Large vessel occlusion stroke contributes to disability and mortality out of proportion to its incidence. Over time it was noted that intravenous thrombolysis alone was not sufficient for this stroke type. Slowly, endovascular approach and mechanical clot retrieval have come out to be the biggest advances in the field of neurology as well as modern medicine. Although the careful selection of patients is needed as standardized by landmark trials. At the same time, thrombectomy is now being studied in patients excluded by previous trials and is seemingly coming out to be effective in the vast majority of patients with large vessel occlusions. Further, techniques and devices are getting refined day by day to achieve the maximum possible benefit.

Keywords: Ischemic stroke, mechanical thrombolysis, thrombectomy, thrombolytic therapy

INTRODUCTION

Although intravenous thrombolysis (IVT) revolutionized the treatment and became the standard of care in ischemic stroke, there are several drawbacks. First, there is a relatively small time window within which treatment has to be initiated. Second, stroke due to large vessel occlusion (LVO) portends a poor prognosis, and recanalization rates even with IVT are poorer in these patients.[1,2] In one natural history study from Italy, 75% of patients with stroke due to ICA occlusion were either dead or dependent at a mean follow-up of 1.2 years.[3] A systematic review including two different multicenter studies from the US and Europe reported LVO to account for 38.7% of all ischemic strokes, still accounting for 61.6% of post-stroke death and 95.6% of mortality.[4] A large study including five high volume centers from India reported arterial occlusion or >50% stenosis in 42.7% of patients.[5] A study using transcranial doppler showed recanalization rates after intravenous thrombolysis in the terminal internal carotid artery and proximal middle cerebral artery to be 6% and 30% respectively.[6] Similarly, G J del Zoppo et al.[6] had found angiographic recanalization rates in ICA, M1 MCA, M2 MCA, and M3 MCA occlusions after intravenous duteplase to be 8.7%, 35.3%, 53.8%, and 65.9%, respectively.

It was recognized for a long time that IVT alone was not sufficient and more effective therapy is needed for ischemic stroke types which are more devastating than lacunar strokes. PROACT-II, published in 1999, was one of the earliest randomized trials favoring the endovascular treatment approach, where 180 patients with stroke due to MCA occlusion were randomized to receive intra-arterial recombinant prourokinase (r-pro-UK) plus IV heparin or IV heparin alone within 6 hours of onset. Favorable outcome i.e., Modified Rankin scale of ≤2 at 90 days was achieved in 40% patients in the intervention arm and 25% patients in the control arm (p = 0.04).[7] However, the second trial with r-pro-UK did not complete and thence it did not receive FDA approval.[8] Intra-arterial thrombolysis with various fibrinolytic agents compared to IVT showed favorable results but it was never tested in larger randomized trials.[9]

Eventually, mechanical devices took over the fibrinolytic drugs because of concerns of intracranial hemorrhage. MERCI and later PENUMBRA system were approved by FDA for clot removal in ischemic stroke nearly 15 years ago, but recanalization rates were poor.

Intracranial stent placement was thought to provide high recanalization rates but at the same time concerns regarding the use of antiplatelet agents, hemorrhage, and occurrence of in-stent stenosis were also there.[10] In 2008, Kelly et al.[11] reported successful recanalization of MCA occlusion by partially deployed Enterprise stent leading to temporary endovascular bypass and then retrieval of the stent along with clot. Successful use of stent retrievers for large vessel occlusion stroke from India also dates back to 2010 by Huded et al.[12] Although, subsequent randomized trials comparing endovascular treatment to IVT alone (IMS-3, SYNTHESIS, and MR RESCUE) were negative and had one or the other of the following drawbacks- case selection without vessel imaging, poor workflows, longer stroke onset to reperfusion time.
times, the predominant use of first-generation devices (MERCI or Penumbra) or poor recanalization rates.\textsuperscript{[13,15]} Though these trials were discouraging, they paved the way forward for upcoming positive trials with second-generation devices. It was understood that patients with severe strokes due to large vessel occlusions who do not have large established infarcts can be benefited to great extent by an immediate and better degree of recanalization.\textsuperscript{[16]}

**EVIDENCE FOR THROMBECTOMY**

The current practice of thrombectomy in ischemic stroke is largely based on randomized trials published in and after 2015. All of the trials emphasized intervention by experienced interventionists, faster workflow, and better successful recanalization rates. Inclusion criteria of individual early window trials are summarized in Table 1. Overall, early window trials included adult patients with independent baseline functional state presenting in the early window (mostly <6 hours) after last seen normal and clinically measurable deficits (most were moderate to severe strokes), favorable infarct cores, and large vessel occlusion as confirmed on CT (or MR) angiography. Extended window trials additionally required either clinical-radiological or core-perfusion mismatch to identify patients with salvageable brain tissue. Detailed exclusion criteria of all trials are provided in the supplementary material. Largely, patients with any evidence of intracranial hemorrhage, large infarct cores (defined as either ASPECTS <6 or involvement of >½ territory of a middle cerebral artery), severe hypertension even after medications, severe hypo/hyperglycemia, coagulopathy (defined variably in different trials), pregnancy, limited life expectancy, intracranial tumors (other than small meningioma), suspected septic emboli were excluded. Notably, some of the trials also excluded patients with cervical dissection or proximal cervical occlusions where acute cervical stent might be required. Patients in whom thrombectomy could be initiated within 6 or 5 hours of onset, were included irrespective of infarct volume in MR CLEAN or THRACE trials, respectively.\textsuperscript{[17,18]} In general, criteria were more inclusive compared to those for IVT. Relevant baseline and procedure characteristics are mentioned in Table 2.

Important outcomes are summarized in Figure 1. After the publication of the first and the largest trial MR CLEAN showing the benefit of thrombectomy, other trials (ESCAPE, REVASCAT, SWIFT PRIME, EXTEND 1A, EASI) were stopped prematurely given the ethical concerns.\textsuperscript{[18-22]} All of the trials including patients from vast geographic distribution independently showed significant benefit of mechanical thrombectomy in selected patients. Furthermore, an individual patient-level meta-analysis involving five major early window thrombectomy trials by HERMES collaboration confirmed the benefit of thrombectomy for wide strata of patients.\textsuperscript{[24]} It was shown that patients can be benefited irrespective of age, sex, baseline NIHSS, time from onset (within 7 hours of time window), IVT eligibility, or presence of tandem occlusion. Although, the benefit did not reach statistical significance in patients with young age (<50 years), ASPECTS 0-5, NIHSS ≤10, and M2 occlusions, it tended to favor thrombectomy. The number needed to treat to make one more patient achieve functional independece at 3 months is 10 for thrombolysis in the early time window (<3 hours), while it is 2.6 for thrombectomy as per HERMES.\textsuperscript{[25]} Absolute risk reduction was higher in late window trials (DAWN, DEFUSE 3) compared to most of the early window trials (the late window paradox) and it is likely because of the selection of slow progressors in late window trials while the fast progressors were not excluded in early window trials.

**THROMBECTOMY FOR POSTERIOR CIRCULATION STROKES**

Heterogeneity in symptoms and their onset often leads to relatively later detection of posterior circulation strokes.\textsuperscript{[26]} In all positive landmark thrombectomy trials, except THRACE, posterior circulation strokes were excluded. Although routinely practised in many centers, thrombectomy for vertebro-basilar-PCA occlusions is currently not backed by evidence as in anterior circulation strokes.

The BEST trial included 131 patients (target was 344) within 8 hours of basilar artery occlusion and randomized them to endovascular arm and medical management alone. The primary outcome at 90 days (mRS score ≤3) was achieved by 42% of patients in the endovascular arm and 32% of patients in the control arm (adjusted odds ratio 1.74, 95% confidence interval 0.8-3.7). Symptomatic hemorrhage was higher in the endovascular arm (8% vs 0) and there was no significant difference in mortality at 90 days. Although in the per-protocol analysis, favorable outcome was higher in the endovascular arm (44% vs 25%, adjusted odds ratio 2.9, 95% confidence interval 1.2-7.03).\textsuperscript{[27]} The BASICS trial had randomized 300 patients within 6 hours of basilar artery occlusion to endovascular therapy or medical management alone. The primary outcome at 90 days (mRS score ≤3) was achieved by 44.2% of patients in the endovascular arm and 37.7% in the medical management arm (common odds ratio- 1.18, 95% confidence interval 0.91-1.5).\textsuperscript{[28]} There was no significant difference in mortality at 90 days. These trials are criticized for their slow recruitment, a significant proportion of patients having the unknown time of onset (almost 1/3rd patients in BASICS), the inclusion of patients with significantly higher baseline stroke severity, very low rates of intravenous thrombolysis (in BEST), and poor adherence to treatment allocation. These factors could have led to results that are negative with wide confidence intervals. Basilar Artery Occlusion Chinese Endovascular Trial is further assessing the usefulness of thrombectomy in patients with basilar artery occlusion up to 24 hours after onset.

While the benefit of thrombectomy is not excluded by randomized trials, many observational studies have suggested benefit. A systematic review and meta-analysis including observational studies (with a total of 1172 posterior circulation...
large vessel occlusion and 7726 anterior circulation large vessel occlusion strokes) comparing thrombectomy in posterior versus anterior circulation concluded that thrombectomy can be equally efficient in achieving successful recanalization and favorable outcome in posterior circulation strokes.[29]

Another meta-analysis including 474 patients with posterior circulation occlusion and 3505 patients with anterior circulation occlusion showed that functional independency at 90 days was achieved by 34.8% of patients with posterior circulation occlusions (albeit lower than anterior circulation). Symptomatic hemorrhage was significantly lower in patients with posterior circulation occlusions undergoing thrombectomy (2.23% vs 5.53%).[30] A large prospective nonrandomized cohort study including 829 patients within 24 hours of the onset of basilar artery occlusion showed that functional outcomes at 3 months were significantly improved (mRS score ≤3, 32% vs 9.3%, P < 0.001), and mortality at 3 months was lower (46.2% vs 71.4%, P < 0.001) even when symptomatic ICH was higher (7.1% vs 0.5%, P < 0.001) in patients undergoing thrombectomy compared to patients receiving medical management alone. These findings did not differ after propensity score matching.[31]

One retrospective study including 81 patients with acute basilar artery occlusion showed that factors like lower baseline NIHSS, distal basilar occlusion, better posterior circulation collateral status were significantly associated with better functional outcomes at 3 months. Interestingly, the time from onset to recanalization (even >12 hours) did not show statistical significance in predicting good outcome. Authors concluded that time from onset should not be an absolute criterion for thrombectomy in patients with acute basilar artery occlusion.[32]

An institutional retrospective study including 89 patients with stroke due to vertebro-basilar occlusion showed a favorable outcome (mRS ≤2) at 90 days in 40% of patients and all-cause mortality of 36%. Patients with NIHSS >10, treated within 24 hours of onset, having infarcts not involving bilateral thalami, or more than half of pons/midbrain were more likely to get benefited from endovascular treatment.[33] In one retrospective study from Korea including 82 patients with basilar occlusion who underwent thrombectomy, embolism without vertebral steno-occlusion, embolism with tandem vertebral steno-occlusion and in-situ atherothrombosis accounted for 41%, 34%, and 24% of patients, respectively. Embolism without large artery atherosclerosis was associated with the distal location of the basilar occlusion, shorter procedure times, better successful recanalization rates, and better functional outcomes at 3 months.[34] A prospective study comparing aspiration with stent retriever in basilar artery occlusion showed that a direct aspiration first pass (ADAPT) was associated with higher complete recanalization rates, shorter procedure time, and better clinical outcomes.[35] The TOPMOST study compared mechanical thrombectomy with standard medical management in 186 matched patients with primary posterior cerebral artery occlusion and found that it was safe, feasible, and had significant treatment effects particularly in patients with high baseline NIHSS.[36]

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**Table 1: Inclusion criteria of randomized trials**

| Trial      | Age | Symptom duration | Imaging                     | Occlusion                  | Trait                       | Baseline functional status | mRS score ≤1 | Pre-stroke mRS ≤1 |
|------------|-----|------------------|----------------------------|----------------------------|-----------------------------|----------------------------|---------------|------------------|
| MR CLEAN   | ≥18 | <6 hours         | CTA, MRA, DSA              | MR CLEAN                   | CTA, MRA, DSA              | Pre-stroke mRS ≤1          | Pre-stroke mRS ≤1 |
| ESCAPE     | ≥18 | <6 hours         | CTA, MRA, DSA              | MR CLEAN                   | CTA, MRA, DSA              | Pre-stroke mRS ≤1          | Pre-stroke mRS ≤1 |
| SWIFT PRIME| ≥18 | <6 hours         | CTA, MRA, DSA, RAPID       | MR CLEAN                   | CTA, MRA, DSA              | Pre-stroke mRS ≤1          | Pre-stroke mRS ≤1 |
| PISTE      | ≥18 | <6 hours         | CTA, MRA, DSA              | MR CLEAN                   | CTA, MRA, DSA              | Pre-stroke mRS ≤1          | Pre-stroke mRS ≤1 |
| DAWN       | ≥18 | <6 hours         | CTA, MRA, DSA              | MR CLEAN                   | CTA, MRA, DSA              | Pre-stroke mRS ≤1          | Pre-stroke mRS ≤1 |
| EXTEND IA  | ≥18 | <6 hours         | CTA, MRA, DSA              | MR CLEAN                   | CTA, MRA, DSA              | Pre-stroke mRS ≤1          | Pre-stroke mRS ≤1 |

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Table 2: Baseline and procedure characteristics of randomized trials

| MR CLEAN | ESCAPE | REVASCAT | SWIFT PRIME | EXTEND IA | THRACE | PISTE | EASI | DAWN | DEFUSE 3 |
|----------|--------|----------|-------------|-----------|--------|-------|------|------|----------|
| Total patients (%male) | 500 (58.4%) | 315 (47.1%) | 206 (52.9%) | 196 (51%) | 70 (48.6%) | 412 (53.4%) | 65 (44.6%) | 77 (49.4%) | 206 (45.1%) | 182 (50.5%) |
| Medical management | 267 (58.8%) | 150 (47.3%) | 103 (52.4%) | 98 (47%) | 35 (48.6%) | 208 (50%) | 32 (50%) | 20 (54.1%) | 99 (51.5%) | 90 (49.9%) |
| Intervention | 233 (57.9%) | 165 (47.9%) | 103 (53.4%) | 98 (55%) | 35 (48.6%) | 204 (57%) | 33 (39%) | 18 (45%) | 107 (39.2%) | 92 (50%) |
| Age (years) | | | | | | | | | | |
| Medical management | 65.7* | 67.2* | 66.3* | 70.2* | 68* | 64* | 71* | 70.7* | 71* |
| Intervention | 65.8* | 65.7* | 65* | 68.6* | 66* | 67 | 74* | 69.4* | 70* |
| NIHSS at baseline (median) | 18 | 17 | 17 | 13 | 17 | 14 | 20 | 17 | 16 |
| Medical management | 18 | 17 | 17 | 13 | 17 | 14 | 20 | 17 | 16 |
| Intervention | 17 | 16 | 17 | 17 | 18 | 18 | 18 | 17 | 16 |
| ASPECTS/Infarct core (median/mean) | | | | | | | | | |
| Medical management | 9 | 9 | 8 | 9 | 19.6 | 83% | 9 | 8 | 7.6 ml |
| Intervention | 17 | 17 | 17 | 17 | 18 | 18 | 18 | 17 | 16 |
| Occlusion (% of intervention arm) | | | | | | | | | |
| Intracranial ICA±M1 | 25.7% | 27.6% | 25.5% | 18% | 31% | 12% | 14% | 15% | 20.5% | 34.8% |
| M1 | 66.1% | 68.1% | 64.7% | 67% | 57% | 86% | 76% | 42.5% | 77.6% | 65.2% |
| M2 | 7.7% | 3.7% | 9.8% | 14% | 11% | - | 10% | 13% | - | - |
| A1 or A2 | 0.4% | - | - | - | - | - | - | - | - |
| Basilar | - | - | - | - | 1% | - | 12.5% | - | - |
| IVT | 90.6% | 78.7% | 68% | 95.9% | 100% | 100% | 100% | 62.2% | 13.1% | 8.9% |
| Medical management | 90.6% | 78.7% | 68% | 95.9% | 100% | 100% | 100% | 62.2% | 13.1% | 8.9% |
| Intervention | 87.1% | 72.7% | 77.7% | 100% | 100% | 100% | 100% | 57.5% | 4.7% | 10.9% |
| Onset to groin access (minutes- median) | 260 | 269 | 224 | 210 | 250 | 245 | 11.5 hours |
| Onset to CT | 134, CT to randomization to groin access 51 |
| Onset to randomization 150, randomization to groin access 58 |
| Onset to randomization 12.2 hours, randomization to groin access 16 min |
| Intervention arm | | | | | | | | | |
| Device/technique used | | | | | | | | | |
| Retrievable stents | 81.5% | 86.1% | 93% | 88.8% | 80% | 83% | 68% | 96.7% | 97.4% | 80.4% |
| Others | 2.5% | - | 1.9% | 1% | - | 16%,13% | 32%,19% | 3.3% | 2.8% | 5.4%,27.2% |
| Acute cervical stent | 12.9% | - | 8.7% | 1% | 8.6% | - | - | 13% | - | 13% |
| No intervention | 15.9% | 8.4% | 4.8% | 11.2% | 17.1% | 29% | 3.1% | 25% | 1.9% | 2.1% |
| General anesthesia in the intervention arm | 37.8% | 9.1% | 6.7% | 37% | 33% | 49% | 31% | 6.7% | 10.2% | 28% |

*median; †mean; ‡MERCI, wire disruption, thromboaspiration, intraarterial fibrinolytic, intracranial stenting; ‡‡Aspiration devices; ‡‡‡more than one device/fibrinolytic used
Large core

Irrespective of the time window they present in, patients with large established infarcts were excluded in most of the trials evaluating benefits of thrombectomy as well as IVT in ischemic stroke. Indeed, recanalization in these patients is not expected to lead to as favorable outcomes as in highly selected patients. Simultaneously, the risk of reperfusion injury and hemorrhage leading to further deteriorations might be more in these patients. Though, it is imperative to identify patients (e.g. young, fast progressors) who might get some benefit from highly effective therapies available currently. In an analysis from the STRATIS registry, including 57 patients with ASPECTS of 0-5, functional independence at 3 months was achieved by 28.8% of patients. Symptomatic hemorrhage (7%), as well as mortality (30.8%), was higher compared to patients with ASPECTS 6-10. Though no patients aged >75 years achieved functional independence, 44.8% of patients with age ≤65 years were functionally independent at 3 months.[37] Meyer et al.[38] included 228 patients from the German stroke registry, with stroke due to large vessel occlusion and CT ASPECTS of 0-5. They compared patients after propensity score matching, who had undergone thrombectomy to patients receiving the best medical management alone. A favorable outcome at 90 days (mRS 0-3) was achieved in 27.4% in the thrombectomy group and 25% of patients in the medical management group. Symptomatic ICH and mortality were significantly higher in the thrombectomy group. However, in patients in whom mTICI 3 recanalization was achieved with ≤2 passes, symptomatic hemorrhage as well as mortality were lesser and there was a trend towards the favorable outcome (mRS 0-3 in 42.3%, P = 0.052). The SELECT study included 361 patients with ischemic stroke due to large vessel occlusion to assess concordance/discordance of CT and CT perfusion and their effect on decision making regarding EVT as well as clinical outcome. In patients with discordant profiles on CT and CTP (e.g. one modality showing the favorable core, while other showing unfavorable) also, functional independence was achieved by 38% of patients.[39] Upcoming randomized trials are evaluating the effect of thrombectomy in populations with large infarct cores. (SELECT 2, TESLA, TENSION, LASTE)

Low NIHSS

In a study by Mazya et al.,[40] nearly 25% of patients with low NIHSS (0-5) had large vessel occlusion and non-hemorrhagic early neurologic deterioration (defined as worsening of NIHSS >3) occurred in 30% of patients with ICA occlusions; among patients with early deteriorations, 77% were dead or dependent at 3 months. Similarly, Mokin et al.[41] included 204 patients with NIHSS <8 and large vessel occlusions, out of these 38% were dead or dependent at discharge. In a study by Saleem et al.[42] one-fifth of patients with large vessel occlusion and NIHSS <6 on admission had early neurologic deterioration with a median time of 3.6 hours after the arrival. Elevated blood pressure on admission, positive head-up test, patients presenting early in the time window, and large perfusion deficit are factors hypothesized to portend a poor prognosis and to take into account while decision making for EVT.[43] A recent multicentric cohort study including 729 patients with minor stroke and LVO (basilar, ICA, M1/M2 MCA) showed early deterioration in 12.1% and was strongly associated with poorer outcomes; proximal occlusion and longer thrombus

Figure 1: Important outcomes of randomized trials; Successful recanalization defined as modified TICI 2b or 3 (ESCAPE*- TICI2b or 3), Symptomatic hemorrhage definition used- † ECASS 2, ‡ ECASS, § SITS MOST, || ECASS 3 (not specified in EASI)
were independently associated with early deterioration.\textsuperscript{[44]} In a multicenter matched analysis, immediate thrombectomy was associated with favorable outcomes compared to rescue thrombectomy after deterioration.\textsuperscript{[45]} Meta-analysis of observational studies has shown equivocal conclusions and randomized trials are needed to answer the question.\textsuperscript{[46]} ENDOLOW and MOSTE are ongoing randomized trials aiming to assess the efficacy of thrombectomy in mild strokes.

**Distal/medium vessel occlusions**

Most of the patients included in landmark trials had occlusions of the M1 segment of the MCA. The M1 segment of MCA is considered to extend from origin to its division. The M2 segment extends from division to the origin of cortical branches. However, the definition, as well as anatomy in each patient, varies significantly. In some patients, M2 division can be as big as M1 and can be supplying a significant part of the hemisphere. Similarly, other medium vessel (lumen diameters between 0.75 to 2 mm- M3, M4, A1-A5, P1-P5, PICA, AICA, and SCA) occlusions can lead to significant morbidity or mortality.\textsuperscript{[47]} This can be due to the strategic location of infarcts as well e.g., Wallenberg syndrome. Distal vessel occlusions can occur spontaneously or can complicate the mechanical thrombectomy for large vessel occlusions. Although recanalization rates with IVT are better in distal vessel occlusions, a significant proportion of patients might not get benefited or cannot be offered IVT at all due to small time windows. A study including 258 patients with medium vessel occlusions (M2/3, A2/3, P2/3) from two stroke registries showed that 32.8% of patients could not achieve functional independence despite the best medical management.\textsuperscript{[48]} Currently, randomized evidence for benefit of thrombectomy in medium vessel occlusions is limited to M2 MCA occlusions. In a meta-analysis of data from HERMES collaboration, 130 patients with M2 occlusions were included. Intravenous thrombolysis was administered in 85.1% of patients in the thrombectomy group and 89.1% of patients in the medical management group. Functional independence was achieved by 58.2% of patients in the thrombectomy group and 39.7% in the medical management group. Notably, no patients in the thrombectomy group had symptomatic ICH, while 7.9% in the medical management group had symptomatic ICH.\textsuperscript{[49]} Evidence for thrombectomies in other vessel occlusions is limited but intriguing. The DISCOUNT trial is randomizing patients with distal vessel occlusions (M2/3, A1/2/3, and P1/2/3) to mechanical thrombectomy and medical management arms.

**Pediatric age group**

Although all landmark trials excluded patients less than 18 years of age, mechanical thrombectomy in this age group also appears safe when the cause is either cardioembolic or dissection rather than underlying pathology of cerebral vessels as reported by Bhatti et al.\textsuperscript{[50]}

**Pregnancy**

Although, arterial strokes are less frequent in this subset of patients, large vessel occlusion can have devastating outcomes. Pregnant or lactating patients were excluded in many of the landmark trials in view of concerns of radiation exposure to fetus. A study by Tse et al.\textsuperscript{[51]} assessing radiation exposure to the fetus during mechanical thrombectomy showed that the estimated dose received by fetus following CT brain and mechanical thrombectomy in three pregnant patients was $0.024 \pm 0.018 \ \mu \text{Gy}$ (which was less than diagnostic imaging in trauma cases); patients had excellent neurological outcomes and babies were well at follow up. A large, national in-patient sample from the US during the period of 2012-2018 yielded 180 pregnant/postpartum patients who had undergone thrombectomy; it was shown that 50% of these patients had good functional outcomes at discharge. Although, it was lower compared to non-pregnant patients. At the same time, rates of intracranial hemorrhage were lower and rates of DVT/thromboembolic or pregnancy-related complications were higher in patients undergoing thrombectomy compared to medical management alone. The authors concluded that thrombectomy is a safe and viable option in stroke during pregnancy/postpartum.\textsuperscript{[52]}

**Tandem occlusions**

Occlusion of both extracranial carotid and intracranial large vessel carries a poor prognosis. These patients were excluded in many of the landmark trials. A significant number of patients in other trials were having tandem occlusions and were treated by acute proximal cervical stenting. Although thrombectomy and intracranial recanalization have a proven role, a standardized approach is lacking. Which lesion to treat first and whether to do acute cervical stenting or not, are the questions that remain to be answered. Recently, a pooled analysis of two stroke registries (TITAN and ETIS) including 603 patients with tandem occlusions has shown that patients undergoing stenting had higher odds of successful recanalization and favorable outcome while symptomatic ICH was similar compared to patients receiving angioplasty alone.\textsuperscript{[53]} This benefit was more pronounced in patients with low baseline NIHSS and atherosclerotic occlusion as opposed to dissection. This is likely because of the high bleeding risk in patients with large strokes and better natural history of dissection compared to atherosclerosis, respectively. Another meta-analysis did not find any significant difference between angioplasty alone or stenting group as well as no significant difference with regard to the order of the treatment.\textsuperscript{[54]} EASI-TOC and TITAN are upcoming randomized trials addressing this question.

**Beyond the “window”**

Some patients with large vessel occlusion and good collaterals can have a very protracted course of infarct progression over several days if the arteries are not recanalized. A post-hoc analysis of the DEFUSE-3 trial had found that patients in the medical management arm had similar infarct volumes but persistent penumbral tissue beyond 24 hours while the majority of patients in the endovascular arm did not have penumbra as their vessels were recanalized. Patients in the endovascular arm not having a penumbral profile had significantly higher odds of functional independence.\textsuperscript{[55]} Further trials are needed to
identify patients who might be benefited from thrombectomy beyond 24 hours

**Procedural Variables**

**Successful recanalization**

Given the high-quality data emphasizing the faster and better recanalizations to be associated with better outcomes, better techniques to achieve this are strived for. The “first-pass effect”, defined as complete recanalization with a single thrombectomy pass, has been shown to be an independent predictor of good clinical outcome. The definition of ‘successful’ recanalization is also being reconsidered. Most of the landmark thrombectomy trials used an mTICI score of 2b or greater (>50% reperfusion of affected arterial territory) to be ‘successful’ recanalization. However, it has been shown that clinical outcomes between mTICI 2b and 3 vary significantly. Hence, the expanded TICI grading scale incorporating 7 points is proposed by the HERMES group where a score of 2b67 or higher is considered successful reperfusion (0- no reperfusion; 1- thrombus reduction, no filling of distal arteries; 2a- reperfusion of <50%; 2b50- reperfusion of 50 to 66%; 2b67- reperfusion of 67 to 89%; 2c- reperfusion of 90 to 99% and 3- complete reperfusion).

**Devices/techniques**

Stent-retrievers were the predominantly or exclusively used devices in all the landmark randomized trials mentioned above. Primary devices, as well as adjunctive materials and techniques, are evolving to achieve first-pass complete recanalization in the shortest possible time. A direct aspiration, first pass technique (ADAPT) was compared with stent-retrievers in the observational study including 243 patients; it was found that ADAPT led to better successful recanalization rates (82.3% vs 68.9%), though the use of adjunctive devices was more frequent in ADAPT group and

Figure 2: (1)- Stent retriever with a balloon guide catheter, (2) stent retriever with an aspiration catheter, (3) recanalization of basilar occlusion with ADAPT followed by stent retriever thrombectomy for superior cerebellar artery occlusion. SR- stent-retriever, MC- microcatheter
functional outcomes did not differ. However, randomized control trial (THERAPY) comparing aspiration thrombectomy with medical management alone was negative. The ASTER randomized trial failed to show superiority of aspiration to stent-retriever thrombectomy. While the COMPASS randomized trial finally proved the non-inferiority of aspiration as the first pass. A recent meta-analysis including 15 studies comparing balloon guide catheters to non-balloon guide catheters showed better procedural success (higher rates of first-pass effect and successful recanalization, lower distal emboli) as well as better clinical outcomes (lower symptomatic hemorrhage, higher rates of functional independence at 3 months and lower mortality). There are various combination techniques described with some modifications while the principle remains the same-effective engagement of clot with the device, proximal flow arrest, and flow reversal while retrieving the clot to prevent emboli. All of these (COLUMBRA, CAPTIVE, ARTS, SAVE, ASAP, PROTECT, PROTECT PLUS, BADDASS) report higher successful recanalization rates [Figure 2].

Radial approach

The anatomy of the aortic arch might be unsuitable sometimes to access the vessel of interest through the femoral approach. In these circumstances, alternative approaches like a radial or direct carotid might need to be used. A systematic review and meta-analysis identified 51 patients in whom these approaches were used and found that technical success could be achieved in 84% of patients; there were no complications through radial approach and 7.4% of patients in whom direct carotid access was used had hematoma. The radial approach can be the preferred primary approach as well in selected patients.

Anesthesia

Initial observational studies, as well as meta-analysis from individual patient-level data by HERMES collaborators, had concluded that general anesthesia (GA) for thrombectomy was associated with worse outcomes compared to non-GA groups and the use of GA should be avoided. However, the subsequent three randomized trials (SIESTA, AnStroke, GOLIATH) did not show any difference in primary outcomes between general anesthesia or conscious sedation. The likely reason for the difference is the lack of standardized anesthesia protocols in previous studies. A recent meta-analysis involving four randomized trials even concluded that general anesthesia leads to better recanalization rates and better functional outcomes at three months, as far as sudden drops in blood pressure are avoided by standard anesthesia protocols. Recently, local anesthesia, as opposed to GA or conscious sedation, has evolved to seem promising for better outcomes.

Direct thrombectomy

As shown in HERMES meta-analysis, outcomes in patients undergoing thrombectomy were favorable irrespective of whether they were given IVT or not. This had formulated a question of whether IVT can be skipped ineligible patients as well, as it might lead to more hemorrhagic complication rates and might have financial implications specifically in low and middle-income countries. Initial observational studies addressing this question have led to conflicting conclusions. While recent randomized trials and meta-analyses have concluded that direct thrombectomy can be a reasonable approach. This holds true especially in patients with large clots, higher bleeding risk (large infarcts, basal ganglia infarcts, current antithrombotic use), or in patients requiring acute stenting and can be the preferred approach in patients presenting directly to thrombectomy ready centers.

Conclusions

Mechanical thrombectomy has proven to be one of the strongest treatments modern medicine can offer for any disease condition. Such a strong treatment needs as its companions, a robust pre-hospital and post-discharge systems of care as well to provide the best possible benefit to patients.

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Conflicts of interest

There are no conflicts of interest.

References

1. Dabus G, Linfante I. The natural history of acute ischemic stroke due to intracranial large-vessel occlusion: What do we know? Tech Vasc Interv Radiol 2012;15:2-4.
2. Malhotra K, Gornbein J, Saver JL. Ischemic strokes due to large-vessel occlusions contribute disproportionately to stroke-related death and death: A review. Front Neurol 2017;8:651.
3. Paciaroni M, Caso V, Venti M, Milia P, Kappelle LJ, Silvestrelli G, et al. Outcome in patients with stroke associated with internal carotid artery occlusion. Cerebrovasc Dis 2005;20:108-13.
4. Sylaja PN, Pandian JD, Kaul S, Srivastava MVP, Khurana D, Schwamm LH, et al. Ischemic stroke profile, risk factors, and outcomes in India: The Indo-US collaborative stroke project. Stroke 2018;49:219-22.
5. Saqqur M, Uchino K, Demchuk AM, Molina CA, Garami Z, Calleja S, et al. Site of arterial occlusion identified by transcranial Doppler predicts the response to intravenous thrombolysis for stroke. Stroke 2007;38:948-54.
6. del Zoppo GJ, Poock K, Pessin MS, Wolpert SM, Furlan AJ, Fritser B, et al. Recombinant tissue plasminogen activator in acute thrombotic and embolic stroke. Ann Neurol 1992;32:78-86.
7. Furlan A, Higashida R, Wechsler L, Gent M, Rowley H, Kase C, et al. Intra-arterial prourokinase in acute ischemic stroke. The PROACT II study: A randomized controlled trial. Prolyse in acute cerebral thromboembolism. JAMA 1999;282:2003-11.
8. Jauch EC, Saver JL, Adams HP, Bruno A, Connors JJ (Buddy), Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke. Stroke 2013;44:870-947.
9. Ma Q, Chu C, Song H. Intravenous versus intra-arterial thrombolysis in ischemic stroke: A systematic review and meta-analysis. PLoS One 2015;10:e0116120.
10. Nogueira RG, Schwamm LH, Hirsch JA. Endovascular approaches to acute stroke, part 1: Drugs, devices, and meta-analysis. AJNR Am J Neuroradiol 2009;30:649-61.
11. Kelly ME, Furlan AJ, Fiorella D. Recanalization of an acute middle cerebral artery occlusion using a self-expanding, reconstrainable, intracranial microstent as a temporary endovascular bypass. Stroke 2008;39:1770-3.
12. Huded V, Rajesh KN, Netravathi S, Iyer R. Endovascular treatment for 2008;39:1770-3.
acute ischemic stroke using solitaire stent: Temporary endovascular bypass, a novel technique. Neurol India 2011;59:401-4.

13. Broderick JP, Palesch YY, Demchuk AM, Yeatts SD, Khatri P, Hill MD, et al. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. N Engl J Med 2013;368:893-903.

14. Kidwell CS, Jahan R, Gornbein J, Alger JR, Nenov V, Ajani Z, et al. A trial of imaging selection and endovascular treatment for ischemic stroke. N Engl J Med 2013;368:914-23.

15. Ciccone A, Valvassori L, Nicheltelli M, Sgifo A, Ponzio M, Sterzi R, et al. Endovascular treatment for acute ischemic stroke. N Engl J Med 2016;375:904-13.

16. Nogueira RG, Gupta R, Davalos A. IMS-III and SYNTHESIS expansion trials of endovascular therapy in acute ischemic stroke. Stroke 2013;44:3272-4.

17. Brcadac S, Ducrocq X, Mas JL, Soudant M, Oppenheim C, Moulin T, et al. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): A randomised controlled trial. Lancet Neurol 2016;15:1138-47.

18. Berkhemer OA, Fransen SS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11-20.

19. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thromton J, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 2015;372:1019-30.

20. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 2015;372:2296-306.

21. Saver JL, Goyal M, Bonafe A, Diener H-C, Levy EI, Pereira VM, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 2015;372:2285-95.

22. Campbell BCV, Mitchell PJ, Kleing JI, Dewey HM, Charilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 2015;372:1009-18.

23. Khoury NN, Darsaut TE, Ghostine J, Deschaintre Y, Daneault N, Durocher A, et al. Endovascular thrombectomy and medical therapy versus medical therapy alone in acute stroke: A randomized care trial. J Neurolorad 2017;44:198-202.

24. Goyal M, Menon BK, Zwam WH van, Dippel DWJ, Mitchell PJ, Demchuk AM, et al. Endovascular therapy for acute ischemic stroke: A meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723-31.

25. Vlahos VY, Srivastava MP. Innovations in acute stroke reperfusion strategies. Ann Indian Acad Neurol 2019;22:6-12.

26. Salerno A, Strambo D, Nannoni S, Dunet V, Michel P. Patterns of ischemic posterior circulation strokes: A clinical, anatomical, and radiological review. Int J Stroke 2020;15:443‑9.

27. Liu X, Dai Q, Ye R, Zi W, Liu Y, Wang H, et al. Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): An open-label, randomised controlled trial. Lancet Neurol 2020;19:115-22.

28. Langezaal LCM, van der Hoeven EJRJ, Mont’Alverne FJA, de Carvalho JJF, Lima FO, Dippel DWJ, et al. Endovascular therapy for stroke due to basilar-artery occlusion. N Engl J Med 2021;384:1910-20.

29. Mbroh J, Poli K, Tünnerhoff J, Gomez-Exposito A, Wang Y, Bender B, et al. Comparison of risk factors, safety, and efficacy outcomes of mechanical thrombectomy in posterior vs. anterior circulation large vessel occlusion. Front Neurol 2021;12:936.

30. Wang F, Wang J, He Q, Wang L, Cao Y, Zhang H, et al. Mechanical thrombectomy for posterior circulation occlusion: A comparison of outcomes with the anterior circulation – A meta-analysis. JAT 2020;27:1325-39.

31. Writing Group for the BASILAR Group. Assessment of endovascular treatment for acute basilar artery occlusion via a nationwide prospective registry. JAMA Neurol 2020;77:561-73.

32. Kwak HS, Park JS. Mechanical thrombectomy in basilar artery occlusion: Clinical outcomes related to posterior circulation collateral score. Stroke 2020;51:2045-50.

33. Raymond S, Rost NS, Schafer PW, Leslie-Mazwi T, Hirsch JA, Gonzalez RG, et al. Patient selection for mechanical thrombectomy in posterior circulation: An emergent large-vessel occlusion. Interv Neuroradiol 2018;24:309-16.

34. Baik SH, Park HJ, Kim J-H, Jang CK, Kim BM, Kim DJ. Mechanical thrombectomy in subtypes of basilar artery occlusion: Relationship to recanalization rate and clinical outcome. Radiology 2019;291:730-7.

35. Gory B, Mazighi M, Blanc R, Labreuche J, Piotin M, Turjman F, et al. Mechanical thrombectomy in basilar artery occlusion: Influence of reperfusion on clinical outcome and impact of the first-line strategy (ADAPT vs stent retriever). J Neurosurg 2018;129:1482-91.

36. Meyer L, Stracke CP, Jungi N, Wallocha M, Broocks G, Sporns PB, et al. Thrombectomy for primary distal posterior cerebral artery occlusion: The TOPMOST study. JAMA Neurol 2021;78:434-44.

37. Zaidat OO, Liebeskind DS, JadHAV AP, Ortega-Gutiierrez S, Nguyen TN, Haussen DC, et al. Impact of age and alberta stroke program early computed tomography score 0 to 5 on mechanical thrombectomy outcomes: Analysis from the STRATIS registry. Stroke 2021;52:2220-8.

38. Meyer L, Bechtel M, Bester M, Hanning U, Brekenfeld C, Flottmann F, et al. Thrombectomy in extensive stroke may not be beneficial and is associated with increased risk for hemorrhage. Stroke 2021;52:3109-17.

39. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 2015;372:2296-306.

40. Seners P, Ben Hassen W, Lapergue B, Arquizan C, Hehnder MR, Heron H, et al. Prediction of early neurological deterioration in individuals with minor stroke and large vessel occlusion intended for intravenous thrombolysis alone. Stroke 2021;52:2220-8.

41. Mok M, Masud MW, Dumont TM, Ahmad G, Kass-Hout T, Snyder KV, et al. Outcomes in patients with acute ischemic stroke from proximal intracranial vessel occlusion and NIHSS score below 8. J NeuroInterv Surg 2014;6:413-7.

42. Saleem Y, Nogueira RG, Rodrigues GM, Kim S, Sharashidze V, Frankel M, et al. Acute neurological deterioration in large vessel occlusions and mild symptoms managed medically. Stroke 2020;51:1428-34.

43. McCarthy DJ, Tonetti DA, Stone J, Starke RM, Narayanan S, Lang MJ, et al. More expansive horizons: A review of endovascular therapy for patients with low NIHSS scores. J NeuroInterv Surg 2021;13:146-51.

44. Senes P, Ben Hassen W, Lapergue B, Arquizan C, Hehnder MR, Heron H, et al. Prediction of early neurological deterioration in individuals with minor stroke and large vessel occlusion intended for intravenous thrombolysis alone. JAMA Neurol 2021;78:321-8.

45. Nagel S, Bousslama M, Krause LU, Köpper C, Messer M, Petersen M, et al. Mechanical thrombectomy in patients with milder strokes and large vessel occlusions. Stroke 2018;49:2391-7.

46. Goyal N, Tsiivgoulos G, Malhotra K, Kishaf MQ, Pandhi A, Frohler MT, et al. Medical management vs mechanical thrombectomy for mild strokes: An international multicenter study and systematic review and meta-analysis. JAMA Neurol 2020;77:16-24.

47. Saver JL, Chapaar R, Agid R, Hassan AE, JadHAV AP, Liebeskind DS, et al. Thrombectomy for distal, medium vessel occlusions. Stroke 2020;51:2872-84.

48. Ospel JM, Menon BK, Demchuk AM, Almekhlafi MA, Kashani N, Mayark A, et al. Clinical course of acute ischemic stroke due to medium vessel occlusion and with and without intravenous alteplase treatment. Stroke 2020;51:3232-40.

49. Menon BK, Hill MD, Davalos A, Roos YBWEM, Campbell BCV, Dippel DWJ, et al. Efficacy of endovascular thrombectomy in patients with M2 segment middle cerebral artery occlusions: Meta-analysis of data from the HERMES collaboration. J NeuroInterventional Surg 2019;11:1065-9.

50. Bhatti A, Huded V, Vyas D, Mushtaq M, Kekaptopure M, Hiremath S, et al. Mechanical thrombectomy using retrievable stents in pediatric acute ischemic stroke. Indian Pediatr 2019;56:571-5.

51. Tse GH, Balian V, Charalampatou P, Malikai P, Nayak S, Dyre R, et al. Foetal radiation exposure caused by mechanical thrombectomy in large-vessel ischaemic stroke in pregnancy. Neuroradiology 2019;61:443-9.

52. Diepinigaitis AJ, Sursal T, Morse CA, Briskin C, Dakay K, Kurian C, et al. Mechanical thrombectomy for treatment of acute ischemic stroke.
stroke during pregnancy and the early postpartum period. Stroke 2021;52:3796-804.
53. Anadani M, Marnat G, Consoli A, Papanagiotou P, Nogueira RG, Siddiqui A, et al. Endovascular therapy of anterior circulation tandem occlusions: Pooled analysis from the TITAN and ETIS registries. Stroke 2021;52:3097-105.
54. Wilson MP, Murad MH, Krings T, Pereira VM, O’Kelly C, Rempel J, et al. Management of tandem occlusions in acute ischemic stroke—intracranial versus extracranial first and extracranial stenting versus angioplasty alone: A systematic review and meta-analysis. J Neurointerv Surg 2018;10:721-8.
55. Sarraj A, Mlynash M, Heit J, Pujara D, Lansberg M, Marks M, et al. Clinical outcomes and identification of patients with persistent penumbra profiles beyond 24 hours from last known well. Stroke 2021;52:838-49.
56. Zaidat OO, Castonguay AC, Linfante I, Gupta R, Martin CO, Holloway WE, et al. First pass effect: A new measure for stroke thrombectomy devices. Stroke 2018;49:660-6.
57. Zaidat OO, Yoo AJ, Khatri P, Tomsick TA, von Kummer R, Saver JL, et al. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: A consensus statement. Stroke 2013;44:2650-63.
58. Goyal N, Tsivgoulis G, Frei D, Turk A, Baxter B, Froehler MT, et al. Comparative safety and efficacy of modified TICI 2b and TICI 3 reperfusion in acute ischemic strokes treated with mechanical thrombectomy. Neurosurgery 2019;84:680-9.
59. Liesbeschinsky BS, Bracard S, Guillemin F, Jahan R, Jovin TG, Majoie CB, et al. eTICI reperfusion: Defining success in endovascular stroke therapy. J Neuroradiol Surg 2019;11:433-8.
60. Lapergue B, Blanc R, Guedin P, Decroix J-P, Labreuche J, Preda C, et al. A direct aspiration, first pass technique (ADAPT) versus stent retrievers for acute stroke therapy: An observational comparative study. Am J Neuroradiol 2016;37:1860-5.
61. Mocco J, Zaidat OO, von Kummer R, Yoo AJ, Gupta R, Lopes D, et al. Aspiration thrombectomy after intravenous alteplase versus intravenous alteplase alone. Stroke 2016;47:2331-8.
62. Lapergue B, Blanc R, Gory B, Labreuche J, Duhamel A, Marnat G, et al. Effect of endovascular contact aspiration vs stent retriever on revascularization in patients with acute ischemic stroke and large vessel occlusion: The ASTER randomized clinical trial. JAMA 2017;318:443-52.
63. Turk AS, Siddiqui A, Fifi JT, Leacy RAD, Fiorella DJ, Gu E, et al. Aspiration thrombectomy versus stent retriever thrombectomy as first-line approach for large vessel occlusion (COMPASS): A multicentre, randomised, open label, blinded outcome, non-inferiority trial. Lancet 2019;393:998-1008.
64. Pederson JM, Reierson NL, Hardy N, Touche JC, Medam S, Barrett A, et al. Comparison of balloon guide catheters and standard guide catheters for acute ischemic stroke: A systematic review and meta-analysis. World Neurosurg 2021;154:144-53.e21.
65. Humphries W, Hoit D, Doss VT, Ejiofor I, Frei D, Loy D, et al. Distant aspiration with retrievable stent assisted thrombectomy for the treatment of acute ischemic stroke. J Neuroradiol Surg 2015;7:90-4.
66. McGaggart RA, Tung EL, Yaghi S, Cutting SM, Hemendinger M, Gale HI, et al. Continuous aspiration prior to intracranial vascular embolectomy (CAPTIVE): A technique which improves outcomes. J Neuroradiol Surg 2017;9:1154-9.
67. Massari F, Henninger N, Lozano JD, Patel A, Kuhn AL, Howk M, et al. ARTS (Aspiration-Retriever Technique for Stroke): Initial clinical experience. Interv Neuroradiol 2016;22:325-32.
68. Maus V, Henkel S, Riabikin A, Riedel C, Behme D, Tsogkas I, et al. The SAVE technique: Large-scale experience for treatment of intracranial large vessel occlusions. Clin Neuroradiol 2019;29:669-76.
69. Goto S, Oshtima T, Ishikawa K, Yamamoto T, Shimato S, Nishizawa T, et al. A stent-retrieving into an aspiration catheter with proximal balloon (ASAP) technique: A technique of mechanical thrombectomy. World Neurosurg 2018;109:e468-75.
70. Maeglelein C, Mönch S, Boechk-Behrens T, Lehmk, Hedderich DM, Berndt MT, et al. PROTECT: PrOximal balloon occlusion TogEther with direCt thrombus aspiration during stent retriever thrombectomy-evaluation of a double embolic protection approach in endovascular stroke treatment. J Neuroradiol Surg 2018;10:751-5.
71. Maeglein C, Berndt MT, Mönch S, Kreiser K, Boechk-Behrens T, Lehmk, et al. Further development of combined techniques using stent retrievers, aspiration catheters and BGC: The PROTECTPLUS technique. Clin Neuroradiol 2020;30:59-65.
72. Ospel JM, Volny O, Jayaraman M, McGaggart R, Goyal M. Optimizing fast first pass complete reperfusion in acute ischemic stroke-the BADDASS approach (Ballon guide with large bore distal access catheter with dual aspiration with stent-retriever as standard approach). Expert Rev Med Devices 2019;16:955-63.
73. Scocco AN, Addepalii A, Zhu S, Bentjon J, Jenna SR, Harahallnili N, et al. Trans-carotid and trans-radial access for mechanical thrombectomy for acute ischemic stroke: A systematic review and meta-analysis. Cureus 2020;12:e8875.
74. Sur S, Snelling B, Khandelwal P, Caplan JM, Peterson EC, Starke RM, et al. Transradial approach for mechanical thrombectomy in anterior circulation-large-vessel occlusion. Neurosurg Focus 2017;42:E13.
75. Chen SH, Snelling BM, Sur S, Shah SS, McCarthy DJ, Luther E, et al. Transradial versus transfemoral access for anterior circulation mechanical thrombectomy: Comparison of technical and clinical outcomes. J Neuroradiol Surg 2019;11:874-8.
76. Campbell BCV, van Zwam WH, Goyal M, Menon BK, Dippel DWJ, Demchuk AM, et al. Effect of general anaesthesia on functional outcome in patients with anterior circulation ischaemic stroke having endovascular thrombectomy versus standard care: A meta-analysis of individual patient data. Lancet Neurol 2018;17:47-53.
77. Schönberger S, Uhlmann L, Hacke W, Schieber M, Mundiyapanurath P, Rurucker JC, et al. Effect of conscious sedation vs general anesthesia on early neurological improvement among patients with ischemic stroke undergoing endovascular thrombectomy: A randomized clinical trial. JAMA 2016;316:1986-96.
78. Löwhagen Hendén P, Rentzos A, Karlsson J-E, Rosengren L, Leiram B, Sundeman H, et al. General anesthesia versus conscious sedation for endovascular treatment of acute ischemic stroke. Stroke 2017;48:1601-7.
79. Simonsen CZ, Yoo AJ, Sorensen LH, Juul N, Johnsen SP, Andersen G, et al. Effect of general anesthesia and conscious sedation during endovascular therapy on infarct growth and clinical outcomes in acute ischemic stroke: A randomized clinical trial. JAMA Neurol 2018;75:470-7.
80. Campbell D, Diprose WK, Deng C, Barber PA. General anesthesia versus conscious sedation in endovascular thrombectomy for stroke: A meta-analysis of 4 randomized controlled trials. J Neurosurg Anesthesiol 2021;33:21-7.
81. Katsanos AH, Turc G, Psychogios M, Kaesmacher J, Palaiodimou L, Stefanou MI, et al. Utility of intravenous alteplase prior to endovascular stroke treatment: A systematic review and meta-analysis of RCTs. Neurology 2021;97:e777-84.
Table 1: (Supplementary material)- Exclusion criteria of randomized trials

| MR CLEAN | ESCAPE | REVASCAT | SWIFT PRIME | EXTEND IA | THRACE | PISTE | EASI | DAWN | DEFUSE 3 |
|----------|--------|----------|-------------|-----------|--------|-------|------|------|----------|
| Imaging  | Hemorrhage; ASPECTS 0-5, no minimal collaterals in >50% MCA territory | Hemorrhage; Age <81; ASPECTS CT <7, MR <6 Age ≥81; ASPECTS CT/MR <9 | Hemorrhage; infarcts in >½ MCA territory, ASPECTS <6, carotid dissection/ proximal occlusion, CTP infarct >50 ml | Hemorrhage; Infarcts in >½ MCA territory, carotid dissection | Cervical ICA occlusion/severe stenosis | Hemorrhage; Infarcts in >½ MCA territory, extracranial ICA occlusion | Hemorrhage; established infarcts | Hemorrhage, >½ MCA territory involved, carotid dissection/proximal high-grade stenosis/ occlusion (requiring acute stenting), vasculitis, BP ≥185/110 mmHg (even after medications) | Hemorrhage, ASPECTS <6, flow-limiting carotid dissection, |
| BP       | ≥185/110 mmHg | ≥185/110 mmHg (even after medications) | ≥185/110 mmHg (even after medications) | ≥185/110 mmHg (even after medications) | ≥185/110 mmHg (even after medications) | - | - | - | - |
| Blood glucose | <50/>400 mg/dl | <50/>400 mg/dl | - | - | - | - | - | - | - |
| Hemorrhagic | - | Platelet <30000/µL, ASPECTS CT/MR <9 | Any contraindications for IVT | Hemorrhagic diathesis, INR >1.7, use of heparin in previous 48 hours and abnormal APTT, GpIIb-IIIa in <72 hours | Any contraindications for IVT | Any contraindications for IVT | - | NOACs, heparin within 24 hours allowed (with normal APTT), platelets <50000/µL, Hb <7mmoVL, Hemorrhagic diathesis, INR >3, aPTT ratio >3, Platelets <50000/µL, Hemorrhagic diathesis, INR >3, APTT ratio >3, |
| Previous stroke | Infarct in same territory <6 wks, previous ICH | - | - | - | - | - | - | - | - |
| Others | Major surgery or GI/GU bleed <2 weeks, arterial puncture noncompressible <7d, IAT-head injury <4 wks | Pregnancy, contrast allergy, intracranial dissection, chronic intracranial occlusion | Coma, life expectancy <1 yr, contrast allergy, creatinine >3 mg/dl, pregnancy/lactation, vasculitis, endovascular intervention/major surgery <48 hr, b/l stroke, intracranial tumors | Any contraindications to IVT, Life expectancy <90 days, pregnancy, rapidly improving symptoms, allergy to contrast/ nickel-titanium, life expectancy <1 yr, pregnancy, AVM, aneurysm, cerebral neoplasm | Any contraindications for IVT, any cause prohibiting femoral catheterization | History s/o SAH, vascular access contraindications, life expectancy <3 months, allergy to contrast | History s/o SAH, vascular access contraindications, life expectancy <3 months, allergy to contrast | Head injury <90 days, dementia, seizure at onset (accurate NIHSS NA), Sodium <130, Potassium <3/>6, creatinine >3 mg/dl (except pt on dialysis), pregnancy, lactation, infective endocarditis, aortic dissection, b/l/ multiple territory stroke, cerebral neoplasm, life expectancy <6 months | Pregnancy, allergy to contrast, life expectancy <6 months, seizure at onset (accurate NIHSS NA), Infective endocarditis, tPA use beyond guidelines, cerebral neoplasm, AVM, aortic dissection, multiple territory stroke |