stroke, hemorrhagic stroke, myocardial infarction, or vascular death) at 3 months. The primary safety outcome was combined moderate and severe bleeding, according to the GUSTO definition. Other safety outcomes included intracranial hemorrhage, total mortality, and adverse events (including serious adverse events). Study visits were performed on the day of randomization at Day 21 and Day 90.

Subjects were mean 62.5 years of age and mostly men. Approximately 72% of the enrolled patients had minor stroke; mean time to randomization was 13 hours. At 3 months, the risk of recurrent stroke was significantly lower among patients assigned to clopidogrel plus aspirin compared with those receiving aspirin alone (HR, 0.68; 95% CI, 0.57 to 0.81; p<0.001). More patients on the dual regimen were also free of the secondary outcome of combined events (HR, 0.69; 95% CI, 0.58 to 0.82; p<0.001). Patients on the dual regimen were also less likely to experience a recurrent ischemic stroke (7.9% vs 11.4%; HR, 0.67; 95% CI, 0.56 to 0.81; p<0.0001). The differences on the remaining secondary outcomes of hemorrhagic stroke, myocardial infarction, and cardiovascular death were not statistically different. There was no difference in the rates of severe, moderate, or mild bleeding, or death from any cause. As the greatest separation of the 2 treatment arms appeared to occur during the first 21 days post stroke, the authors suggested that the early period of dual antiplatelet therapy may have been the major cause of superior outcome.

Reversal of Chronic Hypoperfusion to Improve Cognitive Function: The RECON Trial

Written by Emma Hitt, PhD

Carotid artery disease is thought to be one of the causes of cognitive dysfunction, but treatment of the associated cerebral blood flow impairment has never been tested in a randomized controlled trial [Marshall RS et al. *Neurology* 2012]. Randolph S. Marshall, MD, MS, Columbia University Medical Center, New York, New York, USA, reported the results of the Randomized Evaluation of Carotid Occlusion and Neurocognition trial [RECON; NCT00390481].

The RECON trial randomized 41 patients with complete internal carotid artery occlusion and hemispheral transient ischemic attack (TIA) or minor stroke in the territory of the carotid occlusion within 120 days prior to enrollment and positron emission tomography (PET) oxygen extraction fraction (OEF) >1.13, indicating stage II hemodynamic failure. Patients had no prior diagnosis of dementia, Barthel index ≥12/20 at the time of enrollment, and an education level >4 years.

Patients were randomized to receive surgical extracranial-intracranial (EC-IC) bypass plus best medical therapy or medical therapy alone to determine if reversing chronic hypoperfusion with EC-IC bypass can improve cognitive function or prevent its decline. Patients in the surgical arm underwent PET 30 days after surgery to measure OEF ratio. There were no differences in the baseline characteristics of the surgical and medical arms.

All patients received 14 standardized tests as part of the neurocognitive exam at baseline and after 2 years. Left hemisphere-specific, right hemisphere-specific, and global tests were included. Individual tests were Z-scored based on age- and education-matched norms. Composite Z-scores for each patient were determined based on the average Z-score for left hemisphere plus global test scores if the patient had left carotid occlusion, and right hemisphere plus global scores if the patient had right carotid occlusion.

At baseline, there was no difference in cognitive scores between the groups, but the average neurocognitive composite Z-score across all patients was 1.2 standard deviations below the age- and education-adjusted mean (range, –3.7 to –0.3). There was a slight, but not significant, improvement in cognitive score over 2 years for both groups, but no significant difference was found between the surgical and medical arms (Table 1).

Table 1. Unadjusted Cognitive Outcomes by Treatment Group

	Medical (n=15)	Surgical (n=13)	p Value
Change in composite neurocog Z-score	0.2 (SE=0.14)	0.02 (SE=0.25)	0.5 [two-sample t test]
p Value	0.17 [paired t test]	0.9 [paired test]	

In the univariate analysis of factors correlating with cognitive change, presentation with a TIA rather than a stroke (p=0.01), improvement of depression over the 2 years (p=0.02), and a better baseline PET OEF ratio (p=0.04) were associated with cognitive improvement. The first 2 variables were significant in multiple regression.

In the surgical group, the OEF dropped from 1.24 to 1.14. Only 3 out of 13 surgical patients had 30-day PET OEF ratios ≤1.13, and none of the 13 patients achieved an OEF ratio <1.067, which is considered the upper limit of normal. Thus, hemodynamic normalization was not achieved by EC-IC bypass in the RECON cohort.

Dr. Marshall concluded that there was "no evidence to support superiority of EC-IC bypass surgery plus best medical therapy in preserving or improving cognition over medical therapy alone in patients with recently symptomatic carotid artery occlusion and stage II hemodynamic failure." Further investigation with medical interventions or more effective reperfusion interventions is needed.