Carotid Endarterectomy May Improve Cognition

BY LAIRD HARRISON

FROM THE ANNUAL MEETING OF THE CONGRESS OF NEUROLOGICAL SURGEONS

SAN FRANCISCO – Cognitive function improved for most patients in the year after they underwent endarterectomy for carotid stenosis, according to the results of an ongoing prospective study.

Benefits seem to come gradually from improved blood flow, said Dr. Zoher Ghogawala, a neurosurgeon at Yale University in New Haven, Conn. "After 1 month, there was no change in any of the domains we measured," he said. "However, if we followed these patients for a year, there was significant improvement."

'After 1 month, there was no change, [but after] a year, there was significant improvement.'

DR. GHOGAWALA

Although carotid endarterectomy is a well-established technique to treat carotid stenosis as a means of preventing stroke, its effects on cognitive function are poorly understood, Dr. Ghogawala said.

To learn more, he and his colleagues enrolled 36 patients from three sites. To estimate the extent that these patients' circulation was compromised, the researchers generated quantitative phase-contrast magnetic resonance angiography (qMRA) flow maps for their internal and middle cerebral arteries. This technology images blood flow in multiple phases of the cardiac cycle and then calculates volume, velocity, and direction.

The researchers used this technique because conventional MR techniques usually do not show changes in blood flow.

Using these data, they found that 12 patients had middle cerebral artery (MCA) flow impairment (defined as at least 15% less flow than the contralateral side) and 18 had impairment of internal carotid artery flow.

Lower blood flows were associated with a higher rate of stenosis. "It's what you might expect," said Dr. Ghogawala.

Following surgery, new qMRA maps showed improved blood flow in these patients. Of the 12 patients who had preoperative impairment in MCA blood flow, 10 had improved flow after surgery.

After a month, there were no significant improvements in cognitive functioning. But in 29 patients who completed follow-up at 1 year, there was improvement in executive functioning (as measured by the Trail Making Test, Part B), verbal fluency (Controlled Oral Word Association FAS test), and memory (total recall score on the Hopkins Verbal Learning Test).

Scores improved on the Trail Making Test in all 9 patients with improvement in blood flow following surgery, compared with 8 of 20 patients with no improvement.

The presence of a right-sided lesion and impairment in middle cerebral artery blood flow were both significant, independent predictors of improved Trail Making Test scores.

Dr. Ghogawala said that patients with those features may have benefited the most because their cognitive function had been most impaired by their constricted blood flow.

Dr. Ghogawala disclosed that one of his coauthors received research support from VasSol Inc., the company that made the technology for producing the qMRA maps used in the study. Another coauthor owns shares in the company. ■

VIEW ON THE NEWS

Technology May Have Future

This study that may become more important as the debate between CAS and CEA continues and further questions develop regarding intervention vs. medical management for asymptomatic patients. If these findings are reproducible on a larger scale, this might become an important testing modality for asymptomatic patients to determine who might benefit from intervention. If the technology proves successful, it would be very interesting to see if there are differences between CAS and CEA with regard to improvement in cognitive function.

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Stroke History Did Not Alter Dabigatran's Safety, Efficacy

BY JEFF EVANS

FROM THE LANCET NEUROLOGY

Patients with atrial fibrillation who were taking the anticoagulant dabigatran for secondary stroke prevention suffered an ischemic stroke or systemic embolism at a rate similar to patients taking warfarin in a prespecified subgroup analysis of patients from the 2-year RE-LY trial.

This analysis of 3,623 patients was consistent with the overall results found in the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) trial cohort of 18,113 patients. Significant differences in the rates of intracranial bleeding between patients treated with dabigatran and those taking warfarin that had been observed in the overall results of the trial also were seen among those with a history of ischemic stroke or TIA.

"Although the subgroup analyses were not powered to detect whether the effects of dabigatran compared with warfarin varied by subgroup, the overlapping 95% confidence intervals suggest that major variations in the relative effects of the drugs between the patients with or without previous stroke or transient ischemic attack are unlikely," Dr. Hans-Christoph Diener of University Hospital Essen (Germany) and his colleagues wrote (Lancet Neurol. 2010 Nov. 8 [doi:10.1016/S1474-4422(10)70274-X]).

The Food and Drug Administration approved the drug in October at doses of 150 mg and 75 mg for reducing the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. The approval was based on the overall results of the open-label RE-LY trial, which randomized patients with atrial fibrillation to 110 mg or 150 mg dabigatran twice daily or warfarin adjusted to an international normalized ratio of 2.0-3.0.

In the overall trial cohort, a stroke or systemic embolism occurred significantly more often among patients with a previous stroke or TIA (2.38% per year) than in those without such history (1.22% per year).

The primary outcome of stroke or systemic embolism occurred at similar rates between patients with a previous stroke or TIA who took warfarin (2.78% per year), 110 mg dabigatran (2.32% per year), and 150 mg dabigatran (2.07% per year). In the overall study population, the rate of stroke or systemic embolism did not differ among groups, occurring at 1.71% per year in patients on warfarin, 1.54% per year in patients on 110 mg dabigatran, and 1.11% per year in those on 150 mg dabigatran.

In the subgroup, intracranial bleeding occurred at a significantly lower rate in patients who took 110 mg dabigatran, compared with those who took warfarin (0.25% vs. 1.28% per year).

Patients with a history of stroke or TIA who took the 110-mg dose of dabigatran had a significantly lower rate of vascular death and all-cause mortality than did patients who received warfarin, but this effect was not seen in the 150-mg group.

Based on the results in patients with a previous stroke or TIA, the investigators suggested that "150 mg dabigatran might provide better protection against stroke than warfarin, whereas 110 mg dabigatran is as efficacious as warfarin and reduces adverse events (bleeding complications and mortality)." And indeed, the FDA's Cardiovascular and Renal Drugs Committee that evaluated dabigatran in September came to a similar conclusion, although no superiority claim over warfarin could be made. Additionally, the FDA did not include the 110-mg dosage that established noninferiority in its approved dosages, recommending the regimen of 150 mg twice daily, except in patients with impaired renal function, who would take 75 mg twice daily.

Boehringer Ingelheim GmbH funded the study and is marketing dabigatran as Pradaxa. Dr. Diener and some of his authors disclosed financial relationships with this company and others that manufacture or market drugs for the prevention or treatment of stroke. One author is an employee of Boehringer Ingelheim. ■

VIEW ON THE NEWS

Subgroup Analysis Offers Guidance

This subgroup analysis begins to fill the void of data on the benefit of oral coagulation for secondary stroke prevention and the safety of oral coagulation in patients with a previous ischemic stroke or TIA, according to Dr. Deidre A. Lane and Dr. Gregory Y.H. Lip of the University of Birmingham (England).

The analysis offers some guidance to physicians when deciding which dose of dabigatran to prescribe after going through an individualized stroke and bleeding risk assessment.

"Because of the necessary trade-off between stroke prevention and bleeding with both doses of dabigatran, consultation with patients regarding their preferences for treatment dose will be even more important to ascertain their threshold for stroke prevention over increased bleeding risk or vice versa," they wrote.

Editor's Note: The approved dosages and indications differ between the countries in which dabigatran was approved.

DR. LANE AND DR. LIP *wrote their comments in an editorial accompanying the paper (Lancet Neurol. 2010 Nov. 8 [doi:10.1016/S1474-4422(10)70275-1]). Both report having received funding for research and lecturing from manufacturers of drugs used to treat atrial fibrillation, including Boehringer Ingelheim.*