Focused update to guidelines for endovascular therapy for emergent large vessel occlusion: large core and basilar artery occlusion patients

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BACKGROUND
Endovascular therapy (EVT) dramatically improves clinical outcomes for patients with emergent large vessel occlusion (ELVO). Later this year, the Society of NeuroInterventional Surgery (SNIS) Standards and Guidelines Committee will update and supplement the existing SNIS guidelines on ‘Embolectomy for stroke with emergent large vessel occlusion (ELVO)’, ‘Indications for thrombectomy in acute ischemic stroke from emergent large vessel occlusion (ELVO)’, and ‘Current endovascular strategies for posterior circulation large vessel occlusion stroke’.

However, given the importance of recent clinical trials in two specific populations with relatively common and devastating strokes, we summarize some of the new trial data and provide updated recommendations for treatment in a timely manner.

ANTERIOR CIRCULATION STROKES WITH LARGE ISCHEMIC CORE
Thrombectomy has been the standard of care for patients with anterior circulation ELVO and small to medium-sized ischemic cores (ASPECTS [Alberta Stroke Program Early CT Score] scores 6–10 and core volumes <70 mL). However, recent trials, SELECT2, ANGEL-ASPECT, RESCUE-Japan LIMIT, and TESLA have challenged this previous limitation and demonstrated benefit to thrombectomy of the intracranial internal carotid artery (ICA) and M1 middle cerebral artery (MCA) in patients with larger baseline ischemic cores.

The Recovery by Endovascular Salvage for Cerebral Ultra-acute Embolism Japan Large Ischemic Core Trial (RESCUE-Japan LIMIT), a multicenter, open-label, randomized clinical trial in Japan, enrolled 203 patients with either CT or MR ASPECTS between 3 and 5, although MRI was primarily used for triage. The percentage of patients achieving a modified Rankin scale (mRS) score of 0 to 2 at 90 days was 14.0% in the EVT group versus 7.8% in the standard medical management group. The ordinal shift across the range of mRS scores favored endovascular therapy. Furthermore, the incidence of symptomatic intracranial hemorrhage (sICH) was not significantly higher with EVT than with standard medical care.

The Randomized Controlled Trial to Optimize Patient’s Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT2) trial enrolled 352 patients with large core strokes defined as ASPECTS 3–5 or CT perfusion-derived core volume >50 mL. The patients were enrolled from the United States, Canada, Europe, Australia, and New Zealand to undergo EVT and receive standard medical care or to receive standard medical care alone within 24 hours since last known to be well. An interim analysis by the data and safety monitoring board recommended the cessation of recruitment. EVT was associated with a 90-day mRS 0–2 of 20% in the EVT group versus 7% in the standard medical management group. Rates of sICH were similar between the groups. Furthermore, EVT reduced by 50% the number of mRS 5 patients.

The Endovascular Therapy in Acute Anterior Circulation Large Vessel Occlusive Patients with a Large Infarct Core (ANGEL-ASPECT) trial randomized 456 patients in China with ELVO ischemic stroke patients and large core strokes defined as ASPECTS 3–5 but also core volume of 70–100 mL, presenting within 24 hours since last known to be well. A planned interim analysis resulted in early termination on account of the 90-day mRS 0–2 of 30% in the EVT group versus 11.6% in the standard medical management group. Like SELECT2, EVT reduced by 50% the number of mRS 5 patients.

The Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke (TESLA) Trial was presented in May 2023 at the European Stroke Organisation Conference. While TESLA did not meet its primary intention-to-treat analysis of EVT superiority over medical treatment (90-day utility-weighted mRS), multiple secondary efficacy endpoints did favor EVT and its results were broadly in the direction of benefit for thrombectomy. Specifically, EVT was associated with 90-day mRS 0–3 in 30% of patients compared with 20% of medically managed patients (p=0.03, OR 1.6). Similarly, major neurological improvement was 26% in the EVT group and 13% in the medical management group (p=0.0008). EVT treatment effect was smaller in TESLA (9.9%) as compared with RESCUE-Japan LIMIT (18.3%), ANGEL-ASPECT (13.7%), and SELECT2 (19.2%).

Also presented at the 2023 European Stroke Organisation Conference was a patient-level data meta-analysis of over 1000 patients from SELECT2, ANGEL-ASPECT, and RESCUE-Japan LIMIT. MAGNA (Mechanical thrombectomy for large brain infarctions) demonstrated meaningful improvement in mRS shifts (with good outcome defined as either mRS 0–2 or mRS 0–3) for patients with ASPECTS 3, ASPECTS 4, and ASPECTS 5 who underwent EVT. This positive result was also evident for patients with ischemic cores of <70 mL (OR 1.97, 95% CI 1.27 to 3.05), 70–99 mL (OR 1.77, 95% CI 1.30 to 2.39), and 100–149 mL (OR 1.94, 95% CI 1.49 to 2.51). Only in the cohort of patients with ischemic cores of 150 mL or greater did EVT not demonstrate statistically significant benefit (OR 1.2, 95% CI 0.83 to 1.73).

Despite differences in design, methodology, and inclusion/exclusion criteria, all three published trials (SELECT2, ANGEL-ASPECT, RESCUE-Japan LIMIT) demonstrated benefits of EVT on mortality, severe morbidity (reducing the proportion of patients who survive with mRS 5 disability), as well as more traditional good functional outcomes (mRS 0–2). The results of these studies and the more recently reported but not yet published TESLA trial and MAGNA meta-analysis support the use of EVT for ELVO patients.
compared with standard medical management, thus warranting re-examination of our treatment guidelines.12

Updated recommendation
► In patients with anterior circulation ELVO who present within 24 hours after symptoms onset to EVT versus medical therapy. Of note, although the trial was originally designed to have a good outcome designated as mRS 0–4, this was changed to mRS 0–3 after the trial was underway. After 110 patients received thrombectomy and 107 received medical therapy, the trial was stopped early at an interval analysis due to superiority of thrombectomy. Good outcomes were achieved in 46% of thrombectomy patients versus 23% of medical therapy patients (adjusted relative risk [ARR] 1.81, 95% CI 1.26 to 2.60, p<0.001). Similar to BAOCHE, in ATTENTION the sICH rate was low overall but non-significantly higher in the EVT group (5%) compared with the medical group (0%). Mortality at 90 days was lower in the EVT arm (37%) than in the medical arm (53%, ARR 0.66, 95% CI 0.52 to 0.82). Of note, 14% of EVT cases were noted to have a procedural complication, including one death due to arterial perforation.

POSTERIOR CIRCULATION STROKES
Similar to the transition from IMS-III to the post-MR CLEAN era, new data in basilar artery occlusion strokes provide encouraging results regarding improved clinical outcomes. Although the randomized BEST (Basilar Artery Occlusion Endovascular Intervention versus Standard Medical Treatment) and BASICS (Basilar Artery International Cooperating Study) trials did not show a definite benefit of EVT over medical therapy, the newly published BAOCHE (Basilar Artery Occlusion Chinese Endovascular Trial)10 and ATTENTION (Endovascular Treatment for Acute Basilar Artery Occlusion)11 studies suggest that EVT within 12–24 hours of ictus is superior to medical therapy. BAOCHE randomized patients with basilar artery stroke presenting within 6 to 24 hours after symptoms onset to EVT versus medical therapy. Of note, although the trial was originally designed to have a good outcome designated as mRS 0–4, this was changed to mRS 0–3 after the trial was underway. After 110 patients received thrombectomy and 107 received medical therapy, the trial was stopped early at an interval analysis due to superiority of thrombectomy. Good outcomes were achieved in 46% of thrombectomy patients versus 23% of medical therapy patients (adjusted relative risk [ARR] 1.81, 95% CI 1.26 to 2.60, p<0.001) and sICH was uncommon but non-significantly higher in the thrombectomy group (6% vs 1%, RR 5.18, 95% CI 0.46 to 42.18). Mortality at 90 days was non-significantly lower in the thrombectomy group also (31% vs 42%, RR 0.75, 95% CI 0.54 to 1.04).

ATTENTION randomized basilar artery occlusion stroke patients within 12 hours of onset in a 2:1 manner to EVT versus best medical therapy. In total, 226 patients were assigned to the EVT arm and 114 to the medical therapy arm.11 Good functional outcome defined as mRS 0–3 at 90 days was achieved in 46% of the EVT group versus 23% in the medical therapy group (ARR 2.06, 95% CI 1.46 to 2.91, p<0.001). Similar to BAOCHE, in ATTENTION the sICH rate was low overall but non-significantly higher in the EVT group (5%) compared with the medical group (0%). Mortality at 90 days was lower in the EVT arm (37%) than in the medical arm (53%, ARR 0.66, 95% CI 0.52 to 0.82). Of note, 14% of EVT cases were noted to have a procedural complication, including one death due to arterial perforation.

Updated recommendation
► In patients with acute basilar artery occlusion who would meet criteria for BAOCHE or ATTENTION, thrombectomy is indicated (Class I, Level B-R).
► It is reasonable to consider thrombectomy for selected patients with basilar artery occlusion who do not strictly meet criteria for BAOCHE or ATTENTION (Class IIIb, Level C).

In summary, we now have multiple randomized trials showing a benefit to thrombectomy in populations where previously there was a paucity of data. These results justify changes in local patient selection criteria for thrombectomy. Hub and spoke hospital systems should consider incorporating these results in determining which patients are appropriate for transfer to a center capable of performing thrombectomy.

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