The Secondary Prevention of Small Subcortical Strokes Trial: Blood Pressure Intervention Results

Written by Emma Hitt, PhD

Small subcortical strokes (S3), or lacunar strokes, account for >25% of brain infarcts. Although S3 are the most common cause of vascular dementia, no clinical trials have focused on this stroke subtype. Oscar R. Benavente, MD, University of British Columbia, Vancouver, Canada, reported blood pressure (BP) intervention results from the Secondary Prevention of Small Subcortical Strokes Trial [SPS3; NCT00059306].

SPS3 enrolled 3020 patients who had experienced lacunar strokes within 180 days, verified by MRI. The median time from the index event to randomization was 62 days. The mean patient age was 63 years, and 63% were male. Patients who had a cortical stroke, cardioembolic disease, and/or carotid stenosis were not eligible for the trial.

In the BP intervention portion of SPS3, patients were randomized to a higher systolic BP (SBP) target of 130 to 149 mm Hg (higher target group, n=1519) or a lower SBP target of <130 mm Hg (lower target group, n=1501). Antihypertensives were not discontinued at study entry, and BP medications were not specified by the study protocol.

The primary outcome was recurrent stroke. During a mean follow-up of 3.7 years, 277 first recurrent strokes occurred. The secondary outcomes were major vascular events, cognitive decline, or death.

The patients reached target BP at around 6 months. At 1 year, the average SBP for the higher target group was 138 mm Hg compared with 127 mm Hg for the lower target group. At the last observed visit, there was an average difference in SBP between the groups of 11 mm Hg.

For the primary outcome, the lower target group had an approximately 19% reduction in ischemic and hemorrhagic strokes compared with the higher target group, but this trend did not reach significance (HR, 0.81; 95% CI, 0.64 to 1.03; p=0.08). However, when ischemic and hemorrhagic strokes were separated, there was a significant reduction in intracerebral hemorrhage in the lower versus the higher target group (HR, 0.37; 95% CI, 0.15 to 0.95; p=0.03). The reduction in ischemic strokes did not reach significance after separating these events.

There were no significant differences between the lower and higher target groups in the secondary outcomes of major vascular events and death. The safety outcomes between the 2 groups were not significantly different, but more patients in the lower target group had complications due to hypotension (HR, 1.53; 95% CI, 0.80 to 2.93; p=0.20), particularly orthostatic syncope (HR, 2.18; 95% CI, 0.76 to 6.27; p=0.14).

Prof. Benavente said, "Achieving a lower systolic blood pressure target was feasible, safe, and well tolerated." An SBP of <130 mm Hg significantly reduced intracerebral hemorrhage by two thirds, and a lower BP is likely to reduce recurrent stroke by approximately 20%, even though this trend did not reach significance. Although this is the only trial that has used target BP levels as an intervention, the results are consistent with data from previous trials of BP lowering after stroke.

Final Results of the Solitaire FR Thrombectomy for Acute Revascularization: The STAR Trial

Written by Muriel Cunningham

Vitor Mendes Pereira, MD, MSc, University Hospital of Geneva, Geneva, Switzerland, presented the results from the Solitaire FR Thrombectomy for Acute Revascularisation trial [STAR; NCT01327989]. This was a prospective, observational, single-arm, multicenter, core lab-reviewed study conducted in high-volume stroke centers that had extensive mechanical thrombectomy experience. The Solitaire FR, a self-expanding retrievable stent, was utilized as a first-intention device in anterior circulation.

The main inclusion criteria were patients aged 18 to 85 years with a National Institutes of Health Stroke Scale (NIHSS) score of 8 to 30, proximal anterior intracranial vasculature, and presentation within 8 hours of the onset of stroke, with a modified Rankin Scale (mRS) score ≤2 prior to stroke onset. Patients who were participating in another study, were pregnant or nursing, had signs of rapid neurological improvement, suffered a stroke within the previous 30 days, had an unknown time of stroke onset, or had a life expectancy <90 days were excluded. Additionally, any patients with evidence of intracranial hemorrhage, arteriovenous malformation, aneurysm, early ischemic changes, carotid dissection, complete carotid occlusions, vasculitis, or stenosis proximal to the thrombus site were excluded.

Of the 682 patients screened, 471 failed screening and 9 withdrew consent, for a total of 202 patients in the final study population. The median age was 72 years (range, 25 to 86), with 122 (60%) females and 80 (40%) males. The median NIHSS at baseline was 17 (range, 8 to 26). Stroke and procedure characteristics are presented in Table 1.

Table 1. Stroke and Procedure Characteristics

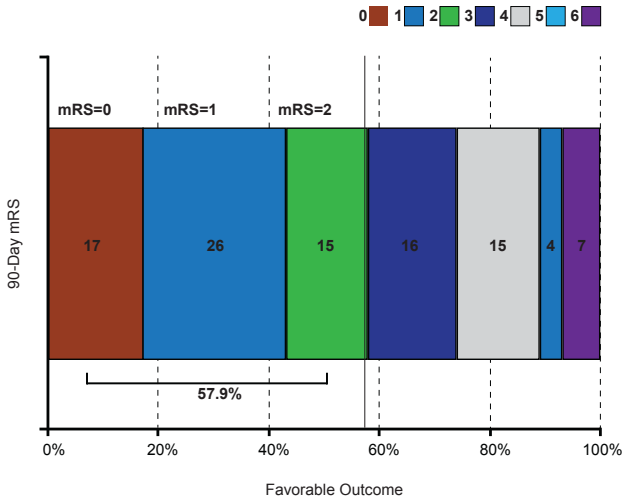
Parameter	n (%)
Combined intravenous rtPA/mechanical thrombectomy	119 (59)
Mechanical thrombectomy only	83 (41)
Time to Treatment	n (%)
0 to 3 hours	50 (25.6)
3 to 4.5 hours	74 (37.9)
>4.5 hours	71 (36.4)
Occluded Vessel (per Core Lab)[a]	n (%)
Internal carotid artery terminal	36 (18)
Middle cerebral artery	160 (82)
M1	131 (67)
M2	28 (14)
M3	1 (0.5)[b]
Procedure Characteristics	Mean±SD (n)
Number of passes	1.5±0.7 (202)
Stroke onset to groin puncture (min)	251±99 (195)
Groin puncture to balloon catheter placement (min)	15±10 (193)
Balloon catheter placement to TICI 2b/3 or final digital subtraction angiogram (min)	29±27 (194)

[a]6 patients could not be evaluated due to incomplete data. [b]Protocol violation. rtPA=recombinant tissue plasminogen activator; SD=standard deviation; TICI=thrombolysis in cerebral infarction.

A total of 188 patients (93%) completed the 90-day follow-up and 14 (7%) died. Per the core lab, 160 patients (79%) met the primary endpoint of revascularization (thrombolysis in cerebral infarction score ≥2b) within 3 passes; 12 patients with missing endpoint data were counted as failures. Eighteen patients (9%) required rescue therapy, and 57.9% had a favorable outcome (mRS score ≤2) at 90 days (Figure 1). Per adjudication by Clinical Events Committee, 38 patients (18.8%) experienced symptomatic intracranial hemorrhage within 24 hours of the procedure. Fifteen patients (7.4%) had a device- or procedure-related serious adverse event.

Prof. Pereira said, "This nonrandomized prospective study suggests that treatment with the Solitaire FR device for intracranial anterior circulation strokes by comprehensive and experienced stroke centers results in a low risk of clinically relevant procedural and device related complications, high revascularization rates, and good clinical outcomes." These results support the further investigation of this device in a randomized controlled trial against best medical treatment.

Figure 1. Modified Rankin Scale Distribution at 90 Days



mRS=modified Rankin Scale.

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Clopidogrel Plus Aspirin Reduces Risk of Recurrent Stroke: The CHANCE Trial

Written by **Phill Vinall**

Transient ischemic attack (TIA) and minor stroke are common cerebrovascular disorders after which there is a high risk of recurrent stroke. Results from the recently completed Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events study [CHANCE] indicate that an early period of clopidogrel plus aspirin reduces the risk of recurrent stroke in these patients without increasing bleeding compared with aspirin alone.

The objective of the CHANCE study was to assess the effects an early 21-day period of clopidogrel plus aspirin versus aspirin alone on reducing the risk of a new stroke when initiated within 24 hours of symptom onset in patients with minor stroke (National Institutes of Health Stroke Score [NIHSS] ≤3) or TIA (ABCD^2 score ≥4). The study design has been published [Wang Y et al. *Am Heart J* 2010]. Yongjun Wang, MD, Beijing Tian Tan Hospital, Beijing, China, presented the 3-month results.

Study participants (n=5170) were randomly assigned to receive clopidogrel (loading dose of 300 mg then 75 mg/day for up to 3 months) plus aspirin (75 mg/day for 21 days; n=2584) or aspirin (75 mg/day for 3 months) plus placebo (n=2586). The primary efficacy outcome was the percentage of new strokes (ischemic or hemorrhagic) at 3 months. The secondary efficacy outcome was a combination of new clinical vascular events (ischemic