and (2) ipsilateral ischemic stroke within 2 years of randomization. For the nonsurgical group and for those randomized to the surgical group who did not receive surgery, the primary measured outcome was the combination of (1) all stroke and death from randomization to randomization plus 30 days and (2) ipsilateral ischemic stroke within 2 years of randomization.

Median (midpoint) follow-up for the surgical group was 723 days; for the nonsurgical group, it was 722 days. The trial was terminated early due to futility. The researchers found that the two-year rates for the primary end point were 21.0 percent (20 events) for the surgical group and 22.7 percent (20 events) for the nonsurgical group, a difference of 1.7 percent. At 30 days, the rates of ipsilateral ischemic stroke were 14.4 percent (14/97) in the surgical group and 2.0 percent (2/98) in the nonsurgical group, a difference of 12.4 percent.

"The lower stroke risk observed in the COSS for the nonsurgical group is similar to the better outcomes observed in more recent studies of patients with medically treated asymptomatic carotid artery stenosis,

ascribed to improvements in medical therapy. These observations reaffirm the hazard of using even the most carefully studied historical controls to infer therapeutic efficacy and the necessity of performing randomized controlled trials to establish clinical benefit. Although improved hemodynamics in participants who survived EC-IC bypass surgery without perioperative stroke was associated with low risk of recurrent stroke, the better-than-expected efficacy of medical therapy in the nonsurgical group was sufficient to nullify any overall benefit of surgery," the authors write.

In an accompanying editorial, Joseph P. Broderick, M.D., of the University of Cincinnati College of Medicine, and Philip M. Meyers, M.D., of Columbia University, New York, write regarding the reimbursement for procedures and devices in clinical practice without evidence of clinical effectiveness.

"Clinical science and reimbursement for delivery of clinical stroke care must be balanced and aligned. Physicians who provide care for patients with stroke must recognize the current lack of evidence for clinical efficacy of endovascular therapy and enroll patients in randomized trials. The review process of the Food and Drug Administration and Centers for Medicare & Medicaid Services (CMS) must be harmonized and should require higher standards of evidence for clinical efficacy prior to clearance or approval of devices for stroke and subsequent reimbursement. Long-term and ongoing reimbursement should be predicated on evidence for equivalent or superior clinical efficacy, and cost-effectiveness should be an important consideration for clinically equivalent therapies. For example, if intravenous tissue plasminogen activator (IV t-PA) is clinically equivalent to endovascular therapy, society will have to weigh the substantially increased costs for equal clinical benefit. If these devices produce better clinical outcomes, appropriate reimbursement, even for more expensive endovascular interventions, should be promptly instituted so appropriate changes in

delivery of care for patients with acute stroke can be expedited."

More information: *JAMA*. 2011;306[18]:1983-1992.

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