Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management Evidence Tables

Seventh Edition, Update 2022

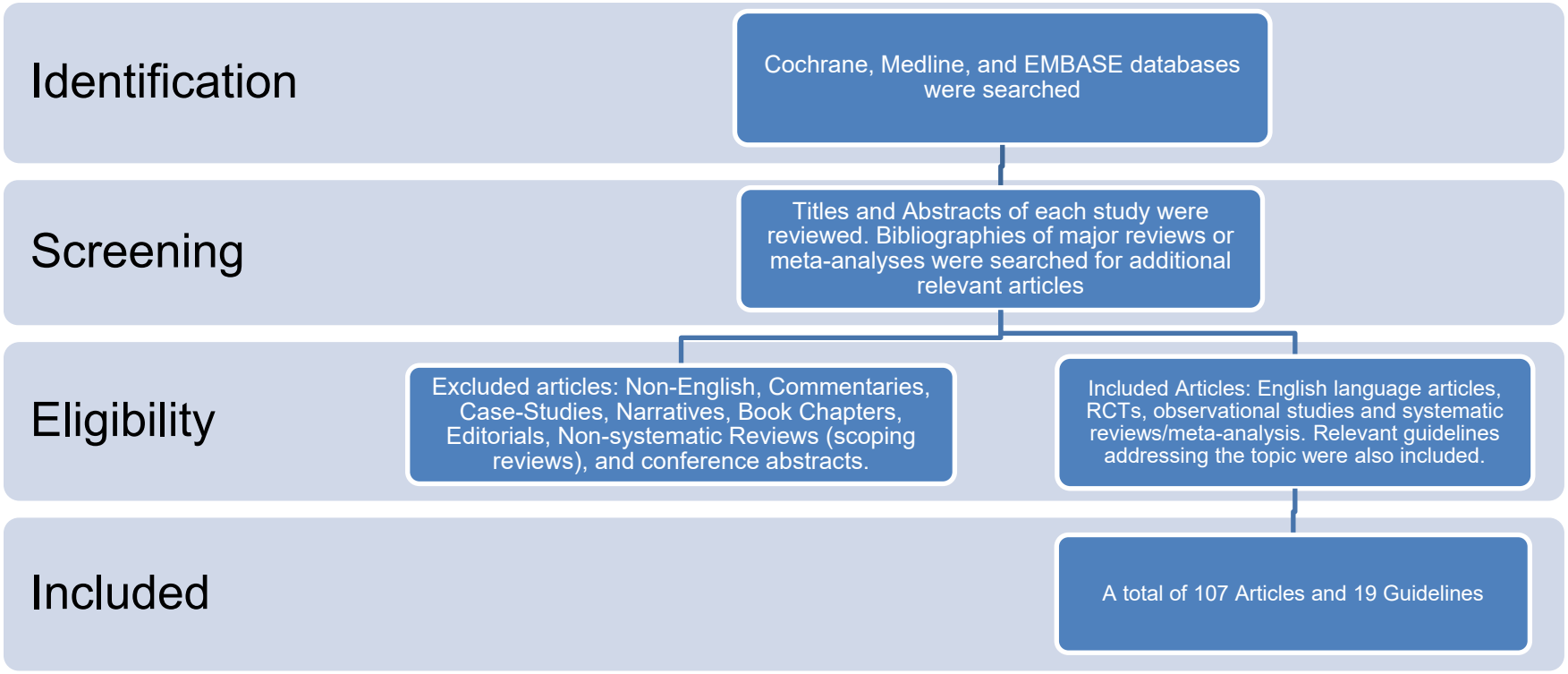
Section 5: Acute Ischemic Stroke Treatment

Endovascular Therapy

Heran M, Shamy M (Writing Group Chairs)
on Behalf of the Canadian Stroke Best Practice Recommendations
Acute Stroke Management Writing Group and in collaboration with the
Canadian Stroke Consortium

Table of Contents

Search Strategy



Pubmed, EMBASE and the Cochrane Central Register of Controlled Trials databases were search using the terms ischemic stroke AND mechanical thrombectomy OR endovascular therapy OR intra-arterial therapy. Titles and abstract of each article were reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. A total of 19 guidelines and 107 articles were included and were separated into separate categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
Turc G, Tsivgoulis G, Audebert H, et al. **EXPRESS: European Stroke Organisation (ESO) – European Society for Minimally Invasive Neurological Therapy (ESMINT) expedited recommendation on indication for intravenous thrombolysis before mechanical thrombectomy in patients with acute ischaemic stroke and anterior circulation large vessel occlusion.** ***Eur Stroke Jl* February 2022;7: I–XXVI.**	PICO 1: For large vessel occlusion acute ischaemic stroke (≤ 4.5 hrs of symptom onset) patients directly admitted to a thrombectomy capable centre and eligible for both treatments, does mechanical thrombectomy alone compared with intravenous thrombolysis plus mechanical thrombectomy lead to: a) a non-inferior proportion of patients with good outcome (mRS 0-2) at 90 days? b) non-inferior or better results on other efficacy outcomes (whole range of the mRS; mRS 0-1; successful reperfusion)? c) a reduction in the risk of adverse events (mortality at 90 days, sICH, any ICH)? d) a reduction in key time metrics? Evidence-base recommendation For patients directly admitted to a thrombectomy-capable centre for an acute ischaemic stroke (≤4.5 hrs of symptom onset) with anterior circulation large vessel occlusion and who are eligible for both treatments, we recommend intravenous thrombolysis plus mechanical thrombectomy over mechanical thrombectomy alone. Both treatments should be performed as early as possible after hospital arrival. Mechanical thrombectomy should not prevent the initiation of intravenous thrombolysis, and intravenous thrombolysis should not delay mechanical thrombectomy. Quality of evidence: Moderate ⊕⊕⊕ Strength of recommendation: Strong ↑↑ Expert consensus statement For patients directly admitted to a thrombectomy-capable centre within 4.5 hours of symptom recognition after wake-up ischaemic stroke caused by anterior circulation large vessel occlusion, we suggest intravenous thrombolysis plus mechanical thrombectomy over mechanical thrombectomy alone in selected patients. The selection criteria for IVT and MT for patients with wake-up stroke are detailed in the corresponding European guidelines. Notably, eligibility imaging criteria for IVT include DWI-FLAIR mismatch or perfusion core/penumbra mismatch.
Berge E, Whiteley W, Audebert H, et al. **European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke.** ***Eur Stroke J* 2021; 6: I-LXII.** **(with respect to EVT-selected)**	1.1 For patients with acute ischaemic stroke of <4.5 h duration, we recommend intravenous thrombolysis with alteplase. Quality of evidence: High ⊕⊕⊕⊕, Strength of recommendation: Strong ↑↑ 2.1 For patients with acute ischaemic stroke of 4.5–9 h duration (known onset time), and with no brain imaging other than plain CT, we recommend no intravenous thrombolysis. Quality of evidence: Moderate ⊕⊕⊕, Strength of recommendation: Strong ↓↓ 4.1 For patients with acute ischaemic stroke on awakening from sleep, who were last seen well more than 4.5 h earlier, who have MRI DWI-FLAIR mismatch, and for whom mechanical thrombectomy is either not indicated or not planned, we recommend intravenous thrombolysis with alteplase. Quality of evidence: High ⊕⊕⊕⊕, Strength of recommendation: Strong ↑↑ 12.1 For patients with acute ischaemic stroke of <4.5 h duration, who used single or dual antiplatelet agents prior to the stroke, we suggest intravenous thrombolysis with alteplase. Quality of evidence: Low ⊕⊕, Strength of recommendation: Strong ↑↑

Guideline	Recommendations
	12.2 For patients with acute ischaemic stroke of <4.5 h duration, who use vitamin K antagonists and have INR ≤1.7 we recommend intravenous thrombolysis with alteplase. Quality of evidence: Low ⊕⊕, Strength of recommendation: Strong ↑↑ For patients with acute ischaemic stroke of <4.5 h duration, who use vitamin K antagonists and have INR >1.7 we recommend no intravenous thrombolysis. Quality of evidence: Very Low ⊕, Strength of recommendation: Strong ↑↑ For patients with acute ischaemic stroke of <4.5 h duration, who use vitamin K antagonists, and for whom the results of coagulation testing is unknown, we recommend no intravenous thrombolysis. Quality of evidence: Very low ⊕, Strength of recommendation: Strong ↑↑ 12.3 For patients with acute ischaemic stroke of <4.5 h duration, who used a NOAC during the last 48 h before stroke onset, and for whom there is no specific coagulation tests available (i.e. calibrated anti-Xa-activity for factor Xa inhibitors, thrombin time for dabigatran, or the NOAC blood concentrations), we suggest no intravenous thrombolysis. Quality of evidence: Very Low ⊕, Strength of recommendation: Strong ↑↑
Liu L, Chen W, Zhou H, et al. **Chinese Stroke Association guidelines for clinical management of cerebrovascular disorders: executive summary and 2019 update of clinical management of ischaemic cerebrovascular diseases.** ***Stroke and Vascular Neurology* 2020; 5(2): 159-176.** **(selected)**	**Patients within 6 hours after AIS—bridging/endovascular treatment.** 1. Mechanical thrombectomy is strongly recommended for patients within 6hours after AIS if they meet all the following criteria: (1) prestroke mRS score of 0–1; (2) causative occlusion of the internal carotid artery (ICA) or middle cerebral artery (MCA) segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6 and (5) ASPECTS of ≥6 (class I, level of evidence A). 2. It is reasonable to initial treatment with intra-arterial thrombolysis within 6hours after AIS caused by occlusions of the MCA for carefully selected patients who have contraindications or no clinical response to the use of IV rt-PA and could not perform mechanical thrombectomy (class IIa, level of evidence B). 3. Endovascular treatment should be performed as soon as possible after its indication. Patients eligible for IV rt-PA should receive IV rt-PA and direct perform bridging treatment for mechanical thrombectomy (class I, level of evidence A). 4. Mechanical thrombectomy should performed as the first-line treatment for patients who have contraindications to the use of IV rt-PA (class IIa, level of evidence A). 5. Stent retrievers is indicated for mechanical thrombectomy as first choice (class I, level of evidence A). Other thrombectomy or aspiration devices approved by local health authorities may be used at the operators' discretion (class IIa, level of evidence B). **Patients within 6–24 hours after AIS—endovascular treatment** 1. In selected patients with AIS within 6–16hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended (class I, level of evidence A). 2. In selected patients with AIS within 16–24hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable (class IIa, level of evidence B). 3. Patients with acute basilar artery occlusion within 6–24hours should be evaluated in centres with multimodal imaging and treated with mechanical thrombectomy or they may be treated within an RCT for thrombectomy approved by the local ethical committee (class IIb, level of evidence B). 4. The benefits of mechanical thrombectomy are uncertain for patients with acute large vascular occlusion for >24hours (class IIb, level of evidence C).

Guideline	Recommendations
Pierot L, Jayaraman MV, Szikora I, Hirsch JA, Baxter B, Miyachi S, Mahadevan J, Chong W, Mitchell PJ, Coulthard A, Rowley HA. **Standards of practice in acute ischemic stroke intervention: International recommendations.** ***Interv Neuroradi.* 2019 Feb;25(1):31-7.**	General recommendations that describe the minimum organization and workload, based on expert consensus, that is necessary for a hospital to practice acute ischemic stroke intervention, including thrombectomy, aspiration, percutaneous transluminal angioplasty, stent implantation, and drug infusion. (same recommendations also published: *J Neurointerv Surg*. 2018 Nov;10(11):1121-1126; *AJNR Am J Neuroradiol*. 2018 Nov;39(11):E112-E117; *Can J Neurol Sci.* 2019 Mar 20:1-6.)
Turc G, Bhogal P, Fischer U, Khatri P, Lobotesis K, Mazighi M, Schellinger PD, Toni D, de Vries J, White P, Fiehler J. **European Stroke Organisation (ESO)–European Society for Minimally Invasive Neurological Therapy (ESMINT) Guidelines on Mechanical Thrombectomy in Acute Ischaemic Stroke. Endorsed by Stroke Alliance for Europe (SAFE).** ***Eur Stroke J*. 2019 Feb 26:2396987319832140.** **(selected)**	There are 15 questions/recommendations in total (Expert opinion statements are also included) In adults with anterior circulation LVO-related acute ischaemic stroke presenting within 6 hours after symptom onset, we recommend MT plus best medical management (BMM), including IVT whenever indicated, over BMM alone to improve functional outcome. Quality of evidence: High; Strength of recommendation: Strong In adults with anterior circulation LVO-related acute ischaemic stroke presenting between 6 and 24 hours from time last known well and fulfilling the selection criteria of DEFUSE-3 or DAWN, we recommend MT plus BMM over BMM alone to improve functional outcome. Quality of evidence: Moderate; Strength of recommendation: Strong In LVO-related ischaemic stroke patients eligible for both treatments, we recommend IVT plus MT over MT alone. Both treatments should be performed as early as possible after hospital arrival. MT should not prevent the initiation of IVT, and IVT should not delay MT. Quality of evidence: Very low; Strength of recommendation: Strong In LVO-related ischaemic stroke patients not eligible for IVT, we recommend MT as standalone treatment. Quality of evidence: Low; Strength of recommendation: Strong In patients with suspected stroke, we cannot make a recommendation on the use of a prehospital scale for improving identification of patients eligible for MT. We suggest enrolling patients in a dedicated randomized controlled trial, whenever possible. Quality of evidence: Very low; Strength of recommendation N/A We do not recommend an upper NIHSS score limit for decision-making on MT. We recommend that patients with high stroke severity and LVO-related acute ischaemic stroke be treated with MT plus BMM, including IVT whenever indicated. These recommendations also apply for patients in the 6-24h time window, provided that they meet the inclusion criteria for the DAWN or DEFUSE-3 studies. Quality of evidence: High; Strength of recommendation: Strong In the 0-6 hour time window, we recommend MT plus BMM (including IVT whenever indicated) over BMM alone in LVO-related anterior circulation stroke patients without evidence of extensive infarct core (e.g. ASPECTS 6 on non-contrast CT scan or infarct core volume 70 ml). Quality of evidence: High; Strength of recommendation: Strong In adult patients with anterior circulation LVO-related acute ischaemic stroke presenting from 0-6 hours from time last known well, advanced imaging is not necessary for patient selection. Quality of evidence: Moderate; Strength of recommendation: Weak

Guideline	Recommendations
Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; on behalf of the American Heart Association Stroke Council. **Guidelines for the early management of patients with acute ischemic stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association** ***Stroke* 2019;50:e344–e418.** **(selected)**	**1.7. Organization and Integration of Components** 2. Mechanical thrombectomy requires the patient to be at an experienced stroke center with rapid access to cerebral angiography, qualified neurointerventionalists, and a comprehensive periprocedural care team. Systems should be designed, executed, and monitored to emphasize expeditious assessment and treatment. Outcomes for all patients should be tracked. Facilities are encouraged to define criteria that can be used to credential individuals who can perform safe and timely intra-arterial revascularization procedures. Class I; LOE C-EO. **3.7. Mechanical Thrombectomy** **3.7.1. Concomitant with IV Alteplase** 1. Patients eligible for IV alteplase should receive IV alteplase even if EVTs are being considered. Class I; LOE A. 2. In patients under consideration for mechanical thrombectomy, observation after IV alteplase to assess for clinical response should not be performed. Class III: Harm; LOE B-R. **3.7.2. 0 to 6 Hours from Onset** 1. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset. Class I: LOE A. 3. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the MCA segment 2 (M2) or MCA segment 3 (M3) portion of the MCAs. Class IIb; LOE B-R. 5. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries. **3.7.3. 6 to 24 Hours from Onset** 1. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended. Class I; LOE A 2. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable. Class IIa; B-R. **3.7.4. Technique** 1. Use of stent retrievers is indicated in preference to the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) device. Class I; LOE A 2. The technical goal of the thrombectomy procedure should be reperfusion to a modified Thrombolysis in Cerebral Infarction (mTICI) grade 2b/3 angiographic result to maximize the probability of a good functional clinical outcome. Class I; LOE A

Guideline	Recommendations
	5. It is reasonable to select an anesthetic technique during EVT for AIS on the basis of individualized assessment of patient risk factors, technical performance of the procedure, and other clinical characteristics. Class IIa; LOE B-R
Eskey CJ, Meyers PM, Nguyen TN, Ansari SA, Jayaraman M, McDougall CG, et al. **American Heart Association Council on Cardiovascular Radiology and Intervention and Stroke Council. Indications for the performance of intracranial endovascular neurointerventional procedures: A Scientific Statement from the American Heart Association.** ***Circulation* 2018;137:e661–e689.** **(selected)**	1. Observing patients after intravenous r-tPA to assess for clinical response before pursuing endovascular therapy is not required to achieve beneficial outcomes and is not recommended. 6. If endovascular therapy is contemplated, a noninvasive intracranial vascular study is strongly recommended during the initial imaging evaluation of the patient with acute stroke but should not delay intravenous r-tPA if indicated. For patients who qualify for intravenous r-tPA according to guidelines from professional medical societies, initiating intravenous r-tPA before noninvasive vascular imaging is recommended for patients who have not had noninvasive vascular imaging as part of their initial imaging assessment for stroke. Noninvasive intracranial vascular imaging should then be obtained as quickly as possible. 9. Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1, (2) AIS receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies, (3) causative occlusion of the ICA or proximal MCA (M1), (4) age ≥18 years, (5) NIHSS score of ≥6, (6) ASPECTS of ≥6, and (7) ability to initiate treatment (groin puncture) within 6 hours of symptom onset.
Stroke Foundation. Clinical Guidelines for Stroke Management 2017. Melbourne Australia (Part 3)	Strong recommendation New For patients with ischaemic stroke caused by a large vessel occlusion in the internal carotid artery, proximal cerebral artery (M1 segment), or with tandem occlusion of both the cervical carotid and intracranial arteries, endovascular thrombectomy should be undertaken when the procedure can be commenced within six hours of stroke onset. Strong recommendation New Eligible stroke patients should receive intravenous thrombolysis while concurrently arranging endovascular thrombectomy, with neither treatment delaying the other. Strong recommendation New In selected stroke patients with occlusion of the basilar artery, endovascular thrombectomy should be undertaken.
Papanagiotou P, Ntaios G, Papavasileiou V, Psychogios K, Psychogios M, Mpotsaris A, Rizos T, Spengos K, Gravanis M, Vassilopoulou S, Gkogkas C. **Recommendations for Mechanical Thrombectomy in Patients with Acute Ischemic Stroke. A Clinical Guide by the Hellenic Stroke Organization.** ***Clin Neuroradiol* 2018; Mar;28(1):145-151.**	1. In patients with significant neurological symptoms due to an ischemic stroke with occlusion of a large vessel of the anterior cerebral circulation, we recommend endovascular treatment (EVT) with mechanical thrombectomy in the first 6 h after the onset of the symptoms (1A). Coexistence of ipsilateral extracranial carotid artery disease is not a contraindication (2B). Beyond the 6-h window, we recommend EVT for selected patients (1A). If no contraindications exist, we recommend that patients are firstly treated with intravenous thrombolysis with alteplase, provided that alteplase can be administered within 4.5 h after the onset of symptoms (1A). 2. Patients who are eligible for intravenous thrombolysis should receive alteplase, even if EVT is planned. The EVT should not delay the administration of alteplase, and vice versa, the administration of alteplase should not delay EVT. If the patient is a candidate for mechanical thrombectomy, we do not recommend waiting for clinical improvement after administration of alteplase (1A). 3. Patients who, based on the clinical setting, are candidates for EVT should be assessed with urgent intracranial computed tomography (CT) angiography or magnetic resonance angiography (1A). Furthermore, in patients who,

Guideline	Recommendations
	based on the clinical setting, are candidates for EVT within the 6–24 h window, we recommended magnetic resonance imaging diffusion-weighted imaging (MRI-DWI) or perfusion CT to select the most suitable patients (1A). 4. In cases where intravenous thrombolysis with alteplase is contraindicated, we recommend mechanical thrombectomy as a first-line therapy for patients with acute occlusion of a large vessel of the anterior cerebral circulation (1B). 5. When there is an indication for mechanical thrombectomy, we recommend that EVT should be performed immediately without any delay, given that the time period from the onset of symptoms to recanalization is significantly correlated with the patient's clinical outcome (1A). 6. Mechanical thrombectomy should aim to achieve TICI (Thrombolysis in Cerebral Infarction) reperfusion grade 2b/3 (1A). 7. We recommend the use of stent-retriever devices or aspiration catheters to perform mechanical thrombectomy (1A) 8. Mechanical thrombectomy can be performed with the patient either under general anesthesia or conscious sedation. Due to the absence of strong evidence in favor of one of these approaches, the final decision should be made on clinical judgment (2B). 9. We recommend the establishment of specialized units that can provide urgent stroke diagnosis and treatment, as well as recruitment of sufficient, specialized and dedicated medical, nursing and paramedical personnel. These centers should offer 24/7 availability of intravenous thrombolysis with alteplase and EVT (1A). 10. In the case of acute occlusion of a large vessel of the anterior cerebral circulation in a patient that has an indication for EVT in a hospital that does not offer this treatment option, we recommend to transfer the patient immediately after intravenous thrombolysis to a center where mechanical thrombectomy can be performed (2B).
Fiehler J, Cognard C, Gallitelli M et al. **European recommendations on organisation of interventional care in acute stroke (EROICAS)** ***Eur Stroke J 2016*; 1(3): 155–170.** **(selected Q1 &Q2/Q14)**	1. What service organization is associated with favorable outcome after thrombectomy? Services should demonstrate established organization at the center to support rapidly instituted IV rtPA use, team organization of a level sufficient to support clinical trial participation, a process for monitoring door-to-needle/ groin puncture, and procedural duration times, and a governance process to ensure that these are reviewed (Quality of evidence: moderate, Strength of recommendation: strong). Services should include a neuroradiological/radiological department with experience with acute CT/ MR interpretation including ASPECTS, and experience with CTA in acute stroke patients as a minimum additional imaging modality (Quality of evidence: Moderate, Strength of recommendation: Strong). Operators and services should conform to minimum requirements for training, certification, caseload and ongoing education for acute neurovascular procedures by national/European neurointerventional/ radiological organizations and national statutory bodies (Quality of evidence: Moderate, Strength of recommendation: Strong). 2. What operator characteristics are associated with favorable outcome after thrombectomy?

Guideline	Recommendations
	Thrombectomies should be performed by physicians competent in intracranial endovascular procedures. Competence in Interventional neurovascular procedures is based on: – Proven capacity to perform, conduct, and interpret standard diagnostic Neuroradiology (CT, MR, multimodal-imaging) for appropriate case selection. – Proven capacity to perform, conduct, and interpret standard intracranial endovascular procedures as well as management skills for procedural complications. – Skills in interdisciplinary management of hemorrhagic and ischemic stroke patients with stroke physicians or neurologists/neurosurgeons in stroke centers. Treatment in the context of an acute stroke unit is an option in geographically remote regions. – Meeting the minimum requirements for training, certification, caseload, and ongoing education for acute neurovascular procedures by national/European neurointerventional/radiological organizations and national statutory bodies (e.g. certification by a European or National Certificate/Diploma/Master). – Continuous updating of the interventional neuroradiology (INR) diagnostic and therapeutic methods and skills. (Quality of evidence: Moderate, Strength of recommendation: Strong).
Wahlgren N, Moreira T, Michel P et al. **Mechanical thrombectomy in acute ischemic stroke: Consensus statement by ESO-Karolinska Stroke Update 2014/2015, supported by ESO, ESMINT, ESNR and EAN.** ***Int J Stroke* 2016;11(1):134-147.** **(selected)**	Mechanical thrombectomy, in addition to intravenous thrombolysis within 4.5 h when eligible, is recommended to treat acute stroke patients with large artery occlusions in the anterior circulation up to 6 h after symptom onset (Grade A, Level 1a, KSU Grade A). – new. Mechanical thrombectomy should not prevent the initiation of intravenous thrombolysis where this is indicated, and intravenous thrombolysis should not delay mechanical thrombectomy (Grade A, Level 1a, KSU Grade A). – changed. Mechanical thrombectomy should be performed as soon as possible after its indication (Grade A, Level 1a, KSU Grade A). For mechanical thrombectomy, stent retrievers approved by local health authorities should primarily be considered (Grade A, Level 1a, KSU Grade A). – new. Other thrombectomy or aspiration devices approved by local health authorities may be used upon the neurointerventionists discretion if rapid, complete and safe revascularisation of the target vessel can be achieved (Grade C, Level 2a, KSU Grade C) – new. If intravenous thrombolysis is contraindicated (e.g. Warfarin-treated with therapeutic INR) mechanical thrombectomy is recommended as first-line treatment in large vessel occlusions (Grade A, Level 1a, KSU Grade A) – changed and updated level of evidence. Patients with acute basilar artery occlusion should be evaluated in centres with multimodal imaging and treated with mechanical thrombectomy in addition to intravenous thrombolysis when indicated (Grade C, Level 4, KSU Grade C); alternatively they may be treated within a randomized controlled trial for thrombectomy approved by the local ethical committee – new. The decision to undertake mechanical thrombectomy should be made jointly by a multidisciplinary team comprising at least a stroke physician and a neurointerventionist and performed in experienced centres providing comprehensive stroke care and expertise in neuroanaesthesiology (Grade C, Level 5, GCP, KSU Grade C). Mechanical thrombectomy should be performed by a trained and experienced neurointerventionist who meets national and/or international requirements (Grade B, Level 2b, KSU Grade B) – changed in level of evidence.
Lavine SD, Cockroft K, Hoh B, et al.	**Physician qualifications** Baseline training and qualifications:

Guideline	Recommendations
Training guidelines for endovascular stroke intervention: an international multi-society consensus document. ***Neuroradiology* 2016; 58: 537-541.**	1. Residency training (in radiology, neurology or neurosurgery) which should include documented training in the diagnosis and management of acute stroke, the interpretation of cerebral arteriography and neuroimaging under the supervision of a board-certified neuroradiologist, neurologist or neurosurgeon with subsequent board eligibility or certification. The residency program and supervising physicians should be accredited according to national standards as they pertain to the countries involved. Those physicians who did not have adequate such training during their residencies must spend an additional period (typically one year) by training in clinical neurosciences and neuroimaging, focusing on the diagnosis and management of acute stroke, the interpretation of cerebral arteriography and neuroimaging prior to their fellowship in neuroendovascular interventions. AND 2. Dedicated training in Interventional Neuroradiology (also termed Endovascular Neurosurgery or Interventional Neurology) under the direction of a Neurointerventionalist (with neuroradiology, neurology or neurosurgical training background), at a high-volume center. It is preferred that this is a dedicated year, which occurs after graduating from residency (i.e., a fellowship). A training program accredited by a national accrediting body is also strongly preferred but not required. Published standards exist for various countries [15–21]. Within these programs, specific training for intraarterial therapy for acute ischemic stroke should be performed, including obtaining appropriate access even in challenging anatomy, microcatheter navigation in the cerebral circulation, knowledge, and training of the use of stroke specific devices and complication avoidance and management. **Maintenance of physician qualifications:** Outcomes should be tracked and recorded. While threshold levels for recanalization, complication rates, etc. have yet to be established, we suggest the following as a minimum: 1. Successful recanalization (modified TICI 2b or 3) in at least 60 % of cases. 2. Embolization to new territory of less than 15 % 3. Symptomatic intracranial hemorrhage (i.e., parenchymal hematoma on imaging with clinical deterioration) rate less than 10 %. **Hospital requirements:** We feel it is critical that the patients be treated in a center, which has 24/7 access to the following: 1. Angiography suites suitably equipped to handle these patients, as well as equipment and capability to handle the complications. 2. Dedicated stroke and intensive care units (preferably dedicated neuro-intensive care unit), staffed by physicians with specific training in those fields. 3. Vascular neurology and Neurocritical care expertise. 4. Neurosurgery expertise, including vascular neurosurgery. 5. All relevant neuroimaging modalities (CT/CTA, MR/ MRA, Trans-cranial Doppler [TCD]), including 24/7 access to CT and MRI.
Intercollegiate Stroke Working Party. Royal College of Physicians. National Clinical guidelines for stroke. 5th Edition 2016, Edinburgh, Scotland	Patients with acute ischaemic stroke and a contraindication to intravenous thrombolysis but not to thrombectomy should be considered for intra-arterial clot extraction (using stent retriever and/or aspiration techniques) if they have a proximal intracranial large vessel occlusion causing a disabling neurological deficit (National Institutes of Health Stroke Scale [NIHSS] score of 6 or more) and the procedure can begin (arterial puncture) within 5 hours of known onset.

Guideline	Recommendations
	Patients with acute ischaemic stroke causing a disabling neurological deficit (a National Institutes of Health Stroke Scale [NIHSS] score of 6 or more) may be considered for intraarterial clot extraction (using stent retriever and/or aspiration techniques, with prior intravenous thrombolysis unless contraindicated) beyond an onset-to-arterial puncture time of 5 hours if: – the large artery occlusion is in the posterior circulation, in which case treatment up to 24 hours after onset may be appropriate; – a favourable profile on salvageable brain tissue imaging has been proven, in which case treatment up to 12 hours after onset may be appropriate. Hyperacute stroke services providing endovascular therapy should participate in national stroke audit to enable comparison of the clinical and organisational quality of their services with national data, and use the findings to plan and deliver service improvements.
Powers WJ, Derdeyn CP, Biller J et al. **2015 AHA/ASA Focused Update of the 2013 Guidelines for the Early Management of Patients with Acute Ischemic Stroke Regarding Endovascular Treatment: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association.** ***Stroke* 2015;46:3024-3039.**	1. Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria (Class I; Level of Evidence A). (New recommendation): (a) prestroke mRS score 0 to 1, (b) acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies, (c) causative occlusion of the internal carotid artery or proximal MCA (M1), (d) age ≥18 years, (e) NIHSS score of ≥6, (f) ASPECTS of ≥6, and (g) treatment can be initiated (groin puncture) within 6 hours of symptom onset 2. As with intravenous r-tPA, reduced time from symptom onset to reperfusion with endovascular therapies is highly associated with better clinical outcomes. To ensure benefit, reperfusion to TICI grade 2b/3 should be achieved as early as possible and within 6 hours of stroke onset (Class I; Level of Evidence B-R). (Revised from the 2013 guideline) 3. When treatment is initiated beyond 6 hours from symptom onset, the effectiveness of endovascular therapy is uncertain for patients with acute ischemic stroke who have causative occlusion of the internal carotid artery or proximal MCA (M1) (Class IIb; Level of Evidence C). Additional randomized trial data are needed. (New recommendation) 4. In carefully selected patients with anterior circulation occlusion who have contraindications to intravenous r-tPA, endovascular therapy with stent retrievers completed within 6 hours of stroke onset is reasonable (Class IIa; Level of Evidence C). There are inadequate data available at this time to determine the clinical efficacy of endovascular therapy with stent retrievers for those patients whose contraindications are time-based or nontime based (eg, prior stroke, serious head trauma, hemorrhagic coagulopathy, or receiving anticoagulant medications). (New recommendation) 5. Although the benefits are uncertain, use of endovascular therapy with stent retrievers may be reasonable for carefully selected patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the M2 or M3 portion of the MCAs, anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries (Class IIb; Level of Evidence C). (New recommendation) 6. Endovascular therapy with stent retrievers may be reasonable for some patients <18 years of age with acute ischemic stroke who have demonstrated large vessel occlusion in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset, but the benefits are not established in this age group (Class IIb; Level of Evidence C). (New recommendation)

Guideline	Recommendations
	7. Although the benefits are uncertain, use of endovascular therapy with stent retrievers may be reasonable for patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score of >1, ASPECTS <6, or NIHSS score <6 and causative occlusion of the internal carotid artery or proximal MCA (M1) (Class IIb; Level of Evidence B-R). Additional randomized trial data are needed. (New recommendation) 8. Observing patients after intravenous r-tPA to assess for clinical response before pursuing endovascular therapy is not required to achieve beneficial outcomes and is not recommended. (Class III; Level of Evidence B-R). (New recommendation) 9. Use of stent retrievers is indicated in preference to the MERCI device. (Class I; Level of Evidence A). The use of mechanical thrombectomy devices other than stent retrievers may be reasonable in some circumstances (Class IIb, Level B-NR). (New recommendation) 10. The use of proximal balloon guide catheter or a large bore distal access catheter rather than a cervical guide catheter alone in conjunction with stent retrievers may be beneficial (Class IIa; Level of Evidence C). Future studies should examine which systems provide the highest recanalization rates with the lowest risk for nontarget embolization. (New recommendation) 11. The technical goal of the thrombectomy procedure should be a TICI 2b/3 angiographic result to maximize the probability of a good functional clinical outcome (Class I; Level of Evidence A). Use of salvage technical adjuncts including intra-arterial fibrinolysis may be reasonable to achieve these angiographic results, if completed within 6 hours of symptom onset (Class IIb; Level of Evidence B-R).(New recommendation) 12. Angioplasty and stenting of proximal cervical atherosclerotic stenosis or complete occlusion at the time of thrombectomy may be considered but the usefulness is unknown (Class IIb; Level of Evidence C). Future randomized studies are needed. 13. Initial treatment with intra-arterial fibrinolysis is beneficial for carefully selected patients with major ischemic strokes of <6 hours' duration caused by occlusions of the MCA (Class I; Level of Evidence B-R). However, these data derive from clinical trials that no longer reflect current practice, including use of fibrinolytic drugs that are not available. A clinically beneficial dose of intra-arterial r-tPA is not established, and r-tPA does not have FDA approval for intra-arterial use. As a consequence, endovascular therapy with stent retrievers is recommended over intra-arterial fibrinolysis as first-line therapy (Class I; Level of Evidence E). (Revised from the 2013 guideline) 14. Intra-arterial fibrinolysis initiated within 6 hours of stroke onset in carefully selected patients who have contraindications to the use of intravenous r-tPA might be considered, but the consequences are unknown (Class IIb; Level of Evidence C). (Revised from 2013 guideline) 15. It might be reasonable to favor conscious sedation over general anesthesia during endovascular therapy for acute ischemic stroke. However, the ultimate selection of anesthetic technique during endovascular therapy for acute ischemic stroke should be individualized based on patient risk factors, tolerance of the procedure, and other clinical characteristics. Randomized trial data are needed (Class IIb; Level of Evidence C). (New recommendation) **Imaging** 1. If endovascular therapy is contemplated, a noninvasive intracranial vascular study is strongly recommended during the initial imaging evaluation of the acute stroke patient but should not delay intravenous r-tPA if indicated.

Guideline	Recommendations
	For patients who qualify for intravenous r-tPA according to guidelines from professional medical societies, initiating intravenous rtPA before noninvasive vascular imaging is recommended for patients who have not had noninvasive vascular imaging as part of their initial imaging assessment for stroke. Noninvasive intracranial vascular imaging should then be obtained as quickly as possible (Class I; Level of Evidence A). (New recommendation) 2. The benefits of additional imaging beyond CT and CTA or MR and MRA, such as CT perfusion or diffusion- and perfusion-weighted imaging, for selecting patients for endovascular therapy are unknown (Class IIb; Level of Evidence C). Further randomized, controlled trials may be helpful to determine whether advanced imaging paradigms employing CT perfusion, CTA, and MRI perfusion and diffusion imaging, including measures of infarct core, collateral flow status, and penumbra, are beneficial for selecting patients for acute reperfusion therapy who are within 6 hours of symptom onset and have an ASPECTS <6. Further randomized, controlled trials should be done to determine whether advanced imaging paradigms using CT perfusion and MRI perfusion, CTA, and diffusion imaging, including measures of infarct core, collateral flow status, and penumbra, are beneficial for selecting patients for acute reperfusion therapy who are beyond 6 hours from symptom onset. (New recommendation)
Toni D, Mangiafico S, Agostoni E, Bergui M, Cerrato P, Ciccone A, Vallone S, Zini A. and Inzitari D. **Intravenous thrombolysis and intra-arterial interventions in acute ischemic stroke: Italian Stroke Organisation (ISO)-SPREAD guidelines.** ***Int J Stroke* 2015;10:1119–1129**	In patients eligible for IVT, intra-arterial reperfusion treatments are not recommended as an alternative. Grade A The techniques of mechanical thrombectomy are recommended within six-hours of stroke onset in patients with occlusion of ICA terminus, middle cerebral artery M1–M2, or anterior cerebral artery A1 who do not respond to or cannot be treated with IVT. Grade B. The techniques of mechanical thrombectomy are recommended within six-hours of stroke onset in patients with occlusion of vertebral artery, basilar artery, or posterior cerebral artery P1 who do not respond to or cannot be treated with IVT. Good practice point.
Alonso de LM, Egido JA, Casado I et al. **Representing the ad hoc committee of the SEN (Sociedad Española de Neurología) Study Group for Cerebrovascular Diseases: Guidelines for the treatment of acute ischaemic stroke.** ***Neurologia* 2014;29(2):102-122.**	Intra-arterial thrombolysis may be useful in patients with large-vessel occlusion stroke, and who are not candidates for intravenous thrombolysis, until 6 hours post-infarct (level of evidence 1b; grade B recommendation). The utility of combined intra-arterial and intravenous treatment has not yet been established, but it may be an option for patients presenting large vessel occlusion who do not respond to intravenous treatment (evidence level 2b; grade B recommendation). Mechanical thrombolysis may be useful until 8 hours post-stroke in patients who are not candidates for intravenous thrombolysis or who have experienced treatment failure (level of evidence 1b; grade B recommendation). At present, endovascular treatment is only recommended when performed in centres with SUs and experience in neurointervention. Ideally, this procedure is performed according to a case registry or clinical study protocol (level of evidence 5; grade D recommendation).
Talke PO, Sharma D, Heyer EJ, et al. **Society for Neuroscience in Anesthesiology and Critical Care Expert Consensus Statement: Anesthetic Management of**	We recommend that the choice of anesthetic technique and pharmacological agents should be individualized based on clinical characteristics of each patient, in close communication with the neurointerventionalist. GA may be preferable in uncooperative or agitated patients or patients with elevated neurological severity who cannot protect their airway (most patients with posterior circulation stroke, depressed level of consciousness, respiratory compromise) (class IIa, level of evidence B).

Guideline	Recommendations
Endovascular Treatment for Acute Ischemic Stroke*Endorsed by the Society of NeuroInterventional Surgery and the Neurocritical Care Society. ***Journal of Neurosurgical Anesthesiology* 2014;26(2):95-108.** **(selected)**	Local anesthesia with sedation and GA are feasible options for patients with anterior circulation stroke who can protect their airway and are cooperative (class IIa, level of evidence B). In all patients receiving local anesthesia with sedation, the anesthesia provider should be prepared to rapidly convert to GA if needed (class IIa, level of evidence C). If GA is chosen, standardized protocols for early postprocedural neurological assessment and extubation should be used to minimize the postextubation risks. There is no recommendation on a specific pharmacologic agent or combination for the provision of sedation or GA. Anesthesia-related procedures should be done as quickly as possible to avoid delay in endovascular treatment.
Minematsu K, Toyoda K, Hirano T et al. **Guidelines for the intravenous application of recombinant tissue-type plasminogen activator (alteplase), the second edition, October 2012: a guideline from the Japan Stroke Society.** ***J Stroke Cerebrovasc Dis* 2013;22(5):571-600.**	It is not recommended to give priority to endovascular therapy over IV alteplase if patients are eligible for the latter (level of evidence IIa; grade of recommendation C2). Local fibrinolytic therapy with urokinase within 6 hours of symptom onset can improve outcomes of MCA occlusion (level of evidence Ia; grade of recommendation B). Mechanical recanalization within 8 hours of symptom onset has been approved for use only in patients who are ineligible for or failed IV alteplase; however, it should be noted that its efficacy and safety are still under review (level of evidence IIa; grade of recommendation C1). Other endovascular therapies have no proven efficacy and safety and therefore should be used only for clinical research purposes (level of evidence IIa; grade of recommendation C1)
Martins SC, Freitas GR, Pontes-Neto OM et al. and Executive Committee from the Brazilian Stroke Society and the Scientific Department Guidelines for acute ischemic stroke treatment: part II: stroke treatment. ***Arq Neuropsiquiatr* 2012;70(11):885-893.**	Although the use of the MERCI device is an acceptable intervention for removal of intra-arterial thrombus in patients carefully selected, its effectiveness in improving prognosis after stroke is still uncertain (Level of Evidence 2, Class B Recommendation). Further clinical trials of this device are required before its role in the emergency management of stroke can be defined.

Evidence Tables

Major Trials

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Mechanical Thrombectomy vs. Best Medical Management (+/- t-PA)					
Bendszus et al. 2019 **NCT03094715** ***Efficacy and Safety of Thrombectomy in Stroke with Extended Lesion and Extended Time Window (TENSION)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	714 patients (maximum planned) aged 18-80 years, with moderate to severe acute ischemic stroke (NIHSS <26), eligible for endovascular therapy, with occlusion of the M1 segment of the MCA and/or the intracranial segment of the distal ICA, with an ASPECT score of 3–5 and in whom treatment can be accomplished within 12 h after stroke onset	Patients are randomized 1:1 to received best medical management (+/- thrombolysis) plus endovascular therapy or best medical management only	**Primary outcome:** Shift in mRS scores at 90 days **Secondary outcome:** Independence (mRS 0-2) at 90 days, death or dependency (mRS 4–6) at 90 days, sICH, adverse events, health-related QoL (PROMIS-10, EQ-5D) ay 90 days, poststroke depression (PHQ) at 90 days, and costs utility assessment	TBA Estimated completion date is September 30, 2024
ISRCTN 19922220 ***Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in The Netherlands for Late arrivals: (MR CLEAN-LATE)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	500 adult patients (planned) with acute ischemic stroke, eligible for endovascular therapy, which can be initiated (groin puncture) between 6 and 24 hours after symptom onset or last seen well < 24 hours including wake-up strokes.	Patients are randomized to received best medical management (+/- thrombolysis) plus endovascular therapy or best medical management only	**Primary outcome:** mRS scores at 90 days **Secondary outcome:** Mortality at 90 days, recanalization at 24 hours, infarct size at 5-7 days or just before discharge, sICH at 24 hours, and 5-7 days after randomization, NIHSS score at 24 hours and 5-7 days after randomization	TBA Trial is expected to run until November 2022

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Yoshimura et al. 2022 **Japan** **RCT** ***Recovery by Endovascular Salvage for Cerebral Ultra-acute Embolism Japan Large IscheMIc core Trial (RESCUE-Japan LIMIT***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒	203 patients ≥18 years, recruited from 41 centres with acute, sizable, large vessel occlusion stroke (ASPECTs score of 3-5) and NIHSS score of ≥6 and a premorbid mRS score of 0-1. Mean age was 76 years, 56% were men. Median baseline NIHSS score was 22. 25% of patients had a previous stroke.	Patients were randomized (1:1) to receive endovascular therapy (EVT) with medical care or medical care alone within 6 hours after they were last known to be well or within 24 hours if there was no early change on fluid-attenuated inversion recovery images. Alteplase (0.6 mg per kilogram of body weight) was used when appropriate in both groups.	**Primary outcome:** mRS score of 0-3 at 90 days **Secondary outcomes:** mRS score of 0-1 and 0-2 at 90 days, ordinal shift analysis of mRS scores at 90 days, improvement of ≥8 points in NIHSS score at 48 hours **Safety outcomes:** sICH at 48 hours, any ICH at 48 hours, death within 90 days	94 patients in each group were included in the per-protocol analysis 27% of patients in both groups received alteplase. A significantly higher percentage of patients in the EVT group had a mRS score of 0-3 at 90 days (31% vs. 12.7%, RR=2.43, 95% CI 1.35–4.37). There were no significant differences between groups in the percentage of patients with mRS scores of 0-1 or 0-2 at 90 days (14.0% vs. 6.9% and 5.0% vs. 2.9%, respectively). There was a positive shift in the ordinal analysis of mRS scores favouring the EVT group (common OR=2.42, 95% CI 1.46–4.01). Significantly more patients in the EVT group experienced neurological improvement at 48 hours (31.0% vs. 8.8%, RR=3.51, 95% CI 1.76–7.00). There were no significant differences between groups for any of the safety outcomes with one exception. The risk of any ICH was significantly higher in the EVT group (58.0% vs. 31.4%, RR=1.85, 95% CI 1.33–2.58).
Mocco et al. 2022 **USA** **RCT** ***PerfusiOn Imaging Selection of Ischemic STroke Patients for EndoVascular ThErapyPOSITIVE Stroke Clinical Trial (POSITIVE)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	750 patients (estimated), aged 18-80 years, with premorbid mRS ≤1, NIHSS ≥8, large vessel proximal occlusion, with evidence of salvageable brain tissue on CT perfusion imaging, presenting within 12 hours of onset of symptoms. Patients who were eligible for IV-tPA therapy were excluded.	Patients were randomized to receive endovascular mechanical thrombectomy (using aspiration or a stent retriever, separately or in combination) or best medical management.	**Primary outcome:** Shift in mRS scores at day 90 **Secondary outcomes:** Distribution of mRS scores according to treatment cohorts (0-8 hours and 0-12 hours) at 90 days, 30 and 90-day mortality, good functional outcome (mRS 0-2) at 90 days), symptomatic ICH and serious adverse events at 90 days.	The trial suspended enrollment with the release of results from the DAWN trial and was stopped after the release of the DEFUSE 3 trial results. 33 patients had been enrolled at the time of suspension.
Albers et al.	Concealed	182 patients, aged 18-90	Patients were randomized to	**Primary outcome:**	Trial was stopped early due to efficacy (476

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
2018, Lansberg et al. 2019, Sarraj et al. 2019, Tate et al. 2019 **USA** **RCT** ***DEFUSE 3***	Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	years, recruited from 38 centres, last been known to be well 6-16 hours earlier, with ICA or MCA-M1 occlusion, and an initial infarct volume <70 ml, a ratio of volume of ischemic tissue to initial infarct volume ≥ 1.8 more, and an absolute volume of potentially reversible ischemia (penumbra) ≥ 15 ml and baseline NIHSS ≥6. Median age was 70.5 years, 50.5% were men. Baseline NIHSS score was 16. Median ASPECTS score was 8. Median time from stroke onset to randomization was 10 h 50 min.	treatment with thrombectomy using an FDA-approved device + medical management (n=92) or medical management alone (n=90).	Distribution of mRS scores at 90 days **Secondary outcome:** Functional independence at 90 days (mRS 0-2) **Primary safety outcomes:** Death within 90 days, sICH at 36 hours **Imaging outcomes:** Infarct volume at 24 hours, lesion growth, reperfusion at 24 hours,	maximum planned). 11% (thrombectomy) and 9% (medical management) of patients were treated with iv. t-PA. The distribution of mRS scores was more favourable for patients in the endovascular group at 90 days (unadjusted common OR=2.77, 95% CI 1.63- 4.70, p<0.001). A significantly higher proportion of patients in the thrombectomy group was independent at 90 days (45% vs. 17%; RR=2.67, 95% CI 1.60-4.48, p<0.001). Mortality at 90 days was 14% for patients in the endovascular group vs. 26% for patients in medical management group (p=0.05). The risks of sICH, early neurological deterioration and parenchymal hematoma type 2 were similar between group (7% vs. 4%, p=0.75; 9% vs. 12%, p=0.44; and 9% vs. 3%, p=0.21, respectively) Median infarct volume and growth at 24 hours were not significantly different: 35 vs. 41 mL, p=0.19 and 23 vs. 33 mL, p=0.08, respectively. Complete recanalization 24 hours was achieved in a significantly higher proportion of patients in the endovascular group (78% vs. 18%, p<0.001). There were 2 procedure-related complications in the thrombectomy group. Serious adverse reactions were reported for 45% of patients in the thrombectomy group vs. 53% in the medical management group (p=0.18). General anesthesia was used in 26% of patients. No differences were found between groups in sub-group analysis (time from stroke to randomization,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					volume of ischemic core, baseline NIHSS, age, sex, ASPECTS, site of occlusion, baseline imaging, atrial fibrillation). **Secondary analysis (Lansberg et al. 2019)** The common OR for improved functional outcome with endovascular therapy, adjusted for age, NIHSS score, and serum glucose was 3.1 (95% CI, 1.8-5.4). There was no interaction between treatment and time to randomization, age, or baseline stroke severity at time of randomization. **Secondary analysis (Sarraj et al. 2019)** Of the 182 patients randomized, 61 were transferred directly to the study site and 121 were transferred from another facility. All outcomes were similar between direct and transfer groups (primary outcome, functional independence, reperfusion, mortality, spontaneous ICH **Secondary analysis (Tate et al. 2019)** Among the 167 patients who did not die during acute hospitalization, median length of hospital stay was significantly shorter in the endovascular group (6.5 vs. 9.1 days, p<0.001). Median time at home during the first 90 days was significantly greater in the endovascular group (55 vs. 0 days, p<0.001). The endovascular group had more favorable living situations at time of discharge, 30 days and 90 days poststroke (all p<0.001).
Nogueira et al. 2018, Jadhav et al. 2019 **USA** **RCT**	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑	206 patients, recruited from 26 centres, ≥18 years with ischemic stroke, last been known to be well 6 to 24 hours earlier, with no previous disability (mRS 0-1) who	Patients were randomized to treatment with thrombectomy with Trevo device + medical management (n=107) or medical management alone (n=99).	**Primary outcomes:** Utility-weighted mRS score and functional independence (mRS 0-2) at 90 days, **Secondary outcomes:**	Trial was terminated early at 31 months (500 maximum planned) after interim analysis when efficacy of thrombectomy was established. The median interval between the time that a patient was last known to be well and randomization was 12.2 hours in the thrombectomy group and 13.3

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
DAWN	ITT: ☑	had either failed IV t-PA therapy (defined as a confirmed persistent occlusion 60 min after administration), or those persons for whom IV t-PA administration was contraindicated, because of late presentation. Imaging criteria: < 1/3 MCA territory involved, occlusion of the intracranial ICA and/or MCA-M1 on MRA or CTA Clinical Imaging criteria: Mismatch (CIM) defined as one of the following on MR-DWI or CTP-rCBF maps: 0-<21 cc core infarct and NIHSS ≥ 10 (and age ≥ 80 years old); 0-<31 cc core infarct and NIHSS ≥ 10 (and age < 80 years old); 31 cc to <51 cc core infarct and NIHSS ≥ 20 (and age < 80 years old). Mean age was 70.0 years, 45% were men. Median baseline NIHSS score was 17.		Early response (day 5-7 or discharge (whichever is earlier), defined as a NIHSS score decrease of ≥10 from baseline or NIHSS score 0 or 1, stroke-related 90-day mortality and all-cause 90-day mortality.	hours in the control group. The median interval between the time the patient was last known to be well and reperfusion was 13.6 hours The mean UW-mRS score was significantly higher in the thrombectomy group (5.5 vs. 3.4, adj difference =2.0, 95% Cr I 1.1-3.0, prob of superiority >0.999). There were no interactions in subgroup analysis (mismatch criteria, sex, age, baseline NIHSS score, occlusion site, interval between time that patient was last known to be well and randomization and type of stroke onset). A significantly higher proportion of patients in the thrombectomy group were independent at 90 days (49% vs. 13%, adj difference= 33, 95% Cred I 21–44, prob of superiority >0.999). A significantly higher proportion of patients in the thrombectomy group experienced an early response and had achieved recanalization at 24 hr (48% vs. 19%, RR=3.0, 95% CI 2-4, p<0.001 and 77% vs. 39%, RR=2.0, 95% CI 2-4, p<0.001, respectively). Median infarct volume was significantly lower at 24 hours post treatment in the thrombectomy group (8 vs. 22 mL, p<0.001). There were no significant differences between groups in the proportions of patients with stroke-related deaths, or all-cause mortality at 90 days (16% vs. 18%, and 19% vs. 18%, respectively). There was no significant difference between groups in the proportion of patients with symptomatic ICH at 24 hours (65 vs. 3%). *Jadhav et al. 2019 (mode of onset)* Modes of onset were wake-up stroke (55.3%, n=114), witnessed onset (12.1%, n=25), and unwitnessed onset (32.5%, n=67) with median times last seen well to randomization of 13.4±3.7,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					10.0±3.7, and 14.1±4.9 hours, respectively. The benefit of thrombectomy was similar across groups, compared with best medical management. The proportions of patients with mRS score of 0-2 at 90 days were: 49.3% vs.10.6% (wake up stroke), 63.6% vs. 21.4% (witnessed onset), and 41.4% vs. 13.2% (unwitnessed stroke). P for interaction=0.79)
Muir et al. 2017 **USA** **RCT** ***PISTE***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	65 patients ≥18 years, with occlusion of the intracranial ICA, M1 segment of the MCA or a single M2 MCA branch, who were eligible to receive intravenous t-PA, started within 4.5 hours of symptom onset. Mean age was 65.5 years, 45% were men.	Patients were to receive best medical therapy with IVT alone (n=32), or to undergo additional (adjunctive) mechanical thrombectomy (MT) with any approved device (n=33), performed by an experienced operator, without delay following t-PA.	**Primary outcome:** Independence (mRS score 0-2) at 90 days **Secondary outcomes:** Excellent recovery (mRS score 0–1), change in the distribution of scores on the mRS; early major neurological improvement (improvement by ≥8 points on the NIHSS or NIHSS of 0 or 1 at 24 hours after stroke)	Trial recruitment was suspended in prematurely, following presentation of other relevant thrombectomy trial results. In ITT analysis, the odds of the primary outcome were not increased significantly for the MT group (51% vs. 40%, adj OR=2.12, 95% CI 0.65- 6.94, p=0.204). The odds were significantly increased in the per protocol analysis (57% vs 35%, OR=4.92, 95% CI 1.23 to 19.69, p=0.021). In ITT analysis, the odds of achieving an excellent outcome were significantly increased for the MT group (OR= 7.63, 95% CI 1.56-37.22, p=0.010). There was no significant difference between groups in the distribution of mRS scores at 90 days.MT was not associated with a significantly increased risk of early neurological improvement, death of symptomatic ICH
Jovin et al. 2015 **Dávalos et al. 2017 (1-year follow-up)** **Spain** **RCT** ***REVASCAT***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	206 patients aged 18-80 years, with premorbid mRS score ≤1, baseline NIHSS score ≥6, ischemic stroke attributable to an occlusion of the internal carotid or proximal MCA (M1) arteries who could be treated within 8 hours of stroke onset. Mean age was 66 years, 55% were male. Median baseline NIHSS score	Patients were randomized to receive mechanical embolectomy with Solitaire FR device + best medical management (n=103), which could include rt-PA or best medical management only, which could include intravenous t-PA (n=103).	**Primary outcome:** Shift in mRS score distribution at day 90 **Secondary outcomes:** Infarct volumes at 24 hours, vessel revascularization at 24 hours, early dramatic response to treatment (defined as a decrease in the NIHSS score of ≥8 from baseline or an NIHSS score of 0 to 2 at	Trial was terminated early (690 planned) after first interim analysis when efficacy of intervention was established. Median time from stroke onset to groin puncture was 269 minutes. Over the range of mRS scores, the odds for improvement by 1 point at 90 days were increased significantly in the intervention group (adj OR=1.7, 95% CI 1.05-2.8) The odds of achieving mRS score of 0-2 at 90 days were increased significantly in the intervention group

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		was 17 in both groups. Median ASPECTS scores were 7 (intervention) and 8 (control)		24 hours), NIHSS score and Barthel Index scores at 90 days and EuroQol **Safety outcomes:** 90-day mortality, symptomatic ICH within 90 days.	(adj OR=2.1, 95% CI 1.1-4.0). The odds of dramatic neurological improvement at 24 hours were increased significantly in the intervention group (adj OR=5.8, 95% CI 3.0-11.1). The median infarct volume was significantly lower in the intervention group (16.3 vs. 38.6 mL, p=0.02). At 90 days, the rates of death and symptomatic ICH were similar between groups (18.4% vs. 15.5% and 1.9% vs. 1.9%, respectively). No treatment effects were noted in planned sub-group analyses of age, baseline NIHSS score, site of occlusion, time to randomization, treatment with t-PA, ASPECTS score. **1-year outcomes** Data for 1 patient (control group) were missing. The odds of improvement in the mRS score across any cut-off point of the mRS were increased significantly for patients in the thrombectomy group (OR=1.80, 95% CI 1.09–2.99). The proportion of patients who were functionally independent (mRS score 0–2) was significantly higher for patients in the thrombectomy group (44% vs. 30%; OR=1.86, 95% CI 95% CI 1.01-3.44). Mean EQ-5D utility index scores were significantly higher for patients in the thrombectomy group at 1 year (0·46 vs. 0.33, MD=0·12, 95% CI 0·03–0·22, p=0·01). One-year mortality was similar between group (23% vs. 24%).
Goyal et al. 2015, Ganesh et al. 2021	Concealed Allocation: ☑ Blinding:	316 patients ≥18 years, with stroke onset <12 hours, NIHSS > 5 at the time of randomization,	Patients were randomized to receive endovascular mechanical thrombectomy, using available devices +/-	**Primary outcome:** Shift in mRS scores at day 90	The trial was stopped early. One patient in the control group crossed over to the endovascular therapy group and 14 patients in the

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Canada **RCT** ***ESCAPE***	Patient ☒ Assessor ☑ ITT: ☑	previously independent in ADL and confirmed symptomatic intracranial occlusion in selected regions of the anterior circulation and moderate-to-good collateral circulation, based on CTA findings. Median age of patients was 70 years, 48% were male. Median baseline NIHSS scores were 16 (intervention) and 17 (control). Median ASPECTS score was 9 (both groups).	intravenous t-PA (intervention group, n=165); or best medical management +/- tPA (control group, n=150).	**Secondary outcomes:** Proportion of patients who achieve: a NIHSS or mRS score of 0-2 or Barthel Index score of 95-100, and proportion patients who are independent (mRS 0-2) vs. dependent (mRS 3-6), EQ-5D, all assessed at day 90.	experimental group did not receive the assigned treatment. Retrievable stents were used in 130/151 patients who underwent an endovascular procedure. Median time from stroke onset to first reperfusion was 241 minutes. 125/150 patients in the control group were treated with iv t-PA. The odds of improvement in mRS score by 1 point were significantly higher among patients in the experimental group (adj OR=3.2, 95% CI 2.0-4.7). The odds of attaining a mRS score of 0-2 at 90 days were higher in the experimental group (adj OR=1.7, 95% CI 1.3-2.2). The odds of a NIHSS score of 0-2 and Barthel Index score of 95-100 were also significantly higher in the experimental group (adj OR=2.1, 95% CI 1.5-3.0 and 1.7, 95% CI 1.3-2.22, respectively). The risk of death was significantly lower in the experimental group (adj RR=0.5, 95% CI 0.-0.8). The risk of large or malignant stroke was significantly lower in the intervention group (adj RR=0.3, 95% CI 0.1-0.7). There was no significant increase in the risk of symptomatic ICH (adj RR=1.2, 95% CI 0.3-4.6). In subgroup analyses, based on age, sex, baseline NIHSS score, baseline ASPECTS, occlusion location, and status with respect to alteplase treatment) or according to the presence or absence of cervical carotid occlusion, all of which favoured the intervention. **Ganesh et al. 2020 (analysis to explore factors associated with infarct size and outcome)** Persons with small post-treatment infarct volume (PIV) (volume ≤25th percentile) and large PIV (volume ≥75th percentile) on 24–48-h CT/MRI were

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					identified, as were those with a good outcome (mRS ≤2) and those with a poor outcome (mRS>3). Independent factors associated with discrepant cases (i.e., patients with 90-day poor outcome/small PIV [n=27] and patients with a good outcome/large PIV [n=12]) were identified using multivariable models. Pre-treatment factors associated with small PIV/poor outcome included increasing age, presence of cancer, and absence of vascular risk factors. Post-treatment factors included increasing NIHSS score at 48 hours and serious adverse events. Pre-treatment factors associated with large PIV/good outcome included younger age, absence of vascular risk factors, and sparing of lentiform nucleus on imaging. Post-treatment factors included lower NIHSS score at 48 hours and absence of serious adverse events.
Berkhemer et al. 2015 **van den Berg et al. 2017 (2-year follow-up)** **Netherlands** **RCT** ***MR CLEAN***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	500 patients from 16 centres, ≥18 years, with NIHSS ≥2 at the time of randomization, a symptomatic anterior proximal artery occlusion in selected regions treatable within 6 hours of stroke onset. Mean age was 65 years. 58.4% male. Median baseline NIHSS scores were 17 (intervention) and 18 (control). Median ASPECTS score was 9 (both groups)	Patients were randomized to receive endovascular treatment with intravenous t-PA or urokinase, and/or intra-arterial (IA) treatment with available devices (n=233) or best medical management only, +/- intravenous t-PA (n=267).	**Primary outcome:** mRS score at day 90 **Secondary outcomes:** Vessel recanalization at 24 hours, infarct size at day 5-7, NIHSS score at 24 hours and 1 week after discharge, EQ-5D and Barthel Index (BI) scores, dichotomized mRS scores (0-1 vs. 2-6, 0-2 vs. 3-6, 0-3 vs. 4-6) at day 90.	89.0% of patients were treated with IV t-PA prior to randomization. 10.7% of patients in the intervention group were also treated with intra arterial t-PA. Retrievable stents were used in 81.5% of patients assigned to IA treatment. IA thrombolytic agents, provided as monotherapy were used in 0.4% of patients. There was a significant shift towards more favourable mRS scores among patients in the intervention group (adj common OR=1.67, 95% CI 1.21-2.30). The odds of more favourable outcome (mRS 0-1 and mRS 0-2) at day 90 were significantly higher among patients in the intervention group (adj OR=2.07, 95% CI 1.07-4.02 and adj OR=2.16, 95% CI 1.39-3.38, respectively). The mean NIHSS score at day 5-7 was significantly

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					lower among patients in the intervention group (2.9 points, 95% CI 1.5-4.3). The odds of a BI score of 19-20 were significantly higher among patients in the intervention group (adj OR=2.1, 95% CI 1.4-3.2). There was no significant difference in the median EQ-5D scores between groups. Patients in the intervention group were more likely to have no evidence of intracranial occlusion on follow-up CTA (adj OR=6.88, 95% CI 4.34-10.94, n=394) and to have a lower median final infarct volume (-19 mL, 95% CI 3-34, n=298). There was no difference in the mean number of serious adverse events between groups at 90 days. There were procedure-related complications in 26 patients (11.2%). There were no treatment-related interaction effects found for any of the pre-specified subgroups (NHISS strata, age ≥80 years, time to randomization, the presence of additional extracranial internal carotid artery occlusion and ASPECTS). **2-year follow-up** Data were available for 391 patients. The distribution of mRS scores favored the intervention group (adjusted common OR=1.68, 95% CI 1.15- 2.45, p=0.007). The odds of an mRS score of 0-2 were significantly higher in the intervention group (37.1% vs. 23.9%, adj OR= 2.21, 95% CI 1.30−3.73, p=0.003). The mean EQ-5D score was significantly higher in the intervention group (0.48 vs. 0.38, p=0.006) The risk of death associated with the intervention was not significantly higher (HR=0.9, 95% CI 0.6-

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					1.2, p= 0.46).
Kidwell et al. 2013 **USA** **RCT** ***MR. RESCUE***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒	118 patients 18-85 years, with NIHSS scores of 6 to 29, with large-vessel, anterior circulation stroke. 58 patients had a penumbral pattern while 68 had a nonpenumbral pattern. Mean age was 65 years, 48% were male, median NIHSS score was 17. 37% received i.v. t-PA	All patients received CT/MRI prior to treatment. Patients were randomized within 8 hours of symptom onset to undergo mechanical embolectomy with the Merci Retriever or Penumbra System (n=70), or standard care (n=57), grouped by penumbra pattern (PP) vs. nonpenumbra pattern (NP) Patients in the embolectomy group could also receive additional treatment with IA t-PA (maximum dose 14 mg).	**Primary outcome:** mRS score at 90 days **Secondary outcomes:** Good outcome at 90 days (mRS score ≤2), mortality ay 90 days, ICH, final infarct volume	Mean time to enrollment was 5.5 hours. 8 patient received adjunctive IA therapy with IA-t-PA. There were no differences between groups in unadjusted or adjusted (age) mean mRS scores at 90 days: Adjusted mean (Penumbra): 3.8 (Embolectomy) vs. 3.4 (Standard care), (Nonpenumbra): 4.3 (Embolectomy) vs. 4.2 (Standard care), p=0.30 There were no differences in the percentage of patients who experienced a good outcome at 90 days. 14% (P-embolectomy) vs. 23% (P-standard care) vs. 9% (NP-embolectomy) vs. 10% (NP-standard care), p=0.48 There were no differences in the percentage of patients who had died at 90 days. 18% (P-embolectomy) vs. 21% (P-standard care) vs. 20% (NP-embolectomy) vs. 30% (NP-standard care), p=0.75. Symptomatic ICH at 7 days: 9% (P-embolectomy) vs. 6% (P-standard care) vs. 0% (NP-embolectomy) vs. 0% (NP-standard care), p=0.24. Asymptomatic ICH at 7 days: 56% (P-embolectomy) vs. 41% (P-standard care) vs. 77% (NP-embolectomy) vs. 60% (NP-standard care), p=0.04. Final infarct volume (median mL): 58.1(P-embolectomy) vs. 37.3 (P-standard care) vs. 172.6 (NP-embolectomy) vs. 217.1 (NP-standard care), p<0.001. Losses to follow-up: embolectomy group n=6, standard care group n=3 Adverse events: 17 procedural complications, 5 of which were serious.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Mechanical Thrombectomy + Intravenous t-PA vs. Intravenous t-PA					
Mocco et al. 2016 **USA** **RCT** ***THERAPY***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	108 patients aged 18-85 years with evidence of a large vessel occlusion in the anterior circulation with a clot ≥ 8 mm in length, NIHSS≥ 8 or aphasic at presentation and eligible to received IV t-PA. Mean age was 68.5 years, 47% were men. Median baseline NIHSS score was 17.5	Patients were randomized to undergo intra-arterial mechanical clot retrieval using primarily the Penumbra system, after receiving standard therapy with IV t-PA (n=55) or IV t-PA only (n=53).	**Primary outcome:** Good functional outcome (mRS score 0-2) at 90 days **Secondary outcomes:** Good clinical outcome at 30 days (decrease of ≥10 points on NIHSS at discharge, or NIHSS score of 0-1 at discharge, or 30-day mRS score 0-2), symptomatic and asymptomatic ICH at 90 days. **Primary safety outcome:** 90-day serious adverse events	Trial enrollment was terminated early after MR CLEAN results were presented. 692 patients were planned. As a result, the trial was not powered to meet the primary endpoint. There was no significant difference between groups in the percentage of patients with a good outcome (38% endovascular vs. 30% t-PA: OR=1.4,95% CI 0.60–3.3), p= 0.44, ITT analysis), or in the percentage of patients with serious adverse events (42% endovascular vs. 48% t-PA, p=0.55). Overall mRS distributions demonstrated better functional outcome for the endovascular group in per-protocol analysis, but not in ITT analysis. There was no significant difference between groups in the percentage of patients with symptomatic ICH 9.3% vs. 9.7%, p=1.0).
Bracard et al. 2016 **France** **RCT** ***THRACE***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	414 patients from 26 centres, aged 18-80 years with an occlusion in the intracranial carotid, the MCA (M1) or the upper third of the basilar artery with onset of symptoms <4 hours and NIHSS ≥ 10 and ≤25 at randomization. Mean age 63 years, 53% were male. Mean NIHSS score 17.4. ASPECTS scores14.3% (0-4), 33.1% (5-7), 52.5% (8-10).	Patients were randomized to receive dual IV t-PA therapy + intra-arterial mechanical clot retrieval with the Merci, Penumbra, Catch or Solitaire devices (n=204) or treatment with IV t-PA only (n=208)	**Primary outcome:** mRS scores at day 90 **Secondary outcomes:** EQ-5D scores and Barthel Index (BI) scores at day 90	Median times from symptom onset to t-PA were 150 minutes (IVT group) and 153 minutes (t-PA group). Median time from symptom onset to thrombectomy was 250 minutes. The odds of achieving mRS score of 0-2 at 90 days were increased significantly in the thrombectomy group (53% vs. 42.1%, OR=1.55, 95% CI 1.05-2.3, p=0.028, NNT=10). Median NIHSS scores at days 7 and 3 months were significantly lower for thrombectomy patients (4 vs. 8, p=0.001 and 2 vs. 4, p=0.01, respectively). The proportion of patients with Barthel Index scores of 95-100 at 3 months was significantly higher in thrombectomy group (92% vs. 79%, p=0.04). Median EQ-5D scores at 3 months were not significantly different (0.64 vs. 0.62, p=0.38).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					There were no differences between groups in the number of patients with symptomatic or asymptomatic hemorrhages at 24 hours. There were no interactions noted in any of the subgroup analyses for the primary outcome (age, sex, diabetes, HTN, hypercholesterolemia, time to randomization, occlusion site, NIHSS baseline score, or ASPECTS score).
Saver et al. 2015 **USA** **RCT** ***SWIFT-PRIME***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	196 patients aged 18-80 years with pre-morbid mRS score ≤ 1, NIHSS ≥ 8 and < 30 at randomization, infarction located in the intracranial internal carotid artery, MCA, or carotid terminus confirmed by CT or MRA, treatment with IV t-PA within 4.5 hours of onset of stroke symptoms and ability to be treated within 6 hours of onset of stroke symptom. Mean age 65.5 years. Median baseline NIHSS score was 17 in both groups.	Patients were randomized to receive intravenous t-PA therapy + intra-arterial mechanical clot retrieval with the Solitaire FR device (n=98) or treatment with intravenous t-PA only (n=98)	**Primary outcome:** Global disability at 90 days (mRS scores) **Secondary outcomes:** All-cause mortality, proportion of patients with mRS score ≤2 at 90 days, change in NIHSS score at 27 ± 6 hours post randomization	Median time from stroke onset to first deployment was 252 minutes. There was a significant shift in mRS scores towards lower scores associated with the endovascular therapy group (p=0.0001). The likelihood of successful reperfusion (>90%) at 27 hours was significantly higher in the endovascular therapy group (82.8% vs. 40.4%, RR=2.05, 95% CI 1.45-2.91, p<0.001). A significantly higher percentage of patients were independent at day 90 (mRS 0-2) (60.2% vs. 35.5%, RR=1.70, 95% CI 1.23-2.33, p=0.001). There was no significant reduction in the risk of death at 90 days associated with the intervention (9.2% vs. 12.4, RR=0.74, 95% CI 0.33-1.68, p=0.50). There was no increased risk of serious adverse events, including symptomatic ICH, parenchymal hematoma and SAH associated with endovascular treatment. No treatment effects were found in subgroup analyses, based on age, sex, baseline NIHSS score, baseline ASPECTS, occlusion location, time to randomization, site of care or geographic location.
Campbell et al. 2015	Concealed Allocation: ☑	70 patients ≥18 years, with anterior circulation	Patients were randomized to undergo mechanical clot	**Primary outcomes:** Reperfusion at 24 hours,	The trial was stopped early (100 planned). 8 patients in the endovascular treatment group did not undergo

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Australia ***EXTEND IA*** **RCT**	Blinding: Patient ☒ Assessor ☑ ITT: ☑	acute ischemic stroke, no baseline NIHSS criteria, eligible for treatment with IV tPA within 4.5 hours of stroke onset, with good premorbid function (mRS 0-2), with evidence of salvageable brain tissue on CT perfusion imaging, who could receive intra-arterial treatment within 6 hours of stroke onset. Mean age was 69 years, 49% were male. Median baseline NIHSS scores were 17 (intervention) and 13 (control).	retrieval with the Solitaire device after receiving standard therapy with intravenous rt-PA (n=35) or intravenous t-PA only (n=35)	favorable clinical response (reduction in NIHSS scores by ≥8 points or score of 0–1) by day 3. **Secondary outcomes:** mRS scores day 90, death within 90 days, symptomatic ICH with 36 hours of treatment and ≥4-point increase in NIHSS from baseline.	the procedure. Median time from stroke onset to groin puncture was 210 minutes. Median reperfusion at 24 hours was significantly higher in the endovascular group (median 100% vs. 37%, p<0.001). Significantly more patients in the endovascular group experienced >90% reperfusion without ICH at 24 hours (89% vs. 34%, p<0.001). A significantly greater proportion of patients in the endovascular group experienced early neurological improvement (80% vs. 37%, p<0.001), and were independent at day 90 (71% vs. 40%, p=0.009). There was a significant shift in mRS scores towards lower scores associated with the intervention group (p=0.006). There were no significant differences between groups in any of the safety outcomes (death, symptomatic ICH or parenchymal hematoma).
Mechanical Thrombectomy vs. Intravenous t-PA					
Ciccone et al. 2013 **Italy** **RCT** ***SYNTHESIS***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	362 patients aged 18 to 80 with confirmed diagnosis of ischemic stroke, with onset of symptoms within 4.5 hours.	Patients were randomized to receive: i) either pharmacological or mechanical thrombolysis with a micro-guide wire, at the discretion of the interventionist following a diagnostic procedure-endovascular therapy (ET) group or ii) intravenous t-PA. Patients in both groups received a t-PA dose of 0.9 mg/kg (max dose 90 mg).	**Primary outcome:** Disability-free survival at 90 days (mRS of <2) **Secondary outcomes:** Percentage of patients with no or mild neurological deficit (NIHSS score ≤6), fatal and nonfatal symptomatic ICH, edema or recurrent stroke, all-cause mortality, neurological deterioration, assessed at 7 days.	Survival without disability: Crude OR= 0.82, 95% CI 0.53 to 1.27, p=0.37 (trend in favour of ET) Adjusted OR (age, sex, stroke severity, +/- atrial fibrillation=0.71, 95% CI 0.44 to 1.14, p=0.16 (trend favours ET) Secondary outcomes for ET vs. t-PA NIHSS scores ≤6: 54% vs. 55%, p=0.89 Neurological deterioration: 9% vs. 7%, p=0.39 Death: 8% vs. 6%, p=0.53 Symptomatic ICH (fatal & nonfatal): 6% vs. 65, p=0.99 Symptomatic edema (fatal and nonfatal): 20% vs. 18%, p=0.53 Recurrent stroke (fatal and nonfatal):2% vs. 2%, p=0.99 All subgroups analyses of primary outcome were negative: age (≤67 vs.>67 yrs), NIHSS score (<11

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					vs. ≥11, time to randomization (0-3 hrs vs. 3-4.5 hrs), time to treatment (0-3 hrs. vs. 3-4.5 hrs vs. >4.5 hrs), atrial fibrillation (+/-),systolic BP (<141 vs. ≥141 mm Hg), diastolic BP (<81 vs. ≥81 mm Hg), antidiabetic therapy (+/-), antiplatelet therapy (+/), stroke territory (anterior vs. posterior circulation), stroke cause (cardiogenic vs. large artery atherosclerosis vs. small vessel disease), centre volume (≥30 vs. <30 patients), major protocol violations (+/-). There was an interaction effect for the subgroup of NIHSS scores, which favoured treatment with intravenous t-PA. Adverse events: The incidence between groups was similar Dropouts: n=0, (15 patients did not receive endovascular treatment, 3 patients did not receive t-PA)
Broderick et al. 2013 **USA** **RCT** ***IMS III***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	656 patients aged 18 to 82 from 58 centres in US, Canada and Europe with confirmed diagnosis of moderate-to-severe ischemic stroke with onset of symptom <3 hours. NIHSSS score ≥ 10 at the time that IV t-PA was begun or an NIHSSS >7 and <10 with an occlusion seen in M1, ICA or basilar artery on CTA at institutions where baseline CTA imaging was standard of care.	All patients received treatment with t-PA (dose of 0.9 mg/kg-max dose 90 mg) and were randomized within 40 minutes of the initiation of treatment to receive the remainder of the total dose of i.v. t-PA (n=222) or endovascular therapy (ET) (pharmacological or mechanical at the discretion of the treating interventionist, n=434).	**Primary outcome:** Disability-free survival at 90 days (mRS of ≤2) **Secondary outcomes:** Death within 7 and 90 days, ICH (symptomatic/asymptomatic) major complication (non-ICH) within 5 days, recurrent stroke within 90 days.	*Trial stopped early (futility)-900 patients were to have been randomized according to the trial protocol % of patients in ET and i.v. t-PA groups with mRS of ≤2 at 90 days: 40.8% vs. 38.7%, absolute adjusted difference of 1.5%, 95% CI -6.1 to 9.1, p>0.05. RR for subgroup of patients with NIHSS scores of 8-19=1.01, 95% CI 0.78 to 1.31, p>0.05 RR for subgroup of patients with NIHSS scores of ≥20=1.37, 95% CI 0.63 to 2.99, p>0.05 Mortality for patients in ET and i.v. t-PA groups: 7 days:12.0% vs. 10.8%, p=0.57 90 days: 19.1% vs. 21.6%, p=0.52 ICH incidence for patients in ET and i.v. t-PA groups Symptomatic:6.2% vs. 5.9%, p=0.83 Asymptomatic: 27.4% vs. 18.9%, **p=0.01** Major (non-ICH) complication within 5 days for patients in ET and i.v. t-PA groups 3.0% vs. 2.3%, p=0.55

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Recurrent stroke within 90 days for patients in ET and i.v. t-PA groups 5.1% vs. 6.3%, p=0.54
EVT in Developing Countries					
Martins et al. 2020 **Brazil** **RCT** ***RESILIENT***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	221 adult patients (690 planned) with a proximal intracranial occlusion in the anterior circulation that could be treated within 8 hours after the onset of stroke symptoms, recruited from 12 public hospitals. Imaging inclusion criteria were ASPECTS ≥6, a baseline infarct volume of <70 mL, a ratio of volume of ischemic tissue to baseline infarct volume ≥ 1.8 or more, and an absolute volume of potentially reversible ischemia (penumbra) of ≥15 mL. Median age was 66 years, 47% were women. Median baseline NIHSS was 18.	Patients were randomized 1:1 ratio to receive standard care + plus mechanical thrombectomy (thrombectomy group) or standard care alone (control group).	**Primary outcome:** Shift in distribution of mRS scores at 90 days **Secondary outcomes:** Favourable outcome (mRS 0-2) at 90 days, 90-day mortality, any ICH, sICH	The trial was stopped early due to efficacy. Approximately 70% of patients were treated with rt-PA (68% thrombectomy; 71.8% control). The distribution of mRS scores favoured the thrombectomy group (common OR=2.28, 95% CI 1.41 to 3.69; P = 0.001). The odds of a favourable outcome were significantly higher in the thrombectomy group (35.1% vs. 20.0%, OR=2.55, 95% CI 1.34-4.88). The odds of death were not reduced significantly in the thrombectomy group (24.3% vs. 30.0%, OR=0.75, 95% CI 0.41 to 1.36). The odds of any ICH or sICH using the SITS-MOST criteria or the ECASS III criteria were not increased significantly in the thrombectomy group. The per-patient costs were estimated to be the equivalent of USD $8,066.85 higher with thrombectomy plus medical treatment than with medical treatment alone.
Observational studies					
Mueller-Kronast et al. 2017 **USA** **STRATIS Registry**	NA	984 patients, recruited from 55 centres who underwent mechanical thrombectomy with either the Solitaire or Mindframe devices, within 8 hours of stroke onset. Patients with a premorbid mRS ≤1 and with a baseline NIHSS score of 8-30, were included. Mean age was	Outcome data from STRATIS registry were compared with results from SEER patient-level meta-analysis.	**Primary outcome:** Good functional outcome at 90 days (mRS ≤2) **Secondary outcomes:** Time metrics	There were no significant differences between groups in age, sex distribution or atrial fibrillation. A significant higher proportion of patients in the STRATIS cohort had hypertension, diabetes and current/prior history of tobacco use. 64.0% of patients received treatment with i.v.-tPA, which was significantly lower than SEER (80.5%, p<0.001). Mean baseline NIHSS score was significantly higher

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		67.8 years, 54.2% were men.			in STRATIS cohort (17.3 vs. 16.6, p=0.042). 56.5% of STATIS patients had a good outcome, which was similar to SEER patients (54.0%, p=0.43). 43.2% had an excellent outcome (mRS≤1), which was significantly higher compared with SEER (35.8%, p=0.01) All cause mortality at 90 days was 14.4%. 1.4% of patients suffered a symptomatic ICH. Median time from puncture to reperfusion was 37 minutes. Reperfusion was achieved in 87.9% of patients, which was significantly higher compared with SEER (76.6%, p<0.001). Mean time from stroke onset to groin puncture was 226.4 minutes, which was significantly shorter compared with SEER (263.1 minutes, p=0.011). Mean time from hospital arrival to groin puncture was 80.1 minutes, which was significantly shorter compared with SEER (122 minutes, p<0.001)

Systematic Reviews & Meta-analyses of EVT vs. Standard Care

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Roaldsen et al. 2021 **Norway** **Cochrane review**	Randomisation and concealment of allocation was adequate in 15 studies. In only one trial were	19 RCTs including 3,793 participants, the majority of whom had large artery occlusion in the anterior circulation. Mean age ranged from 64 to 69 years, 53% were men.	Most trial participants were treated within 6 hours of symptom onset with endovascular thrombectomy. The control condition was best medical care.	**Primary outcome:** Favourable outcome (mRS 0-2) at 90 days **Secondary outcomes:** All-cause mortality, symptomatic intracranial hemorrhage, favourable neurological status (NIHSS	Treatment with EVT was associated with a significantly higher likelihood of favourable outcome (RR=1.61, 95% CI 1.42 to 1.82). High certainty of evidence. 18 RCTs The risk of all-cause mortality at 90 days was significantly lower in the EVT group (RR=0.85, 95% CI 0.75 to 0.97). High certainty of evidence. 19 RCTs

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	both participants and assessors blinded. Risk of bias from selective reporting was low in 13 trials. 4 trials did not analyze data using ITT.			0-1), degree of recanalization, major extracranial hemorrhage	The risk of sICH was not increased significantly in the acute phase or at the end of follow-up (RR=1.46, 95% CI 0.91 to 2.36 and RR=1.05, 955 CI 0.72 to 1.52, respectively). High certainty of evidence. 10 RCTs At the end of follow-up, a significantly higher proportion of patients in the EVT group had favourable neurological status (RR=20.3, 95% CI 1.21 to 3.40). Moderate certainty of evidence. 3 RCTs Successful recanalization was significantly more likely to be achieved in the EVT group (RR=8.25, 95% CI 1.63 to 41.90). Moderate certainty of evidence. 2 RCTs. The benefits of EVT were seen with/without intravenous thrombolysis and were unrelated to age, sex, and time to intervention (although most participants were treated within 6 hours of symptom onset). Benefits were greater with more severe stroke.
Jovin et al. 2022 **USA** ***Analysis Of Pooled Data from Randomized Studies of Thrombectomy More Than 6 Hours After Last Known Well (AURORA)***	NA	6 RCTs including DAWN, DEFUSE 3, ESCAPE, RESILIENT, POSITIVE and REVASCAT, (all described above), which included patients with acute anterior circulation ischemic stroke, who received treatment between 6 and 24 hours after the onset of symptoms. Mean age of participants was 68·6 years, 51·3% were women. Median baseline NIHSS was 16. Median ASPECTS score was 8.	Individual patient-level pooling of data from trials compared treatment with either second-generation thrombectomy devices (stent-retrievers or large bore aspiration catheters, n=266) plus standard medical treatment vs. standard medical treatment alone (n=239).	**Primary outcome:** Disability (defined using mRS) at 90 days **Safety outcomes:** Mortality within 90 days and symptomatic intracerebral hemorrhage (sICH)	The median time from onset to randomisation was 625 min overall. The was a significant shift in the ordinal analysis of mRS scores favouring less disability in the thrombectomy group (adj OR=2·54, 95% CI 1·83–3·54). In subgroup analysis, a stronger treatment effect was noted in patients randomized in the 12–24-hour time window (common OR= 5·86, 95% CI 3·14–10·94) compared with those randomized in the 6–12 hour time window (common OR=1·76, 95% CI 1·18–2·62). The odds of achieving an mRS score of 0-1 or 0-2 at 90 days were both significantly higher in the thrombectomy group (adj OR=2·41, 95% CI 1·07–5·43 and adj OR=3·88, 95% CI1·94–7·78, respectively).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Neither mortality, nor sICH were increased significantly in the thrombectomy group (adj OR=0·96, 95% CI 0·58–1·60 and adj OR=1·74, 95% CI 0·70–4·31, respectively).
Zhao et al. 2020 **China**	8/37 studies received a score of 6 on the Newcastle-Ottawa Scale. Using the Cochrane Risk tool for the RCTs, all trials were assessed as having bias in ≥2 domains	15 RCTs (n=3,694) and 37 observational studies (n=9,090) including persons with acute LVO ischemic stroke in the anterior circulation. RCTs included IMS III, MR RESCUE, SYNTHESIS, EXTEND-IA, MR CLEAN, ESCAPE, SWIFT PRIME, REVASCAT, THERAPY, THRACE, EASI, PISTIE, DAWN, DEFUSE and RESILIENT. The median baseline ASPECTS was >6 in the RCTs.	Studies compared EVT vs. medical management. Observational studies were categorized into 3 groups based on imaging data on admission: mild (NIHSS <6, n=11), severe (ASPECTS <6 or ischemic core ≥50 mL, n=4), and normal stroke for all others (n=22).	**Primary outcomes:** mRS score of 0-2 and mortality at 90 days, sICH at 24 hours.	In the RCTs, the odds of attaining an mRS of 0-2 were significantly higher in the EVT group (OR=1.97, 95% CI, 1.48–2.63). In the observational studies, the overall odds were significantly higher in the EVT group (OR=1.56, 95% CI, 1.32–1.84), in the normal group (OR=1.72, 95% CI, 1.46–2.02) and in the severe group (OR=5.33, 95% CI, 2.22–12.76), but not in the mild group (OR=0.91, 95% CI,0.61–1.37). In the RCTs, the odds of mortality were significantly lower in the EVT group (OR=0.82, 95% CI, 0.69–0.99). In the observation studies, the overall odds of mortally were significantly lower (OR= 0.77, 95% CI, 0.63–0.95) in the normal group (OR=0.71, 95% CI, 0.55–0.92) and in the severe group (OR=0.53, 95% CI, 0.34–0.82), but was significantly increased in the mild group (OR=2.22, 95% CI, 1.26–3.89). In the RCTs, the odds of sICH were not significantly increased with EVT (OR=1.09, 95% CI 0.83–1.45). In the observational studies, the overall odds of sICH were significantly increased with EVT (OR=1.58, 95% CI .29–1.93), in the normal group (OR=1.62, 95% CI, 1.30–2.03) and in the mild stroke group (OR=2.78, 95% CI, 1.24–6.21). The odds of sICH were not increased with EVT in the severe group (OR= 0.93, 95% CI, 0.50–1.71).
Flynn et al. 2017 **UK** **Systematic review & meta-analysis**	NA	8 RCTs (n=1,841) including EXTEND-IA, ESCAPE, REVASCAT, SWIFT PRIME, MR CLEAN, THERAPY, THRACE and PISTE	Trials compared mechanical thrombectomy (stent retriever or aspiration devices) with/without adjuvant intravenous thrombolysis vs. intravenous thrombolysis and other forms of best medical/supportive care	**Primary outcome:** Functional independence (mRS 0-2) at 90 days **Secondary outcomes:** 90-day mortality, symptomatic ICH within 7 days	Using the results from all trials, mechanical thrombectomy was associated with significantly higher odds of functional independence (unadjusted OR=2.07, 95% CI 1.70-2.51, p<0.0001). The odds of 90-day mortality were non-significantly lower for patients in the thrombectomy group (unadjusted OR=0.81, 95% CI 0.61-1.07, p=0.13). The risk of sICH was non-significantly higher in the t-PA only group (unadjusted OR=1.21, 95% CI 0.78-

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					1.88, p=0.40). Time series analysis demonstrated robust evidence for a 30% relative benefit for mechanical thrombectomy for the primary outcome, but not for the outcome of mortality.
Yarbrough et al. 2016 **USA** **Systematic review & Meta-analysis**	NA	9 RCTs (n=23,809 participants) including SYNTHESIS, IMS III (2013, 2014), MR RESCUE, ESCAPE, EXTEND-IA, SWIFT PRIME, REVASCAT	Trials compared endovascular therapies (ET) vs. best medical management using t-PA in patients with acute ischemic stroke caused by anterior circulation occlusion	**Primary outcome:** Favourable outcome at 90 days (mRS 0-2) **Secondary outcomes:** Death at 90 days, symptomatic ICH	The odds of a favourable outcome were significantly increased in the endovascular therapy group (OR=1.75, 95% CI 1.20-2.54). The odds of decreased mortality at 90 days were not significantly reduced in the ET group (OR=0.78, 95% CI 0.57-1.08). The odds of sICH associated with ET were not significantly increased (OR=1.26, 95% CI 0.80-1.98).
Goyal et al. 2016 HERMES Collaborators **International** **Meta-analysis**	NA	Patient-level pooling of results from 5 RCTs (n=1,287) including MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME and EXTEND IA	Trials compared endovascular therapies within 12 hours of proximal anterior artery occlusion using second generation neurothrombectomy devices vs. best medical management	**Primary outcome:** Disability (mRS 0-1) at 90 days **Secondary outcomes:** Functional independence (mRS 0-2) at 90 days, proportion of patients with NIHSS scores of 0-2 at 24 hours, proportion of patients with early neurological recovery (reduction in NIHSS score of ≥ 8 points or score of 0-1, within 24 hours)	The odds of achieving a mRS score of 0-1 at 90 days were significantly higher for patients in the endovascular group (26.9% vs. 12.9%; common OR=2.49, 95% CI 1.84-3.35, p<0.0001). NNT for a one-point reduction in mRS was 2.6. The odds of achieving a mRS score of 0-2 at 90 days were significantly higher for patients in the endovascular group (46.0% vs. 26.5%; common OR=2.35, 95% CI 1.85-2.98, p<0.0001). The odds of having a NIHSS score of 0-2 at 24 hours were significantly higher for patients in the endovascular group (21.0% vs. 8.3%; common OR=2.91, 95% CI 2.06-4.12, p<0.0001). The risks of 90-day mortality, symptomatic ICH and parenchymal type 2 hematoma were not significantly increased in the endovascular group. There were no significant treatment effects based on pre-specified subgroups including: age, sex, NIHSS, site of intracranial occlusion, intravenous alteplase received or ineligible, ASPECTS, time from onset to randomisation, or the presence of tandem cervical carotid occlusion.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Saver et al. 2016 HERMES Collaboration **International** **Meta-analysis**	NA	As above	Pooled analyses were conducted to examine the timeframe in which endovascular treatment is associated with benefit, and to investigate the effect of treatment delay	**Primary outcome:** Degree of disability at 3 months, assessed across 6 levels of mRS, with ranks 5 and 6 combined into a single worst outcome rank **Secondary outcomes:** Functional independence (mRS 0-2) and excellent outcome (mRS 0-1) at 3 months	At 90 days, the mean mRS score among patients in the endovascular therapy group was 2.9, and 3.6 for patients in the medical therapy group. Compared with medical therapy, the odds of better disability outcomes at 90 days (mRS scale distribution) associated with endovascular therapy declined with longer time from symptom onset to arterial puncture: 2 hrs: cOR=3.13, 95% CI 2.06 to 4.76 3 hrs: cOR= 2.79, 95% CI 1.96 to 3.98 4 hrs: cOR=2.49, 95% CI 1.79 to 3.47 5 hrs: cOR= 2.22, 95% CI 1.55 to 3.16 6 hrs: cOR=1.98, 95% CI 1.30 to 3.00 7 hrs: cOR=1.76, 95% CI 1.06 to 2.92 8 hrs: cOR= 1.57, 95% CI 0.86 to 2.88 The point at which endovascular therapy was not associated with a significantly better outcome was 7 hours and 18 minutes. Compared with medical therapy, the odds of functional independence associated with endovascular therapy declined with longer time from symptom onset to arterial puncture: 3 hrs: cOR= 2.83, 95% CI 2.07 to 3.86 6 hrs: cOR=2.32, 95% CI 1.56 to 3.44 8 hrs: cOR=2.03, 95% CI 1.03 to 3.99 Among 390 patients who achieved substantial reperfusion with endovascular thrombectomy, each 1-hour delay to reperfusion was associated with a less favorable degree of disability (OR= 0.84, 95% CI,0.76 to 0.93) and less functional independence (OR=0.81, 95% CI 0.71 to 0.92).
Campbell et al. 2016 SEER Collaboration **International** **Meta-analysis**	NA	Patient-level pooling of results from 4 RCTs (n=787) including ESCAPE, REVASCAT, SWIFT PRIME and EXTEND IA	Trials compared endovascular therapies using the Solitaire device predominantly vs. best medical management	**Primary outcome:** Functional outcome at 90 days (using ordinal analysis of mRS scores) **Secondary outcomes:** Independence at 90 days (mRS 0-2), excellent	Treatment with Solitaire device was associated with a significant improvement in the ordinal analysis of mRS (adjusted common OR=2.7, 95% CI 2.0-3.5, p<0.0001). NNT to improve by 1 mRS point was 2.5. Treatment with Solitaire device was associated with both a significantly greater likelihood of independence and excellent functional outcome at

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				functional outcome at 90 days (mRS 0-1), early neurological improvement (reduction in NIHSS score of ≥ 8 points or score of 0-1, within 24 hours), sICH and all-cause mortality at 90 days Analyses were adjusted for age, sex, baseline stroke severity, site of occlusion, t-PA treatment, ASPECTS and time from onset to randomization	90 days (adj common OR=3.1, 95% CI 2.2-4.4, p<0.0001 and adj common OR=3.0, 95% CI 2.1-4.3, p<0.0001, respectively). Treatment with Solitaire device was associated with both a significantly greater likelihood of early neurological improvement (adj common OR=4.8, 95% CI 3.5-6.7, p<0.0001 Treatment with the Solitaire device was not associated with a significant increase in death, sICH or parenchymal hemorrhage. No interactions were observed in planned subgroup analyses of age, sex baseline NIHSS score, site of occlusion, tandem cervical carotid occlusion, t-PA treatment, ASPECTS and time from onset to randomization
Balami et al. 2015 **UK** **Systematic review & meta-analysis**	NA	8 RCTs (n=2,423) comparing endovascular therapies with best medical management following ischemic stroke. Results from ESCAPE, EXTEND-IA, IMS III, SYNTHESIS, MR. RESCUE, SWIFT-PRIME, REVASCAT and MR. CLEAN were included.	Additional subgroup analysis based on baseline ASPECTS (0-4, 5-7 and 8-10)	**Primary outcome:** Favourable outcome (mRS 0-2) at 90 days **Secondary outcomes:** sICH and all-cause mortality at 90 days, mRS 0-3 at 90 days	Patients in the endovascular group were more likely to have a good outcome (OR=1.56, 95% CI1.32-1.85, p<0.0001 [fixed effects], OR=1.71, 95% CI 1.18-2.48, p=0.005 [random effects]. The risks of sICH or mortality were not significantly increased/decreased (OR=1.03, 95% CI 0.71-1.49 and OR=0.84, 95% CI 0.67-1.05, p=0.12, respectively). Patients in the endovascular group were more likely to have mRS of 0-3 at 90 days (OR=1.68, 95% CI 1.18-2.40, p=0.004). In subgroup analysis of 4 trials that included stratified ASPECTS data for the primary outcome, the odds of a favourable outcome were significantly increased in the endovascular group for patients with ASPECTS of 8-10 (OR=2.10, 95% CI 1.61-2.73, p<0.0001) and 5-7 (OR=2.04, 95% CI 1.25-3.32). Only one trial was included in the 0-4 group.
Fargen et al. 2014	NA	6 RCTs (n=1,903) comparing endovascular therapies with best	Analyses were conducted for studies in which patients with confirmation	**Primary outcome:** Good functional outcome (mRS 0-2) at 3 months	**Results from the 5 LVO trials:** Endovascular therapy was associated with significantly improved odds of a good recovery

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
USA **Systematic review & meta-analysis**		medical management following ischemic stroke. Results from PROACT II, MELT, IMS III, SYNTHESIS, MR. RESCUE and MR. CLEAN were included. Mean/median NIHSS scores at the time of randomization varied from 13-17.4	of large vessel occlusion (LVO) were included (n=5), and for all studies where patients were included regardless of the confirmation of LVO (n= 6).	**Secondary outcomes:** mRS scores of 0-1 and 0-3 at 3 months, mortality at 3 months and shift in mRS scores at 3 months	(OR=1.67, 95% CI 1.29-2.16, p<0.0001). Endovascular therapy was also associated with significantly increased odds of mRS score of 0-1 and 0-3 (OR=1.93, 95% CI 1.39-2.68 and OR=1.46, 95% CI 1.16-1.85, respectively), and a shift in mRS scores (mean 3.35 vs. 3.73, p<0.0001), but not a decrease in mortality (OR=0.80, 95% CI 0.60-1.07). **Results from all 6 trials:** Endovascular therapy was associated with significantly improved odds of a good recovery (OR=1.27, 95% CI 1.04-1.54, p=0.018). Endovascular therapy was also associated with significantly increased odds of mRS score of 0-3 (OR=1.25, 95% CI 1.04-1.51), and shift in mRS scores (mean 3.16 vs. 3.42, p=0.003) but not in mRS 0-1 (OR=1.22, 95% CI 0.97-1.53) or decrease in mortality (OR=0.96, 95% CI 0.76-1.22).
Singh et al. 2013 **USA** **Systematic review & meta-analysis**	NA	5 RCTs s (n=1197 patients) comparing the efficacy of endovascular therapy (ET), with or without IV tPA to IV thrombolysis in patients with acute stroke Trials included: SYTHESIS, IMS III, Mr. Rescue (counted as 2 studies, details below), SYNTHESIS pilot study (Ciccone et al. 2010) & Sen et al. 2009 Median NIHSS scores of subjects ranged from were 13 to 21.	Treatment contrasts included: Intra-arterial (IA) t-PA vs IV t-PA (n=4) and mechanical thrombolysis + IA t-PA (n=2)	**Primary outcome:** Improvement in mRS scores at 3 months **Secondary outcomes:** All-cause mortality, sICH	There were no significant differences between groups for any of the outcomes. The proportions of patients with mRS scores of 1, 2 and 3 did not differ at 3 months. The percentage of patients (ET vs. control) were 28.3% vs. 28.3% (mRS=1), 40.1% vs. 39.5% (mRS=2) and 58.0% vs. 56.5% (mRS=3). 18.0% of patients in the ET group had died compared with 17.1% in the control group. The incidence of sICH was similar between groups (5.9% vs. 6.1%). In subgroup analysis restricted to patients with severe stroke (NIHSS score ≥20), and including the results from 3 trials, there were no significant differences between groups in the proportion of patients who had experienced an excellent (mRS≤1) or good outcome (mRS≤2); however, patients in the ET group were more likely to have achieved a fair outcome (mRS≤3) RR=1.41, 95% CI 1.00-1.99,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					p=0.05.
Adjunctive Intra-arterial Thrombolysis					
Diprose et al. 2021 **New Zealand** **Systematic review & meta-analysis**	Risk of bias was moderate in all studies	5 studies including 1,693 patients with acute ischemic LAO, recruited from 2010-2017. Median/median age was 67 years, 51% were men. Median NIHSS score range was 14-20.	Studies compared combined EVT + adjunctive IAT (IA alteplase or urokinase, n=269) with EVT only (n= 1,424).	**Primary outcomes:** Symptomatic ICH, 90-day mortality, successful reperfusion, 90-day good functional outcome (mRS 0-2)	Intravenous thrombolysis was administered to between 19.4% and 75.0% of patients. The odds of sICH were not significantly higher in the EVT+IAT group (6.0% vs. 6.4%, OR=0.61, 95% CI 0.20–1.85), nor were the odds of mortality (21.3% vs. 24.7%, OR=0.77, 95% CI 0.54–1.10). The odds of successful reperfusion were not significantly higher in the EVT+IAT group (80.7% vs. 84.0%, OR=1.05, 95% CI 0.52–2.15). The odds of good functional outcome were higher in the EVT+IAT group (45.4% vs. 39.6%, OR=1.34, 95% CI 1.00–1.80, p=0.053)

Sex Differences

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Casetta et al. 2022 **Italy** **Retrospective study** ***The Italian Registry of Endovascular Thrombectomy in Acute Stroke (IRETAS)***	NA	3,422 patients included in the IRETAs database who had undergone EVT treatment since 2011	The outcomes of women vs. men were compared in the original cohort (1621 men and 1801 women) and in a propensity-matched cohort of 1,150 men and women. Analyses were adjusted for adjust for age, history of hypertension, diabetes, dyslipidemia, atrial fibrillation (AF), smoking status, NIHSS and ASPECTS score at entry, stroke etiology according	**Primary outcomes:** Functional independence (mRS 0-2) at 90 days, death, symptomatic ICH at 24 hours, and TICI 2b–3	In the whole cohort, women were significantly younger than men (72.4 vs. 68.7 years), were more likely to have a history of hypertension (66% vs. 58.6%), and AF (41.7% vs. 28.6%). Men were more likely to have diabetes (17.4% vs. 13.7%), dyslipidemia (25.3% vs. 21.7%) and to be ever smokers (24.9% vs. 10.0). Time metrics (terms onset to groin puncture time and onset to revascularization/end of the procedure time) were similar for men and women. Median baseline NIHSS at admission was the same (median 17). M1 occlusion was more frequent in women (69.0% vs. 60.5%). The proportion of patients who underwent combined treatment (i.v. thrombolysis followed by thrombectomy) was similar between the two groups (51.5% vs. 49.8%).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			to the TOAST definition, site of occlusion, type of treatment, onset to groin puncture and onset to final recanalization time.		In the matched cohort, mean age was 70 years. In both the whole cohort and matched-pair cohort, the odds of functional independence given EVT treatment were significantly higher in women (OR= 1.19, 95% CI 1.02–1.38 and OR=1.25, 95% CI 1.04-1.51, respectively). Women were less likely to die in the whole cohort (OR=0.75, 95% CI 0.62–0.90), but not in the matched-pair cohort (OR=0.81, 95% CI 0.63–1.02). The odds of TICI 2b–3 were significantly higher in women (OR=1.18, 95% CI 1.03–1.38) in the whole cohort analysis, but not in pair-matched analysis (OR=1.19, 95% CI 0.92–1.36). The odds of sICH were not significantly lower in women in either analysis. In subgroup analysis, women who received combined treatment had significantly better outcomes than men (higher odds of functional independence, full recanalization and lower odds of death).
Bala et al. 2022 **Canada** **Retrospective studies**		608 patients included in the SOLSTICE (Selection of Late-Window Stroke for Thrombectomy by Imaging Collateral Extent) Consortium who had suffered a large vessel occlusion and undergone EVT between 6 and 24 hours.	Differences in outcomes between men (n=301) and women (n=307) were compared.	**Primary outcomes:** Independence at 90 days (mRS score of ≤2) and ordinal shift in mRS scores **Secondary outcomes:** Successful reperfusion, 90-day mortality and symptomatic intracranial hemorrhage (sICH	Mean age of women was significantly higher in women (72 vs. 68 years, p=0.02). Baseline NIHSS score was 15 in women vs. 16 in men (p=0.35). The frequency of tandem occlusions was significantly lower in women (14% vs. 22.9%, p=0.005). There were no differences between the groups in mean process times (e,g, time from onset to ED door). There were no significant differences between groups in imaging type received, ASPECTS score, occlusion site, baseline perfusion volume, favorable collateral profile or favorable perfusion profile.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					43.5% of women were independent at 90 days compared with 46.4% of men (p=0.48). There were no significant differences between groups on any of the secondary outcomes. There was a significant interaction between sex and age for 90-day mortality (P for interaction=0.003) and sICH (P for interaction=0.017), with men having an increased likelihood of sICH and death with advancing age compared with women. The effect was strongest for age > 80 years.
Chalos et al. 2019 **The Netherlands** **Pooled analysis**	NA	Data from 7 RCTs (MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME, REVASCAT, THRACE, and PISTIE), were included.	The outcomes of men (n=929) vs. women (n=833) who received EVT vs. medical management, were compared. Analyses were adjusted for age, baseline NIHSS, time from onset to randomization, diabetes, prior stroke, occlusion location, intravenous tPA use, and collateral grade	**Primary outcome:** mRS score at 90 days **Secondary outcomes:** Excellent functional outcome (mRS 0–1) and functional independence (mRS, 0–2) at 90 days, NIHSS score at 24 hours, mortality, symptomatic ICH	Women were significantly older (70 vs. 66 years), smoked less often (30% vs. 44%), and had higher collateral grade (grade 3: 46% vs. 35%). When treatment groups were combined (EVT + medical management), there were no significant differences between men and women for any of the outcomes. The median mRS score at 90 days for both men and women in the EVT group at 90 days was 3. Among both men and women in the EVT group, 48% achieved functional independence, while 30% of women and 29% of men achieved an excellent outcome. In ordinal shift analysis of mRS scores at 90 days, the effect of EVT was similar in women (adjusted common OR=2.13, 95% CI 1.47–3.07) and men (acOR=2.16, 95% CI, 1.59–2.96). P for interaction of 0.926. For all other outcomes, the results for men and women in EVT and medical management groups, were similar).
Demeestere et al. 2010	NA	198 patients with anterior circulation LVO ischemic stroke, and NIHSS score	Differences in imaging and functional outcomes between men (n=107)	**Primary outcome:** mRS score at 90 days.	Women were significantly older than men (mean 68 vs. 64 years, p = 0.05).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Belgium ***CRISP*** **Prospective study**		≥5 treated with endovascular therapy within 18 hours from last known well time.	and women (n=91) were compared.	**Secondary outcomes:** Independence (mRS 0-2), poor outcome (mRS 5-6) and mortality at 90 days. **Imaging outcomes:** Day 1 DWI lesion volume and ischemic core growth between baseline and day 1.	Women had significantly smaller perfusion lesion volumes (median Tmax > 6s lesion volume 105 mL vs 149 mL, p < 0.001) and smaller median penumbral volumes (96 mL vs. 129 mL, p = 0.001), with no significant difference in ischemic core volume. There were no significant differences between sexes in median procedure times (onset to perfusion imaging, onset to groin puncture, or onset to end of procedure. The shift in mRS scores at 90 days was more favourable for women (adj common OR= 1.79, 95% CI 1.04 - 3.08; p = 0.04). The proportion of patients with mRS score of 0-2 did not differ between the sexes (59.3% [women] vs. 48.6 [men]), but significantly fewer women had a poor outcome (9.9% vs. 22.4%, adj OR=0.29, 95% CI 0.10 -0.81). Median core infarct growth was significantly lower in women (15 mL vs. 29 mL, p < 0.01). Women had significantly smaller median final infarct volumes (26 mL vs. 50 mL, p < 0.01).

Mechanical Thrombectomy for Mild Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
NCT04167527 **RCT** ***Endovascular Therapy for Low NIHSS Ischemic Strokes (ENDOLOW)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	200 patients (estimated) aged ≥18 years, with acute ischemic stroke based on clinical diagnosis (NIHSS 0-5), and complete occlusion of the intracranial ICA, M1, or an "M1-like" M2 vessel with or without	Patients are randomized to received EVT, initiated within 8 hours of symptom onset or best medical management	**Primary outcomes:** Ordinal shift analysis of mRS scores at 90 days, sICH at 36 hours **Secondary outcomes:** Good outcome (mRS 0-2) at 90 days, excellent outcome 9mRS 0-1) at	TBA Estimated study completion date is January 2023

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		tandem cervical lesion on imaging and baseline infarct core of either: baseline ASPECTS ≥6, or baseline infarct core volume of < 70cc.		90 days, early neurological deterioration (increase in NIHSS of ≥4 points) at 24 hours, 90-day mortality	
NCT03796468 **RCT** ***Minor Stroke Therapy Evaluation (MOSTE)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	824 patients (estimated) aged ≥18 years, with clinical signs of an acute ischemic stroke and proven anterior circulation intracranial large vessel occlusion with baseline NIHSS score of 0-5 and ASPECT ≥ 6	Patients are randomized to received EVT or best medical management	**Primary outcome:** 90-day all-cause mortality **Secondary outcomes:** Favourable outcome (mRS 0-2) at 90 days, neurological deterioration (increase of ≥10 NIHSS points within 24 hours), sICH, quality of life (QoL) and cognitive function at 90 days	TBA Estimated study completion date is Feb 2022.
Goyal et al. 2020 **USA** **Retrospective study + meta-analysis**	Risk of bias was low in the studies included in the systematic review	251 adult patients with acute large vessel, mild ischemic stroke (NIHSS <6) recruited from 16 centres between 2013-2017. Mean age was 65 years, 46.2% women.	The outcomes of patients treated with best medical management (BMM, including treatment with intravenous thrombolysis [IVT]) and mechanical thrombectomy (MT, with or without pretreatment IVT, were compared. In tandem, a systematic review was conducted of all trials which enrolled patients with mild ischemic stroke (NIHSS<6) and compared BMM vs. MT.	**Primary outcomes:** Functional independence (mRS 0-2 at 3 months), favourable outcome (mrS 0-1 at 3 months) **Secondary outcomes:** Neurological improvement during hospitalization (baseline NIHSS score - discharge NIHSS score), reperfusion, 3-month all-cause mortality, sICH and asymptomatic ICH	Median baseline NIHSS scores were 4 (MT) and 3 (BMM). 54% of MT patients vs. 41.5% of BMM patients received IVT. Successful reperfusion was achieved in 84.5% of patients in the MT group. LOS was 5 days for MT group vs. 4 days for BMM (p=0.002). In analyses adjusted for age, admission NIHSS score, pretreatment with IVT, admission glucose, admission SBP, collateral status, and ASPECTS sore on baseline neuroimaging, there were no significant differences between groups with the exception of an increased risk of asymptomatic ICH in the MT group (OR= 11.07, 95% CI 1.31-93.53, =0.03). 4 trials were identified in the systematic review. In adjusted analysis, there was no differences between groups in the odds of favourable functional outcome or functional independence at 3 months (using the

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					results from 3 studies), 3-month all-cause mortality (using the results from 2 studies), or sICH (using the results from 2 studies).

Endovascular Therapy for Basilar Artery Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Clinical Trials & RCTs					
NCT04751708 (Tao et al. 2022) **China** **RCT** ***Endovascular Treatment for Acute Basilar Artery Occlusion – a Multicenter Randomized Clinical Trial (ATTENTION)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT:☑	342 adult patients (planned) who sustained a basilar artery occlusion within the previous 12 hours and had a baseline NIHSS score of ≥10.	Patients were randomised 2:1 to receive best medical management (BMM) + additional endovascular thrombectomy (EVT) vs. BMM alone. Patients in both groups received intravenous t-PA within 4.5 hours of symptoms onset and antiplatelet drugs, anticoagulation, or their combinations EVT procedures could include mechanical thrombectomy, intra-arterial thrombolysis, balloon angioplasty, stent implantation, or any combination of above procedure	**Primary outcome:** Favourable functional outcome (mRS score 0-3) at 90 days **Secondary outcomes:** Excellent functional outcome (mRS score 0-2) at 90 days, mRS ordinal shift analysis at 90 days, NIHSS score at 24-72 hours and at 5-7 days or discharge, EQ5D-5L and Barthel index scores at 90 days. **Safety outcomes:** Symptomatic ICH + deterioration of 4 points or more on the NIHSS from baseline, or from the lowest NIHSS value between baseline and 24 hours, or death within 90 days	Preliminary results, as presented at the ESO conference May 2022. The risk of the primary outcome was significantly higher in the EVT group (46.0% vs 22.8%; adjusted relative risk (adj RR) = 2.1, 95% CI 1.5 to 3.0, NNT=4) The risk of an excellent outcome was significantly higher in the EVT group (33.2% vs 10.5%: adj RR= 3.2, 95% CI 1.8 to 5.4, NNT=4.4). The risk of 90-day mortality was significantly lower in the EVT group (36.7% vs 55.3%: adj RR= 0.7, 95% CI 0.5 to 0.8, NNT=5.4). The risk of symptomatic ICH, defined using the SITS-MOST criteria was significantly higher in the EVT group (5.3% vs 0%, NNT=19).
NCT02737189 **China** **RCT** ***Basilar Artery***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑	318 patients (planned) aged 18-80 years, with posterior circulation acute ischemic stroke who can be randomized within 6-24 hours from symptom	Patients were randomised 1:1 to receive best medical management (BMM) + additional mechanical thrombectomy (MT) vs. BMM alone.	**Primary outcome:** Favorable outcome (mRS 0-3) at 90 days **Secondary outcomes:** Dramatic early favorable	Preliminary results, as presented at the ESO conference May 2022. Based on data from 217 patients, the odds of a favourable outcome were significantly higher in the thrombectomy group (46.6% vs. 24.3%, adjusted

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Occlusion Chinese Endovascular Trial (BAOCHE)	ITT:?	onset/last seen well, confirmed through CTA, MRA or angiogram. Baseline NIHSS score ≥6, and premorbid mRS score of <2.		response (NIHSS of 0–2 or improvement ≥8 points) at 24 hours, dichotomized mRS score (0–2 vs. 3–6 and 0-4 vs.5-6) at 90 days, ordinal mRS shift analysis at 90 days, Barthel Index (BI) at 90 days, NIHSS at 90 days, MoCA at 90 days, EuroQol/ EQ-5D and SF-36 at 3 months, 6 months and 12 months **Safety outcomes:** Mortality at 90 days, symptomatic intracranial hemorrhage (SICH) at 24 hours.	OR=2.92, 95% CI 1.56-5.47). NNT=4.5. 90-day mortality was 30.9% in the MT group vs. 42.1% in the BMM group (RR=0.73, 95% CI 0.51-1.05). SICH was not significantly higher in the MT group using either SITS-MOST or ECASS II criteria (5.9% vs. 1.1% and 8.8% vs. 2.2%, respectively).
Tao et al. 2022 **China** **Registry data** ***Endovascular treatment for acute Basilar Artery Occlusion – A multicenter randomized controlled trial (ATTENTION)***	NA	2,134 adults aged ≥18 years, recruited from 48 comprehensive stroke centres with basilar artery occlusion sustained within the previous 24 hours and an NIHSS score of ≥12 at the time of imaging. Median age was 65 years, 67.7% were men. Median baseline NIHSS score was 21.	Patients were assigned 2:1 to receive best medical management (BMM, n=1,672) + mechanical thrombectomy (MT) vs. BMM only (n=462). BMM included intravenous t-PA, antiplatelet drugs, anticoagulation, or combinations of these treatments	**Primary outcome:** Favourable functional outcome (mRS score 0-3) at 90 days **Secondary outcomes:** Excellent functional outcome (mRS score 0-2) at 90 days, mRS ordinal shift analysis at 90 days, NIHSS score at 24-72 hours and at 5-7 days or discharge, EQ5D-5L and Barthel index scores at 90 days. **Safety outcomes:** Symptomatic ICH + deterioration of 4 points or more on the NIHSS from baseline, or from the lowest NIHSS value	The primary outcome occurred more frequently in the EVT group (40.4% vs. 28.5%, adjusted RR=1.42, 95% CI, 1.19–1.65; absolute risk difference, 11.8%, 95% CI, 6.9–16.7. The interaction term for NIHSS was significant. The risk of the primary outcome was higher in persons with NIHSS score ≥10 (vs. <10). Significantly more people in the EVT group had an excellent outcome (33.8% vs 23.1%; adjusted RR=1.45, 95% CI, 1.17–1.73; absolute risk difference, 10.4%, 95% CI, 5.6–15.1%). The ordinal shift in mRS scores favoured the EVT group (adjusted common OR=1.58, 95% CI, 1.27–1.96). Similar results were reported in the propensity-matched analyses. Mortality was significantly lower in the EVT group (adjusted RR=0.78, 95% CI, 0.69–0.88; absolute

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				between baseline and 24 hours, or death within 90 days	risk difference, −10.3%, 95% CI, −15.8 to −4.9). The risk of sICH was significantly higher in the EVT group (5.2% vs. 0.9%, adjusted RR=7.77, 95% CI, 2.56–23.59; absolute risk difference, 4.5%, 95% CI, 3.2–5.8).
Langezaal et al. 2021 **The Netherlands** **RCT** ***Basilar Artery International Cooperation Study (BASICS)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	300 patients, aged <85 years, recruited from 23 centres in 7 countries with CTA or MRA confirmed basilar occlusion and a NIHSS score of ≥10. Criteria was relaxed 4 years into the trial to allow older patients and those with less severe strokes to participate. Mean age was 68 years, 34.5% were women. Mean NIHSS score was 22.	Patients were randomised 1:1 to receive best medical management (BMM) + additional mechanical thrombectomy (MT) vs. BMM alone. MT was initiated within 6 hours from estimated time of event.	**Primary outcome:** Favorable outcome (mRS 0-3) at 90 days **Secondary outcomes:** Excellent outcome (mRS 0-2) at 90 days, mRS score at 90 days and 1 year, EQ-5D at 90 days and 1 year, improved early response to treatment as determined by a reduction in NIHSS by 5 points or more at 24 hours, Symptomatic intracranial hemorrhage (sICH), 90-day mortality	Intravenous thrombolysis was used in 78.6% of the patients in the endovascular group and in 79.5% of those in the medical group. Endovascular treatment was initiated at a median of 4.4 hours after stroke onset. A favorable functional outcome occurred in 68 of 154 patients (44.2%) in the endovascular group and 55 of 146 patients (37.7%) in the BMM group (RR=1.18; 95% CI, 0.92 to 1.50). There was no significant difference between groups in the percentage of patients who experienced an excellent outcome (35.1% [MT] vs. 30.1% [BMM], RR=1.17, 95% CI 0.87 to 1.57). The distribution of mRS scores at 90 days did not differ between groups. sICH occurred in 4.5% of the patients after endovascular therapy and in 0.7% of those after medical therapy (RR=6.9;95% CI, 0.9 to 53.0); mortality at 90 days was 38.3% and 43.2%, respectively (RR=0.87; 95% CI, 0.68 to 1.12). There were no significant differences between groups on any of the other secondary outcomes.
Yang et al. 2020 **China** **Prospective study** ***EVT for Acute Basilar Artery Occlusion Study***	NA	829 consecutive patients with acute radiologically confirmed BAO admitted to 47 comprehensive stroke centers across 15 provinces in China between January 2014 and May 2019. Median age was 65 years, 74%	Patients were divided into groups and received standard medical treatment (SMT) plus EVT (n=182) or SMT alone (n=647). SMT could include IVT with rt-PA or urokinase, antiplatelet drugs, systematic anticoagulation, or	**Primary outcomes:** Shift in mRS scores at 90 days **Secondary outcomes:** Favourable outcome at 90 days (mRS 0-3), sICH, 90-day mortality	644 patients (77.7%) had severe deficits; 185 patients (22.3%) had mild to moderate deficits. The odds of a favourable shift in mRS scores at 90 days were significantly higher in the EVT group (common OR=3.08, 95% CI 2.09-4.55, p <.001). The odds of a favourable outcome were significantly higher in the EVT group (32% vs. 9.3%, adj OR=

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
(BASILAR)		were men. Median NIHSS score was 27.	combinations of these medical treatments.		4.70, 95% CI, 2.53-8.75; p < 0.001; NNT for 1 additional patient to be able to walk unassisted was 4.4). 90-day mortality was significantly higher in the SMT group (71.4% vs. 46.2%; adj OR= 2.93, 95% CI 1.95-4.40, p<0.001). 7.1% of patients in the EVT group had a sICH vs. 0.5% in the SMT group. In 1:1 propensity score matching analysis including 167 patients, the results for primary and secondary outcomes were similar.
Liu et al. 2020 **China** **RCT** ***Basilar Artery Occlusion Endovascular Intervention versus Standard Medical Treatment (BEST)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	131 adult patients presenting within 8 hours of vertebrobasilar occlusion to 28 centres in China from April 27, 2015, and Sept 27, 2017. Median age was 62 years in the intervention group and 68 years in the control group. 73% of the intervention group were men vs. 80% in the control group. Baseline NIHSS scores were 32 in the intervention group and 26 in the control group.	Patients were randomized (1:1) to receive endovascular therapy + standard medical therapy (intervention group) or standard medical therapy alone (control group).	**Primary outcome:** Favourable outcome (mRS 0-3) at 90 days **Secondary outcomes:** Functional independence (mRS 0-2) at 90 days, 90-day mortality, sICH	The trial was terminated early due to excessive crossovers (77 patients of 65 randomized to the intervention group received the intervention while 54 of 66 patient allocated to the control group received standard treatment) and low enrollment (the number of patients planned was 344). In ITT analysis, the percentage of patients with a favourable outcome was not significantly higher in the intervention group (42% vs.32%; adjusted [age and baseline NIHSS] OR=1·74, 95% CI 0·81–3·74, p=0.23). Similarly, the percentage of patients who were functionally independent was not significantly higher in the intervention group (33% vs. 28%, adj OR=1·40, 95% CI 0·64−3·10, p=0.48), nor was the ordinal shift in mRS scores favouring lower scores (adj OR=1·36, 95% CI 0·72−2·55). In both the per protocol and as treated analyses, the percentage of patients with a favourable outcome was significantly higher in the intervention group (44% vs. 25%, adj OR=2·90, 95% CI 1·20−7·03 and 43 vs. 27%, adj OR=3·02, 95% CI 1·31−7·00, respectively). In both the per protocol and as treated analyses, the percentage of patients who were functionally independent was significantly higher in the

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					intervention group. There were no significant differences between groups in the odds of 90-day mortality (33% vs. 38%, OR=0·80, 95% CI 0·37–1·64, p=0·54) or the percentage of patients with sICH (8% vs. 0%, p=0.08). There was a significant interaction (p<0.01) between treatment and site of occlusion, whereby patients with vertebral artery infarcts had significantly lower odds of a favourable outcome with standard medical treatment alone (OR=0.04, 95% CI 0.01-0.88, n=12) and patients with basilar artery occlusion had significantly higher odds of a favourable outcome with intervention treatment (OR=2.13, 95% CI 1.00-4.56, n=119).
Systematic Reviews					
Katsanos et al. 2021 **Canada** **Systematic review**	Risk of bias in 1 RCT was low and could not be assessed adequately in the other due to lack of access to the full text publication.	5 studies (two RCTs, including BEST and BASILAR and 3 observational cohorts) including a total of 1,098 patients.	Trials compared EVT vs. best medical management (BMM)	**Primary outcome:** mRS score ≤3 points at 3 months **Secondary outcomes:** mRS score ≤2 points at 3 months, all-cause mortality at 3 months, ordinal shift analysis of mRS scores at 3 months, symptomatic intracranial hemorrhage (sICH) in follow-up neuroimaging.	The was no significant difference between groups in the primary outcome (RR= 0.97, 95% CI: 0.64-1.47). The certainty of the evidence was very low. There was heterogeneity such that the direction of the effect was different for observational studies and RCT, favouring EVT in RCTs and BMM in observational studies, although in neither case was statistical significance reached. There were no significant differences between groups for the proportion of patients with mRS scores of 0-2 at 3 months, all-cause mortality or functional outcome (shift analysis), with significant heterogeneity. The risk of sICH was significantly higher in the EVT group (RR=5.42, 95%CI: 2.74-10.71).

Bridging Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Clinical Trials Using Intravenous Alteplase (t-PA)					
Mitchell et al. 2022 **Australia** **RCT** ***Direct Endovascular Clot Retrieval Versus Standard Bridging Thrombolysis with Endovascular Clot Retrieval (DIRECT-SAFE)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	295 patients (780 planned), recruited from 25 hospitals ≥18 years of age, with small to moderate early ischemic changes on non-contrast CT and occlusion of the intracranial internal carotid artery, MCA artery (M1 or M2), or basilar artery confirmed by vascular imaging (CTA or MRA), who could receive intravenous thrombolytic within 4.5 hours of stroke onset. Median age was 69 years, 43% were women. Median NIHSS score was 15. Median ASPECTs score was 10.	Patients were randomized to receive mechanical thrombectomy only or mechanical thrombectomy plus intravenous alteplase (83%) or tenecteplase (17%). Endovascular thrombectomy had to commence within 90 min of randomisation.	**Primary outcome:** mRS score 0-2 at 90 days (the lower boundary of the 95% CI for the primary outcome was set at –0·10) **Secondary outcomes:** mRS 0-1 at 90 days, all-cause mortality at 90 days, early neurological improvement successful reperfusion (mTICI 2b-3), symptomatic ICH	Recruitment was halted early on the recommendation of the DSMB. In the ITT analysis, 55% of patients in the direct thrombectomy group and 61% of patients in the bridging therapy group achieved the primary outcome (risk difference –0·051, 95% CI –0·160 to 0·059; adjusted OR= 0·75, 95% CI 0·45 to 1·24), p=0·19 for non-inferiority; p=0·26 for superiority of bridging therapy. In subgroup analysis, region was found to be the only significant effect modifier, with Asian patients more likely to achieve the primary outcome when treated with bridging (57% vs. 34%, adjusted OR=0·42, 95% CI 0·21–0·86). 42% of patients in the direct thrombectomy group and 48% of patients in the bridging therapy group had a mRS score of 0-1 at 90 days (adjusted OR=0·76, 95% CI 0·46 to 1·24). 60% of patients in the direct thrombectomy group and 68% of patients in the bridging therapy group had early neurological recovery (adjusted OR=0·73, 95% CI 0·45 to 1·18). There were no significant between groups in the distribution of mRS scores at 90 days (common OR=0·85, 95% CI 0·56–1·27). Reperfusion was successful in 89% of patients in both groups. 90-day mortality was 15% in the thrombectomy only group vs.16% of patients in the bridging group (adjusted OR=0·92, 95% CI 0·46 to 1·84). Symptomatic ICH occurred in 1% of patients in each group

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Fischer et al. 2022 **Germany** **RCT** ***Bridging Thrombolysis Versus Direct Mechanical Thrombectomy in Acute Ischemic Stroke (SWIFT DIRECT)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	423 adult patients, recruited from 42 centres who were eligible for thrombolysis +/- endovascular therapy with NIHSS score of ≥ 5 and < 30 and ASPECTS ≥ 4, with occlusion of the intracranial internal carotid artery (ICA), the M1 segment of the middle cerebral artery (MCA), or both confirmed by baseline CT or MR imaging who could receive alteplase within 4.5 hours after stroke symptom onset and could undergo thrombectomy within 75 minutes of randomization. Median age was 72 years, 51% were women. Median NIHSS score was 17.	Patients were randomized 1:1 to treatment with mechanical thrombectomy or treatment with intravenous alteplase (0.9 mg/kg) followed by mechanical thrombectomy.	**Primary outcome:** mRS score of 0-2 at 90 days (the lower boundary of the 95% CI for the primary outcome was set at –0·12%) **Secondary outcomes:** 90-day mortality, ordinal shift analysis of mRS scores at 90 days, 24-hour NIHSS scores, successful reperfusion (mTICI 2b-3), symptomatic ICH at 24 hours.	57% of patients in the thrombectomy alone group achieved the primary outcome compared with 65% of patients assigned to intravenous alteplase plus thrombectomy (adjusted risk difference −7·3%, 95% CI −16·6 to 2·1, lower limit of one-sided 95% CI −15·1%, crossing the non-inferiority margin of −12%). In subgroup analysis, age was found to be the only significant effect modifier, with patients younger than 70 years more likely to achieve the primary outcome when treated with thrombectomy plus thrombolysis (84% vs. 65%, risk difference -18.9, 95% CI -32.2% to -5.7%). 90-day mortality was 11% in the thrombectomy only group vs. 9% of patients in the thrombectomy plus alteplase group (risk difference 2·3%, 95% CI −3·2 to 7·8). Mean change in NIHSS score at 24 hours was -9 in the thrombectomy only group vs. -10 in the thrombectomy plus alteplase group (mean difference 0·92, 95% CI −0·59 to 2·42). There were no significant between groups in the distribution of mRS scores at 90 days (common OR=0·75, 95% CI 0·53–1·06). Successful reperfusion was less common in patients assigned to thrombectomy alone (91% vs. 96%, risk difference −5·1%, 95% CI −10·2 to 0·0, p=0·047). Symptomatic ICH occurred in 2% of patients in the thrombectomy only group vs. 3% of patients in the thrombectomy plus alteplase group (risk difference −1·0%, 95% CI −4·8 to 2·7). The risk of serious adverse events was similar between groups (28% vs. 26%).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
LeCouffe et al. 2021 **MR CLEAN–NO IV Investigators** **The Netherlands** **RCT**	Concealed Allocation: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☒	539 patients admitted to one of 20 hospitals with ischemic stroke who were eligible to receive intravenous alteplase and EVT. Median age was approximately 70 years, 57% were men. Median baseline NIHSS score was 16.	Patients were randomized (1:1) to receive EVT alone or intravenous alteplase followed by EVT (the standard of care). The specified noninferiority margin of the lower boundary of the 95% confidence interval of the common odds ratio was 0.8.	**Primary outcome:** Shift in mRS score at 90 days, analyzed for superiority and then for noninferiority **Safety outcomes:** Death from any cause and symptomatic intracerebral hemorrhage (ICH) were the main safety end points.	The median mRS score in the EVT group was 3 and 2 in the alteplase plus EVT group. The adjusted common OR was 0.84 (95% CI 0.62 to 1.15; p=0.28), which showed neither superiority nor noninferiority of EVT alone. Mortality was 20.5% in the EVT group vs. 15.8% in the alteplase plus EVT group (adjusted OR=1.39; 95% CI, 0.84 to 2.30). Symptomatic ICH occurred in 5.9% in the EVT group vs. 5.3% in the alteplase plus EVT groups (adjusted OR=1.30; 95% CI, 0.60 to 2.81).
Suzuki et al. 2021 **Japan** **RCT** ***The Direct Mechanical Thrombectomy in Acute LVO Stroke (SKIP)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	204 patients aged 18-85 years with acute ischemic stroke due to LVO, recruited from 23 hospital from January 1, 2017, to July 31, 2019. Median age was 74 years, 62.7% were men. Median NIHSS was 18.	Patients were randomized (1:1) to undergo mechanical thrombectomy alone or combined intravenous thrombolysis with alteplase (0.6-mg/kg dose) plus mechanical thrombectomy.	**Primary outcome:** Favourable outcome (mRS score 0-2) at 90 days, analyzed for non-inferiority at a margin of 0.74. **Secondary outcomes:** Shift in mRS scores at 90 days, mortality at 90 days, successful reperfusion defined as an eTICI score of 2b to 3, recanalization, defined as modified Mori scale score of 2 to 3. **Safety outcomes:** Any ICH and symptomatic ICH	Favorable outcome occurred in 60 patients in the mechanical thrombectomy alone group and 59 patients in the combined intravenous thrombolysis plus mechanical thrombectomy group. There was no significant between-group difference (Diff=2.1%, 1-sided 97.5% CI, −11.4% to ∞; OR=1.09, 1-sided 97.5% CI, 0.63 to ∞, p = .18 for noninferiority). Mechanical thrombectomy alone was not associated with a favorable shift in the distribution of the mRS score at 90 days (OR=0.97, 1-sided 97.5% CI, 0.60 to ∞; noninferiority p = .27). There were no significant differences between groups for mortality (8 vs. 9) or successful reperfusion after mechanical thrombectomy (90.1% vs. 93.2%). The frequency of any ICH was significantly higher in the mechanical thrombectomy plus alteplase group (55.5% vs. 33.7%), but there was no significant difference in sICH (7.9% vs. 11.7%) at 36 hours, using the NINDs criteria.
Zi et al. 2021 **China** **RCT** ***Direct***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑	234 patients (970 planned), aged ≥ 18 years with an acute ischemic stroke, eligible for IV alteplase treatment within 4.5 hours of onset,	Patients were randomized (1:1) to undergo endovascular thrombectomy alone or combined IV thrombolysis (0.9 mg/kg dose) and	**Primary outcome:** Functional independence (mRS score 0-2) at 90 days, analyzed for non-inferiority. The lower margin of the 97.5% CI limit was set at	The trial was terminated early due to efficacy, when endovascular thrombectomy alone was shown to be noninferior. 54.3% of patients in the endovascular thrombectomy alone group achieved functional independence vs.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Endovascular Thrombectomy vs Combined IVT and Endovascular Thrombectomy for Patients with Acute Large Vessel Occlusion in the Anterior Circulation (DEVT)	ITT: ☑	and with an occlusion of the intracranial ICA or the first segment of the MCA, recruited from 33 sites from May 20, 2018, to May 2, 2020). Median age 70 years, 56.4% were men. Median NIHSS score was 16.	endovascular thrombectomy.	10%. **Secondary outcomes:** Shift in mRS scores at 90 days, excellent functional outcome (mRS 0-1), successful reperfusion defined as an eTICI score of 2b to 3, recanalization, defined as modified Arterial Occlusive Lesion score of 2 or 3 and EQ-5D-5L at 90 days. **Safety outcomes:** sICH within 48 hours, 90-day mortality, procedure-associated complications	46.6% in the combined treatment group (difference= 7.7%; 1-sided 97.5% CI, −5.1% to ∞; p = .003 for noninferiority). There were no significant differences between groups for any of the secondary or safety outcomes.
Yang et al. 2021 **China** **RCT** ***Direct Intraarterial Thrombectomy in Order to Revascularize Acute Ischemic Stroke Patients with Large Vessel Occlusion Efficiently in Chinese Tertiary Hospitals: A Multicenter Randomized Clinical Trial (DIRECT-MT)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	656 adult patients recruited from 41 sites with acute ischemic stroke from large-vessel occlusion in the anterior circulation, without pre-existing disability (mRS <2). Median age was 69, 56% were men. Median NIHSS score was 17.	Patients were randomized (1:1) to undergo endovascular thrombectomy using a stent retriever as the primary device, alone or endovascular thrombectomy preceded by intravenous t-PA at 0.9 mg per kilogram of body weight, administered within 4.5 hours after symptom onset (combination-therapy group).	**Primary outcome:** mRS score at 90 days, analyzed for non-inferiority at a margin of 0.8 of the lower limit of the 95% CI. **Secondary outcomes:** Death within 90 days, successful reperfusion before thrombectomy, NIHSS score at 24 hours and at 5 to 7 days (or at hospital discharge) **Safety outcomes:** All hemorrhages and symptomatic intracranial hemorrhages	There was no significant difference between groups in the median mRS score at 90 days (3 vs.3, common OR=1.07, 95% CI 0.81 to 1.40). There were no significant differences between groups in the proportions of patients with mRS scores of 0-1, 0-2, 0-3, 0-4, or 0-5. There were no significant differences between groups in the median NIHSS score at 24 hours (12 vs. 12) or at 5-7 days (8 vs. 8). There were no significant differences between groups in the percentage of patients with eTICI score of 2b, 2c, or 3, assessed on final angiogram (79.4% vs. 84.5%), or the percentage of patients with recanalization at 24–72 hours (85.1% vs. 89.1%) There were no significant differences between groups on any of the safety outcomes, or adverse reactions.
Observation Studies Using Intravenous t-PA					

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Smith et al. 2020 **Canada** **Retrospective studies**	NA	15, 832 patients admitted to 555 hospitals in the US from February 1, 2019, to June 30, 2020, treated with EVT for acute ischemic stroke (onset within the previous 6 hours). Median age was 72.0 years, 50.1% were women. Baseline median NIHSS score was 16.	The outcomes of patients treated with (n=10,548) and without (n=5,284) intravenous alteplase, were compared.	**Primary outcomes:** Discharge destination, independent ambulation at discharge, mRS score at discharge, hospital mortality, cerebral reperfusion according to modified Thrombolysis in Cerebral Infarction grade (TICI), and sICH.	Patients treated with alteplase were younger (median 70 vs. 74 years), less likely to have a history of atrial fibrillation (25% vs. 51%), to have a history of previous stroke or TIA (16.8% vs. 31.8%) or prior heart failure (12.3% vs. 18.3%). The risk of in-hospital mortality was significantly lower in the alteplase group (11.1% vs. 13.9%; adj OR=0.83, 95% CI 0.77-0.89). Significantly more patients in the alteplase group were discharged home (34.4%. vs. 27.5%; adj OR=1.29, 95% CI 1.23-1.36), could ambulate independently at discharge (38.7% vs.30.4%; adj OR=1.33, 95% CI 1.26-1.40), had a mRS score of 0-2 (28.5% vs. 20.7%; adj OR=1.36, 95% CI 1.29-1.44) and were more likely to have TICI reperfusion grades ≥2b (90.9% vs. 88.0%; adj OR=1.39, 95% CI 1.28-1.50). Significantly more patients in the alteplase group had sICH (6.5% vs. 5.3%).
Using Tenecteplase					
Campbell et al. 2020 **Australia/NZ** **RCT** ***EXTEND-IA TNK-2***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	300 adult patients, recruited from 27 centres, with ischemic stroke due to occlusion of the intracranial internal carotid, basilar, or middle cerebral artery who were eligible to receive intravenous thrombolysis. Pre-morbid mRS score ≤3. Mean age was 72.7 years, 53% were men. Median NIHSS score was 17.	Patients were randomized 1:1 to receive 2.5 or 4.0 mg/kg intravenous tenecteplase given as a bolus prior to endovascular thrombectomy	**Primary outcome:** Substantial reperfusion (the restoration of blood flow to greater than 50% of the involved territory or an absence of retrievable thrombus). **Secondary outcomes:** mRS scores at 90 days, early neurological improvement (a reduction of ≥ 8 points or a score of 0 or 1 on the NIHSS at 72 hours) **Safety outcomes:** Death, symptomatic intracranial hemorrhage (sICH) within 36 hours of	The percentage of participants with ≥50% reperfusion of the previously occluded vascular territory was the same in each group (19.3% vs. 19.3%, unadjusted risk difference, 0.0% [95% CI, −8.9% to −8.9%]; adjusted risk ratio, 1.03 [95% CI, 0.66-1.61]; P = .89). Median mRS score was 2 in both groups at day 90 (p=0.73). The percentage of patients who were functionally independent at 90 days did not differ between groups (59% [0.40] vs. 56% [0.25], p=0.40). The percentage of patients who achieved substantial early neurological deficit improvement did not differ significantly between groups (68% [0.40] vs. 62% [0.25], p=0.39).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				treatment	Mortality was 17% in 0.40 group and 19% in the 0.25 group, p=0.35. sICH incidence was 4.7% in 0.40 group vs.1.3% in the 0.25 group, p=0.12.
Systematic Reviews of Bridging with t-PA prior to EVT					
Podlasek et al. 2021 **UK** **Systematic review & meta-analysis**	All trials were at low risk of bias	4 RCTs (DEVT, DIRECT-MT, MR-CLEAN NO-IV and SKIP) comprising 1,633 patients. Mean age was 70 years, 57% were men. Mean baseline NIHSS score was 16.5.	The clinical and procedural outcomes of patients treated with direct mechanical thrombectomy (n=817) and bridging therapy (n=816), were compared.	**Primary outcome:** Good functional outcome at 90 days (mRS≤ 2) **Secondary outcomes:** Excellent functional outcome (mRS ≤1), mortality, any intracranial hemorrhage, symptomatic ICH, successful reperfusion (thrombolysis in cerebral infarction ≥2 b), and procedure-related complications.	The odds of a good functional outcome were not significantly higher in the direct MT group (OR=1.02, 95% CI 0.84-1.25). The absolute risk difference was 1% (95% CI: -4% to 5%). The lower 95% CI fell within the strictest noninferiority margin of -10%. The odds of an excellent outcome were not increased significantly with direct MT (OR=1.08, 95% CI 0.86-1.36). The odds of mortality were not increased significantly with direct MT (OR=1.06, 95% CI 0.82-1.37). The odds of any ICH were reduced significantly with direct MT (OR=0.65, 95% CI 0.49-0.86). The odds of successful reperfusion were significantly higher in the bridging group (80.9% vs. 76.5%), OR=0.76, 95% CI 0.60–0.97).
Wang et al. 2021 **China** **Systematic review & meta-analysis**	All studies except one had a low risk of bias in at least 4/6 domains using the Quality in Prognostic Studies tool	30 studies including 7,191 patients admitted to hospital following admission for acute ischemic stroke, eligible for EVT for LVO.	Studies compared pretreatment bridging with intravenous thrombolysis before EVT with direct EVT	**Primary outcomes:** Functional independence (mRS 0-2) at 90 days, 90-day mortality, successful recanalization (modified Thrombolysis in Cerebral Ischemia score 2b-3) after procedure, symptomatic ICH	The odds of functional independence were significantly higher in the bridging group (OR=1.43 95% CI, 1.28–1.61). The odds of 90-day mortality were significantly lower in the bridging group (OR=0.67, 95% CI, 0.60–0.75). The odds of successful recanalization were significantly higher in the bridging group (OR=1.23, 95% CI, 1.07–1.42). The odds of sICH were not significantly higher in the bridging group (OR=1.01, 95% CI 0.86–1.19). The results were similar for all outcomes when using propensity matching and when restricted to persons with anterior circulation strokes.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hui et al. 2020 **China** **Network meta-analysis**	Most of the trials were judged to be at high risk of bias	17 RCTs including 3,236 adult patients with LVO acute ischemic stroke. Multi-site trials included EMS, ESCAPE, EXTEND-IA, IMS III, MR. CLEAN, PISTIE, REVASCAT, SWIFT PRIME, and SYNTHESIS. Since first generation devices and trials where <50% of the patients were treated with IVT, MR RESCUE, DAWN and DEFUSE 3 were excluded.	Trials compared recanalization techniques including IAT vs IVT (n=4), IVT+MT vs IVT (n=8), IVT+IAT vs IAT (n=2), IAT+ IVT vs. IVT (n=2), MT vs IVT+IAT (n=1). In addition to traditional data pooling methods, the surface under the cumulative ranking curve (SUCRA) probability was used to indicate the probability of an intervention being the most effective intervention. Values range between 0% and 100%, with higher values indicating a higher likelihood that an intervention might be the best.	**Primary outcomes:** Functional independence (mRS 0-2) at 90 days **Secondary outcome:** Successful recanalization confirmed by angiography. **Safety outcomes:** All-cause mortality at the end of the follow-up period and sICH.	IVT+MT was associated with significantly higher odds of functional independence compared with IVT alone (OR=2.07; 95% credible interval [CI], 1.61–2.66). In the SUCRA plots, IVT+MT was ranked as the treatment associated with the best functional outcome (98.85%), followed by IAT (41.28%), IVT+IAT (38.70%), and IVT (21.17%). IVT+MT was not associated with significantly lower odds of mortality at 90 days compared with IVT alone (OR=0.84; 95% CI, 0.63-1.11). There were no significant differences between treatment strategies for any of the other comparisons (IVT +MT vs, MT, IVT vs. MT, IVT+IAT vs. MT, IAT vs. MT, IVT+MT vs. IAT, IVT+MT vs. IVT+IAT, IVT+IAT vs. IAT, IVT vs. IAT, IVT+IAT vs. IAT). In the SUCRA plots, IVT+MT had an 83.89% chance of being the safest treatment with the lowest rate of all-cause mortality at 90 days, which was higher than IVT+IAT (57.98%), IVT (53.93%), IAT (41.35%), and MT (12.84%). None of the treatment strategies were associated with an increased risk of sICH at 30 hours (IVT vs. IAT, IVT+IAT vs. IAT, IVT+MT vs. IVT, IVT+IAT vs. IVT+MT, IVT+MT vs. IAT, IVT vs. IVT+IAT). In the SUCRA plots IVT was the most favorable treatment to avoid sICH (66.10%), followed by IVT+IAT (57.99%), IVT+MT (41.41%), and IAT (34.51%). MT+ IVT was associated with higher likelihood of successful recanalization rate compared with IVT.
Phan et al. 2019 **International** **Network meta-**	6 factors assessing risk of bias were assessed. All	12 studies (5 RCTs, 7 prospective cohort) published up to May 2017 including 3,161 patients. RCTs included	The outcomes of patients who received 1) direct EVT within the thrombolysis window with no contraindications to	**Primary outcomes:** Good functional outcome (mRS 0-2) at 90 days, all-cause mortality at 90 days	*Good functional outcome* There was no significant difference between groups for the comparisons of DEVT vs. IVEVT (OR= 1.11; 95% CI 0.75 to 1.66), DEVTc vs IVEVT (OR= 1.30; 95% CI 1.00 to 1.79), DEVT vs DEVTc (OR=1.45;

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
analysis	RCTs were considered at low risk of bias. All but one of the prospective studies had ≥1 factor indicating clear or unclear risk of bias	EXTEND-IA, SWIFT PRIME, THERAPY, THRACE, and PISTIE	thrombolysis (DEVT, n=248), 2) direct EVT secondary to contraindications to thrombolysis (DEVTc, n=878), 3) EVT in addition to thrombolysis (IVEVT, n=1516); and (4) thrombolysis without EVT (IVT, n=519), were compared.	**Secondary outcomes:** Symptomatic ICH (sICH), asymptomatic ICH (aICH), reperfusion	95% CI 0.93 to 2.35), DEVTc vs. IVT (OR=1.52; 95%CI 0.96 to 2.33). The odds of a good outcome were increased significantly given IVENT vs. IVT (OR= 1.97; 95% CI 1.42 to 2.78) and with DEVT vs. IVT (OR=2.19; 95% CI 1.32 to 3.75). *Mortality* There was no significant difference in 90-day mortality between all treatments, including DEVT vs IVEVT (OR= 0.77; 95% CI 0.53 to 1.05), IVEVT vs DEVTc (OR= 0.78; 95% CI 0.50 to 1.20), and IVEVT vs IVT (OR= 0.76; 95%CI 0.48 to 1.18). *sICH* There were no significant differences between all treatment groups. *aICH* The odds of aICH were significantly lower for DEVT vs. IVEVT (OR=0.47, 95% CI 0.29 to 0.76). There were no significant differences between groups for any of the other pairings. *Reperfusion* The odds of successful reperfusion were significantly higher for DEVT vs. IVEVT (OR=1.73; 95% CI 1.04 to 2.94) and for DEVT vs. DEVTc (OR= 2.03; 95% CI 1.16 to 3.59)
Katsanos et al. 2019 **Greece** **Systematic review & meta-analysis**	The overall Newcastle–Ottawa scale score was 267/342 (78%), considered to represent overall high quality.	38 eligible observational studies, including 11,798 LVO patients who received EVT treatment. Mean age was 68 years, 50% were women	Studies compared pretreatment bridging with intravenous thrombolysis before EVT (56%) with direct EVT	**Primary outcome:** Functional independence (mRS score of 0-2) at 90 days **Secondary outcomes:** 3-month mortality, any intracranial hemorrhage, shift in mRS scores	Bridging was associated with a significantly higher likelihood of functional independence (adjusted OR = 1.55, 95% CI = 1.26–1.91) and lower odds of 3-month mortality (adjusted OR = 0.80, 95% CI = 0.66–0.97. There was no significant difference between the groups symptomatic intracranial hemorrhage (adjusted OR = 0.87, 95% CI = 0.61–1.25), or shift in mRS scores at 3 months (adj OR=1.24, 95% CI 0.89–1.74).

Neuroprotectants + Endovascular Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hill et al. 2020 **Canada** **RCT** ***ESCAPE-NA1***	Concealed Allocation: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	1,105 adult patients, previously independent with acute ischemic stroke, baseline NIHSS score >5, ASPECTS > 4, and vascular imaging showing moderate-to-good collateral filling, recruited between March 1, 2017, and Aug 12, 2019 from 48 acute care hospitals in 8 countries. Mean age was 71 years, 50% were men. Median NIHSS score was 17.	Patients were randomized (1:1) to receive a single dose of IV nerinetide (2·6 mg/kg, up to a maximum dose of 270 mg) or saline placebo prior to EVT +/- IV t-PA.	**Primary outcome:** Good outcome (mRS 0-2) at 3 months **Secondary outcomes:** Good neurological outcome, (NIHSS of 0–2), functional independence (Barthel Index ≥95), excellent functional outcome (mRS 0-1) and mortality	59.2% of patients in the placebo group and 60.1% of patients in the intervention group received IV t-PA. 337 (61·4%) patients who received nerinetide and 329 (59·2%) placebo patients achieved a good outcome (adjusted RR= 1·04, 95% CI 0·96–1·14; p=0·35). The percentage of patients with NIHSS of 0-2 was similar between groups (placebo 57·6% vs. intervention 58.3%, adj RR=1·01, 95% CI 0·92 to 1·11). The percentage of patients with BI score ≥95 and excellent outcome was similar between groups (placebo 60.3% vs. intervention 62.1%, adj RR=1·03, 95% CI 0·94 to 1·12 and placebo 40.6% vs. intervention 40.4%, adj RR= 0·98, 95% CI 0·85 to 1·12). Mortality was similar between groups (placebo 14.4% vs. intervention 14.4%. adj RR=0·84, 95% CI 0·63 to 1·13). There was a significant effect modification whereby patients in the intervention group who did not receive IV t-PA had better outcomes. (good outcome: RR=1·18, 95% CI 1·01 to 1·38; mortality: RR=0·66, 95% CI 0·44 to 0·99). The number of patients with serious adverse events was similar between groups.

Trials Comparing Devices/Approaches

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Turk et al. 2019 **USA** **RCT** ***COMPASS Trial: A Direct Aspiration First Pass Technique*** **(non-inferiority trial)**	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	270 patients recruited from 15 sites presenting with an acute ischaemic stroke from large vessel occlusion, occurring within 6 hours of symptom onset and an Alberta Stroke Program Early CT Score>6. Mean age was 71.5 years, 50% were men. Median NIHSS score was 17.	Patients were randomized 1:1 to receive direct aspiration as first pass thrombectomy (Penumbra) or a stent retriever (Solitaire or Trevo)	**Primary outcome:** mRS score of 0-2 at 90 days, shift in distribution of mRS scores, time to TICI ≥2b **Safety outcomes:** Intracranial hemorrhage within 90 days, asymptomatic ICH within 24 hours, parenchymal hematoma type 2 hemorrhage within 36 hours of randomisation, clinically significant complications, all-cause mortality at 3 months	70% of patients received pre-procedure t-PA. The percentage of patients achieving an mRS score of 0-2 was 50% compared with 52% in the stent retriever group. Aspiration was non-inferior to stent retriever (p=0.0014). The result was similar in the per-protocol analysis (55% vs. 52%, p for non-inferiority=0.0028) The shift in distribution of mRS scores did not differ significantly between groups. Median time to TICI ≥2b was significantly shorter in the aspiration group (22 vs. 33 minutes, p= 0·0194). There were no significant differences between groups for any of the safety outcomes. Procedural costs were lower in the aspiration group (mean US$4,541)
Lapergue et al. 2017 **France** **RCT** ***The Contact Aspiration vs Stent Retriever for Successful Revascularizatio n (ASTER) trial***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	381 patients recruited from 8 sites with suspected ischemic stroke secondary to occlusion of the anterior circulation, within 6 hours of onset of symptoms. Mean age was 69.9 years, 45.7% were women. Mean NIHSS score was 16.2	Patients were randomized 1:1 to undergo either contact aspiration (intervention) or stent retriever (control) thrombectomy as the first line intervention. The study was designed to demonstrate the superiority of first line contact aspiration over stent retriever	**Primary efficacy outcome:** Successful revascularization (modified TICI score of 2b or 3) at the end of all endovascular procedures **Secondary outcomes:** Overall distribution of mRS scores at 90 days, change in NIHSS score at 24 hours, all-cause mortality at 90 days, and procedure-related serious adverse events	65.6% of patients received pre-procedure t-PA. Median time from symptom onset to arterial puncture was 227 minutes. There was no significant difference in successful revascularization rates at the end of the procedure (85.4% for contact aspiration vs 83.1% for stent retriever (OR=1.20, 95% CI 0.68-2.10, p=0.53). There were no significant differences between groups for any of the secondary outcomes
Nogueira et al. 2012 **USA** **TREVO-2 Non-inferiority study**	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☑	178 patients aged 18 to 85 years with ischemic stroke who had failed IV t-PA therapy or for those whom treatment with IV t-PA was contraindicated, NIHSS scores of 8-29 Angiographic	Patients were randomized to undergo thrombectomy with either the Merci Retriever (n=90) or the Trevo Stentriever (n=88)	**Primary outcome:** Efficacy-Revascularization success (TICI flow of ≥2 of the occluded territory) Safety- adverse events **Secondary outcomes:** Time to revascularization,	Successful revascularization was achieved by more patients in the Trevo group (86% vs. 60%, RR=4.22, 95% CI 1.92 to 9.69, p<0.0001). A good outcome was achieved by more patients in the Trevo group (40% vs. 22%, RR=2.39 95% CI 1.16 to 4.95, p=0.013).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT		confirmation of a persistent large vessel occlusion in the internal carotid, middle cerebral (M1 and/or M2 segments), basilar and/or vertebral arteries Treatable within 8 hours of symptom onset.		good outcome at 90 days (mRS score of ≤2), all-cause mortality at day 90, symptomatic ICH within 24 hours of procedure.	There were no differences in adverse events between groups (Trevo vs. Merci). Symptomatic ICH: 7% vs. 9%, p=0.78 Vessel perforation: 0 vs. 1%, p=1.00 Death within 24 hrs.: 2% vs. 0, p=0.243 Death at 90 days: 33% vs. 24%, p=0.185 Neurological deterioration at 24 hrs: 16% vs. 22%, p=0.342 Losses to follow-up: n=1 (Merci group)
Saver et al. 2012 **USA** **RCT** ***SWIFT***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	113 patients aged 22-85 years, with clinical signs consistent with moderate-to-severe ischemic stroke, with NIHSS scores of 8-30, and able to be treated within 8 hours of stroke symptoms onset and were ineligible for, or failed t-PA therapy.	Patients were randomized to undergo thrombectomy with either the Solitaire Device (n=58) or Merci Retriever (n=55). An additional 32 roll-in patients were allocated to the SOLITAIRE group	**Primary outcome:** Efficacy-Revascularization success (TICI flow of ≥2 of the occluded territory) with no ICH Safety- adverse events **Secondary outcomes:** Good neurological outcome at 90 days (mRS score of ≤2) (or pre-stroke mRS) Improvement in NIHSS scores at 90 days of ≥10 points, mortality symptomatic ICH	Among randomized patients, a greater percentage in the SOLITAIRE group achieved the primary efficacy endpoint (61% vs. 24%, OR=4.87, 95% CI 2.14 to 11.10, p<0.0001 (non-inferiority). Good neurologic outcome was achieved by significantly more patients in the SOLITAIRE group (58% vs. 33%, OR=2.78, 95% CI 1.25 to 6.22, p=0.0001 (non-inferiority). Median mRS score at 90 days was lower among patients in the SOLITAIRE group (3 vs. 4, p=0.035). Mortality: Fewer patients in the SOLTAIRE group had died at day 90 (17% vs. 36%, p=0.02 (superiority) Symptomatic ICH: Trend towards fewer incidences in SOLITAIRE group (2% vs. 11%, p=0.057). Losses to follow-up or withdrawals: n=3 SOLITAIRE, n=7 MERCI Adverse events: No study-device related (9% SOLITAIRE vs. 16% MERCI, p=0.26) or procedure related (14% vs. 16%, p=1.00) differences in serious adverse events between groups.

Blood Pressure Targets to Reduce the Risk of Bleeding Following EVT

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Mazighi et al. 2021 **France** **RCT** ***Blood Pressure Target in Acute Stroke to Reduce hemorrhaGe After Endovascular Therapy (BP-TARGET)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	324 adult patients with successful reperfusion after a thrombectomy procedure (2b-3 TICI score) for acute ischemic LVO stroke, recruited from 4 centres. Median age was 77 years, 51% were women. Median NIHSS score was 17.	Patients were randomized 1:1 to receive antihypertensive treatment to reach and maintain a SBP target of < 130 mm Hg or 130-185 mm Hg for 24 hours post EVT.	**Primary outcome:** Any ICH between 24 and 36 hours post procedure **Safety outcomes:** Symptomatic ICH between 24 and 36 hours post procedure, hypotensive events, all-cause mortality at follow-up	The mean SBP during the first 24 h after reperfusion was 128 mm Hg in the intensive target group and 138 mm Hg in the standard target group. The odds of the primary outcome were not significantly lower in the intensive target group (42% vs. 43%, OR=0·96, 95% CI 0·60–1·51; p=0·84). The odds of the symptomatic ICH within 24-36 hours were not significantly lower in the intensive target group (11% vs. 7%, OR=1.68, 95% CI 0·75–3·77). The odds of all-cause mortality were not reduced significantly in the intensive target group (21% vs. 16%, OR=1·46, 95% CI 0·80 to 2·63). The frequency of hypotensive events was not significantly higher in the intensive target group (8% vs. 3%, OR=2·53, 95% CI 0·86 to 7·41).
Anadani et al. 2020 **USA** **Retrospective study**	NA	1,019 patients recruited from 8 comprehensive stroke centres following successful revascularization (mTICI 2b-3) with EVT for LVO. Mean age varied across groups from 64-70 years, 47-52% were women.	Patients were divided into 3 groups based on SBP goal in the first 24 hours after EVT (<140 mmHg, [n=540] <160 mm Hg [n=142] and <180 mmHg [n=337]), and their outcomes compared using propensity score analysis.	**Primary outcome:** Good clinical outcome (mRS 0-2) at 90 days **Secondary outcomes:** sICH, all-cause 90-day mortality, rescue therapy with hemicraniectomy during hospitalization	Mean SBPs (mmHg) across the 3 groups were 126 (<140 mmHg), 135 (<160 mmHg) and 133 (<180 mmHg). The percentages of patients with SBP below goal targets in each group were 90%, 86% and 93%. The percentages of patients with a good clinical outcome were 52% (<140 mmHg), 52% (<160 mmHg) and 44% (<180 mmHg). Compared with the <180 mmHg group, the odds of a good clinical outcome were significantly higher in the <140 mmHg group (adj OR=1.53, 95% CI 1.07–2.19). The odds of all-cause mortality were reduced significantly in the <160 mmHg group vs. <180 mmHg group (adj OR=0.42, 95% CI 0.22–0.82). The odds of a hemicraniectomy were reduced significantly in the <140 mmHg group compared with

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					the <180 mmHg group (adj OR=0.18, 95% CI 0.16–0.21) In subgroup analyses including only patients with admission SBP≥140 mmHg, the odds of a good clinical outcome were significantly higher in the <140 mmHg group compared with the <180 mmHg group (adj OR=1.75, 95% CI 1.07–2.85) and in the <160 mmHg group compared with the <180 mmHg group (adj OR=2.30, 95% CI 1.17–4.52). The odds of all-cause mortality were reduced significantly in the <140 vs. <180 mmHg groups and in the <160 vs. <180 mmHg groups.
Rasmussen et al. 2020 **Denmark** **Retrospective study**	NA	365 adult patients with anterior-circulation ischemic stroke, enrolled in 3 RCTs (SIESTA and ANSTROKE, and GOLIATH trial) assessing anesthetic strategy for EVT between February 2014 and February 2017. Mean age was 71.4 years, 44.6% were women. Median NIHSS score was 17.	The association between intraprocedural hypotension and hypertension and neurological outcome, was examined.	**Primary outcome:** mRS score at 90 days	A cumulated period of a minimum of 10 minutes with mean atrial plod pressure (MABP) of <70 mm Hg MABP and with a continuous episode of minimum 20 minutes with <70 mm Hg MABP were associated with a shift toward higher 90-day mRS scores (adjusted OR, 1.51; 95% CI, 1.02-2.22 and adjusted OR, 2.30; 95% CI, 1.11-4.75, respectively). The corresponding to a number needed to harm (NNTH) were 10 and 4. A cumulated period of a minimum 45 minutes with MABP of > 90 mm Hg and a continuous episode of minimum 115 minutes with > 90 mm Hg MABP, were associated with a shift toward higher 90-day mRS scores (adjusted OR, 1.49; 95% CI, 1.11-2.02 and adjusted OR, 1.89; 95% CI, 1.01-3.54, respectively). The corresponding NNTH were 10 and 6.
Cho et al. 2019 **South Korea** **Retrospective study**	NA	378 patients treated with EVT due to large vessel occlusion in the anterior circulation at a comprehensive stroke centre between January 2011 and September 2016. Mean age was 70 years, 54.2% were men. Median baseline NIHSS	BP was measured hourly during the first 24 hours after admission. Associations between various SBP and DBP parameters, including mean (an average of values), standard deviation (SD), maximum, coefficient of	**Primary outcome:** Good outcome (mRS 0-2) at 3 months **Secondary outcomes:** Excellent functional outcome (mRS 0-1) at 3 months, sICH and death Fully adjusted model was	313 patients (82.8%) achieved successful reperfusion after EVT. 149 patients achieved a good outcome. Initial SBP and DBP were 138.7 and 76.9 mmHg, respectively. Mean SBP and DBP over the first 24 hours following EVT were 127.6 and 70.6 mmHg. In a fully adjusted model, using data from all patients, higher systolic SV was associated with a

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		score was 12.	variation (CoV) and successive variation (SV), and outcomes were examined.	adjusted for age, male sex, NIHSS score, SBP mean, onset to groin puncture time, TOAST, occlusion site, IVT, recanalization, hypertension, diabetes, atrial fibrillation, prior stroke, smoking, SBP, DBP, and glucose.	reduced likelihood of achieving good outcome (each 10% increase, OR=0.41, 95% CI 0.20–0.82, p=0.01). Among patients who were successfully revascularized, higher systolic SV was also associated with a reduced likelihood of achieving good outcome (each 10% increase, OR=0.28, 95% CI 0.12–0.65, p=0.003). The same pattern of results was observed for diastolic SV, whereby increasing SV was associated with reduced odds of a good outcome among all patients and those who were successfully reperfused. Outcomes across the entire ordinal range of the mRS were independently associated with systolic SV and mean SBP. Higher mean SBP [every 10-mmHg increase], common cOR=1.25, 95% CI 1.09–1.43 and systolic SV [every 10% increase, cOR 2.50 (1.61–3.88)] values were associated with a higher likelihood of worse mRS scores at 3 months, with similar results were observed for DBP parameters. In a model adjusted for age, sex, NIHSS score, SBP mean, onset to groin puncture time, TOAST, occlusion site, IVT, and recanalization, there were no associations between any of the SBP parameters and sICH. Mean SBP was 158.8 mmHg in patients who did not develop sICH and was 158.2 mmHg for patients who did. In a model adjusted for age, sex, NIHSS score, SBP mean, onset to groin puncture time, TOAST, occlusion site, IVT, and recanalization, using data from all patients, higher systolic SV was associated with an increased risk of death (each 10% increase, OR=1.10, 95% CI 1.20–1.192, p=0.01). Among patients who were successfully revascularized, higher systolic SV was also associated with an increased likelihood of death (each 10% increase, OR=1.13, 95% CI 1.04–1.23, p=0.01).
Mistry et al. 2019	NA	485 patients recruited from 12 comprehensive stroke centers from	The 24-hour post procedure threshold of peak SBP that best	**Primary outcome:** Dichotomized 90-day mRS score representing a good	mRS data were available for 446 patients, of which 186 (42%) had a good outcome.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
USA **Prospective study** ***Blood Pressure after Endovascular Therapy for Ischemic Stroke (BEST)***		November 2017 to July 2018 with LVO, treated with EVT. Median age was 69 years, 51% were women. Median baseline NIHSS was 16	discriminated primary outcome, was identified.	(0–2) versus bad (3–6) outcome **Secondary outcomes:** Any ICH, sICH (associated with ≥4 points increase in NIHSS from baseline to 24 hours), change in the mRS distribution, and early neurological recovery (NIHSS 0–1 or 8 points decrease in NIHSS from baseline to 24 hours)	A peak SBP of 158 mmHg was the point that best discriminated between a good and bad outcome (52% sensitivity, 68% specificity; area under the curve 0.61, 95% CI, 0.56–0.66, P<0.001). A peak SBP of >158 mmHg was associated with significantly increased odds of a bad outcome in unadjusted analysis (66% vs. 47%; OR=2.24, 95% CI 1.52–3.29, p<0.01), but not in adjusted analysis (OR=1.29, 95% CI 0.81–2.06, p=0.28). As a continuous variable, SBP>158 mmHg was associated with bad outcome in unadjusted (OR= 1.02, 95% CI 1.01–1.03, p=0.79), but not adjusted analysis (OR=1.00, 95% CI 0.99–1.01, p=0.79). The odds of early neurological recovery were significantly lower in patients with a peak SBP >158 in unadjusted (OR=0.68, 95% CI 0.47–0.99, p=0.04) but not adjusted analysis (OR=0.90, 95% CI 0.58–1.39, p=0.63). The odds of any ICH or sICH were not increased significantly in patients with peak SBP>158 mmHg in unadjusted, or adjusted analysis.
Cernik et al. 2019 **Czech Republic** **Retrospective study**	NA	690 patients recruited from 2 centres between 2010 and 2016 and treated with EVT for MCA, ICA or basilar artery acute ischemic stroke. Mean age was 71 years, 51% were men. Median baseline NIHSS score was 17.	The outcomes of patients with median of SBP <140mm Hg and ≥140mm Hg within the first 24 hours after EVT, were compared	**Primary outcome:** Good outcome (mRS 0-2) at 90 days **Secondary outcomes:** Complete recanalization, any ICH, sICH, mortality at 7 and 90 days	There were no significant differences between groups (<140 vs. ≥140 mm Hg) in the percentage of patients with complete recanalization (66.2% vs. 62.1%, p=0.26), any ICH (27.4% vs. 30.6%, p=0.36), sICH (5.1% vs. 5.1%, p=0.98), or 7-day mortality (7.7% vs. 9.2%, p=0.47). A significantly higher percentage of patients in the <140 mmHg group had a good outcome at 90 days (53.7% vs. 41.4%, p=0.001). A significantly lower percentage of patients in the <140 mmHg group and were dead at 90 days (23.4% vs. 32.2%, p=0.01). Patients with good outcome had a significantly lower median SBP and median of maximal recorded SBP compared with those with poor outcome (131 vs

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					140mm Hg, P<0.0001).
Goyal et al. 2017 **USA** **Retrospective study**	NA	217 patients who underwent EVT for LVO, treated at a tertiary care stroke center from July 2012 to January 2016. Mean age was 62 years, 50% were men. Median baseline NIHSS score was 16. Mean admission SBP and DBP were 158- and 90-mm Hg.	Hourly SBP and DBP recording were obtained for all patients during the first 24 hours following EVT. Univariable and multivariable logistic regression models were used to evaluate associations between minimum, mean, and maximum SBP and DBP levels during the first 24 hours following EVT. Among 145 patients who achieved complete revascularization, patients were stratified into 3 groups based on post-EVT achieved BP goals: <140/90 mm Hg (intensive, n=10), <160/90 mm Hg (moderate, n=36), and a permissive hypertension group defined as <220/120 mm Hg or <180/105 mm Hg when pretreated with IV thrombolysis (n=94). Group outcomes were compared.	**Primary outcome:** Functional independence (mRS 0-2) at 3 months **Secondary outcomes:** sICH and 3-month mortality	65% of patients were treated with IV t-PA prior to EVT. Mean maximum SBP and DBP were significantly lower in patients who were functionally independent at 3 months (163 vs. 179 mmHg, p<0.001 and 91 vs. 97 mmHg, p=0.008, respectively). Mean maximum SBP and DBP were significantly lower in patients who were alive at 3 months (166 vs. 184 mmHg, p<0.001 and 93 vs. 98 mmHg, p=0.014, respectively). There were no significant differences between groups in mean SBP or DBP associated with the development of sICH. A 10 mm Hg increment in maximum SBP was an independent risk factor for lower odds of 3-month functional independence (OR=0.70; 95% CI 0.56–0.87) and higher odds of 3-month mortality (OR= 1.49; 95% CI 1.18–1.88). There was no significant association between maximum DBP levels and 3-month mortality or functional independence. Using the permissive hypertension group as the reference category, the odds of functional independence were not increased significantly in either the intensive or moderate blood pressure groups. Using the permissive hypertension group as the reference category, the odds of 3-month mortality were significantly reduced in the moderate BP group (OR=0.08, 95% CI 0.01–0.054, p= 0.010), but not compared with the intensive BP group (OR=1.00, 95% CI 0.99–1.01, p= 0.999).

Anesthetic Management for Endovascular Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Systematic Reviews & Meta-analyses					
Tosello et al. 2022 **Brazil** **Cochrane review**	The overall risk of bias was high in 4 trials, unclear in 2 trials and low in one trial.	7 RCTs including 982 participants. Mean age was 71.2, years, 56.8% were men. About 72% received IV r-tPA before EVT. Mean NIHSS score was 16.1.	All participants were randomized to receive general anesthesia (GA) vs. non-GA (local anaesthesia, conscious sedation anaesthesia or monitored anaesthesia care).	**Primary outcomes:** Functional outcome at the end of scheduled follow-up, neurological impairment **Secondary outcomes:** Stroke-related mortality, intracranial hemorrhage, target artery revascularisation status	*Early outcomes* There was no significant difference between groups in NIHSS scores at 48 hours (MD= –0.29, 95% CI –1.18 to 0.59; 7 studies, 982 participants; low-certainty evidence) The risk of stroke-related mortality was not reduced significantly with GA (RR= 0.98, 95% CI 0.52 to 1.84; 3 studies, 330 participants; low-certainty evidence), The risk of all intracranial haemorrhages was not reduced significantly with GA (RR 0.92, 95% CI 0.65 to 1.29; 5 studies, 693 participants; low-certainty evidence) GA was associated with significantly better likelihood of artery revascularisation (RR=1.10, 95% CI 1.02-1.18; 7 studies, 982 participants; moderate-certainty evidence) GA was associated with a decreased risk of adverse events (RR=0.21, 95% CI 0.05-0.79; 2 studies, 229 participants; low-certainty evidence). *Long-term outcomes* The likelihood of having a good functional outcome (mRS ≤2) at 90 days was not significantly greater in the GA group (RR=1.21, 95% CI 0.93 to 1.58; 4 studies, 625 participants; low-certainty evidence). The risk of stroke-related mortality was not reduced significantly with GA (RR= 0.88, 95% CI 0.64 to 1.22; 6 studies, 843 participants; low-certainty evidence),
Campbell et al. 2021 **New Zealand**	The risk of bias was assessed as low in all 4	4 RCTs including SIESTA, AnSTROKE, GOLIATH and CANVAS (pilot) (n=408). Mean	All participants were randomized to receive general anesthesia (GA) vs. conscious sedation	**Primary outcomes:** Successful recanalization (TICI score of 2b to 3) and good functional outcome	The odds of successful recanalization and good functional outcome were significantly higher in the GA group (OR=2.14, 95% CI 1.26-3.62, p=0.005 and OR=1.71, 95% CI: 1.13-2.59; P=0.01,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	trials	patient age ranged from 63.5 to 72.5 years, 56.6% were men. Mean baseline NIHSS from 13.5 to 18.5.	(CS) during thrombectomy	(mRS 0-2) at 3 months. **Safety outcomes:** Intracerebral hemorrhage and 3-month mortality.	respectively). For every 7.9 patients receiving GA, one more achieved good functional outcome compared with those receiving CS. There were no significant differences between groups in intracerebral hemorrhage (OR: 0.61, 95% CI: 0.20- 1.85; P=0.38) or 3-month mortality (OR: 0.62, 95% CI: 0.33-1.17; P=0.14).
Schönenberger et al. 2019 **Germany**	The risk of bias was assessed as low in all 3 trials	3 single centre RCTs (SIESTA, AnSTROKE and GOLIATH), including adult participants with acute ischemic stroke in anterior circulation with baseline NIHSS scores of ≥10. Details of all trials described below.	All participants were randomized to receive general anesthesia vs. procedural sedation during thrombectomy	**Primary outcome:** Ordinal shift in distribution of mRS scores at 3 months **Secondary outcomes:** There were 15 secondary outcomes including 4 clinical, 2 imaging, 9 care process outcomes, and 5 adverse events.	General anesthesia (GA) was associated with a more favorable shift in mRS scores at 3 months (cOR=1.58, 95% CI 1.09 to 2.29, p=0 .02). GA was also associated with higher odds of patients with mRS scores of 0-2 and 0-3, at 3 months (OR=2.16, 95% CI 1.31 to 3.54 and OR=1.73, 95% CI 1.06 to 2.82, respectively). The odds of successful reperfusion (mTICI score of 2b or 3) were significantly higher in the GA group (OR=1.84, 95% CI 1.12 to 3.01) GA was not associated with decreased mortality, infarct growth or early neurological improvement. The risk of hypotension (<20% from baseline) was significantly higher in the GA group (OR=4.3, 95% CI 2.6 to 7.1) as was the risk of BP variability (>180 or <120 mm Hg; OR=2.4, 95% CI 1.5 to 3.9). 21 patients converted from procedural sedation to GA.
Campbell et al. 2018 HERMES Collaborators **International** **Patient-level meta-analysis**	NA	7 RCTs (n=1,764 patients), including MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME, REVASCAT, PISTE and THRACE. The mean age of patients who were randomized to the mechanical thrombectomy group was	The method of anesthesia for those patients undergoing mechanical thrombectomy was identified. The outcomes of patients who received general anesthesia (GA, n=236) were compared with patients who	**Primary outcome:** mRS score at 90 days **Secondary outcomes:** Proportion of patients with mRS score of 0-2 and 0-1 at 90 days, early neurological improvement (reduction of NIHSS score ≥8 points at 24 hours, or NIHSS score of 0-	Patients who received GA were significantly younger (63.8 vs. 66.3 years, p=0.015), had a significantly lower median baseline ASPECTS score (7 vs. 8, p=0.0005), and were randomized sooner (179 vs. 184 min, p=0.04). The outcomes of all patients who received thrombectomy, regardless of method of anesthesia were better than those who received standard care.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		65.5 years, 53% were men. Median NIHSS score was 17.	received non-GA methods (n=561).	1), 90-day mortality, symptomatic ICH	The odds of improved outcome using non-GA versus GA were significantly greater in ordinal analysis of the mRS, after adjustment for baseline prognostic factors (common OR=1.53 95% CI 1.14–2.04, p=0·0044). For every 100 patients treated under GA versus no GA, 18 patients would have worse functional outcome, including 10 who would not achieve functional independence. The odds of achieving a mRS score of 0-1 and 0-2, and in early neurological improvement were significantly higher for non-GA patients. The odds of 90-day mortality or sICH were not increased significantly in the non-GA group. The proportions of patients with successful reperfusion (≥50%) did not differ between groups (75% vs. 76%). Mean stroke onset to reperfusion time was similar between groups (GA 302 min vs. non-GA 288 min, p=0.57).
Brinjikji et al. 2017 **USA**	NA	22 studies, including 4,716 patients who had undergone endovascular therapy for revascularization following acute stroke	The outcomes of patients who received conscious sedation or local anesthesia (i.e non-general anesthesia, non-GA, n=2,897) were compared with those who had undergone general anesthesia (GA, n=1,819)	**Primary outcome:** Good functional outcome (mRS ≤2) at 90 days following treatment **Secondary outcomes:** Successful recanalization rate, 90-day mortality, vascular complications, respiratory complications, procedure time	GA was associated with significant lower odds of favorable functional outcome (OR=0.58; 95% CI, 0.48–0.64). The effect was maintained after adjustment for baseline NIHSS scores GA was associated with significantly higher odds of 90-day mortality (OR=2.02, 95% CI 1.66–2.45), vascular complications (OR= 1.43, 95% CI, 1.01–2.03), and respiratory complications (OR=1.70, 95% CI, 1.22–2.37). There was no significant difference in successful recanalization rates between groups. GA was associated with significantly higher odds of vascular complications, respiratory complication and symptomatic ICHs. Time to groin puncture was significantly longer in the

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					GA group (WMD=14.2 minutes, 95% CI, 9.47–18.9). Procedure time was statistically significant shorter in the GA group (WMD= −4.6, 95% CI, −8.76 to −0.51).
Brinjikji et al. 2015 **USA**	NA	9 studies, including 1,956 patients who had undergone endovascular therapy for revascularization following acute stroke	The outcomes of patients who received conscious sedation (n=1,142) were compared with those who had undergone general anesthesia (n=819)	**Primary outcome:** Good functional outcome (mRS ≤2) at 90 days following treatment **Secondary outcomes:** Successful recanalization rate, asymptomatic and symptomatic intracranial hemorrhage (ICH), death, vascular complications, respiratory complications, procedure time, time to groin puncture, time from symptom onset to recanalization	Patients undergoing general anesthesia had: Lower odds of good functional outcome (OR = 0.43; 95% CI, 0.35-0.53) Higher odds of death (OR = 2.59; 95% CI, 1.87-3.58) Higher odds of respiratory complications (OR = 2.09; 95% CI, 1.36-3.23) Lower odds of successful angiographic outcome (OR = 0.54; 95% CI, 0.37-0.80). There were no significant differences between groups for the outcomes of asymptomatic or symptomatic ICH or vascular complications. There were no differences between groups in mean time to groin puncture, (136 vs. 54 minutes, p=0.24), mean procedure time (104 vs. 89 minutes, p=0.280 or time from symptom onset to revascularization (329 vs 354 minutes, p=0.17). Pre-intervention NIHSS scores were available from 6 studies; in those, patients receiving general anesthesia had a higher average NIHSS score.
Trials					
NCT03263117 ***SEdation Versus General Anesthesia for Endovascular Therapy in Acute Ischemic Stroke (SEGA)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	260 adult patients aged 18-80 years, (planned) with large intracranial vessel occlusion to be treated with EVT, NIHSS of 6-30. Time of from stroke symptom onset of last seen normal to start of EVT (defined as groin puncture) ≤ 16 hours.	Patients will be randomized 1:1 to receive general anesthesia or conscious sedation. The protocol does not specify a combination of drugs that must be used for either group	**Primary outcome:** mRS score at 90 days **Secondary outcomes:** mRS 0-2 at 90 days, recanalization, NIHSS at 24-36 hours, mortality, EQ-5D at 90 days, sICH, in-hospital mortality	TBA Estimated study completion date is Feb 28, 2023.
NCT03229148	Concealed Allocation: ☑	332 patients (planned), recruited from 10 centres	Patients were randomized 1:1 to	**Primary outcome:** Functional independence	Results presented at ESC May 2022.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
France **RCT** ***Anesthesia Management in Endovascular Therapy for Ischemic Stroke (AMETIS)***	Blinding: Patient ☒ Assessor ☑ ITT: ☑ (modified)	with acute anterior circulation ischemic stroke with indication to receive endovascular thrombectomy. Mean age was 72 years, 71% were women. Median baseline NIHSS was 16. 48% of patients received thrombolysis treatment.	receive general anesthesia or conscious sedation. In both groups a SBP between 140 and 180 mmHg was maintained and SpO2 maintained between 94 and 98%.	(mRS 0-2) at 90 days and absence of major periprocedural complications within 7 days **Secondary outcomes:** Procedure-related serious adverse events, pneumonia, MI, cardiogenic pulmonary edema, progression to malignant stroke, median ordinal mRS score at 90 days, 7 and 90-day mortality and clinically important results	The primary composite outcome occurred in 28.2% of patients in the general anesthesia group vs. 36.2% in the conscious sedation group (RR=1.29, 95% CI 0.91-1.82). There were no significant differences between groups with the exception of a higher frequency of hypotension in the general anesthesia group (87.4% vs. 44.9%, RR=0.51, 95% CI 0.42-0.63). 10.9% of conscious sedation patients converted to general anesthesia.
Cappellari et al. 2020 **Italy** **Retrospective study**	NA	4,429 adult patients enrolled in the Italian Registry of Endovascular Treatment in Acute Stroke between January 2011 and December 2017. Median age was 73 years, 50.5% were men. Median NIHSS score was 18.	The outcomes of patients who received general anesthesia (GA, n=2013) versus conscious sedation (CS, n=1285) and local anesthesia (LA, n=1131) were compared, following adjustment for unbalanced variables	**Primary outcomes:** Excellent functional outcome (mRS 0–1), favorable functional outcome (mRS 0–2), and death at 3 months. **Radiological outcomes:** Successful recanalization (TICI score 2b/3), complete recanalization (TICI score 3), any type of intracerebral hemorrhage (ICH).	Compared with LA, the odds of an excellent and good recovery were significantly lower with GA (32.7% vs. 38.1%; OR=0.714, 95% CI 0.515–0.990 and 42.5% vs. 52.4%; OR=0.769, 95% CI 0.566–0.998, respectively). There were no significant differences in the proportions of patients with excellent or good functional outcomes who received GA or CS. There were no significant differences between the comparisons of GA vs. CS and GA vs. LA for the outcomes of death, successful recanalization or complete canalization. The odds of any ICH were significantly reduced in the GA group compared with the CS group (22.1% vs. 27.3%, OR=0.591, 95% CI 0.452–0.773) and compared with LA (22.1% vs. 29.5%; OR=0.539, 95% CI 0.398–0.730).
Goldhoorn et al. 2020 **The Netherlands** **Mr CLEAN Registry**	NA	1,376 patients included in the Mr CLEAN registry from March 16, 2014, until June 15, 2016.	The outcomes of patients who received local anesthesia only (LA, n=821), general anesthesia (GA, n=381), or conscious sedation (CS, n=174), were	**Primary outcome:** Shift in mRS scores at 90 days **Secondary outcomes:** Good functional recovery (mRS score 0-2 at 90 days),	Compared with LA, both GA and CS were associated with worse outcomes (adjusted common ORs of 0.75; 95% CI 0.58–0.97 and 0.45; 95% CI 0.33–0.62, respectively). The odds of a good functional outcome were significantly lower for CS patients compared with LA

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			compared, adjusting for age, sex, prestroke mRS score, baseline NIHSS score, collaterals, and time from onset to arrival at intervention center	successful reperfusion (eTICI score ≥2B), sICH, ischemic stroke progression (decline in NIHSS score ≥4), pneumonia, and mortality at 90 days.	patients (OR=0.35, 95% CI 0.23–0.54). The odds of stroke progression and pneumonia were significantly increased in CS patients compared with LA patients (OR= 1.82, 95% CI 1.10–3.02 and OR=2.23, 95% CI 1.44–3.48, respectively). The odds of mortality were significantly increased in both GA and CS patients compared with LA (OR= 1.39, 95% CI 1.00 to 1.93 and OR= 1.96, 95% CI, respectively). CS was associated with worse outcomes compared with GA (shift in mRS [common OR=0.60, 95% CI 0.42–0.87], good functional outcome [OR= 0.44, 95% CI 0.27–0.71], and increased odds of pneumonia [OR= 2.51, 95% CI 1.50–4.20])
Sun et al. 2020 **China** **Pilot RCT** ***Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke (CANVAS) trial***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑ (modified)	40 patients ≥18 years, recruited from a single site who were eligible for endovascular treatment and if stroke occurred ≤6 hours from the onset of symptoms and who were previously functionally independent (mRS 0 to 2). Patients with GCS score <8 were excluded. Median age was 65 years, 65% were men. 10% of patients received t-PA.	Patients were randomized to undergo the thrombectomy procedure using general anesthesia (GA, n=20) or conscious sedation (CS, n=20)	**Primary outcomes:** Recruitment, conversion from CS to GA **Secondary outcomes:** mRS score at 90 days, favourable outcome (mRS 0-2) at 90 days, NIHSS score at 7 days, successful perfusion (mTICI 2b-3), 90-day mortality	4 patients were converted to GA. There were no significant differences between groups in mean mRS scores at 90 days (2.4 vs. 3.1), or in the percentage of patients with a favourable outcome (55% vs. 50%). Successful reperfusion was higher in the GA group (95% vs. 65%; p=0.048). Mean NIHSS scores at 7 days did not differ significantly between groups (8.9 vs. 10.6). There were no deaths at 90 days in the GA group and 2 in the CS group.
Simonsen et al. 2018 **Denmark** ***General or Local Anesthesia in Intra Arterial Therapy (GOLIATH)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	128 patients ≥18 years, recruited from a single site who were eligible for endovascular treatment, and in whom groin puncture could be performed within 6 hours from symptom onset or time from last seen well. A DWI MRI scan was	Patients were randomized to undergo the thrombectomy procedure using general anesthesia (GA, n=65) or conscious sedation (CS, n=63)	**Primary outcome:** Infarct growth **Secondary outcomes:** mRS at 90 days, successful reperfusion (mTICI 2b-3), 24-hour NIHSS and	75% of patients were treated with i.v t-PA, and 13%, with intra-arterial t-PA. Baseline median infarct volumes were similar between groups (GA 10.5 vs. CS 13.3 mL, p=0.26). Final median infarct volume was significantly smaller in the GA group (22.3 vs. 38.0 mL, p=0.04). Median infarct growth was 8.2 mL in the GA group and 19.4 in the CS group (p=0.10).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		required to establish baseline infarct volume. Patients with infarct volumes >70 mL, were excluded. Mean age was 71.4 years, 51.6% were men. Median NIHSS score was 18.			A significantly higher proportion of patients in the GA group experienced successful reperfusion (76.9% vs. 60.3%, p=0.04). Median 24-hour NIHSS score was 6 in the GA group and 10 in the SC group (p=0.19). There was a shift towards lower mRS scores at 90 days associated with GA (OR=1.91, 95% CI 1.03-3.56). There were no significant differences between groups in process times, with one exception. The median time from arrival at the neurointerventional suite to groin puncture was significantly longer in the GA group (24 vs. 15 min, p<0.001). 6.2% of patients in the GA group type 2 parenchymal hemorrhage vs. 4.8 in the CS group. 90-day mortality did not differ significantly between groups (GA 7.7% vs CS 12.7%, p=0.35).
Löwhagen Hendén et al. 2017 **Sweden** **RCT** ***AnStroke Trial (Anesthesia During Stroke)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	90 patients ≥18 years, who were eligible for endovascular treatment within 8 hours of ischemic stroke onset. Median age was 72 years, 54% were men. Median NIHSS score was 18.	Patients were randomized 1:1 to undergo the thrombectomy procedure using general anesthesia (GA) or conscious sedation (CS)	**Primary outcomes:** mRS score at 90 days, early neurological improvement **Secondary outcome:** Good outcome (mRS 0-2 at 90 days)	77% of patients received IV rt-PA. Successful recanalization was achieved in 91% of patients. There were no differences between groups in any of the procedural time intervals. Median mRS score at 90 days was similar between groups (3 vs. 3, p=0.51) There were no significant differences between groups in the proportion of patients with a good outcome at 3 months (42% vs. 40%, p=1.00), or in the distribution of mRS scores at 90 days (p=0.64). The NIHSS score shifts at 24 hours, day 3, and hospital discharge, as well as cerebral infarction volume at day 3, ASPECTS at day 3, hospital

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					mortality, and incidence of a new stroke at 3 months, were similar for both groups. There were no differences between groups in complications.
Schönenberger et al. 2016 **Germany** **RCT** ***Sedation vs Intubation for Endovascular Stroke Treatment (SIESTA)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	150 patients, admitted to a single institution with a severe ischemic stroke (NIHSS ≥10), appropriate for mechanical thrombectomy. Mean age was 71.5 years, 60% were men. Mean baseline NIHSS sore was 17.	Patients were randomized to undergo the thrombectomy procedure using general anesthesia (GA, n=77) or conscious sedation (CS, n=73)	**Primary outcome:** Early neurological improvement (change in NIHSS score between admission and 24 hours) **Secondary outcomes:** 47 pre-specified clinical, logistical, feasibility, complications and safety outcomes	At 24 hours post treatment, the mean NIHSS score decreased from 16.8 to 13.6 in the GA group, and from 17.2 to 13.6 in the CS group. The mean difference in decline (adjusted for baseline NIHSS) between the groups was not significant (−0.4, 95% CI, −3.4 to 2.7; p=0.82). Of 5 clinical outcomes, one was associated with a significant difference between groups. A significantly higher percentage of patients in the GA group had a good outcome (mRS 0-2) at 3 months (37% vs. 18.2%, p=0.01). Of 7 logistical outcomes, two were associated with significant differences between groups. Mean door-to-arterial puncture time and mean duration of procedure time was significantly shorter for patients in the CS group. There were no differences between groups in any complications before or during the procedure.
Van den Berg et al. 2015 **The Netherlands** **Retrospective study**	NA	348 patients, admitted to one of 16 Dutch hospitals from 2002-2013 who were participants of the MR CLEAN trial.	The outcomes of patients who received treatment using general anesthesia (GA, n=278) were compared with those using non-GA (n=70)	**Primary outcomes:** Good clinical outcome (mRS 0-2) at discharge, in-hospital mortality, full recanalization, procedural complications, post procedural complications, including symptomatic and asymptomatic ICH	Patients who received GA were significantly younger (mean 57 vs. 62 years, p=0.03) and were less likely to have atrial fibrillation (16.4% vs. 29.3%, p=0.03). The proportion of patients who experienced a good outcome was significantly higher in the non-GA group (25.9% vs. 14.3%, p=0.04; however, after adjusting for prognostic factors, the result was no longer significant (OR=1.9, 95% CI 0.89-4.24). There was no significant difference in the number of patients who died in hospital (non-GA 16.5% vs. GA 21.4%, p=0.34). There was no significant difference in the number of patients who had full recanalization (TICI 2b/3: non-

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					GA 42.6% vs. GA 48.6%, p=0.37). There were no significant differences between groups in the frequency of procedural or post procedural complications. Post procedure, there were significantly more patients in the GA group with hyper/hypothermia, delayed extubation and ventilation-associated complications
Davis et al. 2012 **Canada** **Retrospective study**	NA	97 patients who received endovascular therapy following acute ischemic stroke from a single institution (January 2003 to September 2009). Mean age was 62.5 years, 70% were male. Median NIHSS score was 9	The outcomes of patients who received general anesthesia (GA, n=48) were compared to those who received local anesthesia (LA, n=48). For patients managed with local anesthesia, conscious sedation, when required, was provided with intermittent doses of midazolam (2.5 mg) and fentanyl (25 mcg) every 15 to 30 minutes.	**Primary outcome:** Good outcome (mRS 0-2) at 3 months	A higher proportion of patients in the LA group experienced a good outcome at 3 months (60% vs. 15%, < 0.001). The risk of a good outcome for patients who received LA was significantly higher (RR=03.2,95% CI 1.5-6.8). The risk of mortality was significantly higher in the GA group (RR=2.3, 95% CI 1.1-3.7, p=0.039) Independent predictors for good neurologic outcomes were local anesthesia, systolic blood pressure <140 mmHg and lower baseline NIHSS scores.
Abou-Chebl et al. 2010 **USA** **Retrospective study**	NA	980 patients at 12 stroke centres who underwent intra-arterial therapy (ITA) for acute stroke were recruited from 2005 to 2009. Mean age was 66 years, median NIHSS score of 17.	The outcomes of patients who achieved a good clinical outcome (mRS 0-2, n=355) were compared to those with a poor outcome (mRS3-6, n=625). Independent predictors of a good outcome were identified. The following data were collected: Demographic variables, stroke severity (NIHSS) use of intravenous tissue-type plasminogen activator use of general anesthetic (GA), time to groin puncture, location	**Primary outcome:** Good outcome (mRS 0-2) at 3 months	Successful recanalization was achieved in 68% of patients; of which 37% achieved good outcome Overall mortality: 31% Symptomatic hemorrhage: 9.2% Asymptomatic hemorrhage: 24.7% 428 (44%) patients were placed under GA before the procedure. Compared with patients who had conscious sedation, GA patients were more likely to have carotid terminus occlusions (25% vs. 15%, p<0.01), and were more likely to have higher baseline NIHSS scores (17±5 vs.16±6, p<0.01) There was no difference in the mean time to treatment between groups (306±133 versus 296±172 minutes, *P*<0.09) There were no differences between groups in the numbers of patients who experienced a symptomatic

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			of thrombus (including tandem occlusions), technical aspects of the procedure (devices and pharmacologic agents used), recanalization grade, time to recanalization, post procedural hemorrhage, and 90-day outcomes		or asymptomatic ICHs (27% vs. 24%, p<0.22 and 9.3% vs.9.1%, p<0.82, respectively) Use of GA was an independent predictor of poor clinical outcome. Use of a stent was associated with good outcome. Lack of recanalization (TIMI score o f0 or 1), older age, higher initial NIHSS score, and post-procedural asymptomatic or symptomatic hemorrhage were associated with a poor clinical outcome. After controlling for age, NIHSS score, time to groin puncture, time to recanalization, recanalization status, and presence of hemorrhage, patients placed under GA were at a significantly higher risk of a poor outcome (OR=2.46; 95% CI 1.54 to 3.92; *P*<0.0001)

Perioperative Use of Antithrombotics for Endovascular Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Van der Steen et al. 2022 **The Netherlands** **RCT** **(2x3 factorial)** ***Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN-MED)***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒ (modified ITT, including persons who deferred consent or died before consent could be asked)	663 patients aged ≥18 years, with a large, anterior large vessel occlusion, in whom revascularization could occur within 6 hours, recruited from 15 centres. Median age was 73 years, 53% were men. Median baseline NIHSS score was 15. 18% of patients had a previous stroke.	Patients were randomly assigned (1:1) to receive periprocedural intravenous aspirin (300 mg bolus) or no aspirin, and randomly assigned (1:1:1) to receive moderate-dose unfractionated heparin (5000 IU bolus followed by 1250 IU/h for 6 h), low-dose unfractionated heparin (5000 IU bolus followed by 500 IU/h for 6 h), or no unfractionated heparin. Treatment groups (n) • No treatment 153	**Primary outcome:** mRS score at day 90 (ordinal shift analysis) **Secondary outcomes:** NIHSS score at 24 hours and 5-7 days, or hospital discharge, reperfusion **Safety outcomes:** Symptomatic ICH, any ICH	The trial was halted prematurely due to safety concerns. 628 patients were included in the modified ITT. There was a non-significant shift towards worse functional outcomes (higher mRS scores) for patients who received aspirin (vs. no aspirin, (adjusted common OR=0·91, 95% CI 0·69–1·21) and for those allocated to unfractionated heparin (vs. no unfractionated heparin, adjusted common OR=0·81, 95% CI 0·61–1·08). Patients who received moderate dose unfractionated heparin had significantly worse outcomes compared with persons who received no heparin (adjusted common OR=0·42, 95% CI 0·18–0·99) but not for those who received low-dose unfractionated heparin (vs. no heparin; OR=0.86, 95% CI 0·64–1·16).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			• Aspirin 156 • Low dose heparin 161 • Aspirin + low-dose heparin 147 • Moderate dose heparin 22 • Aspirin +moderate dose heparin 24		The odds of complete recanalization at 24 hours were significantly higher among those who received unfractionated heparin (vs. no heparin; OR=1·89, 95% CI 1·16–3·09). There were no significant differences in the median NIHSS scores (aspirin vs. no aspirin and heparin vs. no heparin) at 24 hours or 5-7 days. Compared with patients who did not receive aspirin, the odds of symptomatic ICH were significantly higher in the aspirin group (adjusted OR=1.95, 95% CI 1.13-3.35). The odds of symptomatic ICH were also higher in patients who received heparin (vs. no heparin, adjusted OR=1·98, 95% CI 1·14–3·46). The risk of any ICH was not significantly greater in patients who received aspirin (vs. no aspirin) or heparin (vs. no heparin).

Risk of Contrast-Induced Nephropathy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Prasad et al. 2014 **USA** **Retrospective study**	NA	158 patients who received a dose of contrast material (CM) of 75 to ≥250 associated with neuroendovascular procedures, at a single institution from 2001-2013. Mean age was 54 years, 65% women. Patients with chronic kidney disease or glomerular filtration rate (GFR) ≤30 mL/min, were excluded	Preprocedure and postprocedure serum creatinine levels obtained within 48 hours of the procedure were obtained. The glomerular filtration rate (GFR) and creatinine clearance (CC) were estimated. Mean values were compared between patients who received low CM doses of 75-249 mL (n=79) and high CM doses ≥250 mL (n=79).	**Primary outcome:** Incidence of Contrast-induced nephropathy (CIN), defined as ≥50% increase in serum creatinine from baseline measurement, or ≥ 0.3 mg/dL increase of at either 24 or 48 hours after the procedure.	Doses of CM in the high-dose group 250-299 mL; 36 patients (46%) 300-399 mL: 29 patients (37%) 400-499 mL: 9 patients (11%) ≥500 mL 5 patients (6%) The change in serum creatinine over time was not significantly different between the control group and high-dose cohort (p=0.32). There were no cases of CIN in the low-dose group and 4 cases, in the high-dose group. At 24 hours, the increase from baseline in creatinine levels among the 4 CIN cases was 0.38, 0.35, 0.13 and 0.33 mg/dL. The corresponding relative

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					increases were: 23%, 42%, 17% and 48%. At 48 hours, the increase in creatinine levels among the 4 CIN cases was 0.90, 0.18, 0.45 mg/dL, and were not available for 4th patient. The corresponding relative increases were: 55%, 21%, 60% and were not available for 4th patient. 48%. No patient that developed CIN required dialysis.
McDonald et al. 2013 **USA** **Retrospective study**	NA	157,140 CT scans from 53,439 patients admitted to a single institution from 2000-2010, who underwent an unenhanced or intravenous contrast enhanced abdominal, pelvic, and/or thoracic CT scan, with before and after procedure serum creatinine levels available.	The incidence of acute kidney injury (AKI), defined as a rise in maximal observed SCr of ≥0.5 mg/dL over baseline in the 24–72 hours after the CT scan, was compared between patients who received contrast enhanced scans and those who received noncontrast scans, using 3 types of statistical analyses (propensity matching using full dataset, with stratification for low, medium and high-risk groups, based on baseline SCr, propensity matching using a reduced dataset including the most recent scan [n=53,439] and a counterfactual analysis [n=8,530] , which included patients who had enhanced and unenhanced scans)	**Primary outcome:** AKI	The odds of AKI in patients who received enhanced CTs were not significantly increased. Using the full dataset (1:1 matching, based on risk factors for contrast material induced nephropathy) Low risk group: OR=0.94, 95% CI 0.85-1.04 Medium risk group: OR=0.97, 95% CI 0.87-1.09 High-risk group: OR=0.79, 95% CI 0.66-0.95 When using the inverse-weighting method and the odds weighting method, the odds AKI were not significantly increased for any risk group. Using the reduced dataset (single scan patients only), the odds of AKI in patients who received enhanced CTs were not significantly increased 1:1 matching analysis Low risk group: OR=0.93, 95% CI 0.76-1.13 Medium risk group: OR=0.97, 95% CI 0.81-1.16 High-risk group: OR=0.91, 95% CI 0.66-1.24 When using the inverse-weighting method and the odds weighting method, the odds AKI were not significantly increased for any risk group. In the counterfactual analysis dataset, the odds of AKI in patients who received enhanced CTs were not significantly increased (OR=0.97, 95% CI 0.79-1.18, p=0.65).
Sharma et al. 2013 **USA**	NA	194 consecutively admitted patients who received contrast-enhanced imaging,	Each patient received approximately 150 ml of non-ionic low-osmolar contrast agent during the	**Primary outcomes:** Incidence of contrast-induced nephropathy (CIN), defined as ≥50% increase in	There were 3 cases of CIN at 48 hours post procedure. One patient who developed an increased Cr level

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Retrospective study		associated with endovascular treatment for acute ischemic stroke (2006-2010). Mean age was 65 years, 48% were male. No patient was excluded based on renal function (3 patients were on chronic hemodialysis). Mean serum creatinine level was 1.09 md/dL	procedure.	serum creatinine (Cr) from baseline measurement, or ≥ 0.3 mg/dL increase of at either 24 or 48 hours after the procedure	had a known history of chronic renal insufficiency (Cr>1.5 mg/dl) and two had baseline Cr levels within the normal range.
Loh et al. 2010 **USA** **Prospective study**	NA	99 consecutively admitted patients to a single institution from 2002-2008, who had undergone endovascular treatment following acute ischemic stroke, and in whom a pre-procedural serum creatinine (Cr) and a 48-hour post procedural were available for review. Mean age was 65 years, 46% were men	The characteristics of patients who developed acute kidney injury were compared with those who did not.	**Primary outcome:** Incidence of acute kidney injury (AKI), defined as defined as ≥50% increase in serum creatinine (Cr) from baseline measurement, or ≥ 0.3 mg/dL increase of at either 24 or 48 hours after the procedure	For all patients, the mean preangiography and postangiography serum Cr levels were both 0.9± 0.3 mg/dL (p=0 .4 compared with admission creatinine). The average creatinine change was 4.6% at 48 hours. The mean volume of contrast was 189 ± 71 mL. There were 3 cases of AKI. The absolute (and relative) changes in creatinine levels were: 0.4 mg/dL (+33.3%), 0.3 mg/dL (+27.3%), and 1.0 mg/dL (+76.9%). All 3 patients died. The mean baseline serum Cr level was higher in AKI patients (1.2 vs. 0.9, p=0.023)

Cost-Effectiveness of Endovascular Treatment

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
van den Berg et al. 2022 **The Netherlands** **RCT (Societal perspective)**	NA	Data from the MR CLEAN trial were used.	The cost-effectiveness of medical treatment vs. medical treatment + endovascular therapy (+/- iv t-PA) was evaluated. Health care costs ($USD) were estimated using unit costing (acute care, hospital admission,	Cost-effectiveness of endovascular therapy: functional independence (mRS 0-3), cost gained/QALY	The mean per-persons cost of treatment with EVT was $126,494 (95% CI, $113,962–$140,320) compared with $143,331 (95% CI, $130,509–$155,558) in the medical treatment group. The mean between-group difference was −$16,839 (95% CI, −$38,113 to $5,456) per patient. Significantly more patients in the EVT group achieved functional independence (37.2% vs.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			hospital care, home care, consultations) and out-of-pocket expenses incurred by the patient over the 2-year study period.		23.9%, absolute difference = 13.3% [95% CI, 4.0%–22.0%]). Patients in the EVT group generated 0.99 (95% CI, 0.89–1.09) QALYs compared with 0.83 (95% CI, 0.75–0.91) in the medical treatment group. The mean difference was 0.16 QALYs (95% CI, 0.04–0.29, p=0.01). Endovascular treatment dominated standard treatment with $18,233 saved per extra patient with a good outcome and $105,869 saved per additional QALY.
Sevick et al. 2021 **Canada** **RCT (Societal perspective)**	NA	Data from the ESCAPE trial were used.	A decision analytic tree and a Markov model was used to estimate the lifelong costs/cost-effectiveness of thrombectomy (EVT) compared with best medical management (BMM) using patient-level microcosting for 3-months, and the literature, beyond 3 months.	Cost-effectiveness of endovascular therapy: cost gained/ QALY	Average 3-month costs for EVT were $53,918 and $46,739 for BMM. Compared with best medical management, over 3-months, the cost per QALY was $201,243 for EVT. When the time horizon was shortened to 1 year, EVT remains cost savings compared to standard of care (~$15,376 per QALY gained with EVT). Over the lifetime, EVT was both more effective and less costly than BMM (-$91).
Aronsson et al. 2016 **Sweden** **RCT (Healthcare payer perspective)**	NA	Data from ESCAPE, EXTEND-IA, MR CLEAN, REVASCAT and SWIFT PRIME trials were used	A decision analytic model (Markov model) was used to estimate the lifelong costs of thrombectomy using the characteristics of patients in the 5 large RCTs, plus data from long-term observational studies. Costing (adjusted for inflation) and population data from Sweden were used. 90-day outcome data from the 5 trials were extrapolated to a lifelong time horizon based on mortality and stroke recurrence from	Cost-effectiveness of endovascular therapy: cost gained/ QALY A threshold value of $10,000/QALY gained was used as a reference to determine whether the treatment was cost-effective	Pooling the results from the 5 trials, total costs/patient were: $70,088 (thrombectomy) vs. $70,309 (best medical management): Difference of $-221 (favours thrombectomy) Total life years gained were: 8.21 (thrombectomy) vs. 7.81 (best medical management) Gain of 0.4 for thrombectomy QALYs were: 2.59 (thrombectomy) vs.1.60 (best medical management). Difference of 0.99 (favours thrombectomy) Cost/QALY gained =US$-233 Among the individual trials the Cost/QALY gained

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			published data.		(US$): ESCAPE: 2,780 EXTEND IA: 256 REVASCAT: -7,793 SWIFT-PRIME: -2,996
Kunz et al. 2016 **Netherlands** **Cost-effectiveness analysis**	NA	Data from ESCAPE, EXTEND-IA, MR CLEAN, REVASCAT and SWIFT PRIME trials were used	A decision analytic model (Markov model) was used to estimate the 30-year costs of endovascular therapy (EVT) compared with standard care using the characteristics of patients in the 5 large RCTs. Costs were based on Leppert et al. 2015. Transition probabilities were based on meta-analysis of Goyal et al. 2016	Cost-effectiveness of endovascular therapy: cost gained/ QALY A willingness to pay threshold was set at $50,000/QALY gained	Overall, over 30 years, EVT was cost-effective compared with standard care. Incremental cost was $4,938, incremental effectiveness 1.59 QALY; incremental cost-effective ratio (ICER) was $3,100/QALY. In all subgroups including stroke severity, time from stroke onset, ASPECTS score and site of occlusion, EVT remained cost-effective. The least favourable ICERs were associated with the subgroups of M2 location (ICER $28,812) and ASPECTS score of 0-5 (ICER $14,273)
Leppert et al. 2015 **USA** **Economic analysis study**	NA	A theoretical cohort of patients ≥65 years, admitted to hospital following acute ischemic stroke	A decision analytic model was used to estimate the lifetime (30 year) costs and outcomes (mRS 0-6 at 90 days) associated with the additional costs of intra-arterial therapy (IAT) compared with t-PA alone for the treatment of acute ischemic stroke. Inputs were based, in part, of data from MR CLEAN IAT was considered to be cost-effective if the incremental cost-effectiveness ratio was <$50,000/QALY	Additional cost of IAT per QALY	Total lifetime costs of IAT and alternative therapy for base case were $140,055 and $130,144. IAT was associated with 3.80 QALYs and alternative treatment with 3.10 QALYS ICER=$$9,.911/0.7**=$14,137/QALY** In one-way sensitivity analysis, compared with the standard care arm, the least unfavorable, unfavorable, and most unfavorable scenarios produced ICERs of $41, 816, $56,146, and $132,128, respectively. In 97.6% of simulations, IAT was the dominant treatment, or was the preferred treatment based on the willingness to pay threshold.
Turk et al. 2014 **USA**	NA	171 patients who had undergone intra-arterial treatment (IAT) following stroke from 2008-2012	Patient, procedural and diagnostic costing information associated with IAT was collected by	Procedural costs	The Penumbra system was used in 144 cases (84.2%) and achieved recanalization in 41.7% of cases. Stent retrievers were successful as the primary device for achieving recanalization in 70.1%

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Retrospective study			chart review. Thrombectomy devices were categorized as Penumbra aspiration system thrombectomy (group P) or stent retriever (group S).		of cases. The mean cost across both groups was $11,926.45 (minimum cost=$3,296, maximum cost=60,872) The mean cost for Group P was $11,158 per patient, ranging from $3,296 to $60,872. The mean cost for Group S was $16,021 per patient, ranging from $9,601 to $35,724.

Early Repatriation Following EVT

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Griffin et al. 2020 **Ireland** **Retrospective study**	NA	435 patients consecutively admitted to a single specialized institution who underwent thrombectomy from January 2016 to June 2018, of whom 352 were transferred back to a local region primary care centres (LRG) and 83 to a remote region (RRG). Median age was 70 years, 52% were men. Median NIHSS was 16, median ASPECTS was 9.	Patients from the LRG were repatriated immediately following EVT to the primary care centre, while RRG patients were repatriated to the PSC within 24hours. The outcomes of these patients were examined.	**Primary outcome:** Good functional outcome (mRS 0-2) at 90 days, mortality	Good functional outcome was achieved by 47% of patients and was significantly higher in the RRG (57% vs. 45%, p=0.034). 90-day mortality was 19% and was significantly higher in the LRG (21% vs. 10%, p=0.024). Median door to CT time was significantly shorter in the LRG (28 vs. 38 minutes, p=0.003). Median onset to t-PA time was significantly shorter in the LRG (133 vs. 165 minutes, p=0.015) as was the median onset to groin puncture and onset to reperfusion time (256 vs. 405 minutes, p=0.001 and 295 vs. 431, p=0.001, respectively). In the LRG, 91% (n=322) were repatriated to their referring institution immediately after the procedure. 30 patients (9%) were admitted to the endovascular stroke centre (ESC), due to the development of intracranial haemorrhage (n=10), the need for immediate ICU admission (n=7) or decompressive craniectomy (n=4). Good clinical outcome was significantly lower in the ESC group (20% vs. 47%, p=0.006), with similar mortality (27% vs. 20%, p=0.377).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					In the RRG, 67% (n=56) were repatriated within 24hours. 27 patients (33%) admitted to the ESC. The most common reason for admission included general observation (n=7), intracranial haemorrhage post-EVT (n=6) and the need for mechanical intubation either pre- or post-EVT (n=5). Good clinical outcome was significantly lower in the ESC group (65% vs. 41%, p=0.042). Mortality was significantly higher in the ESC group (22% vs. 4%, p=0.007).

First Pass Effect

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Aubertin et al. 2021 **France** **Prospective study**	NA	280 patients included in the Endovascular Treatment in Ischemic Stroke (ETIS) Registry with basilar artery occlusion who underwent thrombectomy from 6 participating centres. Mean age was 63.9 years, 61% were men.	The outcomes of patients who achieved recanalization after first pass, defined as mTICI score, 2c or 3, with no rescue therapy (first-pass effect [FPE]), were compared with those who did not.	**Primary outcome:** Good clinical outcome at 90 days (mRS score 0-2) **Secondary outcomes:** Excellent clinical outcome (mRS 0-1) and mortality at 90 days	FPE was achieved in 93 patients (33.2%). The odds of a good or excellent outcome were increased significantly in FPE patients (50.0% vs. 29.2%, adj OR=4.01, 95% CI 1.94-8.25 and 40.2% vs. 23.8%, adj OR=2.81, 95% CI 1.40-5.62, respectively). Mortality and procedural complications were significantly lower in FPE patients (26.1% vs. 49.2%, adj OR=0.25, 95% CI 0.14-0.76 and 9.7% vs. 22.5%, adj OR=0.34, 95% CI 0.14 to 0.76, respectively).
Di Maria et al. 2021 **France** **Prospective study**	NA	1,832 patients treated with EVT for isolated anterior intracranial occlusions included in the Endovascular Treatment in Ischemic Stroke (ETIS) registry. Mean age was 69.8 years 47.9% were men. Median admission NIHSS score was 18.	The outcomes of patients who achieved complete/near recanalization after the first pass with a stent retriever or aspiration device were compared patients without first-pass effect.	**Primary outcome:** Change in NIHSS score at 24 hours, favourable outcome (mRS 0-2), excellent outcome (mRS 0-1) and mortality. **Safety outcomes:** Any hemorrhage, sICH, procedural complications	After a first pass of device, near to complete recanalization (mTICI 2c/3) was achieved in 417 patients (22.8%). The odds of increasing change in NIHSS scores, favourable and excellent outcomes were all significantly higher in first-pass patients. The odds of mortality, hemorrhage and procedural complications were all significantly lower in first-pass patients.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Significant predictors of first pass effect were increasing age, lower SBP, MCA-M1 occlusion, higher DWI-ASPECTS at admission, local anesthesia, and combined first-line device strategy (i.e., aspiration catheter+ stent retriever).
Flottmann et al. 2021 **Germany** **Prospective study**	NA	1,225 patients from the prospective German Stroke Registry included between June 2015 and April 2018, who had undergone EVT. Mean age 73 years, 53.1% were women. Median NIHSS score on admission was 15, median ASPECTS on admission imaging was 9.	Independent factors, including the number of passes, required to achieve successful reperfusion, (TICI score of 2b or 3) associated with functional independence at day 90 were identified, adjusting for age, baseline NIHSS score and ASPECTS.	**Primary outcome:** Functional independence (mRS 0-2) at 90 days.	The median number of retrievals was 2 (minimum: 0, maximum: 20). 41% of patients achieved successful reperfusion on first pass. Of these, 49.4% had a good outcome. As the number of passes increases, with one exception the odds of functional independence decreased. The odds of good clinical outcome associated with the number of passes required were: First pass adj OR= 6.45, 95% CI, 4.0–10.4 Second pass adj OR= 4.56, 95% CI, 2.7–7.7 Third pass adj OR=3.16, 95% CI, 1.8–5.6 Fourth pass adj OR=1.70, 95% CI 0.74–3.92 Fifth pass adj OR= 2.90, 95% CI 1.11–7.59 Sixth pass adj OR=0.82, 95% CI 0.32–2.14

Operator/Hospital Volumes

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Stein et al. 2021 **USA** **Retrospective study**	NA	13,335 Medicare patients (≥65 years) with acute ischemic stroke treated with mechanical thrombectomy by 2,754 proceduralists at 641 hospitals from January 1, 2016, to December 31, 2017.	Regression models were developed to determine whether total cases (hospital cases or proceduralist cases) were independent predictors of inpatient mortality, good outcome (defined as a discharge destination of home or transfer to inpatient rehabilitation), and 30-day readmission.	**Primary outcome:** In-hospital mortality, good outcome, 30-day readmission	For every 10 more proceduralist cases, patients had i) 4% lower odds of inpatient mortality (adjusted OR=0.96, 95% CI 0.95–0.98), ii) 3% greater odds of a good outcome (adjusted OR=1.03, 95% CI, 1.02–1.04), with no significant association with odds of 30-day readmission. For every 10 more hospital cases, patients had i) 2% lower odds of inpatient mortality (adjusted OR=0.98, 95% CI, 0.98–0.99), ii) 2% greater odds of a good outcome (adjusted OR=1.02, 95% CI, 1.01–1.02]), with no significant association with odds of 30-day readmission.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Odds of inpatient mortality were 11% lower at a proceduralist threshold of 5 cases (OR=0.89, 95% CI 0.79–1.00), progressively decreasing to an OR of 0.73 (95% CI, 0.60–0.89) at 40 cases. At a hospital volume threshold of 55 cases, the odds of inpatient mortality were significantly lower (OR=0.84, 95% CI 0.74–0.96). Odds of good outcome were statistically significant at every proceduralist volume. At a threshold of 20 cases, there were 15% greater odds of good outcome (OR=1.15, 95% CI, 1.06–1.25), progressively increasing to 1.26 (95% CI 1.11–1.44) at 40 cases. At a hospital volume level of 25 cases, the odds of a good outcome were significantly increased (OR=1.12, 95% CI 1.03–1.22). At 60 cases, the odds of a good outcome were increased by 19% (OR=1.08–1.32). The odds of hospital readmission were not reduced by increasing hospital volumes or proceduralist volumes.
Zhu et al. 2021 on behalf of the ETIS Registry and Study Collaborators **France** **Retrospective study**	NA	4,012 persons with acute ischemic stroke admitted to one of 7 centres, who had undergone a mechanical thrombectomy (MT) procedure. Mean age was 70.0 years, 55% were women.	The association between experience (# of procedures performed) among 36 operator (analyzed as a continuous variable) and outcome was examined.	**Primary outcome:** Duration of procedure **Secondary outcomes:** Final angiographic recanalization according to the modified (TICI) classification, first-pass complete recanalization (modified TICI score of 2c or 3 after a single pass of thrombectomy) and the frequency of severe procedural complications (defined as arterial perforation or arterial dissection)	A total of 4,516 MT procedures were performed (median of 97.5/operator). Overall median MT duration was 40.0 minutes. Recanalization success (TICI score≥ 2b) was achieved in 80% of patients. In multivariable analysis, higher operator experience was associated with a significantly shorter procedural duration (β estimate, −3.98, 95% CI, −5.1 to −2.8). Each 10-procedure increase was associated with significantly greater recanalization success (estimate= 1.02, 95% CI 1–1.04). After adjustment for general anesthesia, occlusion location, age and tPA use, there was no effect of operator's experience on overall first-pass complete

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					recanalization frequency. There was no association between operator's experience and perforation or arterial dissection.

EVT Complications

Study/Type	Main Findings	
Jadhav et al. 2018 **Topical review** **USA**	**Complication**	**Treatment**
	Contrast allergy	Pretreat with 50 mg IV diphenhydramine and 200 mg IV methylprednisolone; supplemental oxygen; intravenous epinephrine, diphenhydramine (H1 antagonist), hydrocortisone, and ranitidine (H2 antagonist); intravenous fluid resuscitation and epinephrine infusion (if hypotensive); intubation (if severe laryngeal edema)
	Access-site hematoma and pseudoaneurysm	Establish hemostasis, reestablish arterial flow, vascular repair, initiate blood transfusion, thrombin injection, or direct surgical repair of symptomatic pseudoaneurysms, watchful waiting (if stable)
	Vessel vasospasm	Remove catheter/device, infusion of calcium channel blocker (5–10 mg of intra-arterial verapamil, 2.5 mg of intra-arterial nicardipine), balloon angioplasty (if severe)
	Vessel perforation	Reduce SBP to <140 mm Hg, reverse coagulopathies, transfuse platelets if indicated, watchful waiting (if extravasation is self-limited), inflate balloon at site of extravasation to achieve hemostasis; if extravasation persists, advance microcatheter to the site of perforation and deliver liquid embolic agent (Onxy, glue) or coils to achieve hemostasis. If tear is discrete, vessel patency may be preserved, but in most cases, vessel sacrifice is necessary; postprocedural CT to assess for hemorrhage, edema, and hydrocephalus; Extensive intraventricular hemorrhage and hydrocephalus may warrant CSF diversion with EVD; extensive parenchymal hematoma with mass effect and edema may warrant clot evacuation and decompressive craniectomy.
	Vessel dissection or intrinsic residual stenosis	If not flow limiting or not severely narrowing, medical therapy with antithrombotics and permissive hypertension; if high concern for vessel occlusion, consider acute stent placement with loading of intravenous antiplatelet agents (eg, 180 µg/kg of eptifibatide) and postprocedural loading with 325 mg aspirin and 600 mg clopidrogel via enteral access
	BP control	If reperfusion achieved, aim for moderate or normal BP goal of SBP <140 or 160 mm Hg; if reperfusion not achieved, permissive hypertension with SBP <180 or 220 mm Hg
	Glucose control	Aim for normoglycemia (<180 mg/dL or 10 mmol/L)
	Temperature control	Aim for euthermia; benefit of hypothermia remains unproven
	Tracheostomy	Consider early in patients with severe bulbar weakness or large infarct with midline shift

Abbreviations

ASPECTS: Alberta Stroke Program Early CT Score	CA: concealed allocation	CI: confidence interval
HR: hazard ratio	LVO: large vessel occlusion	ITT: intention-to-treat

NA: not assessed	NIHSS: National Stroke Institutes of Health Stroke Scale	OR: odds ratio
QALY: quality-adjusted life year	RR: relative risk	TICI: thrombolysis in Cerebral Infarction

Reference List

Writing Group for the BASILAR Group Group. Assessment of endovascular treatment for acute basilar artery occlusion via a nationwide prospective registry. *JAMA Neurol* 2020; 77: 561-573.**NEW**

Abou-Chebl A, Lin R, Hussain MS, et al. Conscious sedation versus general anesthesia during endovascular therapy for acute anterior circulation stroke: Preliminary results from a retrospective, multicenter study. *Stroke* 2010;41(6):1175-1179.

Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *New Eng J Med* 2018; 378:708-718.

Anadani M, Arthur AS, Tsivgoulis G, et al. Blood pressure goals and clinical outcomes after successful endovascular therapy: A multicenter study. *Ann Neurol* 2020; 87: 830-839.

Aubertin M, Weisenburger-Lile D, Gory B et al. First-pass effect in basilar artery occlusions: Insights from the Endovascular Treatment of Ischemic Stroke Registry. *Stroke*. 2021 52:3777–3785.**NEW**

Bala F, Casetta I, Nannoni S et al. Sex-related differences in outcomes after endovascular treatment of patients with late-window stroke. *Stroke.* 2022 Feb;53(2):311-318. **NEW**

Balami JS, Sutherland BA, Edmunds LD et al. A systematic review and meta-analysis of randomized controlled trials of endovascular thrombectomy compared with best medical treatment for acute ischemic stroke. *Int J Stroke* 2015;10(8):1168-78.

Bendszus M, Bonekamp S, Berge E, et al. A randomized controlled trial to test efficacy and safety of thrombectomy in stroke with extended lesion and extended time window. *Int J Stroke* 2019;14(1):87-93. **NEW**

Berkhemer OA, Fransen PS, 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(1):11-20.

Bracard S, Ducrocq X, Mas JL, et al. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): A randomised controlled trial. *Lancet Neurol* 2016;15(11):1138-1147.

Brinjikji W, Murad MH, Rabinstein AA, Cloft HJ, Lanzino G, Kallmes DF. Conscious sedation versus general anesthesia during endovascular acute ischemic stroke treatment: A systematic review and meta-analysis. *Am J Neuroradiol* 2015;36(3):525-529.

Brinjikji W, Pasternak J, Murad MH, Cloft HJ, Welch TL, Kallmes DF, et al. Anesthesia-related outcomes for endovascular stroke revascularization: A systematic review and meta-analysis. *Stroke* 2017;48(10):2784-91.

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* Mar 7;368:893-903.

Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med* 2015;372:1009-18.

Campbell BC, Hill MD, Rubiera M et al. Safety and efficacy of solitaire stent thrombectomy: Individual patient data meta-analysis of randomized trials. *Stroke* 2016;47(3):798-806.

Campbell BC, van Zwam WH, Goyal M et al. Effect of general anaesthesia on functional outcome among patients with anterior circulation ischaemic stroke undergoing endovascular thrombectomy versus standard care: A meta-analysis of individual patient data from seven randomised controlled trials. *Lancet Neurol* 2018;17(1):47-53.

Campbell D, Diprose WK, Deng C, et al. General anesthesia versus conscious sedation in endovascular thrombectomy for stroke: A meta-analysis of 4 randomized controlled trials. *J Neurosurg Anesthesiol* 2021 Jan;33(1):21-27.2019. **NEW**

Campbell BCV, Mitchell PJ, Churilov L, Yassi N, Kleinig TJ, Dowling RJ, et al. Effect of intravenous tenecteplase dose on cerebral reperfusion before thrombectomy in patients with large vessel occlusion ischemic stroke: The EXTEND-IA TNK Part 2 randomized clinical Trial. *JAMA.* 2020;323(13):1257-1265. **NEW**

Cappellari M, Pracucci G, Forlivesi S, et al. General anesthesia versus conscious sedation and local anesthesia during thrombectomy for acute ischemic stroke. *Stroke* 2020; Jul;51(7):2036-2044. **NEW**

Casetta I, Fainardi E, Pracucci G, Saia V, Sallustio F, da Ros V, Nappini S, Nencini P, Bigliardi G, Vinci S, Grillo F. Sex differences in outcome after thrombectomy for acute ischemic stroke. A propensity score-matched study. *Eur Stroke J* 2022; 7(2): 151–157. **NEW**

Cernik D, Sanak D, Divisova P, et al. Impact of blood pressure levels within first 24 hours after mechanical thrombectomy on clinical outcome in acute ischemic stroke patients. *Journal of NeuroInterventional Surgery* 2019; 11: 735-739. **NEW**

Chalos V, de Ridder IR, Lingsma HF, et al.; HERMES collaborators. Does sex modify the effect of endovascular treatment for ischemic stroke? *Stroke* 2019; 50: 2413–2419. **NEW**

Ciccone A, Valvassori L, Nichelatti M, Sgoifo A, Ponzio M, Sterzi R, et al. Endovascular treatment for acute ischemic stroke. *N Engl J Med* 2013 Mar 7;368(10):904-13.

Christoforidis GA, Mohammad Y, Kehagias D, Avutu B, Slivka AP. Angiographic assessment of pial collaterals as a prognostic indicator following intra-arterial thrombolysis for acute ischemic stroke. *Am J Neuroradiol* 2005; 26(7):1789-1797.

Davalos A, Cobo E, Molina CA, et al. Safety and efficacy of thrombectomy in acute ischaemic stroke (REVASCAT): 1-year follow-up of a randomised open-label trial. *Lancet Neurol* 2017;16(5):369-376..

Davis MJ, Menon BK, Baghirzada LB, et al. Anesthetic management and outcome in patients during endovascular therapy for acute stroke. *Anesthesiology* 2012;116(2):396-405.

Demeestere J, Christensen S, Mlynash M, Federau C, Albers GW, Lemmens R, Lansberg MG. Effect of sex on clinical outcome and imaging after endovascular treatment of large-vessel ischemic stroke. *J Stroke Cerebrovasc Dis* 2021;30(2):105468**. NEW**

Diprose WK, Wang MTM, Ghate K, et al. Adjunctive intra-arterial thrombolysis in endovascular thrombectomy. A systematic review and meta-analysis *Neurology* 2021; 96(4):1135-1143. **NEW**

Di Maria F, Kyheng M, Consoli et al; ETIS investigators. Identifying the predictors of first-pass effect and its influence on clinical outcome in the setting of endovascular thrombectomy for acute ischemic stroke: Results from a multicentric prospective registry. *Int J Stroke*. 2021 Jan;16(1):20-28. **NEW**

Fargen KM, Neal D, Fiorella DJ, Turk AS, Froehler M, Mocco J. A meta-analysis of prospective randomized controlled trials evaluating endovascular therapies for acute ischemic stroke. *J Neurointerv Surg* 2015; 7(2):84-89.

Fischer et al. SWIFT DIRECT CollaboratorsThrombectomy alone versus intravenous alteplase plus thrombectomy in patients with stroke: an open-label, blinded-outcome, randomised non-inferiority trial. *Lancet* 2022; 400(July 9): 104–15. **NEW**

Flottmann F, Brekenfeld C, Broocks G, et al. Good clinical outcome decreases with number of retrieval attempts in stroke thrombectomy. *Stroke* 2021 Jan;52(2):482-490. **NEW**

Flynn D, Francis R, Halvorsrud K, Gonzalo-Almorox E, Craig D et al. Intra-arterial mechanical thrombectomy stent retrievers and aspiration devices in the treatment of acute ischaemic stroke: A systematic review and meta-analysis with trial sequential analysis. *Eur Stroke J* 2017; 2(4):308-318.

Ganesh A, Menon BK, Assis ZA, Demchuk AM, Al-Ajlan FS, Al-Mekhlafi MA et al. Discrepancy between post-treatment infarct volume and 90-day outcome in the ESCAPE randomized controlled trial. *Int J Stroke* 2021 Jul;16(5):593-601. **NEW**

Goldhoorn RB, Bernsen MLE, Hofmeijer J et al. Anesthetic management during endovascular treatment of acute ischemic stroke in the MR CLEAN registry. *Neurol* 2020; 94: e97-e106. **NEW**

Goyal M, Menon BK, van Zwam WH et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016;387(10029):1723-31.

Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med* 2015;372(24):1009-1018.

Goyal N, Tsivgoulis G, Pandhi A, et al. Blood pressure levels post mechanical thrombectomy and outcomes in large vessel occlusion strokes. *Neurol* 2017; 89: 540-547.

Goyal N, Tsivgoulis G, Malhotra K, Ishfaq MF, 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.**NEW**

Griffin E, Murphy S, Sheehan M, et al. Early repatriation post-thrombectomy: a model of care which maximises the capacity of a stroke network to treat patients with large vessel ischaemic stroke. *J Neurointerv Surg* 2020; 12: 1166-1171. **NEW**

Hill MD, Goyal M, Menon BK, et al. Efficacy and safety of nerinetide for the treatment of acute ischaemic stroke (ESCAPE-NA1): A multicentre, double-blind, randomised controlled trial. *Lancet* 2020; 395: 878-887. **NEW**

Hui W, Wu C, Zhao W, et al. Efficacy and safety of recanalization therapy for acute ischemic stroke with large vessel occlusion. *Stroke* 2020; Jul;51(7):2026-2035.. **NEW**

Jadhav AP, Molyneaux BJ, Hill MD, Jovin TG. Care of the post-thrombectomy patient. *Stroke*. 2018 Nov;49(11):2801-2807.

Jadhav AP, Aghaebrahim A, Jankowitz BT et al. Benefit of endovascular thrombectomy by mode of onset: Secondary analysis of the DAWN trial. *Stroke*. 2019 Nov;50(11):3141-6. **NEW**

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(24): 2296-2306.

Jovin TG, Nogueira RG, Lansberg MG et al. Thrombectomy for anterior circulation stroke beyond 6 h from time last known well (AURORA): A systematic review and individual patient data meta-analysis. *Lancet*. 2022; 399(10321): 249–58. **NEW**

Kamal N, Benavente O, Buck B, et al. Good is not good enough: the benchmark stroke door-to-needle time should be 30 minutes. *Can J Neurol Sci*. 2014;41(6):694-6.

Katsanos AH, Malhotra K, Goyal N, et al. Intravenous thrombolysis prior to mechanical thrombectomy in large vessel occlusions. *Ann Neurol* 2019; **86:** 395–406. **NEW**

Katsanos AH, Safouris A, Nikolakopoulos S, Mavridis D, Goyal N, Psychogios MN et al. Endovascular treatment for basilar artery occlusion: A systematic review and meta-analysis. *Eur J Neurol*. 2021 Jun;28(6):2106-2110. **NEW**

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.

Kunz WG, Hunink MG, Sommer WH, et al. Cost-effectiveness of endovascular stroke therapy: A patient subgroup analysis from a US healthcare perspective. *Stroke* 2016;47(11):2797-2804.

Langezaal LCM, van der Hoeven EJRJ, Mont'Alverne FJA, et al. Endovascular therapy for stroke due to basilar-artery occlusion. *New Eng J Med* 2021; 384: 1910-1920. **NEW**

Lansberg MG, Mlynash M, Hamilton S, et al. Association of thrombectomy with stroke outcomes among patient subgroups: secondary analyses of the DEFUSE 3 randomized clinical trial. *JAMA Neurol* 2019;76(4):447-453. **NEW**

Lapergue B, Blanc R, Gory B, 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.

LeCouffe NE, Kappelhof M, Treurniet KM, et al; MR CLEAN–NO IV Investigators. A randomized trial of intravenous alteplase before endovascular treatment for stroke. *N Engl J Med*. 2021 Nov 11;385(20):1833-1844. **NEW**

Leppert MH, Campbell JD, Simpson JR, Burke JF. Cost-effectiveness of intra-arterial treatment as an adjunct to intravenous tissue-type plasminogen activator for acute ischemic stroke. *Stroke* 2015;46(7):1870-1876.

Liu X, Dai Q, Ye R, et al. Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): an open-label, randomised controlled trial. *Lancet Neurol* 2020; 19: 115-122. **NEW**

Loh Y, McArthur DL, Vespa P, et al. The risk of acute radiocontrast-mediated kidney injury following endovascular therapy for acute ischemic stroke is low. *Am J Neuroradiol* 2010;31(9):1584-1587.

Löwhagen Hendén P, Rentzos A, Karlsson JE, Rosengren L, Leiram B, Sundeman H, et al. General anesthesia versus conscious sedation for endovascular treatment of acute ischemic stroke: the AnStroke trial (anesthesia during stroke). *Stroke* 2017;48:1601–1607.

Martins SO, Mont'Alverne F, Rebello LC, et al. Thrombectomy for stroke in the public health care system of Brazil. *New England Journal of Medicine* 2020; 382: 2316-2326. **NEW**

Mazighi M, Richard S, Lapergue B et al. BP-TARGET investigators. Safety and efficacy of intensive blood pressure lowering after successful endovascular therapy in acute ischaemic stroke (BP-TARGET): A multicentre, open-label, randomised controlled trial. *Lancet Neurol*. 2021 Apr;20(4):265-274. **NEW**

McDonald RJ, McDonald JS, Bida JP, et al. Intravenous contrast material-induced nephropathy: causal or coincident phenomenon? *Radiology* 2013;267(1):106-118.

Menon BK, d'Esterre CD, Qazi EM, Almekhlafi M, Hahn L, Demchuk AM et al. Multiphase CT Angiography: A new tool for the imaging triage of patients with acute ischemic stroke. *Radiology* 2015;275(2):510-20.

Mistry EA, Sucharew H, Mistry AM, et al. Blood pressure after endovascular therapy for ischemic stroke (BEST): A multicenter prospective cohort study. *Stroke* 2019; 50: 3449-3455. **NEW**

Mitchell P. DIRECT-SAFE Investigators. Endovascular thrombectomy versus standard bridging thrombolytic with endovascular thrombectomy within 4·5 h of stroke onset: an open-label, blinded-endpoint, randomised non-inferiority trial. *Lancet* 2022; 400(July 9):116–25. **NEW**

Mocco J, Zaidat OO, Von Kummer R, Yoo AJ, Gupta R, Lopes D, Frei D, Shownkeen H, Budzik R, Ajani ZA, Grossman A. Aspiration thrombectomy after intravenous alteplase versus intravenous alteplase alone. *Stroke* 2016;47(9):2331-8.

Mocco J, Siddiqui AH, Fiorella D et al. POSITIVE: Perfusion imaging selection of ischemic stroke patients for endovascular therapy. *J Neurointerv Surg*. 2022 Feb;14(2):126-132. **NEW**

Mueller-Kronast NH, Zaidat OO, Froehler MT, Jahan R, Aziz-Sultan MA, Klucznik RP, et al. systematic evaluation of patients treated with neurothrombectomy devices for acute ischemic stroke: Primary results of the STRATIS Registry. *Stroke* 2017;48(10):2760-8.

Muir KW, Ford GA, Messow CM, Ford I, Murray A, Clifton A et al; PISTE Investigators. Endovascular therapy for acute ischaemic stroke: The Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE) randomised, controlled trial. *J Neurol Neurosurg Psychiatry* 2017 Jan;88(1):38-44.

Nogueira RG, Lutsep HL, Gupta R, Jovin TG, Albers GW, Walker GA, et al. Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): A randomised trial. *Lancet* 2012;380(9849):1231-40.

Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *New Eng J Med* 2018; 378:11-21.

Phan K, Dmytriw AA, Lloyd D, et al. Direct endovascular thrombectomy and bridging strategies for acute ischemic stroke: a network meta-analysis. *J Neurointerv Surg* 2019; 11: 443-449. **NEW**

Podlasek A, Dhillon PS, Butt W, Grunwald IQ, England TJ. Direct mechanical thrombectomy without intravenous thrombolysis versus bridging therapy for acute ischemic stroke: A meta-analysis of randomized controlled trials. *Int J Stroke* 2021 Aug;16(6):621-631. **NEW**

Prasad V, Gandhi D, Stokum C, Miller T, Jindal G. Incidence of contrast material-induced nephropathy after neuroendovascular procedures. *Radiology* 2014;273(3):853-858.

Rasmussen M, Schönenberger S, Hendèn PL, Valentin JB, Espelund US, Sørensen LH et al. Blood pressure thresholds and neurologic outcomes after endovascular therapy for acute ischemic stroke: an analysis of individual patient data from 3 randomized clinical trials. *JAMA Neurol*. 2020 May 1;77(5):622-631. **NEW**

Roaldsen MB, Jusufovic M, Berge E, Lindekleiv H. Endovascular thrombectomy and intra-arterial interventions for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2021, Issue 6. Art. No.: CD007574. **NEW**

Sarraj A. Outcomes of thrombectomy in transferred patients with ischemic stroke in the late window: A subanalysis from the DEFUSE 3 Trial. *Lancet Neurol* 2019;76(6):682-689. **NEW**

Saver JL, Jahan R, Levy EI, Jovin TG, Baxter B, Nogueira RG, et al. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): A randomised, parallel-group, non-inferiority trial. *Lancet* 2012;380(9849):1241-9.

Saver JL, Goyal M, Bonafe A, Diener HC, 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(24):2285-9.

Saver JL, Goyal M, van der Lugt A, Menon BK, Majoie CB, Dippel DW et al.HERMES Collaborators. Time to treatment with endovascular thrombectomy and outcomes from Ischemic stroke: a metaanalysis. *JAMA* 2016;316:1279–88.

Schönenberger S, Uhlmann L, Hacke W, Schieber S, Mundiyanapurath S, Purrucker JC, Nagel S, Klose C, Pfaff J, Bendszus M, Ringleb PA. 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(19):1986-96.

Schonenberger S, Henden PL, Simonsen CZ et al. Association of general anesthesia vs procedural sedation with functional outcome among patients with acute ischemic stroke undergoing thrombectomy: A systematic review and meta-analysis. *JAMA* 2019; 322: 1283-1293. **NEW**

Sevick LK, Demchuk AM, Shuaib A, Smith EE, Rempel JL, Butcher K, Menon BK, et al. A prospective economic evaluation of rapid endovascular therapy for acute ischemic stroke. *Can J Neurol Sci* 2021; 48(6): 791 – 798. **NEW**

Sharma J, Nanda A, Jung RS, Mehta S, Pooria J, Hsu DP. Risk of contrast-induced nephropathy in patients undergoing endovascular treatment of acute ischemic stroke. *J Neurointerv Surg* 2013;5(6):543-545.

Simonsen CZ, Yoo AJ, Sørensen LH, Juul N, Johnsen SP, Andersen G, Rasmussen M. 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(4):470-477.

Singh B, Parsaik AK, Prokop LJ, Mittal MK. Endovascular therapy for acute ischemic stroke: A systematic review and meta-analysis. *Mayo Clin Proc* 2013;88:1056-1065.

Smith EE, Zerna C, Solomon N, Matsouaka R, Mac Grory B, Saver JL et al. Outcomes after endovascular thrombectomy with or without alteplase in routine clinical practice. *JAMA Neurol* 2022;79(8):768-776.

Stein LK, Mocco J, Fifi J, Jette N, Tuhrim S and Dhamoon MS. Correlations between physician and hospital stroke thrombectomy volumes and outcomes: A nationwide analysis. *Stroke* 2021;52:2858–2865. **NEW**

Sun J, Liang F, Wu Y, et al. Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke (CANVAS): Results of the CANVAS Pilot Randomized Controlled Trial. J *Neurosurg Anesthesiol*. 2020;32:41–47. **NEW**

Suzuki K, Matsumaru Y, Takeuchi M, Morimoto M, Kanazawa R, Takayama Yet al. SKIP Study Investigators. Effect of mechanical thrombectomy without vs with intravenous thrombolysis on functional outcome among patients with acute ischemic stroke: The SKIP randomized clinical trial. *JAMA.* 2021 Jan 19;325(3):244-253. **NEW**

Tao C, Qureshi A, Yin Y, Li J, Li R, Xu P et al. Endovascular treatment versus best medical management in acute basilar artery occlusion strokes: Results from the ATTENTION multicenter registry. *Circulation* 2022 Jul 5;146(1):6-17.

Tao C, Li R, Zhu Y, Qun S, Xu P, Wang L, Zhang C, Liu T, Song J, Sun W, Wang G. Endovascular treatment for acute Basilar Artery Occlusion–a multicenter randomized controlled trial (ATTENTION). *Int J Stroke* 2022;146(1): 6–17. **NEW (Protocol)**

Tate WJ, Polding LC, Kemp S, Mlynash M, Heit JJ, Marks MP, Albers GW, Lansberg MG. Thrombectomy results in reduced hospital stay, more home-time, and more favorable living situations in DEFUSE 3. *Stroke* 2019; 50: 2578-2581. **NEW**

Tosello R, Riera R, Tosello G, Clezar CNB, Amorim JE, Vasconcelos V, Joao BB, Flumignan RLG. Type of anaesthesia for acute ischaemic stroke endovascular treatment. *Cochrane Database of Systematic Reviews* 2022, Issue 7. Art. No.: CD013690.

Turk AS, III, Campbell JM, Spiotta A et al. An investigation of the cost and benefit of mechanical thrombectomy for endovascular treatment of acute ischemic stroke. *J Neurointerv Surg* 2014;6(1):77-80.

Turk AS III, Siddiqui A, Fifi JT, 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. **NEW**

van den Berg LA, Koelman DL, Berkhemer OA, et al. Type of anesthesia and differences in clinical outcome after intra-arterial treatment for ischemic stroke. *Stroke* 2015;46(5):1257-1262.

van den Berg LA, Dijkgraaf MG, Berkhemer OA, et al. Two-year outcome after endovascular treatment for acute ischemic stroke. *N Engl J Med* 2017;376(14):1341-1349.

van den Berg LA, Berkhemer OA, Fransen PSS et al; MR CLEAN Investigators. Economic evaluation of endovascular treatment for acute ischemic stroke. *Stroke* 2022 Mar;53(3):968-975. **NEW**

van der Steen W, van de Graaf RA, Chalos V et al; MR CLEAN-MED investigators. Safety and efficacy of aspirin, unfractionated heparin, both, or neither during endovascular stroke treatment (MR CLEAN-MED): An open-label, multicentre, randomised controlled trial. *Lancet*. 2022 399(10329):1059-1069. **NEW**

Wang Y, Wu X, Zhu C, et al. Bridging thrombolysis achieved better outcomes than direct thrombectomy after large vessel occlusion. *Stroke* 2021; 52: 356–365. **NEW**

Weber R, Reimann G, Weimar C, et al; Neurovascular Net Ruhr. Outcome and periprocedural time management in referred versus directly admitted stroke patients treated with thrombectomy. *Ther Adv Neurol Disord*. 2016;9(2): 79-84.

Yang P, Zhang Y, Zhang L, et al. Endovascular thrombectomy with or without intravenous alteplase in acute stroke. *New Eng J Med* 2021; 382: 1981–1993. **NEW**

Yarbrough CK, Ong CJ, Beyer AB, Lipsey K, Derdeyn CP. Endovascular thrombectomy for anterior circulation stroke: Systematic review and meta-analysis. *Stroke* 2015;46(11):3177-3183.

Yoshimura S, Sakai N, Yamagami H, Uchida K, Beppu M, Toyoda K et al. Endovascular therapy for acute stroke with a large ischemic region. *N Engl J Med* 2022; 386:1303-1313.

Zhao Z, Zhang J, Jiang X, et al. Is Endovascular treatment still good for ischemic stroke in real World?: A meta-analysis of randomized control trial and observational study in the last decade. *Stroke*. 2020 Nov;51(11):3250-3263. **NEW**

Zi W, Qiu Z, Li F, Sang H, Wu D, Luo W. DEVT trial investigators. Effect of endovascular treatment alone vs intravenous alteplase plus endovascular treatment on functional independence in patients with acute ischemic stroke: The DEVT randomized clinical trial. *JAMA.* 2021 Jan 19;325(3):234-243. **NEW**