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COMMENTARY STROKE/NEUROINTERVENTIONS

Recent Evidence of Large-Core Thrombectomy in Acute Ischemic Stroke—Certainties and Uncertainties

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Introduction

Manuscript of Commentary

Endovascular thrombectomy (EVT) has become the standard of care for ischemic stroke caused by large-vessel occlusion (LVO). Depending on the timing of presentation, stroke severity and perfusion imaging, current guideline recommends EVT for patients presenting within (1) a 6-h window with an Alberta Stroke Program Early Computed Tomography (ASPECT) score of ≥ 6 or (2) a 6-to-24-h window with clinical-core or core–penumbra mismatch [1]. Nonetheless, the most devastating form of ischemic stroke with large infarct cores was underrepresented in the pivotal clinical trials that set current guideline recommendations. Fortunately, emerging clinical evidence has shed light on large-core stroke thrombectomy and at the same time requires judicious interpretation and implementation in clinical practice.

Three recent randomized control trials (RCT) investigated the efficacy and safety of EVT in LVO strokes with large infarct core: The RESCUE-Japan LIMIT showed benefits of EVT in Japanese patients with LVO who had an MRI-ASPECT 3–5 within a 6-h window, or MRI-ASPECT 3–5 with no FLAIR signal changes in a 6-to-24-h window. EVT achieved a higher rate of modified Rankin scale (mRS) of 0–3 (31% vs 12.7%) compared to best medical treatment [2]. ASPECT-ANGEL showed that among Chinese patients with a CT-ASPECT 3–5, or CT-ASPECT 0–2 with an infarct core 70-100 mL, EVT achieved a shift of mRS toward better outcome. Patients received EVT had a higher rate of mRS 0–3 compared to medical management (47% vs. 33.3%) [3]. SELECT-2 showed EVT was beneficial in a cohort with large infarct core that consisted of predominately the black and white race. Patients who received EVT had a shift of mRS toward better outcome. Rate of mRS 0–2 was higher compared to medical management (20% vs 7%) [4]. RESCUE-Japan LIMIT and ANGEL-ASPECT reported higher risks of intracerebral hemorrhage in the EVT group.

The three RCTs above conferred a clear message that EVT benefited many patients outside the current EVT selection criteria across different ethnicities. Despite the differences among these trials, the inclusion criteria were generally an ASPECT 3–5 or infarct core of < 100 mL within a 24-h window. In fact, the median infarct core volumes of the ANGEL-ASPECT and SELECT-2 cohorts were $\sim$ 60 mL and $\sim$ 80 mL, respectively, which were

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remarkably larger than that of the DAWN and DEFUSE3 trials (7-10 mL). Nonetheless, patients presented 12–24 h after symptom onset were underrepresented in these new trials as the median onset-to-randomization time was 3–9 h, with vast majority of the participants presented < 12 h. Furthermore, a secondary analysis of RESCUE-Japan LIMIT suggested that EVT for LVO with MRI-ASPECT ≤ 3 may not improve functional outcome [5]. Therefore, while it is evident that patients with large infarct cores benefited from EVT within a 12-h window, further efforts should be made on evaluating the effect of EVT in patients with late presentation, and those with an ASPECT score of ≤ 3 on CT. Other important areas to look into include the effects of LVO etiology, imaging modality, eloquent brain regions and neuroprotective agents on the effectiveness of large-core thrombectomy.

In terms of cost-effectiveness, the trials demonstrated 35–50% reduction in severe disability (mRS 4–5), which incurs the highest cost in post-stroke care. Future studies should elucidate the cost-effectiveness of large-core thrombectomy in different income regions, considering the cost of thrombectomy, advanced imaging, neurosurgical input and socioeconomic burden that severe disability brings about.

The additional large-core thrombectomy trials (NCT03805309, NCT03094715, and NCT03811769) may hopefully answer some of the above uncertainties. Meanwhile, the robust data of large-core thrombectomy prompt the need for guideline revision, with unifying criteria that are easily interpretable by disciplines involved in hyperacute stroke care. On the other hand, more resource should be allocated on diversion, triage and periprocedural care due to the expanding EVT indications.

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Declarations

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