What's New in Vascular Neurology

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If one were to summarize recent developments in vascular neurology, the highlights would be that promising procedures for preventing recurrent stroke failed to beat medical treatment [1–3], early aggressive blood pressure reduction after an index stroke was associated with a suggestion of harm [4, 5], one antithrombotic treatment worked, another did not, premature antithrombotic therapy discontinuation was detrimental [6–8], and organized stroke care was associated with better clinical outcomes [9, 10].

Severe atherosclerotic stenosis (70–99%) of the major intracranial arteries is a major cause of stroke, even with traditional medical therapy. The Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial investigated the safety and efficacy of intensive medical management (guideline-based vascular risk factor modification) alone versus medical management with percutaneous transluminal angioplasty and stenting (PTAS) in patients with an ischemic stroke or transient ischemic attack (TIA) within the prior month [1]. SAMMPRIS was prematurely stopped because an interim review showed that within 30 days after enrollment, the rate of stroke or death was significantly higher in the PTAS group (14.7%) than in the medical management group (5.8%). These results indicate that intensive risk factor management and not PTAS should be the preferred treatment strategy for recently symptomatic patients with severe intracranial atherosclerotic stenosis. Another group of stroke patients at high risk for recurrent strokes are those with symptomatic atherosclerotic internal carotid artery occlusion and hemodynamic cerebral ischemia. Carotid Occlusion Surgery Study (COSS) investigators evaluated whether or not extracranial-intracranial

al bypass surgery added to best medical therapy reduced subsequent ischemic stroke in patients with recently symptomatic atherosclerotic internal carotid artery occlusion and hemodynamic cerebral ischemia [2]. The COSS was terminated early for futility: 2-year rates for the primary end point were 21.0% for the surgical group versus 22.7% for the nonsurgical group ($p = 0.78$). It would thus appear that extracranial-intracranial bypass surgery does not reduce the risk of recurrent stroke compared to medical management. The role of patent foramen ovale (PFO) closure to prevent recurrent stroke in patients with a cryptogenic stroke has been controversial. The CLOSURE trial group examined the efficacy of closure with a percutaneous device versus medical therapy alone in patients with a cryptogenic stroke or TIA and a PFO [3]. The incidence of the primary end point (stroke, TIA, death) at 2 years was 5.5% in the closure group versus 6.8% in the medical therapy group ($p = 0.37$). Given these results, PFO closure with a percutaneous device does not seem to offer greater clinical benefit than medical therapy alone.

The premier modifiable risk factor for recurrent stroke is elevated blood pressure (BP). Based on epidemiologic data, the benefits of lowering BP after any stroke may extend to levels as low as 115 mm Hg. However, few studies have investigated this issue early after a recent stroke. However, in one randomized trial, investigators evaluated whether careful BP lowering with candesartan for the initial 7 days would be beneficial in acute ischemic or hemorrhagic stroke patients with high BP (systolic BP ≥ 140 mm Hg) [4]. By 6 months, rates of the composite vascular end point (vascular death, myocardial infarction or stroke) did not differ significantly between treatment groups, and the candesartan group showed a trend

towards a higher rate of poor functional status. Another study (post-hoc observational analysis) examined the association of low-to-normal BP versus normal-to-high BP with recurrent stroke among recent ischemic stroke patients [5]. This study found that low-to-normal BP was associated with a higher risk of recurrent stroke compared to normal-to-high BP, and this difference was especially pronounced within the first 6 months after the index stroke. Together, these results suggest that actively lowering BP within the first 7 days after an acute stroke does not confer clinical benefit; therefore, clinicians should not be too aggressive with BP reduction during the early period after a stroke (up to 6 months) and should probably aim to lower the level to just BP <140/90 mm Hg.

Atrial fibrillation is an important contributor to stroke risk, and warfarin has been the mainstay of preventive therapy for several decades. Although extremely cheap, warfarin use is associated with substantial variability: there are many drug/food interactions and the need exists for blood monitoring. Perhaps, not surprisingly, warfarin is underused in clinical practice. Apixaban, an oral inhibitor of factor Xa, was evaluated in a head-to-head randomized clinical trial with warfarin among patients with atrial fibrillation [6]. After 1.8 years, the primary outcome (stroke or systemic embolism) rate per year was 1.27% for apixaban versus 1.60% for warfarin ($p < 0.001$); major bleeding was 2.13% for apixaban versus 3.09% for warfarin ($p < 0.001$). A separate antithrombotic trial investigated recent noncardioembolic stroke or TIA patients randomized to receive terutroban (a selective thromboxane-prostaglandin receptor antagonist) or aspirin [7]. The study was stopped after 28 months for futility. The pri-

mary outcome (ischemic stroke, myocardial infarction or vascular death) occurred in 11% of each group. In an analysis of the Health Improvement Network, a UK primary care database comprising individuals aged 50–84 years, compared those with a first prescription for low-dose acetylsalicylic acid for the secondary vascular prevention over a mean of 3.4 years with current users of low-dose acetylsalicylic acid; those who discontinued treatment 31–180 days before the index date had a significantly increased overall risk of ischemic stroke/TIA (relative risk 1.40; 95% confidence interval 1.03–1.92) [8].

Finally, an analysis of the Get with the Guidelines®-Stroke data set, comprised of acute ischemic stroke patients treated with thrombolysis within 3 h of symptom onset, showed that in-hospital mortality was lower (odds ratio 0.78; 95% confidence interval 0.69–0.90; $p < 0.0003$) for patients with door-to-treatment times ≤ 60 min versus patients with door-to-needle times > 60 min, thus confirming the need to improve the timeliness of reperfusion in acute ischemic stroke [9]. In an observational study that compared mortality at New York State hospitals with and without designated stroke centers, short- and long-term mortality rates after the index stroke were better at hospitals with stroke centers than at those without (10.1 vs. 12.5% at 30 days; 22.3 vs. 26.0% at 1 year; $p < 0.001$ for both comparisons) [10]. Both of these studies suggest that there may be great value in adopting strategies to enhance quality/processes of inpatient stroke care. As may be seen from the foregoing recent results, medical treatment still provides the best stroke outcomes in most instances, while the quest for promising preventive procedures continues.

References

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