Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management Evidence Tables

Acute Ischemic Stroke Treatment

Endovascular Therapy

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ACUTE STROKE MANAGEMENT Writing Group

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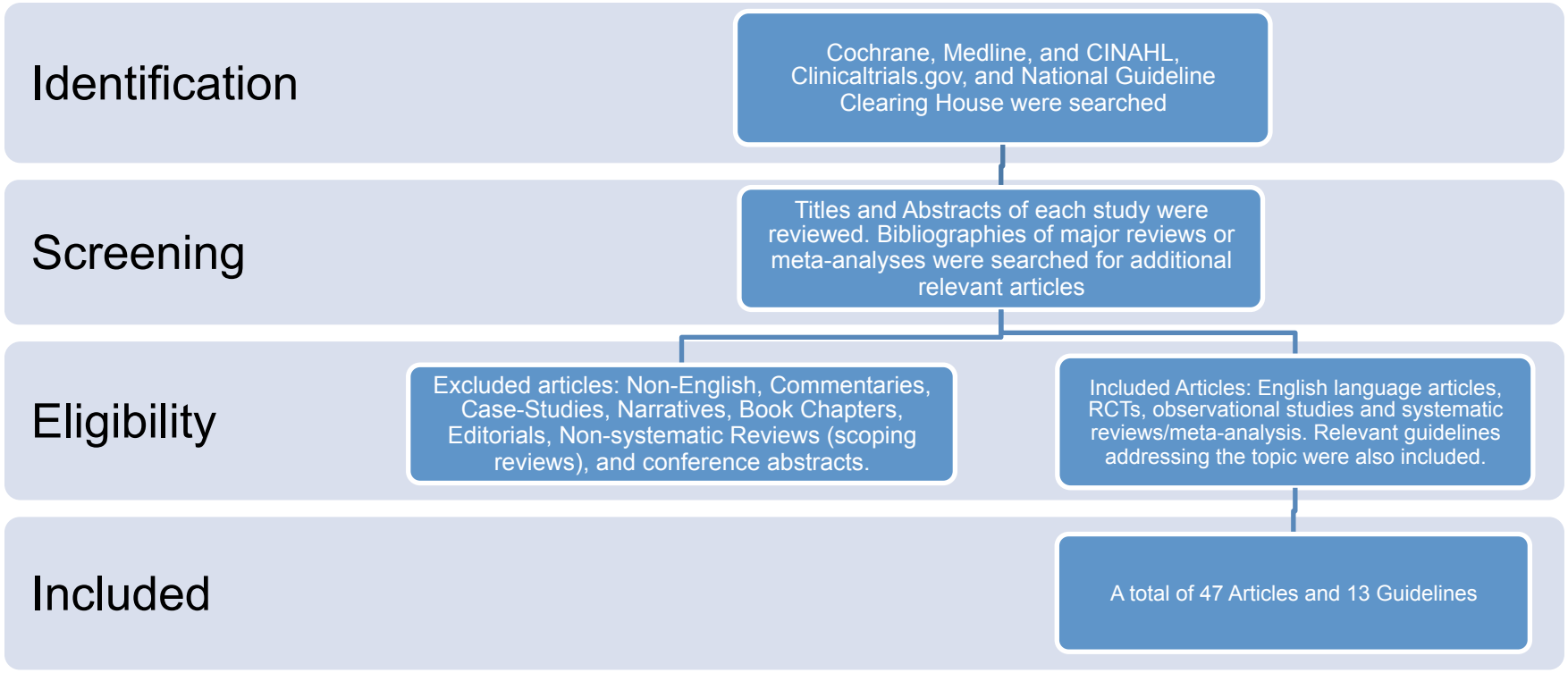
Search Strategy



Cochrane, Medline, and CINAHL, Clinicaltrials.gov, and National Guideline Clearing House were search using medical subject. 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 13 guidelines and 47 articles were included and were separated into separate categories designed to answer specific questions.

Published Guidelines

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. **2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke.* 2018; Mar;49(3):e46-e110** **(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** 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. 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. 4. 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. Class IIb; LOE C-EO. 6. Although its benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score >1, ASPECTS<6 or NIHSS score<6, and causative occlusion of the internal carotid artery (ICA) or proximal MCA (M1). Additional randomized trial data are needed. Class IIb; LOE B-R. 7. 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 8. 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; LOE B-R. 9. The technical goal of the thrombectomy procedure should be reperfusion to a modified Thrombolysis in Cerebral Infarction (mTICI) 2b/3 angiographic result to maximize the probability of a good functional clinical outcome. Class I; LOE A 10. As with IV alteplase, 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 within the therapeutic window. Class I: LOE B-R. 11. Use of stent retrievers is indicated in preference to the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) device. Class I; LOE A. 16. It is reasonable to select an anesthetic technique during endovascular therapy for AIS on the basis of

Guideline	Recommendations
	individualized assessment of patient risk factors, technical performance of the procedure, and other clinical characteristics. Further randomized trial data are needed. Class IIa; LOE B-R.
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, 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

Guideline	Recommendations
	(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? 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).

Guideline	Recommendations
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.
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. 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.

Guideline	Recommendations
	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) 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

Guideline	Recommendations
	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. 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

Guideline	Recommendations
	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)
Irish Heart Foundation **Stroke Thrombolysis Guidelines Version 2.0 (March 2015)** **Available at: http://www.stroke.ie/media/pub/advocacy/thrombolysisguidelines/thrombolysis_version_2_0_2015_final.pdf**	Interventional Thrombectomy Recent trials - MR CLEAN, ESCAPE, EXTEND-IA , SWIFT-PRIME have shown a positive benefit towards thrombectomy in selected patients. Each patient with the criteria below should be discussed with the local interventional neuro-radiologist on call. Indications for Discussion with Neuro-Radiology Centre 1. Clinical examination consistent with acute ischaemic stroke. 2. Non contrast CT brain showing no infarct or evidence of early acute small core infarct (ASPECTS >4) 3. CTA if available showing large vessel occlusion (Intracranial or extracranial ICA, M1 or M2 middle cerebral or basilar artery). 4. Suitable or unsuitable for IV thrombolysis. If suitable, start immediately but do not wait to see the effect before calling neuroradiology. The time frame < 6 hours from last known well, but a time frame of up to 12 hours was occasionally used in the ESCAPE. Patients with a basilar artery occlusion (not included in above trials) can be considered up to 24 hours, and occasionally longer if stuttering symptom onset.
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.**	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

Guideline	Recommendations
***Neurologia* 2014;29(2):102-122.**	neurointervention. Ideally, this procedure is performed according to a case registry or clinical study protocol (level of evidence 5; grade D recommendation).
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.
Lansberg MG, O'Donnell MJ, Khatri P, Lang ES, Nguyen-Huynh MN, Schwartz NE, Sonnenberg FA, Schulman S, Vandvik PO, Spencer FA, Alonso-Coello P, Guyatt GH, Akl EA. **Antithrombotic and thrombolytic therapy for ischemic stroke: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines.** ***Chest 2012* Feb;141(2 Suppl):e601S-36S.**	2.3. In patients with acute ischemic stroke, we suggest against the use of mechanical thrombectomy (Grade 2C)

Evidence Tables

Major Trials

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Campbell et al. 2018 **Australia** **RCT** ***EXTEND-IA TNK***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	202 patients, ≥18 years, recruited from 13 centres, who were eligible to receive intravenous thrombolysis within 4.5 hours after the onset of ischemic stroke and had cerebral lesions that could be treated with intraarterial clot removal, which could commence within 6 hours of stroke onset. Pre-morbid mRS score ≤3. The original entry criteria requiring CT-perfusion mismatch for anterior circulation strokes, was removed after 80 patients. Mean age was 71 years, 55% were men. Median NIHSS score was 17.	Patients were randomized 1:1 to receive intravenous tenecteplase (0.25 mg per kilogram of body weight; maximum dose, 25 mg) or alteplase (0.9 mg per kilogram; maximum dose, 90 mg).	**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 ICH (sICH) within 36 hours of treatment	At initial angiographic assessment, a significantly higher number of patients in the tenecteplase group achieved substantial reperfusion (22% vs. 10%, incidence difference=12%, 95% CI 2- 21, p=0.002 for noninferiority, adjusted incidence ratio=2.2, 95% CI 1.1-4.4; p=0.03 for superiority and adjusted OR=2.6, 95% CI 1.1-5.9; p=0.02 for superiority). Thrombectomy was not performed in patients who met the primary outcome of reperfusion except for one patient in the tenecteplase group. The median mRS score at 90 days was significantly lower in the tenecteplase group (2 vs. 3, common OR=1.4, 95% CI 1.0-2.8, p=0.04). The percentage of patients who were functionally independent or who had achieved an excellent outcome, did not differ between groups. The percentage of patients who experienced early neurological improvement did not differ between groups (71% vs. 68%, p=0.70). There were 10 deaths in the tenecteplase group vs. 18 in the alteplase group (adj OR=0.4, 95% CI 0.2-1.1, p=0.08). There was 1 sICH in each group.
Albers et al. 2018 **USA** **RCT** ***DEFUSE 3***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	182 patients, aged 18-90 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	Patients were randomized to treatment with thrombectomy using an FDA-approved device + medical management (n=92) or medical management alone (n=90).	**Primary outcome:** Distribution of mRS scores at 90 days **Secondary outcome:** Functional independence at 90 days (mRS 0-2)	Trial was stopped early due to efficacy (476 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

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		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.		**Primary safety outcomes:** Death within 90 days, sICH at 36 hours **Imaging outcomes:** Infarct volume at 24 hours, lesion growth, reperfusion at 24 hours,	(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, volume of ischemic core, baseline NIHSS, age, sex, ASPECTS, site of occlusion, baseline imaging, atrial fibrillation).
Nogueira et al. 2017 **USA**	Concealed Allocation: ☑ Blinding:	206 patients, recruited from 26 centres, ≥18 years with ischemic stroke, last been known to	Patients were randomized to treatment with thrombectomy with Trevo device + medical	**Primary outcomes:** Utility-weighted mRS score and functional independence (mRS 0-2) at 90 days,	Trial was terminated early at 31 months (500 maximum planned) after interim analysis when efficacy of thrombectomy was established.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT ***DAWN***	Patient ☒ Assessor ☑ ITT: ☑	be well 6 to 24 hours earlier, with no previous disability (mRS 0-1) who 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 me. Median baseline NIHSS score was 17.	management (n=107) or medical management alone (n=99).	**Secondary outcomes:** 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.	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 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 sub group 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%).
Muir et al. 2017 **USA**	Concealed Allocation: ☑	65 patients ≥18 years, with occlusion of the intracranial ICA, M1	Patients were to receive best medical therapy with IVT alone (n=32), or to	**Primary outcome:** Independence (mRS score 0-2) at 90 days	Trial recruitment was suspended in prematurely, following presentation of other relevant thrombectomy trial results.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT ***PISTE***	Blinding: Patient ☒ Assessor ☑ ITT: ☑	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.	undergo additional (adjunctive) mechanical thrombectomy (MT) with any approved device (n=33), performed by an experienced operator, without delay following t-PA.	**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);	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
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**	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑	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	Patients were randomized to receive dual IV t-PA therapy + intra-arterial mechanical clot retrieval with the Merci, Penumbra, Catch or Solitaire devices	**Primary outcome:** mRS scores at day 90 **Secondary outcomes:** EQ-5D scores and Barthel	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

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
THRACE	ITT: ☑	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).	(n=204) or treatment with IV t-PA only (n=208)	Index (BI) scores at day 90	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). 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 sub group analyses for the primary outcome (age, sex, diabetes, HTN, hypercholesterolemia, time to randomization, occlusion site, NIHSS baseline score, or ASPECTS score).
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 was 17 in both groups. Median ASPECTS scores were 7 (intervention) and 8 (control)	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 24 hours), NIHSS score and Barthel Index scores at 90 days and EuroQol	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 (adj OR=2.1, 95% CI 1.1-4.0). The odds of dramatic neurological improvement at 24

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Safety outcomes: 90-day mortality, symptomatic ICH within 90 days.	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) was 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%)
Saver et al. 2015 **USA** **RCT** ***SWIFT-PRIME***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑	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,	Patients were randomized to receive intravenous t-PA therapy + intra-arterial mechanical clot retrieval with the Solitaire FR device (n=98) or treatment with	**Primary outcome:** Global disability at 90 days (mRS scores) **Secondary outcomes:** All-cause mortality, proportion of patients with	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).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: ☑	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.	intravenous t-PA only (n=98)	mRS score ≤2 at 90 days, change in NIHSS score at 27 ± 6 hours post randomization	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 sub group 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 **Australia** ***EXTEND IA* RCT**	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	70 patients ≥18 years, with anterior circulation 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	Patients were randomized to undergo mechanical clot retrieval with the Solitaire device after receiving standard therapy with intravenous rt-PA (n=35) or intravenous t-PA only (n=35)	**Primary outcomes:** Reperfusion at 24 hours, 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 trial was stopped early (100 planned). 8 patients in the endovascular treatment group did not undergo 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

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		13 (control).			(p=0.006). There were no significant differences between groups in any of the safety outcomes (death, symptomatic ICH or parenchymal hematoma).
Goyal et al. 2015 **Canada** **RCT** ***ESCAPE***	Concealed Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	316 patients ≥18 years, with stroke onset <12 hours, NIHSS > 5 at the time of randomization, 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).	Patients were randomized to receive endovascular mechanical thrombectomy, using available devices +/- intravenous t-PA (intervention group, n=165); or best medical management +/- tPA (control group, n=150). *One patient excluded due to improper consent procedures	**Primary outcome:** Shift in mRS scores at day 90 **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.	The trial was stopped early. One patient in the control group crossed over to the endovascular therapy group and 14 patients in the experimental group did not received 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 sub groups analyses, based on age, sex, baseline NIHSS score, baseline ASPECTS, occlusion location, and status with respect to alteplase treatment) or

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					according to the presence or absence of cervical carotid occlusion, all of which favoured the intervention.
Berkhemer et al. 2014 **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 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 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

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					patients (11.2%). There were no treatment-related interaction effects found for any of the pre-specified sub groups (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 0.6-1.2, p= 0.46).
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. IVt-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 vs.

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					≥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 Drop outs: n=0, (15 patients did not receive endovascular treatment, 3 patients did not receive i.v. 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 Recurrent stroke within 90 days for patients in ET

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					and i.v. t-PA groups 5.1% vs. 6.3%, p=0.54
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.**

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Losses to follow-up: embolectomy group n=6, standard care group n=3 Adverse events: 17 procedural complications, 5 of which were serious.
Trials Ongoing or Terminated but Results Not published as of December 2018					
NCT01852201 **POSITIVE Stroke Clinical Trial** **USA** **RCT**	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.	TBA
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 67.8 years, 54.2% were men.	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 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).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					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)

CA: concealed allocation; ITT: intention-to-treat

Systematic Reviews & Meta-analyses

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
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 0.78-1.88, p=0.40). Time series analysis demonstrated robust evidence

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					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 sub groups including: age, sex, NIHSS, site of intracranial occlusion, intravenous alteplase received or ineligible, ASPECTS, time from onset to randomisation, and presence of tandem cervical carotid occlusion.
Saver et al. 2016 HERMES Collaboration	NA	As above	Pooled analyses were conducted to examine the timeframe in which	**Primary outcome:** Degree of disability at 3 months, assessed across 6	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.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
International **Meta-analysis**			endovascular treatment is associated with benefit, and to investigate the effect of treatment delay	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	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 functional outcome at 90 days (mRS 0-1), early neurological improvement	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 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).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				(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	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 sub group 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 sub groups 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 **USA**	NA	6 RCTs (n=1,903) comparing endovascular therapies with best medical management following ischemic stroke.	Analyses were conducted for studies in which patients with confirmation of large vessel occlusion (LVO) were included	**Primary outcome:** Good functional outcome (mRS 0-2) at 3 months **Secondary outcomes:**	**Results from the 5 LVO trials:** Endovascular therapy was associated with significantly improved odds of a good recovery (OR=1.67, 95% CI 1.29-2.16, p<0.0001).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Systematic review & meta-analysis		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	(n=5), and for all studies where patients were included regardless of the confirmation of LVO (n= 6).	mRS scores of 0-1 and 0-3 at 3 months, mortality at 3 months and shift in mRS scores at 3 months	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 the 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, p=0.05.

Trials Comparing Devices

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Nogueira et al. 2012 **USA** **TREVO-2** **Non-inferiority study** **RCT**	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 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.	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, good outcome at 90 days (mRS score of ≤2), all-cause mortality at day 90, symptomatic ICH within 24 hours of procedure.	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). 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** **SWIFT** **RCT**	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

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					adverse events between groups.

CA: concealed allocation; ITT: intention-to-treat

Anesthetic Management for Endovascular Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Systematic Reviews & Meta-analyses					
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 65.5 years, 53% were men. Median NIHSS score was 17.	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 received non-GA methods (n=561).	**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 0-1), 90-day mortality, symptomatic ICH	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. 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 (cOR=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. There 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,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					p=0.57).
Brinjikiji et al. 2017 **USA** **Systematic Review & Meta-analysis**	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 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).
Brinjikiji et al. 2015 **USA** **Systematic Review & Meta-analysis**	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

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					(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					
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 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.	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). 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	Concealed	90 patients ≥18 years,	Patients were	**Primary outcomes:**	77% of patients received IV rt-PA.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hendén et al. 2017 **Sweden** **RCT** ***AnStroke Trial (Anesthesia During Stroke)***	Allocation: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	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.	randomized 1:1 to undergo the thrombectomy procedure using general anesthesia (GA) or conscious sedation (CS)	mRS score at 90 days, early neurological improvement **Secondary outcome:** Good outcome (mRS 0-2 at 90 days)	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 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** ***Sedation vs Intubation for Endovascular Stroke Treatment (SIESTA)*** **RCT**	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.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					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-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

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					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 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	**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 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)

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).	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 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	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

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			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)		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** **Retrospective study**	NA	194 consecutively-admitted patients who received contrast-enhanced imaging, 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	Each patient received approximately 150 ml of non-ionic low-osmolar contrast agent during the procedure.	Incidence of Contrast-induced nephropathy (CIN), 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	There were 3 cases of CIN at 48 hours post procedure. One patient who developed an increased Cr level 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.	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
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 published data.	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 (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. Cost 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 sub groups 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 sub groups of M2 location (ICER $28,812) and ASPECTS score of 0-5 (ICER $14,273)
Leppert et al.	NA	A theoretical cohort of	A decision analytic model	Additional cost of IAT per	Total lifetime costs of IAT and alternative therapy for

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
2015 **USA** **Economic analysis study**		patients ≥65 years, admitted to hospital following acute ischemic stroke	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	QALY	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** **Retrospective study**	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 chart review. Thrombectomy devices were categorized as Penumbra aspiration system thrombectomy (group P) or stent retriever (group S).	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% 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.

Bridging Therapy Using a Drip & Ship Model

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Gerschenfeld et	NA	159 patients ≥ 18 years,	The outcomes of patients	**Primary outcome:**	Median process times from patients in the

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
al. 2017 **France** **Retrospective study**		admitted to 2 hospitals (one primary stroke centre [PSC] and one comprehensive stroke centre [CSC]) with a large vessel occlusion of the M1 or M2 MCA, treated with intravenous t-PA. and who were eligible for mechanical thrombectomy (MT), within 6 hours after symptom onset. Median age was 72 years, 54% were men. Median baseline NIHSS score was 16.	who received MT following t-PA, using the drip and ship model (PSC, n=100) were compared with patients who underwent MT using the mother ship (MS) model (CSC, n=59).	Favourable outcome (mRS ≤2) at 3 months **Secondary outcomes:** Substantial recanalization (TICI 2B or 3) and symptomatic intracranial hemorrhage (sICH)	mothership group were all significantly shorter (onset to needle, onset to puncture, needle to puncture and onset to recanalization). There was no significant difference between groups in the proportion of patients with a favourable outcome (50.8% MS vs. 61% DS, p=0.82 after adjusting for baseline NIHSS score, DWI-ASPECTS, and general anesthesia), or recanalization (79.7% DS vs. 84% MS, p=0.59 using same adjustments). There was no significant difference between groups in the proportion of patients with sICH (3.4% MS vs. 2.0% DS, p=0.65) or median discharge NIHSS scores (6 MS vs. 4 DS, p=0.46).
Weber et al. 2016 **Germany** **Retrospective study**	NA	643 patients consecutively admitted from 2012-2013, to 17 stroke units with acute ischemic stroke treated with intravenous thrombolysis and/or thrombectomy. Median age was 71 years, 50% were men. Median baseline NIHSS sore was 15.	The outcomes of patients treated in house at 8 centres with expertise to perform endovascular procedures (n=300) were compared with those of patients from 9 centres who had been transferred from another hospital to undergo mechanical thrombectomy (n=343).	**Primary outcome:** In-hospital mortality and mortality at 3 months **Secondary outcomes:** Functional outcome at 3 months (mRS 0-2) and peri-procedural times	50.3% of patients in the in-house received bridging therapy with t-PA vs. 46.9% of referred patients (p=0.39). Canalization (TICI 2B or 3) was achieved in 73.9% of in-house patients and 76.3% of referred patients (p=0.67). Median periprocedural times were significantly shorter for in-house group (e.g., symptom onset to groin puncture 150 vs. 233 min, p<0.001). 3-month mortality data were available for 76.4% of patients. There was no significant difference between groups in the proportion of patients with in-hospital mortality (14.8% in-house vs. 11.7%, referred p = 0.26) or 3-month mortality (21.9% in-house vs. 24.1% referred, p=0.53). Functional outcome data were available for 63% of patients. There was no significant difference between groups in the proportion of patients with a good outcome at discharge (46% in-house vs. 35.1%, referred; p value not reported) or at 3-months (44.0% in-house vs. 35.7% referred,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					p=0.08).

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