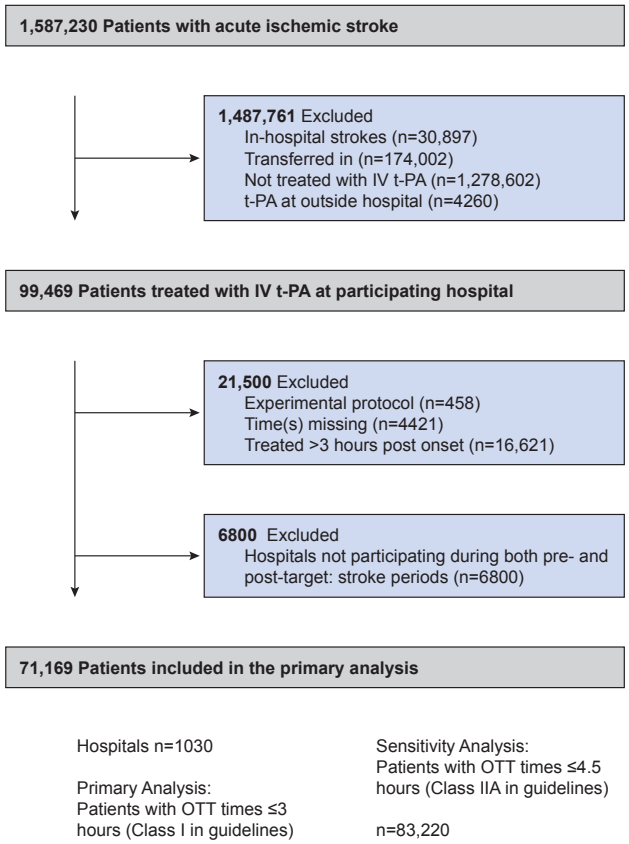
profiles included a balance of men and women, median age 72 years, who were of white, Hispanic, and black origins. Of the stroke patients treated with t-PA (n=71,169) 27,319 were pre-intervention and 43,850 were postintervention patients from 1030 GWTG-Stroke participating hospitals (Figure 1).

Prior to the study's initiation in 2009, 15.6% of hospitals had DTN rates of ≤60 minutes in ≥50% of t-PA-treated stroke patients. Median time was 74 minutes in Quarter 4 of 2009, immediately prior to the start of the Target: Stroke initiative. The study's DTN goal was subsequently met by 46.7% of the participating hospitals by 2013 (p<0.0001) and by 53.3% of patients by Quarter 3, 2013 (p<0.0001). The program's goal of DTN times of ≤60 minutes was achieved within 4 years as opposed to the originally projected 15 years.

Figure 1. Selection of Study Population for Target: Stroke



IV=intravenous; OTT=onset to treatment; t-PA= tissue plasminogen activator.

With a target of achieving a more rapid administration of t-PA, there were initial concerns centered on the shorter DTN times as related to rushed overall assessments for acute ischemic stroke patients. The Target: Stroke Initiative research revealed that rapid reperfusion therapy in acute ischemic stroke can be done with process reductions and improved outcomes.

Blood Pressure Variability After ICH Predicts Poor Outcomes

Written by **Mary Mosley**

The Second Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial [INTERACT2; Anderson CS et al. *N Engl J Med* 2013] showed that early, target-driven (<140 mm Hg) lowering of systolic blood pressure (SBP) was safe and improved functional outcomes compared with guideline-directed BP management (SBP, <180 mm Hg). A post hoc analysis has now shown that within individual variability in SBP during the first 24 hours and days 2 to 7 following acute intracerebral hemorrhage (ICH) predicts outcome, with a linear relationship between the degree of systolic BP variability (BPV) and risk of death or major disability at 90 days (defined as an mRS score of 3 to 6) [Manning L et al. *Lancet Neurol* 2014].

During the hyperacute (first 24 hours) and acute (Days 2 to 7) phases, a higher level of maximum SBP also predicted a poor outcome. These BP findings were independent of mean SBP, said Lisa Manning, MD, University of Leicester, Leicester, United Kingdom, who presented the results.

INTERACT2 was an international, multicenter (21 countries, 144 hospitals), randomized, controlled trial of 2839 patients with spontaneous ICH and an SBP ≥150 mm Hg. BP was measured five times on Day 1, and twice daily on Days 2 to 7. In this analysis 2645 patients were included in Study 1, concerned with the effect of BPV during Day 1 on outcome, and 2347 in Study 2, concerned with BPV during Days 2 to 7. Mean age was 64 years, 63% were men, and 69% to 73% were from the Chinese region.

The key BPV index was the standard deviation of SBP (SD-SBP) derived using all available BP measurements in the two study periods. Three logistic regression models were used to determine the association between BPV and outcomes. Model 1 adjusted for age, sex, and randomized treatment. Model 2 adjusted for these, plus region, high NIHSS, and hematoma volume, and Model 3 further adjusted for mean SBP.

The primary outcome was death or major disability at 90 days. To determine the strength of associations, patients were divided into quintiles of SD-SBP, and the lowest quintile was the reference point. In the hyperacute phase in Model 1, there was a linear association between systolic BPV and risk of the primary outcome (p<0.001). In Model 3, the odds ratio (OR) was 1.41 for the highest quintile of BPV (95% CI, 1.05 to 1.90; p=0.017). In the acute phase, the association between systolic BPV and the primary outcome persisted, although it was slightly

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