EXTEND-IA: Endovascular Therapy Improves Outcomes in Large Vessel Ischemic Stroke

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Bruce C.V. Campbell, MD, Royal Melbourne Hospital, Department of Medicine, University of Melbourne, Melbourne, Australia, presented data from the investigator-initiated EXTEND-IA study [Campbell BCV et al. *N Engl J Med*. 2015], demonstrating the benefit of endovascular therapy in patients with large vessel occlusion stroke.

According to Dr Campbell, who presented the EXTEND-IA results on behalf of co-principal investigator Dr Peter Mitchell and co-chairs Dr Stephen Davis and Dr Geoffrey Donnan, previous trials comparing endovascular therapy and intravenous tissue plasminogen activator (tPA) for patients with ischemic stroke produced conflicting results. With this in mind, EXTEND-IA was a multicenter trial conducted in Australia and New Zealand to determine whether the use of advanced imaging, superior devices, and earlier intervention could improve patient outcomes. The study compared the effect of endovascular therapy after intravenous tPA vs tPA alone for ischemic stroke, using computed tomography (CT) perfusion imaging selection. It aimed to select patients with proven major vessel occlusion and salvageable ischemic tissue (irreversibly injured ischemic core volume < 70 ml) who were most likely to respond favorably to reperfusion.

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Eligibility criteria included the ability to receive tPA within 4.5 hours of the onset of anterior circulation ischemic stroke, and occlusion of the internal carotid artery or of the middle cerebral artery that was accessible to stent thrombectomy. Participants were randomized to receive tPA alone or tPA plus endovascular stent thrombectomy with the Solitaire FR flow restoration device.

The primary end points were the proportion of ischemic tissue that had undergone reperfusion at 24 hours on CT or magnetic resonance perfusion imaging, and early neurologic recovery (defined as a reduction of 8 or more points on the National Institutes of Health Stroke Scale, or reaching a score of 0 or 1 by day 3). A key secondary outcome was analysis of modified Rankin Scale (mRS) at 90 days.

The trial was stopped early, with 70 of the planned 100 participants enrolled, after analysis prompted by the release of positive results in the MR CLEAN study [Berkhemer OA et al. *N Engl J Med*. 2015]. The Data Safety Monitoring Committee terminated the trial when this early analysis showed significant efficacy on the co-primary outcome. Reperfusion of the ischemic tissue was increased in the intervention group compared with the control group (100% vs 37%; $P < .0001$), as was early neurologic improvement (80% vs 37%; $P = .002$). In addition, independent functional outcome (mRS 0 to 2) at 90 days was 71% in the intervention group, compared with 40% in the control group ($P < .01$). No safety concerns were identified during the study, with no significant differences in the incidence of adverse events between the groups, said Dr Campbell.

The results of this trial showed that, in a group of patients with large vessel occlusion screened and selected for having salvageable tissue, early mechanical stent thrombectomy after tPA treatment resulted in faster and more complete tissue reperfusion. This led to improved early neurologic recovery and enhanced functional outcome at 3 months.

Dr Campbell noted that the early termination of this trial did pose limitations. It created the potential for overestimation of the effect size, and the small sample size also precluded subgroup analysis. Nevertheless, he stressed that the data were statistically robust and unequivocal in demonstrating that tPA combined with early stent thrombectomy improve patient outcomes. In the context of the 4 positive randomized trials now reported, stent thrombectomy should be the new standard of care for patients with large vessel occlusion stroke.