weaker, said Dr. Manning, with an OR of 1.57 in Model 3 (95% CI, 1.14 to 2.17; p=0.012). Discrimination analyses showed that maximum SBP in the hyperacute phase and SD-SBP in the acute phase were the best predictors of outcome.

These are the first data to show the prognostic value of BPV after ICH. Large fluctuations in SBP and episodic hypertension after ICH represent an increased risk of poor outcome. The rapid lowering of elevated BP early after ICH is important, plus ensuring smooth and sustained control over several days, said Dr. Manning, which may require tailoring the frequency and intensity of BP monitoring.

Poststroke Cognitive Decline Not Reduced by Aggressive Blood Pressure Lowering or Dual Antiplatelet Therapy

Written by **Mary Mosley**

Neither aggressive blood pressure (BP) lowering nor dual antiplatelet therapy (DAPT) with aspirin and clopidogrel reduced the rate of cognitive decline after a lacunar stroke, said Oscar R. Benavente, MD, University of British Columbia, Vancouver, British Columbia, Canada, who presented the results for this secondary outcome from the Secondary Prevention of Small Subcortical Strokes Trial [SPS3; NCT00059306].

In the international, multicenter SPS3 study, patients with a lacunar stroke, as verified by magnetic resonance imaging, were randomized in a 2x2 factorial design to a lower systolic BP (SBP; <130 mm Hg; n=1501) or higher SBP target (130 to 149 mm Hg; n=1519) and to clopidogrel 75 mg or placebo. All patients received aspirin 325 mg daily. BP management was open label. The median time to randomization from the index event was 62 days.

The lower BP target was associated with a nonsignificant reduction in the primary endpoint of all strokes (HR, 0.81; 95% CI, 0.64 to 1.03; p=0.08) and disabling and fatal strokes (HR, 0.81; 95% CI, 0.53 to 1.23; p=0.32), as well as a significant reduction in intracerebral hemorrhage (HR, 0.37; 95% CI, 0.15 to 0.95; p=0.03) [The SPS3 Study Group. *Lancet* 2013].

At study entry, the BP levels in the lower and higher target groups, respectively, were 144/78 mm Hg and 145/80 mm Hg. At 1 year, the difference in SBP between the groups was 11 mm Hg (127 and 138 mm Hg, respectively) and was maintained to study end. The mean Mini-Mental State Examination (MMSE) was 28 and the mRS score was 66% to 67%. The mean age of the patients was 63 years.

Cognitive assessments were conducted at study entry and annually thereafter by blinded, certified examiners using eight tests covering most cognitive domains. However, the cognitive abilities screening instrument (CASI) was the main test used to determine the benefit of the study interventions. Scores were normalized using published norms for age, sex, education, and region. Linear mixed models were fit to determine whether changes over time differed by BP group. Importantly, cognitive testing results after a recurrent stroke were excluded.

In this analysis, 2916 patients with a baseline assessment were included, with nearly 11,000 total assessments. On average, there were 3.3 assessments per patient, with a range of 1 to 9 assessments.

The overall mean CASI z-scores ranged from –0.59 at study entry to –0.39 at Year 5 to 1.11 at Year 8. The average change in the CASI z-score from study entry to Year 1 was 0.11 (SD=0.84) and from study entry to Year 3 was 0.15 (SD=0.97). This modest decrease in the z-score was not significant, said Prof. Benavente. No interaction was seen between BP treatment (p=0.30) or DAPT (p=0.95), and CASI z-score, even after adjustment. No interaction was seen for the four interventions and CASI z-score (p=0.26).

In this cohort of lacunar stroke patients, a modest nonsignificant decline in cognitive function was observed over the first year. Concluding that neither intervention modified the rate of cognitive decline, Prof. Benavente stated the age and mean MMSE of the cohort and the mean follow-up of only 3.6 years must be considered.

Chromosome 7 Linked to Intracranial Aneurysm in Novel Genetic Finding

Written by **Mary Mosley**

Joseph P. Broderick, MD, University of Cincinnati, Cincinnati, Ohio, USA, reported that a region on Chromosome 7 was associated with intracranial aneurysm (IA) in a Dutch discovery sample used in a genomewide association study (GWAS). This new finding was replicated in another Dutch sample (but not in a Finnish sample), and in a meta-analysis of the samples conducted by Dr. Broderick and colleagues.

There is substantial evidence for a genetic role in IA, and Dr. Broderick stated that this evidence is the strongest for any type of stroke. There is also genetic evidence for other Mendelian diseases associated with IA, such as polycystic kidney disease and Ehlers-Danlos. About 10% of patients with IA have a first-degree relative with a history of subarachnoid hemorrhage, and there is a high rate of intracranial hemorrhage amongst patients with familial

IA (FIA). The location of IA is genetically mediated in FIA families and in twin studies. Prior GWAS studies have shown regional associations on chromosomes 4, 8, 9, 10, 12, 13, 18, and 20.

The Dutch discovery sample included 2644 white patients (male, 28%) from six different populations, and 2548 controls (male, 38%) from five different populations, including patients from the Atherosclerosis Risk in Communities study. The mean age of IA onset was 53.3 years in the discovery sample and 57.9 years in the control sample.

The GWAS of the Dutch discovery sample revealed two peaks; one at chromosome 9 and the other at chromosome 7. In the chromosome 9 region, the CDKN2BAS, or the ANRIL gene, is most pronounced, and the reason it causes an aneurysm is a matter of great discussion, said Dr. Broderick, even though this region has been linked to aneurysms in the brain and abdomen, and to myocardial infarction, among other outcomes, showing that there are many phenotypes within this region.

Further, there was an overlap between the location of the primary association for IA on chromosome 7 and that for ischemic stroke reported by Matarin and colleagues. The association for the former had genomewide significance, while the latter did not. Another overlap was found between a tertiary location found on chromosome 7 and that for large vessel ischemic stroke that reached genomewide significance [International Stroke Genetics Consortium. *Nat Genet* 2012].

Although there was replication in the Dutch cohort, there was no replication in the Finnish cohort, although it was in the right direction, said Dr. Broderick, and there was genomewide significance in the meta-analysis.

The findings in this study may represent another overlap of a gene region associated with large vessel ischemic stroke and with IA, such as chromosome 9p21 - ANRIL, which has been clearly documented, said Dr. Broderick. This suggests that genetic risk factors associated with large vessel pathophysiology may present with different stroke phenotypes. More GWAS, exome sequencing, and functional studies are needed to further delineate the genetic underpinnings of IA.